Trends-in-Medicine

November 2009

by Lynne Peterson and D. Woods

SUMMARY

Ophthalmologists and their patients are feeling the impact of the recession, but things don't appear to be getting worse. ♦ LASIK surgery appears to have bottomed and is likely to remain flat for the next 6-12 months. ♦ Premium IOLs have lost a little market share overall, but within their niche, Alcon's new ReStor 3.0 is a big improvement and is luring customers from Bausch & Lomb's Crystalens HD, which many doctors view as worse than the old Crystalens 5.0. Abbott's Tecnis has mostly replaced ReZoom but is a minor player. ♦ Doctors are very interested in femtosecond cataract surgery, and LenSx, LensAR, and OptiMedica are leading the way. ♦ The glaucoma device pipeline doesn't look very promising. Generic latanoprost is expected to take huge market share. ♦ Retina surgeons are waiting for the results of the CATT head-to-head study of Avastin and Lucentis in wet AMD while investigating a number of potential new treatments for dry AMD. ♦ Autofluorescence is the hot new topic in imaging, picking up things that current OCT does not. ♦ Financial issues – especially Medicare reimbursement and healthcare reform – are a big concern, but ophthalmology appears in a better position than some other medical specialties.

Trends-in-Medicine
Stephen Snyder, Publisher
2731 N.E. Pinecrest Lakes Blvd.
Jensen Beach, FL 34957
772-334-7409 Fax 772-334-0856
www.trends-in-medicine.com
TrendsInMedicine@aol.com

AMERICAN ACADEMY OF OPHTHALMOLOGY (AAO)

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Attendance at AAO this year was up over last year, and ophthalmologists were spending a lot of time on the exhibit floor, which made vendors happy. However, there were three separate exhibit areas, and some vendors did better than others with this layout. Doctors were very interested in new technology on display, but spending seemed to be limited to must-have items.

Asked why exhibit floor traffic appeared stronger at AAO than at other recent medical conferences, Dr. David Parke II, the new executive vice president/CEO of the AAO, said, "At the entrance to the exhibit hall, we have some things posted explaining the new rules (about no or limited give-aways)…And every member who registered got in their packet a sheet of paper explaining the new conflict of interest rules. We did that because, as confusing as it is for − the leadership of the Academy and the leadership of other societies − we live with these issues…But the average ophthalmologist in practice is wondering what's going on…And that leads to frustration and confusion. We've been trying to educate our membership, and once people understand it, the frustration goes away. Some people have come up to me and said they like it because people aren't pushing little give-aways at them. Now, the conversations (on the exhibit floor) are more focused to the issues at hand, and people are always hungry for the exhibit floor. There may also be another factor…The conjecture is that the longer the regulations are in place, the more people will understand how to function within them…not only physicians but industry. What we have tried to do is not only educate members but also establish very clear policies. We have spent a lot of time developing what I think are robust policies."

The impact of the recession

Asked about their purchase plans over the next year, most doctors are taking a very conservative approach but buying what they need. A few said they plan to purchase things like an optical coherence tomography (OCT).

When Medicare patients reach the Medicare Part D coverage gap – the donut hole – they are either discontinuing their medications (usually without telling their doctor) or switching to a generic where that is available, even if the doctor prefers the branded product.

Would a pharma keep patients on the brand drug during this donut hole if it offered a rebate? Ophthalmologists said it would help, but the rebate would have to be substantial. Comments included:

- "Some patients ask for samples and generics, but there aren't generics for some conditions."

- "Patients listen to me, and I believe brands make a difference. So, rebates would help (some) brand use… But with generic Xalatan (Pfizer, latanoprost for glaucoma), a rebate won't be helpful if the generic is priced low enough."
- "Mostly patients switch to a generic. Patients are very cost conscious today. The value of a rebate depends on how much it is…But brand matters."
- "The effect of the donut hole is significant and discontinuations are higher than what has been reported. There is also some movement from brand to generic. A rebate might not be enough. We need to get rid of the donut hole."
- "Patients won't admit they are not taking their medication, but I suspect they are. They always ask about generics, even if they aren't in the donut hole. A rebate would have to be significant."
- "Patients are asking for more samples, and some are switching to a generic. I already see a lot of rebates. I'm not sure if it helps the brand, but people like the coupons."
- "I'm starting to see more and more generic use…and personally, I'm using more and more generics…I imagine rebates would help keep patients on the brand. I've shifted many people to generic because of (the donut hole problem)."

Cataract and Refractive Surgery

At AAO last year, ophthalmologists said the refractive surgery market was very weak, with volume off 40%-50% in 4Q08 and expected to get even worse. This year, refractive surgeons reported the market appears to have bottomed and is holding fairly steady. Unless the economy worsens, they expect LASIK volume to remain relatively flat for the next 6-12 months. A Florida doctor said, "We are trying to get a refractive practice going, and it is slow. We just got a laser in the last year."

Doctors also insisted that there has been no impact on LASIK procedures from patient complaint issues or the collaborative study the FDA, the National Eye Institute (NEI), and the Department of Defense are conducting to examine the impact of LASIK on quality of life. There also was no buzz or concern about this study at the meeting. The goal of the LASIK Quality of Life Collaboration Project is to identify factors that can affect quality of life following LASIK and potentially reduce the risk of adverse effects. The three phases of this project are:

1. Design and implementation of a web-based questionnaire to assess patient opinions of LASIK outcomes and the effect on their quality of life. This phase started in July 2009.
2. Evaluation of the quality of life and satisfaction following LASIK by patients at the Naval Medical Center San Diego. This is still in the planning stage.
3. A national, multicenter clinical trial to study the impact on quality of life following LASIK in the general population, including subpopulations who may be vulnerable to adverse effects from the procedure. This is still in the planning stage.

This study hasn't had an effect on LASIK volume, but it has created noise, which is "distracting." As one surgeon put it, "It can't be helpful."

Dave Harmon of ***Market Scope*** estimates that LASIK volume will total 850,000-880,000 procedures this year, down 15%-20% from 2008, and down ~40% from the 1,427,000 performed in 2000.

One of the rumors circulating at AAO was that TLC Vision is about to go under. It seems certain that TLC will be delisted from the NASDAQ.

In this environment, excimer laser sales are minimal – except for Alcon's deal with LCA-Vision to replace their Ladar-Vision excimer lasers with WaveLight's Allegretto lasers. In terms of procedure share, Visx reportedly is holding steady at ~60%, but Alcon/ WaveLight is growing at the expense of Technolas. Nidek has hardly any U.S. procedure share.

Premium Intraocular Lenses (pIOLs)

pIOLs – advanced multifocal lenses for cataract and refractive lens exchange (RLE) patients − have been slow to catch on. Despite heavy marketing, they still are used in a very small segment of cataract patients. ***Market Scope***'s Harmon estimates that 67% of RLEs use a pIOL (~80,000 lenses a year) but only 5.8% of cataract patients, which is down from ~7%. The decrease is blamed on the recession. Over the next year, doctors said pIOL use is likely to stay relatively flat but is very dependent on what happens to the economy.

In this smaller, if not still shrinking, pIOL market, Alcon's ReStor 3.0 is the market leader, and it has helped Alcon regain market share from B&L/eyeonics' Crystalens. Some doctors described the earlier ReStor 4.0 as "not as good" as Crystalens 5.0, but they said ReStor 3.0 is better than both Crystalens 5.0 and the newer Crystalens HD. As one expert put it, "ReStor 4.0 was not forgiving at all, but 3.0 is." Alcon vice president Douglas MacHatton said, "The (clinical) results (with ReStor 3.0) are astonishing and have doubled the number of people achieving 20/20 vision or better. That's pretty astonishing… It's a tremendous technology story. It's a harder lens to sell to an individual because there are some compromises − there will be glare and some halos − but the quality of vision (is great), with 95% of people achieving 20/40 or better at all distances and 85% achieving 20/30."

But ReStor 3.0 is not the only reason that the use of Crystalens has dropped. Crystalens users complained that Crystalens HD is not as good as Crystalens 5.0, and several said they have gone back to using the 5.0, abandoning the HD. However, B&L reportedly has another version, the Crystalens AO, coming, and doctors familiar with it think it could be a winner. It reportedly is a "marriage of Crystalens and AO technology." It will be on the 5.0 platform but is supposed to be more flexible.

Currently, Harmon estimated that ReStor has ~52% market share, with Abbott/AMO's Tecnis and ReZoom at ~8%, and Crystalens at 40%. Tecnis is picking up a ***little*** share, but, as expected, ReZoom use has all but gone away.

One thing that is ***not*** differentiating these lenses or affecting lens choice is injector. Abbott, Alcon, and B&L all have good injectors, doctors said.

Ophthalmologist comments on pIOLs included:

- *New Jersey:* "The Crystalens 5.0 was good. The HD has some issues with predictability and long-term performance. There is some irregular astigmatism and distortion, so patients are not as stable…The new ReStor 3.0 has a much better image quality (than the ReStor 4.0)…ReStor came back (in use) because the new version is better, and the new Crystalens is worse."
- *Hawaii:* "I'm not using any premium IOLs, and I have no plans to start. Patient expectations are great, and if you are not a LASIK surgeon, you have to refer touch-ups out, and that adds to the cost for patients, which makes them unhappy. Patients are not anxious to spend money on premium IOLs either."
- *California #1:* "The new Crystalens HD is not as good as the old Crystalens 5.0. Tecnis has a possible role in mix/match with the ReStor 3.0; there is more glare but more reading ability than with two ReStors."
- *Pennsylvania:* "I'm going back to the Crystalens 5.0 from the HD. The HD near vision solution was an extra nipple, but it is so small that it is not obvious to the naked eye, and any decentration is causing distortion that is not resolvable."
- *California #2:* "People may start getting disillusioned with the ReStor 3.0 because the glare/halo rate will increase with the end of daylight savings time as people start driving home at night."

A number of new pIOLs are in development, including:

- **Rayner**, a British IOL maker, may be the sleeper company in the pIOL market. Keep an eye on this company.
- **Lenstec's Tetraflex**, a foldable acrylic accommodating lens.
- **Abbott's Synchrony**, which doctors assume was the reason Abbott acquired Visiogen. This is the new lens generating the most excitement. Several experts predicted this lens will help Abbott gain traction in the pIOL market. Synchrony uses a unique dual optic design to, theoretically, give more accommodative amplitude (range of vision) than single optic designs such as Crystalens. However, the current design requires a larger incision size than Crystalens.

Monofocal lenses

With the slow uptake of pIOLs, most cataract surgeons continue to use monofocal lenses. In that market, Alcon's toric lens is doing well. Alcon's MacHatton said, "For refractive surgeons to do cataract surgery, their business model blends well with premium IOLs, but for the more focused cataract surgeon who only does cataract surgery, it's hard to make that transition quickly, and the toric lens is good for them." Dr. James Salz of Los Angeles had cataract surgery himself this year, and he explained why he chose a monofocal lens, "I didn't choose to have a presbyopia-correcting implant because I wanted the best possible distance vision with the lowest risk of problems with glare, halos, contrast sensitivity, and posterior capsule opacification, and I don't mind wearing glasses… I didn't want even a 5% chance of glare/halos. I will get an aspheric toric lens for my other eye when that is done."

Phakic IOLs

Ophthalmologists questioned at AAO generally had little enthusiasm for phakic IOLs – either Staar Surgical's Visian or Abbott's Verisyse/Artisan. There also were no indications that use of, or interest in, either is likely to pick up. A New Jersey doctor said, "Phakic IOLs are a limited market because we don't want to put them in someone too old or too young. You need a very high myope with money. It is a limited market, a niche for 30-40-year-olds with money."

Alcon's one-piece, acrylic, foldable phakic IOL, the AcrySof Phakic, was approved in Europe in 2008, and the company is expected to submit it to the FDA for approval in 2010. It is not a toric, like Visian. U.S. ophthalmologists are starting to talk about AcrySof Phakic, and interest is increasing. Dr. Salz, who participated in an AcrySof Phakic study, said, "I'm excited about it…I really like that…Our results with it are just fantastic. Once it is available, it may become the phakic IOL of choice. It is easy to put in, the complication rate is low, and they are not seeing cataracts. Cell loss at three years is acceptable…We are hoping that maybe, maybe Alcon might get approval (in the U.S.)."

FEMTOSECOND CATARACT SURGERY

The hot news at AAO was femtosecond cataract surgery (also referred to as "femtosecond laser-assisted cataract surgery" or FLACS) – using a femtosecond laser as an adjunct, not a replacement for phacoemulsification (phaco). This is a different femto from that used to make a flap for LASIK; it is set to a much deeper depth (~7,500 microns vs. 1,200 microns). Current femtos cannot be used the way they are for this; it takes a new femto machine, so it opens up a whole new market.

Dr. William Rich, the AAO's medical director for health policy, cautioned, "People have to realize that you can take a cataract out with an $80,000 machine, a $200,000 machine, or scissors, and you get the same results…So, you need a value added outcome to justify different modalities. People fail to realize I get one payment for cataract surgery; there has to be a remarkable breakthrough (to justify any increased cost)…With femto LASIK, doctors could increase the cost to patients to cover their cost."

This is why many proponents of femto cataract surgery are suggesting that, at least initially, it will be focused on the premium IOL market, where an up charge might be acceptable.

The current steps in a cataract procedure are:

- Incision.
- Capsulorhexis (making an opening to allow access to the interior part of the lens).
- Phacoemulsification that uses ultrasound to fracture, pulverize the lens which is then sucked out, leaving the capsular bag intact.
- IOL insertion into the capsular bag.
- Limbal relaxing incisions (LRIs) in patients with astigmatism.

While phaco is a very successful procedure, there are some potential problems, including incision leaks that lead to endophthalmitis, irregular capsulorhexis causing a problem with the posterior capsule, corneal edema or burn, decentration of the IOL, and irregularity of LRI results. The goal of the femto is to make a very precise incision at the proper position and at a uniform depth and to more reliably correct astigmatism. Dr. William (Buddy) Culbertson of Bascom Palmer Eye Institute in Miami said, "The goal of FLACS is to increase safety, improve precision, automate undependable components such as capsulorhexis, incisions, LRIs, and to make it easier for the doctor and the patient by softening the lens…In some cases, you could just bypass (phaco-)emulsification and just remove the softened lens…It is sort of a laser chopping or splitting of the lens…Or, you can emulsify the (pieces) with minimal phaco energy."

Some experts are suggesting that FLACS eventually will replace phaco entirely, but most experts described it more as an adjunct, saying that it will be used with current phaco machines. Likewise, some experts predicted FLACS will be used primarily for patients getting a premium IOL, saying that will ensure better IOL results, while other experts predicted FLACS will be used for all cataract patients because of its ease and precision.

The potential advantages of FLACS are improved safety, increased precision, and enhanced reproducibility. The disadvantages are cost and increased time – perhaps another 5 minutes per patient, at least initially. California refractive surgeon Dr. Salz said that FLACS "may increase the time for really skilled cataract surgeons" but is likely to save 10-15 minutes per procedure for cataract surgeons who currently need an hour for the procedure, "Those who are taking an hour will save a lot of time…I personally think (FLACS) is the next big trend that will revolutionize cataract surgery."

The big question may be how cataract surgeons will pay the added device cost – likely to be an initial machine fee plus per procedure charges. Medicare is unlikely to cover it, but doctors will be able to up charge patients getting premium IOLs for it.

Dr. Culbertson said there are also several other potential uses for this type of femto, including sub-Bowman's relaxing incisions, customized capsulorhexis that integrate with an IOL ("capsule in the lens"), complex cataract incisions, toric IOL orientation, and helping with lens refilling surgery.

Three companies definitely have FLACS machines in development – LenSx, LensAR, and OptiMedica – and Alcon/WaveLight is "thinking about it." Abbott also may be working on this in the background.

LENSX – already FDA approved

This is the first company to get FDA approval for a femtosecond cataract procedure. In September 2009, LenSx received 510(k) approval for capsulotomy, but the company does not plan to launch its device for about a year, apparently wanting additional indications first. Although LenSx didn't even have a booth at AAO, it does hope to showcase its femto at AAO 2010. CEO Dr. Ron Kurtz, himself an ophthalmologist, explained, "Generally, you don't have a booth until you are ready to launch your product…We are launching the product in the fourth quarter of 2010." He insisted this year-long wait to launch was not a delay, pointing out that the company was only incorporated in 2007, "So, we are bringing the product to market in less than three years. The approval is one of the steps…There may be additional approvals."

Although he said that he doesn't know enough about the other two systems in the works to make a comparison, Dr. Kurtz said, "Our system has the most experience. More than 250 sighted patients have been treated to date…It has an integrated

imaging function, which allows the surgeon to plan the procedure and perform it with very high precision."

Asked if the LenSx system is designed to be used alone or with phaco, he said, "It could be used in both situations. There may be situations where the two would work collaboratively to perform the cataract surgery, and there may be situations where phaco is not required…The phacoemulsification device is used to fragment and remove (the lens). Our device fragments the lens, can perform the capsulotomy, and can perform corneal incisions…You can use the aspiration function on the phaco machine. You still have to have that device; ours does not have an integrated phaco in it, and it wouldn't be wise to do that right now."

Asked in what cases it would be used alone, Dr. Kurtz said, "People often use the term phaco to refer to the entire cataract procedure. When I use it, I mean the ultrasound energy. You don't necessarily need ultrasound energy."

Asked how much time using the machine would add to a cataract procedure, Dr. Kurtz said, "It shouldn't add any procedure time to the actual surgical procedure. Time for the (actual) procedure should decrease. There is an additional step prior to that, which is the laser portion, and that is not necessarily performed in the operating room. In our current trials, we are performing that step in an anteroom, and the patient then goes on to the surgical suite…We don't open the eye. The eye is still closed and intact. The patient can undergo the laser procedure and then be prepped for the operating room procedure to remove the lens material."

An incision is made, but the incision is not open until the surgeon opens it mechanically. Dr. Kurtz explained, "We can create an incision, but the incision still needs to be opened mechanically…The laser is transmitted through the cornea and through the transparent lens. No incision is required to deliver the laser energy."

Asked about estimates that the femto would add 2-5 minutes to the procedure for experienced doctors but cut 10-15 minutes for less experienced cataract surgeons, Dr. Kurtz said, "We need to get out and see how that actually works in practice, but that's a fair assumption. One has to remember that two or three or five minutes that one is adding to the procedure are not necessarily on the operating table. We're not necessarily adding to the operating room (OR) time. There may be an intermediate step from preop to the OR, so a patient can have the LenSx procedure performed, but that should not add time. In fact, it potentially could reduce time by reducing the amount of work that the surgeon has to do."

Asked how the company can sell this machine or add to procedure costs with a per patient disposable charge, given that Medicare reimbursement for cataract surgery is ~$600 (per eye), Dr. Kurtz said that focusing on cataract patients getting premium IOLs will give doctors a way to up charge for the procedure and cover costs (or even make a profit), "The current focus is on the patient-pay refractive cataract surgery market, so the device is intended for − and will be demonstrated to improve − the refractive outcome for those procedures. It will be part of that suite of services that refractive cataract surgeons offer their patients…All-LASIK cataract surgery is a term that can be used, but for right now, since this involves a series of individual procedures, we are calling it femtolaser-assisted cataract surgery…I'm not sure that patients understand what a femtosecond is. We can call it laser refractive cataract surgery because that's really what it is, and it fits very well with laser vision correction…Patients have been asking for laser cataract surgery for decades, and this is something that doctors can explain to their patients with success…I think it will be a premium (cost) relative to standard cataract surgery, but that will be determined in the market."

Besides premium IOLs, the machine could be used for incisional surgeries, astigmatic keratotomy (AK), LRIs, and some other advanced IOLs that are not premium IOLs. Dr. Kurtz added, "Certainly, it could be used for the corneal incisions."

This femto laser will mostly be used in hospitals and ambulatory surgery centers (ASCs), not doctors' offices, but many ASCs are owned at least partially by ophthalmologists. Dr. Kurtz said, "In some ways it's an easier market because the surgeons are more concentrated. There are more surgeons per surgical center than there were for LASIK, where it tended to be more individual practices, so in that sense it can be easier for this technology…Precision almost always wins − and always in ophthalmology − because the eye is an optical instrument…Clearly, with manual procedures we can't do certain things…(A laser) will continue to dominate over purely mechanical procedures because of the predictability, accuracy, and reproducibility…The (cataract) market is developing as a refractive procedure…The technology that doctors are currently able to offer their patients doesn't attain the level of predictability and reproducibility that one expects in an elective refractive procedure."

LENSAR

This is likely to be the second company with a FLACS system on the market. LensAR submitted its 510(k) application on March 6, 2009, based on clinical trials in Mexico on ~130 eyes. The company is not pursuing a C.E. Mark, concentrating instead on the FDA approval.

Asked how the LensAR device compares to the other two femtosecond cataract lasers, Keith Edwards, director of clinical affairs for LensAR, said, "The lasers are similar, with similar wavelengths. The exact way that you create the beam is different. You are doing what IntraLase does for making flaps and disrupting tissue, but the pattern that you cut is different...We cut a circular pattern, and then we have a lot of options when the lens is fragmented. Basically, what you do is dock the patient to the system, then attach a suction ring, then a cone is attached to that and the laser. You scan the eye

using a modified scheimpflug-type light system. It takes an ~30 seconds or so to do. Once you have the (imaging) information, you decide what size capsulotomy to do and what shape and size fragmentation you want. Then you press the button, and it does it for you. The eye is still intact. What we are doing is (going) to conventional cataract surgery to make the incision, peel off the capsule that you cut and that comes away easily. For the fragmented lens, you aspirate the pieces. You don't use ultrasound. You have the benefit of not bringing the high frequency mobile part of the tip close to the eye."

Edwards said one difference between the LensAR device and the LenSx device is that LenSx "uses OCT for its imaging system, and certainly the patterns that they are cutting for lens fragmentation seem to be different. They seem to be doing a chop cut (like an X) and put circles in to try to soften it from there. We are cutting it into smaller pieces that are able to be sucked out. We've had some cases where you just aspirate, and that's what the surgeons would like."

Asked if there is any danger in fragmenting the lens into smaller pieces, he said, "It's a tradeoff between how much laser energy you want to put in vs. how hard it is to aspirate. You have to calculate whether the total laser energy is safe. We are doing the optimum…combination."

As for the difference between the LensAR laser and OptiMedica's device, Edwards said, "From what we've seen, OptiMedica uses OCT. Every system of imaging has its issues. All have an issue with pupil size (won't image if the pupil isn't big enough). OCT is a full system, but when you can visualize it in the normal way and see the lens in the cornea, it seems to be more intuitive."

Looking ahead, LensAR plans to ask for LRIs as an indication. Edwards said, "LRIs are used to correct corneal astigmatism, and that's becoming important. With premium IOLs you don't want astigmatism, and that (procedure) is currently done manually – cutting an arc top to bottom…So, we are looking at doing those with the laser." Other indications will include clear corneal incisions (CCIs) and fragmentation.

Edwards said that so many doctors visited his tiny booth at AAO to find out about the laser that he was out of business cards, "We've had quite a range of people from Asia, Europe, and the U.S., and we've had a lot of distributors who are interested."

Asked if the device could potentially be used for refractive surgery, he said, "It would be possible to take it a step further and do flaps, but that isn't where we are looking. We're concentrating on cataracts because that is the unique market. IntraLase has the refractive side sewn up."

Asked how difficult it will be to market a new device in the current economy, Edwards said, "In this bad economy we have to come up with a business plan. This is a different market from LASIK. There will be a premium, but you don't want it to be too expensive. Right now, there are no disposables, and we're still working our way through that."

CEO Randy Frey has a background in the area – he founded Autonomous. Frey said, "In cataract surgery, the standard of care is 20/40, and we want to make it 20/20. The success rate at 20/40 is not even 90%; it's between 70% and 90%, and we'd like to see some attention paid to the 20/20 (segment)."

Asked which cataract patients the device will target, Frey said "100% of cataract patients are eligible." However, he said that paying for it will be a problem, "The Medicare side is frustrating." He said that the future may lie in LRIs, "Many cataract surgeons do LRIs, and those who do usually do not charge for them (because of the variability of results). We have the potential to make a big difference in predictability in refractive outcomes of refractive cataract surgery. There is a tremendous amount of value in LRIs."

OPTIMEDICA

OptiMedica is likely to be No. 3 to market with a cataract femto. CEO Mark Forchette said that the company has not yet filed a 510(k) application, "We are in a research and evaluation process, and we are moving through the proper steps… There are a lot of elements to this system that are important. It's all about precise positioning, and there are things with the way that you manage imaging, the way you dock the patient, and the precision with which you deliver the segmentation. We believe that we have advantages in each of those steps that we will work through."

Forchette said that the femto cataract area "is a fantastic new space." His company's approach to fragmentation is to break the lens into cubes, "They're bigger than phaco, but they are not quadrants. We give (doctors) the option. They can be quadrants, or they can easily break into aspiratable cubes, and that's the physicians' customization capability."

Forchette said that OptiMedica is aiming to address two areas in particular with its cataract femto:

- **Safety** – addressing the posterior capsule rupture rate. "It's addressable, and there are ways to improve the safety of procedures by addressing that with precise capsulotomy and not leaving some of those things maybe to variations of freehand surgery."
- **Precision** – assuring precise positioning of the lens implant, especially in terms of premium IOLs. "Physicians are clearly going to see that precision."

Asked who will benefit from femtosecond cataract surgery, Forchette said, "The benefits are clearly applicable to all but most likely will be utilized for premium IOL patients. That is the business model." He said that there will be "some type of consumable element" to the price, and that is where the recurring revenue will be as opposed to in the just selling the device itself. There will be a device element and a consumable element, no click fees.

Asked if the device would be an adjunct to phaco, Forchette said, "Our objective is to provide a technology that makes everyone better versions of themselves. If you think about it, precision of capsulorhexis in precise positioning makes every one of those (IOL) companies more capable of delivering the benefit…to patients…Phaco technology is not going to go away, but it might be greatly reduced…The phacoemulsification platform will have a vital role; it is not going to go away …They are complimentary technologies, and depending on how the physician elects to manage that case, they'll manage the utilization of them appropriately for each patient."

Forchette said that doctors will be able to use the OptiMedica femto no matter which phaco machine they are using, "This is technology that is…a new category. It is going to replace manual steps. We are addressing the most manual technologically demanding steps in a cataract removal procedure, and this overlays the existing phaco capability."

The onlookers

➢ **ALCON/WAVELIGHT.** Alcon VP MacHatton said, "We are interested in the technology. We're very well aware of it, and we're familiar with how it works. The challenge is: How do you incorporate it into a surgical practice? How does it add economic value? Can you charge more? Can you get reimbursed?"

MacHatton noted that most doctors already have a phaco machine, "That's not to diminish it. Phaco came almost out of nowhere…I think that it's always interesting to look at new technologies that provide better refractive results. You want to be able to have a lens or lens system that can give you vision across all three areas, and it's never one piece; it's the whole system. A femtosecond cataract removal (system) would be interesting, but is it really ready?"

➢ **ZIEMER OPHTHALMIC SYSTEMS.** Ziemer is not working on a femtosecond cataract laser. President/CEO Frank Ziemer said, "Not for the moment, but, of course, we are following this very closely. We want to understand what is going on. We are doing market research and looking at the technical side in order to understand what is going on…It is not merely a technical question of if we can do this; it is a question of what the business model would look like. Would it be a good business? It sounds like a good idea. There are a lot of questions, but definitely it is an interesting approach."

THE COMPANIES

Big pharma

Several knowledgeable sources said that big pharmas – particularly Bristol-Myers Squibb and Sanofi-Aventis – have been sniffing around the ophthalmology area. Alcon's MacHatton offered several reasons that big pharmas are interested in the eye care business right now, "This is a concentrated niche that has steady demand, that is age-related across consumer, surgical, and pharmaceutical products. Not a lot of industries have that so you get balance…You don't have a market for hip and knee (replacements) in China; that will take years. But it's not going to be 20 years before people in China get cataract surgery…The other reason is affordability. Most eye care treatments are very affordable, and when you amortize over someone's life the cost of cataract surgery, which is $2,000 per eye, the average person will pay $200 a year for a surgery that will result in the ability to see, which is pretty astonishing. It works the same way for glaucoma surgery."

ABBOTT

Abbott's purchase of AMO appears to be going very well. Generally, people who work there think it is better, a better place to work. AMO reportedly wasn't a healthy climate before Abbott stepped in, with some dysfunction, acrimony, and turnover, and "everyone kind of unhappy." Now, there is still some of this but much less than before.

From a business standpoint, though, Abbott/AMO reportedly has had a very tough time with innovation after losing a lot of IntraLase and Visx talent, but sources said this is starting to change.

ALCON

Alcon VP MacHatton said that what ophthalmologists were most interested in at AAO was advanced IOLs, "That's the thing that is exciting right now. Although the economy is soft and having an impact, and LASIK is down 30%-40% from last year, premium IOL is flat as a category, and that demonstrates what the demand is. A lot of patients are motivated to do it, and they only have one chance to do it."

MacHatton claimed that Alcon has ~30% of the excimer market share in placements and procedures, "We just added 75 (machines) with the LCA-Vision contract. We are pretty pleased because WaveLight is the most modern and advanced technology there is today. It is very reliable." Another Alcon official said that about 340-350 units plus the 75 LCA-Vision lasers have been placed in the U.S. Worldwide, the company has sold 1,300-1,340 excimer lasers.

MacHatton said that "We're working through" the regulatory hurdles to get approval for the company's (WaveLight) femtosecond laser and predicted that it may be rolled out internationally by the end of 2010, with a C.E. Mark expected by the end of 2009. He said that there are no technical problems with the machine and insisted that the plan was not to roll it out sooner.

Falcon Pharmaceuticals, an Alcon affiliate, got FDA approval for a generic version of Allergan's Alphagan (brimonidine) on October 2, 2009. Under an agreement with Allergan, Alcon will pay a royalty to Allergan. Falcon does not plan to launch its brimonidine until January 2010. MacHatton said, "We think there is a good opportunity there because 40% of the U.S. market is still (Alphagan) 0.15%."

What happens to Ciba Vision when and if Novartis completes its purchase of Alcon? In the past, some Alcon sources have resisted the idea of getting into contact lenses – unless forced to do so. But that tone appears to have changed. MacHatton said, "The contact lens business is an interesting area. We know a lot about optics, the surface of the eye, and interaction of the eye with devices, but it's a challenging area. It goes through periods where technology drives increased sales, demand, and differentiation, and five years or three or two years later, everybody is on the same plane. They can push out millions of these buttons every month, and it becomes commoditized. The opportunity that exists that we would see from a developmental standpoint, for the first time, is taking the leader in solution development − which is us − and combining it with a leading (contact lens) platform. Some would argue for a silicon hydrogel lens and to tailor that solution lens interface to optimize or improve comfort and the wearability of the lens. Why is it that people drop out of lenses in their mid-40s? One reason is presbyopia, and another is comfort…Both reasons definitely push the people out of lenses. You have two million people who leave the (contact lens) market, and two million who enter it. So, you have a flat market except for emerging markets on an international level. What we see is extending the wear-life of patients beyond 21-45 years of age to maybe 14-60 or 65 years old – just push it out. If you can push that wear-life out, you can turn it into a growing area. We think that it's important to do that, to bring together these technologies and design solutions and lenses as a system."

ALLERGAN

The reports were that Allergan is looking to get into the device side of ophthalmology as well as the drug side.

BAUSCH & LOMB

The company appears still to be in disarray, and Crystalens is losing market share.

CARL ZEISS MEDITEC

At AAO Zeiss was emphasizing:

- **Forum, its "solutions" approach to data management.** Forum stores all diagnostic patient data, providing a paperless diagnostic and surgical workflow.

Forum was launched internationally at ESCRS, and it was launched in the U.S. at AAO. Forum, which is considered a PACS Class II device, has FDA approval. Dr. Ludwin Monz, a member of Zeiss's Board of Management, said, "We are transforming our company to be the solutions provider for the eye care industry. We can provide solutions and products that allow doctors to reorganize their workflow, which gives them better efficiency."

Zeiss is going beyond just connecting different devices, putting the various "puzzle pieces" together to combine imaging devices, surgical devices, technical services and support, connectivity, consulting/practice building, and training. Zeiss's platform for doing this is Forum, an advanced ophthalmic image and report management solution that is DICOM compatible. It links diagnostic instruments and OR devices. It can send information bidirectionally to an electronic medical record. It is reportedly the only web-based PACS system in eye care. Dr. Monz said, "I believe DICOM will be the standard in ophthalmology. It has already been accepted widely…DICOM originally came from radiology, but it has now been adapted for ophthalmology. It is our firm belief it will be the standard of the future."

Shawn Dastmalchi, PhD, director of U.S. informatics business at Zeiss, added, "DICOM has been adopted by the camera imaging side of ophthalmic devices. Interoperability is key to those products, and we believe it will be key to all ophthalmic devices…Most Zeiss diagnostic instruments now provide bidirectional DICOM communication. There hasn't been a DICOM archiving system to take full advantage of that, and we are now in the lead in this area. We believe our open standard approach will draw more third party devices to this area…If a third party device is not DICOM, Forum still interoperates with it as long as that device is a networkable device – if that device has a way to be put on the network and export out information from it. Then we could pull that information into Forum."

How long does it take a typical practice to convert? Dr. Dastmalchi estimated about three days for the typical office – one day to install, one day to train, and a third day to observe and do additional training.

Asked about how different EMRs interact with Forum, Dr. Dastmalchi said, "There is quite a bit of variability on the EMR side...from the standpoint of what they believe is the core of their technology and what features they want to present to customers…As a result, the level of interoperability with us varies…It often takes a release cycle on their (EMR) part to make the interface with Forum made available to customers…At the end of the day we would like for us to get beyond just linking EMR client software to Forum Viewer, but for the sake of data consistency, that modality works with scheduling to start with the EMR, so that is an area on which we put a lot of emphasis."

Asked if Forum can interact with Medicare and other payers, Dr. Dastmalchi said, "The billing component is the part the practice management (system) handles. Practice management systems handle billing…In the future, open standards such as DICOM Modality Performed Procedure Step (MPPS) will better integrate Forum with practice management systems, but that is not in place today…That is the domain of practice management system providers."

Zeiss officials wouldn't discuss costs for Forum except to say pricing is "highly modular" and "very competitive in the marketplace."

➢ **New products:**

- Cirrus HD-OCT-400, an enhanced high definition OCT with faster imaging software.
- OPMI Lumera 700 with Resight, a new surgical microscope for cataract and retinal (posterior segment) surgery, and the Callisto OR planning system.

Zeiss officials claimed their excimer laser, Mel 80, is "progressing well." Dr. Monz said, "We strongly believe in the femtosecond technology – how it can be expanded in time to also replace the excimer laser." So far, about 20 Mel 80s have been placed in the U.S. and another 420 outside the U.S. The Mel 80/VisuMax Workstation femtosecond laser is currently being evaluated at 4 U.S. sites. Outcomes of the FLEx all-in-one LASIK procedure performed outside the U.S. are expected to be presented during the American Society of Cataract and Refractive Surgery (ASCRS) meeting in 2010.

Asked about plans for all-femtosecond refractive surgery, eliminating the excimer laser, a Zeiss official said, "That is not available yet. These are studies we are doing…We believe that a femtosecond laser has the potential to replace an excimer laser at some point in time…Technically, it clearly has the potential. The results we have so far support that…It will not only replace it; we believe it will have advantages because the refractive surgery may be done less invasively…It could reduce the size of the incision…You don't produce a full flap, just an incision, and remove the material. If that is possible, it has some major advantages…But that is in the future."

TECHNOLAS PERFECT VISION

Chief commercial officer Mike Riding said that the company's new relationship with Bausch & Lomb "is going very well. We are toward the end of our formative year and have been through the trauma of trying to create a new company. The organization is fully in place and predominantly represented by people who came out of Bausch & Lomb running the refractive business, plus the skills of people in 20/10, so we have completed that (transition). One of the last milestones was getting our own computer system. After nine months of running transactions through Bausch & Lomb, we are now running our transactions ourselves."

Riding agreed with others at the conference that it is not obvious that there is any economic recovery, at least in the ophthalmic sector, "The question is: Are we at the bottom or will we see more dip down? I'm hearing a number of doctors saying that the inquiry levels are rising in the U.S., but some of that might be wishful thinking…We're assuming that we might get 5% improvement next year in the U.S. market."

However, Riding said that things look brighter in emerging markets such as China, where procedure volumes are expected to increase 10%-20% next year. Other emerging markets include India, Russia, the Middle East, Brazil, and Latin America. Riding said, "Sales of machines will go up very significantly next year. Most of this year we didn't push (the femtosecond). We wanted to refine it…We're at the point right now where the technology is ready to go, and we have filled the books. We wanted to wait to take it to market in a controlled way. The procedure that we're doing is not approved in the U.S. It's to correct presbyopia. IntraCor finished its initial trial, received a C.E. Mark in April (2009), and we will be beginning FDA studies at the beginning of the year (2010)."

Asked if Technolas Perfect Vision is working on a femtosecond machine for cataract surgery, Riding said, "The technology is suitable but we are not looking at that today because we have other priorities. Our goal is to become specialists of the cornea. IntraCor is our primary focus. There are other applications in the cornea (that we are looking at) as well."

Technolas Perfect Vision will present its study proposal to the FDA in December 2009, and it is recruiting centers. Riding said that the study is planned to begin in mid-2010, "The procedure is painless, takes 15 seconds, and the recovery time is two hours," he emphasized.

Riding said that another procedure that he believes will come to maturity is presbyLASIK, "If you have a refractive error and have worn spectacles, but you are also perhaps in your 40s or 50s and become presbyopic, this is a solution. Other solutions have been on the market but are not good enough, and we will be coming to market next year (with our solution)."

GLAUCOMA

Most glaucoma specialists questioned at AAO said the recession has had minimal impact on their practice, and patient volume is holding steady – and expected to remain flat over the next 6-12 months − but patients have become much more cost conscious. Comments included:

- *California #1:* "Patients are more concerned with the cost of medications and their ability to comply as a result of the recession, and hospitals are reluctant to buy new equipment, saying they can't buy because of the expected Medicare cuts."
- *Virginia:* "Some patients lost their insurance, so we wind up seeing people for free, but patient volume is steady. The drugs are very expensive. The companies have needy patient plans, but they take an incredible amount of work, and there is a really high bar to get over, and the copays can be too high, so patients don't buy the drugs."
- *California #2:* "My patient volume is holding steady, even gradually coming back a little."
- *New Jersey:* "Most of my patients are Medicare patients, so I haven't seen any effect from the recession on my patient volume or my practice."
- *Pennsylvania:* "There has been an increase in patients not wanting to buy expensive medications or pay for visual field tests, but my patient volume is flat."

- *Georgia:* "Patient volume is holding steady."
- *Oregon:* "There was a dip in patient volume earlier this year (2009), but that was more related to general ophthalmology. Glaucoma volume has been steady for us."

GLAUCOMA MEDICATIONS

Worldwide Market for Glaucoma Medications

Country	Market share (% of units sold March 2008-March 2009)
U.S.	15.2%
Japan	13.7%
Germany	7.6%
France	6.9%
Italy	5.7%
Other	50.9%

Dr. Janet Betchkal of Jacksonville FL said that it is a "hard sell" convincing glaucoma patients to take their medication, "We have to convince patients they need to do this. The benefits of treatment are very difficult for patients to understand. You have to get patients to 'buy' what you are 'selling.' The patient has to buy in."

How do ophthalmologists choose among the available medications? Dr. Betchkal said that most data show the FDA-approved prostaglandins have similar efficacy, so the choice is based on personal experience, patient tolerance, cost, samples (which are very important), and pharmacy dispensing methods.

The prostaglandin market

In the U.S., the most commonly prescribed glaucoma medication is a prostaglandin: Pfizer's Xalatan (latanoprost), Alcon's Travatan and Travatan Z (travoprost), and Allergan's Lumigan (bimataprost). Prostaglandins account for 42.9% of U.S. glaucoma prescriptions, and Xalatan has the largest piece of the prostaglandin market. However, Xalatan will go generic in 2011, and ophthalmologists questioned at AAO estimated that the overwhelming majority of their patients will switch from all the branded prostaglandins to generic latanoprost, though the impact will be greatest on Xalatan. Cost is a huge issue for many glaucoma patients, and several sources referred to prostaglandins as "liquid gold," costing the equivalent of $900-$1,140 an ounce (compared to ~$1,000 for gold)." Dr. Betchkal said, "The price is going down, and that will shake up and turn upside down our market. If you don't believe cost will be the driving force, just look at what is happening in Washington right now."

Other comments on the outlook for generic latanoprost included:

- *Tennessee:* "Right now 20% of my prostaglandin patients are on Xalatan, and that will increase to more than 60% when a generic is available. No insurance company will allow a brand unless a patient fails generic Xalatan first, and I think they all have equivalent efficacy."
- *California:* "Half of my prostaglandin patients are on Xalatan. When generic Xalatan is available, there will be more marketing for non-preservative Travatan Z. The (prostaglandin brand) marketing won't be on pressure control but on side effects and tolerability. In a year, half of my patients will probably be on a generic. There is a shift going on now to beta blockers because of cost, and generic Xalatan will increase prostaglandin use…But this depends on how good the generic Xalatan is. Pred Forte brand (Allergan, prednisolone acetate) and generic prednisolone are absolutely not equivalent."
- *Virginia:* "Only about 25% of my patients are on Xalatan because it is a Tier 3 drug. In one year if the generic is really cheaper, 90% of my patients will be on the generic. I'm very conscious of what patients pay."
- *Veterans Administration doctor:* "The VA has a contract for travoprost, and I'm sure they will go to the generic when it is available…If it is just as effective, pharmacists will be forced to use the generic."
- *Georgia:* "About 25% of my patients are now on Xalatan, and the majority are on Lumigan. A year after generic Xalatan is available, 75% will be on the generic. Some patients who are doing well and don't want to switch will stay on the brand, but I think all the prostaglandins are pretty equivalent."
- *Pennsylvania:* "Half my patients are on Xalatan, and even if a generic Xalatan is available, only about 10%-15% of patients will go on that. I'll stay with the brand. I like brands better than generics. But I may change some Lumigan patients to generic Xalatan because of the red eye with Lumigan."
- *New York:* "From 60% to 70% of my patients are on Xalatan. A year after it is available, about 10% of my patients will be on generic Xalatan, and that will be all former Xalatan (brand) patients – unless the insurance companies force it…Patients tend to buy what the insurance company says. I've seen patients paying a $70 copay when they can buy a drug full-price for $68 somewhere other than where the insurance company recommends."

MERCK/SANTEN's tafluprost

This is a prostaglandin without a preservative. It is in Phase III trials in the U.S.

ALLERGAN's Combigan (brimonidine + timolol)

Ophthalmologists said they are using Combigan, but generally for <5% of glaucoma patients. Use is likely to increase over the next 6-12 months, but still remain <10% of glaucoma patients. One doctor cited cost as a factor, "Combigan is very

expensive, and people are reluctant to stay on it when they see the cost. But there is a place for it. In a year, I might be using it for 5% of patients." Another said, "Combigan is getting on more formularies. That has been an issue, but there has been some improvement. But it will still be a small number of patients on it because it doesn't always work." An Idaho doctor said, "I use a little Combigan – ~5% of glaucoma patients – but my use is holding pretty steady." A North Carolina doctor added, "My use is ***slowly*** going up, but I'm doing a lot of lasers."

Neuroprotection

Will there ever be a neuroprotective agent for glaucoma? Dr. Stuart McKinnon of Duke University said probably not in the next 10 years but maybe in his lifetime, "Neuroprotection is not quite ready for prime time, but recent findings show considerable promise for the development of targeted therapies."

What is most promising at this point? Dr. McKinnon emphasized:

1. **Anti-amyloid beta.** Although Allergan's memantine did not show any benefit in glaucoma, Johnson & Johnson's Razadyne (galantamine) has shown some neuroprotective ability in a rat model.
2. **Complement C1q inhibitors.**
3. **Tumor necrosis factor-alpha (TNF-α).**

GLAUCOMA DEVICES

There was no device pipeline talk at Glaucoma Subspecialty Day, and doctors asked about this suggested it is because nothing in development looks particularly promising or practice-changing. Rather, they said there has been a lot of disappointment with the devices in development. The AAO's Dr. Rich cautioned, "One of the issues with glaucoma and the device industry is that it is harder and harder to find people to pay for device development and developing the clinical data… I have concern about access to capital to develop the separately needed innovations in surgical glaucoma care when the number of surgeries is so few…How to get enough capital involved to get the patient volume and peer review literature? How to get it when no one pays for it? I think we will have to think carefully about an orphan device industry approach – a concept I've been thinking about. New devices have financially struggled…There hasn't been a breakthrough…Will it chill further development? I'm concerned about the long-term commitment of people with capital to fund needed innovation that we are starting to see. I think it is something policymakers in Washington will have to consider."

EyeLight's ELT (excimer laser trabeculostomy)

With the ELT procedure a surgeon inserts a 500-µm probe through a corneal incision, and its laser is brought into contact with the inferior/nasal trabecular meshwork on the side of the eye opposite the paracentesis. Non-thermal, 308 nm excimer laser energy is delivered, excising the trabecular meshwork, juxtacanalicular trabecular meshwork, and the inner wall of Schlemm's canal without damaging the outer wall or collector channels. In current protocols, the doctor creates 5-10 openings.

Dr. Michael Berlin of UCLA, who developed ELT, said the procedure enables pneumatic canaloplasty; it is like a glaucoma shunt without a device or foreign body. ELT has been approved in Europe, but the company needs a partner to develop a second-generation device and get it through the U.S. regulatory process. Dr. Berlin is optimistic about the FDA pathway, "There is a lot of precedent for laser use in the eye at 810 nm; that is already accepted and proven. Lasers are also approved for dermatology and cardiology…We use a 308 nm laser…The issue is safety and not efficacy, so we believe a shorter trial or a 510(k) approach is what the FDA will require…This is a parallel to (NeoMedix's) Trabectome (a minimally-invasive surgical procedure for glaucoma), which got approval easily."

How difficult is the procedure to do? Dr. Berlin said, "The first generation requires similar skill to that required for the Glaukos device (iStent), which is too difficult for the average cataract surgeon – and in the U.S. cataract surgeons do most of this surgery. But the second-generation ELT device will be much more user-friendly. It will be like LASIK was before and after tracking." An Arizona doctor said, "I have to see it in the hands of others (other than Dr. Berlin) to see if they can duplicate the results."

Glaukos's iStent

Glaukos already has submitted iStent to the FDA and is hoping for a January or February 2010 advisory committee meeting.

A poster at AAO reported on a rather disappointing study on this device of iStent, a heparin-coated titanium stent. GC001a was a prospective, uncontrolled, European (Italy, Germany, Netherlands, and Portugal) study of 45 glaucoma patients with intraocular pressure (IOP) >21 mmHg who had failed prior glaucoma surgery such as trabeculectomy (91%) or who were deemed likely to fail filtration surgery (9%) who got just one iStent.

Of the 45 patients in the study, only 28 (62%) completed the 24-month follow-up. The per protocol efficacy analysis included only 17 patients, and at Month 24 it showed:

- A mean decrease of 11.3 mmHg in IOP (from 28.8 mmHg to 17.5 mmHg).
- 32.8% of patients had "substantial" reduction in mean IOP.
- 94.1% of patients had IOP ≤21 mmHg. Of patients with IOP ≤21, 43.8% (7 of 16) were using no medications.
- Medication use was decreased an average of 0.9, which was statistically significant but less than the expected.

The intent-to-treat safety analysis included 28 patients, and 25 of these had a total of 45 adverse events. The most significant was IOP failure on two consecutive study visits after Month 3, which occurred in 17 of the 28 patients. Of these, 15 had to have surgical intervention (trabeculectomy). Other device or procedure-related adverse events were high, and this was blamed on the surgeon learning curve and on one site that reportedly enrolled patients who were too refractory.

The lead investigator, Dr. Carlo Traverso of Italy, had no real explanation for the high dropout rate, and he noted, "I am not promoting this as the new wonder thing." He said he would not use iStent in patients with ocular hypertension, "The ideal patients are those with primary open angle glaucoma (POAG) with early-to-moderate stage disease and an increase in IOP that responds poorly to medications…I would use it in 15%-20% of glaucoma patients. This is a niche…but in the 15% of patients range. It does ***not*** compete with filtration, just medications."

iStent has a C.E. Mark and is being sold in Europe, but sales have been light. The company is doing a "controlled rollout with invitation only" training. Dr. Traverso said he isn't using iStent outside of clinical trials, "I work in a university hospital. I use iStent where I get the funds for a trial. It is difficult to get permission to buy."

Dr. Traverso said the procedure is "demanding," particularly with the "snorkel" shape device which was used in this trial. However, he said the new design is a straight-line design which should be easier for doctors to implant.

Safety Results with iStent

Adverse events	Number of patients
Stent lumen obstruction	2 patients
Malpositioned stent with subsequent repositioning/additional implant	2 patients
Anterior chamber collapse (peri-operative)	2 patients
Malpositioned stent	1 patient
Shallow anterior chamber/iridotomy due to closed angle	1 patient
Excessive bleeding in anterior chamber	1 patient
IOP failure treated with trabeculectomy	15 patients
BCVA loss ≥2 lines	8 patients
Cataract progression	6 patients
Infection localized to external ocular surface	1 patient

The iStent was redesigned after this study to make it easier to implant with less trauma to surrounding tissue.

In contrast, significant safety issues were not reported in a larger, 240-patient, prospective, randomized, multicenter (29 site) trial of cataract surgery ± iStent in patients with mild-to-moderate open-angle glaucoma. The results looked positive in this pivotal U.S. trial, but experts still were *very* critical of the data insisting that clinical utility was not shown. There did not appear to be any significant safety issues as with the earlier European trial. Rather, the issues with this trial appear to be:

1. Failure to lower IOP more than could be achieved with medication alone, thus not justifying use of a device.
2. Failure to achieve an IOP level in the desired range – ~13 mmHg – even though the trial only aimed at getting pressure ≤21 and did that.
3. Only benefit was a reduction in medication use.
4. An apparent need for a second or third stent to achieve more than medications can, which is what the experts want. In this trial, only one iStent was implanted in each patient, though a trial is underway in Europe testing two and three iStents, but the U.S. program so far is only one stent. Dr. Thomas Samuelson of Minneapolis, the principal investigator and a Glaukos consultant, said that in Canada surgeons are achieving an IOP ~13 mmHg with more than one stent – two in most cases, three sometimes, "We expect to gain improved outflow through one quadrant (of Schlemm's canal) with one stent. For patients who are more refractory, more than one stent (may be needed)." But for now, the approach in the U.S. is just one iStent per patient per procedure.

The iStent is designed to lower IOP in glaucoma patients by creating a permanent bypass through the trabecular meshwork into Schlemm's canal that enhances physiologic flow. The device, which weighs 0.1 mg, is implanted through a clear corneal incision using a disposable inserter after the cataract is removed.

Dr. Samuelson was very upbeat and enthusiastic about the current data, "Coincident cataract and glaucoma surgery is an appealing strategy. Cataract surgery alone is known to lower IOP, yet long-term medications are often required post-operatively to maintain IOP control…Phacoemulsification and trabeculectomy each have completely different mechanisms of IOP reduction (trabecular vs. trans-sclera). Thus combining the two procedures is likely to increase the effect of one or the other on IOP reduction. The iStent and cataract surgery share similar mechanisms."

This trial enrolled patients with symptomatic cataracts who had not had prior glaucoma surgery. Dr. Samuelson reported no difference in safety between the two groups, "We were comparing a safe interventional against an amazingly safe procedure…There was no compromise in safety (with iStent use)…The stent had to be repositioned in 5% of patients – always interoperatively – while one patient in the cataract-only group went on to have a glaucoma procedure…The iStent and cataract surgery enabled significantly more patients to remain medication-free than cataract surgery alone. More than twice as many patients in the iStent group were off medication at one year. In this trial, iStent was shown to provide a positive benefit:risk ratio in patients."

Dr. Samuelson noted these limitations to the study:

- It did not include more advanced or severely uncontrolled glaucoma patients.
- The investigators were **not masked**.
- There is a learning curve for surgeons.
- Schlemm's canal flow is not circumferential.

Physician comments about iStent included:

- "It only makes sense when you are already doing cataract surgery."
- "A single stent is often not effective, but putting in the second or third stent is technically difficult."
- "iStent is easier than canaloplasty or (NeoMedix's) Trabectome (a minimally-invasive procedure that removes a portion of the trabecular meshwork). iStent is probably something that could come down to which economic model is best for doctors – Trabectome's $40,000 device (with a $415 disposable cost per case and a $790 facility fee), or the iStent."
- "It is curious that they put in one stent, and IOP goes down, but if they put in a second or a third stent, there is no further decrease in IOP."
- "People who have put it in say you need more than one stent and that it is not easy to do, but it is a neat idea. I'm disappointed that it doesn't work to the degree people had hoped…The iStent still has some legs and so does canaloplasty, but Solx's gold shunt is over. "

12-Month Results of iStent Trial

Measurement	iStent + phaco n=117	Phaco alone n=123	p-value
Primary endpoint: IOP ≤21 mmHg without medication	73% * (23% more than phaco alone)	50%	<0.001
Secondary endpoint: IOP reduction ≥20% without medication	67% (19% more than phaco alone)	48%	<0.002
Change in IOP from baseline	-8.4 mmHg	-8.5 mmHg	Nss
Patients on IOP lowering medications	15%	35%	<0.05
Postoperative medications	0.2	0.4	<0.05
Adverse events			
Anticipated early postoperative event	13%	12%	---
BCVA loss ≥1 line at ≥3 months	5%	5%	---
Posterior capsular opacification	3%	7%	---
Blurry vision or visual disturbance	1%	5%	---
Iritis	1%	5%	---
Stent repositioning or laser iridoplasty (for stent malposition/obstruction)	5%	N/A	---

*Excludes data after second surgery

REPLENISH's mini drug pump

A small, intraocular drug pump – like a tiny insulin pump – is being developed to deliver metered doses of glaucoma medications directly to the eye over time. Dr. Mark Humayun of the University of Southern California said the device can deliver drugs from 3-9 months with ±2% accuracy. The refillable device is implanted with a minimally invasive procedure using "established surgical procedures."

What's really interesting about this pump is that it can be refilled, using a refill port and a 31 gauge transconjunctival system, with either the same or a ***different*** drug. However, it will only work with Replenish-approved drugs. The refill system reportedly flushes out 99.99% of residual drug in <30 seconds. Dr. Humayun said, "If one drug is not effective, you can put another drug in." In addition, wireless programming allows the doctor to change the timing or quantity of drug dose. The battery can be recharged wirelessly. Preclinical data are scheduled to be published in December 2009 on refilling performed once a month for six months. A check valve prevents backflow.

Dr. Humayun said, "It is looking very intriguing…The pump puts 1/100th of a drop into the eye, and it reduces IOP more than the typical timolol (a beta blocker) drop. It lowers IOP more than Travatan Z (Alcon, travoprost Z) out to four hours, and then Travatan Z is a little better, which tells me we can tweak it and be better (than Travatan Z)…What I would really like is a closed loop control. I think that is very exciting, but that is not in the primary device…I thought it would raise IOP, but we are actually seeing an early decrease in pressure, and the little amount of drug is not being flushed out; it is staying around."

Bench top testing is continuing, with human clinical trials expected to start early next year.

RETINA

Most retina specialists questioned at AAO said the recession has had minimal impact on their practice, but patients have become much more cost conscious, are having trouble paying for medications and copays, and patient compliance is down. Comments included:

- *New York #1:* "The recession has only had a slight impact on my practice. For most retina specialists, 40%-65% of patients are Medicare, so we are more worried about healthcare reform than the recession. I'd be happy to make 10%-15% less if there were real tort reform."
- *Nevada:* "My patient volume is flat to slightly up, especially my surgical volume. Patients want to get things done before they lose their insurance, so there has been a surge in surgery in the last six months."
- *Maryland:* "My patient volume is flat, and I expect it to stay that way for the next six months."

- *California:* "The recession hasn't had much impact recently. It did 6-12 months ago, but I think things are better now – because I'm mostly Medicare. But there has been a dramatic increase in patients asking if things are covered."
- *South Carolina:* "More patients have less money for copays and outstanding bills. I haven't changed anything clinically as a result of the recession, but I have administratively; my front office has had to get tougher with patients."
- *New York #2:* "The jobless rate in my area is about 10%, and whether that will impact patients' ability to pay is a question, but so far my volume is steady."

Dr. Timothy Murray of Bascom Palmer Eye Institute said ophthalmology is the third most expensive practice in medicine, with an average office expense of $250/hour, and retina is the most expensive subspecialty within ophthalmology.

Dr. Murray examined the efficacy and profitability of a hospital-based retinal practice under a grant from NeoVista. He found that over 10 years (from 1999 to 2008):

- Physician operating expenses rose 43.8%, but Centers for Medicare and Medicaid Offices (CMS) reimbursement only increased 9.7%.
- Patient volume increased significantly.
- OCT utilization increased 46%.
- Intravitreal infections increased 25%.
- The retina service contributes significant profits to the hospital and to the ophthalmology department.
- "Ultimately, Bascom Palmer retinal doctors worked harder than ever to maintain – at best – a fiscally neutral department."

American Society of Retina Specialists (ASRS) survey

Every year, ASRS surveys its members, and there were some interesting findings in this year's survey, which had 434 respondents:

- 50% of retina specialist treat only one eye at a time with anti-VEGF injections, while 32% do bilateral injections.
- 74% use OCT primarily to follow patients getting anti-VEGF injections, while 23% use both OCT and fluorescein angiography.
- Initially, 76% do 3.4 anti-VEGF injections, and then base additional injections on lesion activity/vision; while 15% do just one injection and then move to activity/vision-based injections; and 6% inject the eye every 4-6 weeks regardless of lesion activity.
- 66% of doctors do anti-VEGF injections during normal clinic hours, but 17% have a separate injection clinic.
- The treatment of choice for vitrectomized diabetic patients with diffuse diabetic macular edema (DME) is: 33% Avastin (Genentech, bevacizumab), 31% laser, 28% triamcinolone acetonide, and 2% Lucentis (Genentech, ranibizumab).
- The DME treatment with the greatest efficacy (as measured by a visual increase over 1-3 months) is: 56% triamcinolone, 27% Avastin, 9% macular laser photocoagulation, and 3% Lucentis.
- The treatment that provides the greatest efficacy by visual improvement at 1 year is: 54% macular laser photocoagulation, 14% Avastin, 12% triamcinolone, and 4% Lucentis.
- In the last year, 37% have increased their anti-VEGF dosing regimen, 10% have decreased it, and 52% have not changed it.
- To maintain optimal visual acuity outcomes, 36% of retina specialists believe that more than half of wet age-related macular degeneration (AMD) patients require chronic treatment (>6 injections a year), 27% believe 31%-50% of AMD patients need chronic treatment, and 37% believe that fewer than a third of AMD patients need chronic therapy.
- 73% of retina specialists have a financial interest in a nearby ASC.
- If these retina specialists had wet AMD themselves, the treatment of choice would be: 43% Avastin, 41% Lucentis, 11% PDT + an anti-VEGF, and 1% an anti-VEGF + a steroid.
- For a 70-year-old patient with a subfoveal CNV lesion of 1 disc area, 20/100 vision in the affected eye and 20/25 vision in the fellow eye: 56% would administer Avastin, 36% Lucentis, 6% PDT + Lucentis or Avastin, and 1% an anti-VEGF + a steroid.

WET AGE-RELATED MACULAR EDEMA (AMD)

Medicare reimbursement for Roche/Genentech's Avastin (bevacizumab)

On October 1, 2009, Medicare announced, without prior notice, that it was reducing the payment for Avastin from ~$50 to $7.20, effective immediately. Ophthalmologists – and even some members of Congress – immediately went to work trying to convince Medicare to reverse this decision. Medicare saw the light and on October 28, 2009, agreed to reinstate the old reimbursement, but not until January 1, 2010.

Thus, for three months, **retina surgeons will lose ~$33 or more on every Avastin injection they give**. However, members of Congress, ophthalmologists, and the AAO are trying to convince Medicare to either make the change retroactive to October 1, 2009, or at least move up the date.

The new CMS fee does not take into account the compounding fee that ophthalmologists have to pay because Genentech doesn't make vials or syringes with the low dose required for off-label use in AMD, so larger vials packaged for on-label use in oncology have to be repackaged by a compounding pharmacy. Yet, there is precedent for CMS to pay for compounding. There are pain drugs and asthma preparations for which CMS includes the cost of compounding in its reimbursement.

Medicare reimbursement for Avastin was a big topic of discussion at AAO. Dr. George Williams of William Beaumont Hospital in Royal Oak MI provided retina surgeons with an update on the issue. He explained that the new payment (ASP +6%, based on pricing data manufacturers report to the government) is $7.20 for the standard dose used in AMD because the Medicare pricing system does not consider compounding costs.

Dr. Williams said the AAO staff was meeting with CMS staff "almost daily," and officials of AAO and the ASRS had "multiple contacts" with CMS and also directly contacted Medicare carriers. But getting this fixed proved harder than anyone expected. Dr. Williams said, "We thought we had a solution. The initial response (by CMS) was quite positive, and we were told…it would be fixed. Two weeks have passed, and it is still not fixed. AAO and ASRS have a joint effort to show CMS the folly of this policy. We have had contact with more senior CMS officials who may interpret the regulations differently, a Congressional inquiry is underway, we've contacted the media, and there is a grassroots campaign – patient- and ophthalmology-based – talking to patients…We urge you to help with continuing input so policymakers understand the implications of this decision."

The argument on Avastin reimbursement is one in which ophthalmologists are wearing the white hats. Doctors get the same injection fee (~$200) for Lucentis and Avastin, but with Lucentis – and not Avastin − they also get to make money (about $120 per injection) on the drug for "handling, storage, and inventory." Thus, doctors who use Lucentis net about $320 per injection (drug and injection), and those who use Avastin get almost half that – about $167. Dr. Rich estimated that it will cost CMS $1.5 billion a year if physicians stop using Avastin for AMD – and he noted that Avastin use is 25-30:1 vs. Lucentis for eye conditions other than AMD. That is, Lucentis is rarely used off-label except in clinical trials.

What caused CMS to change the policy on Avastin in the first place? Dr. Rich said the Academy doesn't know, and he refused to make any accusations, but he did say, "Someone raised the issue (with CMS) that perhaps Medicare was overpaying for Avastin…The Academy is not making any allegations. We don't know who raised this issue with CMS, but we wish they had talked with us first." Some ophthalmologists suspect Genentech is behind this, but Genentech and CMS have both denied it. Dr. Rich said he believes whoever is responsible will eventually be uncovered.

Dr. Rich, AAO's health policy guru, said that some doctors have switched from Avastin because of the change in reimbursement, "and their patients are obviously apoplectic because they were paying 20% of $40, and now it is 20% of $1,900. Doctors who changed (to Lucentis) are getting tremendous push-back from patients. I do think CMS will change this. It makes no sense. The Academy has strongly suggested this needs to be changed as soon as possible."

He stressed that doctors should continue to use only Avastin compounded by a pharmacy, which 95% or more currently do, "We don't want to encourage anyone to draw up directly from the bottle…The Academy and the ASRS notified everyone that if you do that you almost double the risk of infection… Insurance companies sent out (a notice about the) legal risk… so we think way, way fewer than 1% of people are doing that, and we and the insurance industry feel it is inappropriate to do that."

Asked why it was taking so long to get CMS to fix this, Dr. Rich said, "I'm not sure. They are probably looking for a legal way to do it…The best thing to do is to go back to the previous payment. Keep the little payment ($7.20) for anyone silly enough to draw directly out of the bottle…and then have it more appropriately priced when compounded ($40-$50)."

CATT trial: Avastin vs. Lucentis

While most of the attention has been on the two-year National Eye Institute-sponsored and -run head-to-head trial, CATT, there are six other ongoing trials. CATT is almost fully enrolled (1,130 of 1,200 patients), and enrollment should complete in November 2009 with results from a 1-year interim analysis in early 2011. Unfortunately, the results will not quite be ready for AAO 2010. There were rumors that the trial had trouble enrolling patients, but an investigator insisted that this is not true and that, in fact, enrollment has gone "extremely well."

Asked what results in CATT are needed to affect use of either Lucentis or Avastin, doctors generally indicated that it will take a significant imbalance in favor of one or the other to change current practice. Even if Avastin is significantly better on efficacy and/or safety than Lucentis, there will still be doctors who refuse to use it because it is not FDA-approved, retina specialists said. Typical comments included:

- *New York:* "If they are statistically equivalent, that would give greater comfort in saying these are equivalent. If a patient is doing well with Lucentis, people won't change them, but for new patients, they might use Avastin more. Many retina specialists are very comfortable with Avastin, but others feel there aren't sufficient data on efficacy and safety of Avastin. If there is a non-significant difference in CATT, we would have to discuss the results with patients, but it doesn't mean we would stop using (Avastin if it is numerically but not statistically worse). CATT still won't answer all the questions."

- *California:* "Avastin can't be worse than Lucentis, but if Lucentis is even a little worse, it will cause many people to switch from Lucentis to Avastin."
- *Dr. Abdhish Bhavsar, retina specialist at Phillips Eye Institute, University of Minnesota:* "To have an impact, there has to be a >25%-30% difference between the groups at least. Because if we can solve the cost difference with CMS now (over Avastin reimbursement), still more people will be likely to use Avastin. People using Lucentis may keep using it even if Avastin is superior because it has FDA approval…but if Avastin is close, then people using Avastin will feel much better about using Avastin. If Avastin comes out a little worse, it won't change anything; it would need to be significantly worse to cause people to switch to Lucentis."

The other comparative trials are:

- **IVAN** – a 450-patient trial in the U.K.
- **VIBERA** – a 366-patient German trial.
- **MANTA** – a 320-patient Austrian trial that has not yet started enrolling patients.
- **LUCAS** – a 450-patient trial at 12 sites in Norway.
- **GEFAL** – a 600-patient trial in France that started enrolling patients in June 2009.

What is going on with Avastin and Lucentis use in the U.S.? Avastin has continued to gain market share at the expense of Lucentis, retina specialists said. However, there is a bit of a "pause" in any switches as doctors wait to see what will happen with the Medicare payment decision. About half the doctors questioned at AAO said they would continue to use Avastin, even if the new Medicare rate goes into effect, but the other half said they would be forced to use more Lucentis. Comments included:

- *New York #1:* "Even if Medicare cuts the Avastin reimbursement, I'll keep using it."
- *New York #2:* "I will continue to use Avastin regardless of what Medicare does. Lucentis is just too expensive (for patients). My own economic interest just doesn't enter into the equation when I am with a patient."
- *California #1:* "I'll probably take the hit and keep using Avastin. There is still tremendous financial risk with Lucentis. If I don't get reimbursed for one bottle of Lucentis, that pays for a lot of Avastin."
- *California #2:* "We can't afford to give it (Avastin) away for free, so use of Lucentis will probably increase. But it will be difficult for patients who need it (an anti-VEGF) for off-label use."
- *South Carolina:* "I will continue to use Avastin, but Medicare will make me bitter about Lucentis…Behind the gray curtain (CMS) is the Wizard of Oz from San Francisco (a reference to Genentech) trying to protect (Lucentis)."
- *California #3:* "I'll switch to Lucentis if the Medicare cut in Avastin reimbursement goes through after the ongoing appeal. It is just too much for me to absorb."

Some doctors were complaining about problems with reimbursement with off-label use of both Avastin and Lucentis. A West Coast doctor said, "I got my first denial for Avastin from Blue Cross for a DME patient. Avastin was working for her, but she can no longer afford the cost herself; she's losing her house. The insurance company says it is 'experimental.'"

ROCHE/GENENTECH's Lucentis microparticle formulation

Genentech has licensed SurModics' biodegradable microparticle technology to develop a sustained-release formulation of Lucentis, but Genentech has not yet gotten an investigational device exemption (IDE) to take this new technology into human clinical trials.

BAYER/REGENERON's VEGF-TRAP

Dr. Jeffrey Heier of Boston provided an update, and the message was: There is nothing new at this year's AAO but stay tuned. Regeneron has the marketing rights inside the U.S. and Bayer outside the U.S.

- Two Phase III trials in AMD – enrollment expected to be completed this year in the ongoing VIEW-1 and VIEW-2 trials, with data expected in late 2010.
- Phase II DA VINCI trial in DME − finished enrollment in July 2009, with results expected in 1H10.
- Phase III trial program in central retinal vein occlusion (CRVO) – first patient enrolled in July 2009. This program is two trials: Regeneron's COPERNICUS and Bayer's GALILEO. Patients will be dosed monthly with 2 mg or sham for the first 6 months, then as needed for another 6 months. Results are expected in 2011.

Doctors questioned at AAO about VEGF-TRAP, generally had a wait-and-see attitude, though many said use will really depend on pricing, which has to be substantially lower than Lucentis. A South Carolina retina specialist said, "If the efficacy is the same as Avastin, I'll use Avastin. Even if TRAP is a little better, there will be such a cost difference that people would use Avastin. Our society can't afford Lucentis."

The potential advantages to VEGF-TRAP – which still have to be proven – are:

- **Longer duration** – but only 2-3 months, not the 6 months originally expected.
- **Fewer injections** – but, again, not as many fewer as originally hoped.
- **Perhaps lower cost** – perhaps 10%-20% less than Lucentis but still significantly higher than Avastin.
- **Maybe a *little* more effective.**

Two-year results of the CLEAR-IT trial were presented, and it showed that TRAP reduced the number of VEGF injections patients needed. CLEAR-IT was a 157-patient, 5-arm trial study of different doses and different administration schedules. After the first three months, patients continued on an as needed (PRN) basis using the same dose as in the first three months. In the second year, they were all rolled over to the 2 mg PRN dose.

Dr. David Boyer of Beverly Hills CA reported that, on average, patients required an additional 4.6 injections over the 21-month PRN period, >50% of patients needed ≤4 injections, and 9% of TRAP patients needed no VEGF injections at all after the first three months. However, another expert said that ~9% of patients don't deteriorate without therapy, so the significance of the patients needing no further injections is unclear.

The mean number of days to the first PRN injection was 173 (ranging from 21-616 days). Other findings included:

- 92% had <15 letter loss.
- 30% had ≥15 letter gain.
- 41% had 20/40 or better at 24 months.
- No new safety issues arose. Serious adverse events included five deaths: 1 pancreatic cancer, 1 pulmonary failure, 1 pulmonary hypertension, 1 squamous cell lung cancer, 2 cerebrovascular accidents (one of which was fatal), and 2 myocardial infarctions.

Other experts said they would like to see:

- The results with more frequent dosing (such as monthly injections).
- The results based on the different treatment intervals and dosing.

The key results that doctors are waiting to see are the VIEW-1 and VIEW-2 trials. VIEW-1 data should be available in about a year.

NOVARTIS/QLT's Visudyne (verteporfin)

QLT has been trying to breathe life into photodynamic therapy (PDT) with Visudyne by suggesting it be used to reduce the number of anti-VEGF injections, but nothing at AAO so far is likely to boost PDT use. Dr. Allen Ho from Mid-Atlantic Retina Associates in Pennsylvania reported on the 1-year results of the RADICAL study comparing Lucentis + PDT vs. Lucentis alone. There was no difference between the therapies in visual acuity results. The number of retreatments was numerically but not statistically lower with ½ fluence triple therapy (3.0 months vs. 5.4 months with Lucentis monotherapy), but Dr. Ho suggested this should be investigated further.

Dr. Peter Kaiser of the Cleveland Clinic said a web-based Visudyne registry showed equivalent visual acuity with the combination of Visudyne and Avastin, but the number of Avastin injections were "dramatically" reduced, "In fact, 27% of patients in the registry did not require additional treatment at 15 months average follow-up." He said the "more real world" DENALI study is completed, with results expected in early 2010, looking at reduced fluence + Lucentis vs. standard fluence + Lucentis vs. Lucentis monotherapy.

Radiation therapy

At least two companies are working on radiation therapy systems for treating wet AMD: NeoVista and Oraya. The idea is that by local delivery of low-dose radiation, the number of anti-VEGF injections can be reduced while maintaining their efficacy.

➢ **NeoVista.** The MERITAGE-1 trial compared the combination of targeted, one-time epiretinal delivery of strontium 90 beta radiation (brachytherapy) plus Lucentis vs. Lucentis alone over 12 months. There was no radiation-based retinopathy, the number of intravitreal anti-VEGF injections was reduced, and visual acuity was maintained. A post hoc analysis found that visual acuity actually improved when only pseudophakic patients were examined. The CABERNET trial is now fully enrolled with 450 treatment-naïve patients, and the 340-patient MERITAGE-II trial is ongoing in patients who require persistent, frequent anti-VEGF therapy.

➢ **Oraya's iRay.** This office-based, low-voltage (100 keV) x-ray radiation therapy is a 10-20 minute procedure with no appreciable shielding required. For patients, CEO James Taylor compared the radiation to getting an x-ray in the dentist's office. For doctors, the radiation exposure would be equivalent to ~0.14 mrem/hour or one-quarter of the radiation from a transcontinental airline flight. Each patient would get just one lifetime dose, not repeated exposures. Even though doctors might experiment, after FDA approval, with pulse or repeat dosing at some interval, Oraya is not studying repeat dosing.

Dr. Kaiser reported at AAO on a Phase I pilot study in Mexico City (CLH-001) that tested iRay + Lucentis in 15 anti-VEGF-naïve patients. There were no device-related serious adverse events and no evidence of radiation-related abnormalities, but there were a few device-related adverse events – all superficial keratopathy − which Dr. Kaiser said were due mostly to placement of the eye guide. There was no difference in visual acuity. Anti-VEGF injections were reduced after iRay by an average of 0.9 over 10 months, and ~55% of patients needed no additional anti-VEGF injections. Dr. Kaiser concluded that iRay extends the durability of Lucentis, reduces the number of injections, and appears safe and effective.

Oraya expects to enroll the first patients in a European trial in November, using 16 Gy (but perhaps amending that to include a 24 Gy arm as well). The company also plans to start a pivotal ~450-patient, sham-controlled, masked PMA trial in the U.S. in the first half of 2010 comparing combination therapy to Lucentis alone in patients with at least 3 prior anti-VEGF injections.

After the experience with brachytherapy in cardiology, it is hard to get excited about radiation therapy in non-cancer ophthalmology, and doctors asked about it were dubious. One commented, "This is like Hiroshima-izing someone." Another doctor said, "This is too big a gun. It obliterates everything. I don't believe it will be safe." A third said, "I can't see telling patients we are putting a radioactive problem in their eye. They won't go for it."

However, Taylor, the former CEO/President of Carl Zeiss Meditec, is very optimistic. He said he joined Oraya because his 88-year-old mother has AMD, and, though she is currently doing well on Avastin, he wanted to find something more effective or that would reduce the injection burden. Taylor said, "We are seeing lesions shrink in size. You don't see that with Lucentis and Avastin…And we are seeing scarring ameliorate to a degree…although it is a small number of patients so far."

Asked about the long-term safety of iRay, Taylor said, "I'd be the last person to say we have absolute certainty we know the outcome (with iRay). The comfort comes from the ample data and research from ocular oncology and from some early work done in radiotherapy for AMD that suggest the incidence of radiation retinopathy is low…Years of study in ocular oncology…have given comfort that the doses here (are safe)… We know that AMD has an inflammatory component to it… and we know that AMD causes scarring and building of lesions in the eye that don't respond to anti-VEGF therapy… And we know that radiation is anti-vascularization and anti-fibrotic as well…Lastly, we know that if you combine an anti-VEGF agent with radiation, you get a synergistic effect."

Taylor explained that radiation works best on concentrated lesions in an atmosphere of oxygenation. So, stopping leaking capillaries with an anti-VEGF, tends to make the center of the lesion more robust – and a better target for radiation therapy.

Oraya has worked with radiation and oncology researchers and experts around the country to determine the dose and the approach. The science looks good. And the radiation is not delivered through the cornea but through the sclera. Taylor said one advantage of iRay over NeoVista's therapy is that iRay is robotically delivered while NeoVista has a hand-held system, "We have a robot that is a wonderfully designed sniper, shooting low energy in tightly collimated beams with 3 beams going through the sclera at separate points, all converging at the same point on the fovea." The iRay goal is to deliver either 16 Gy or 24 Gy to a spot 4 mm in diameter centered on the fovea.

The three elements of iRay that Taylor highlighted were:

1. Robotic positioning.
2. Continuous tracking and management of eye motion with the iGuide.
3. Collimation of the beat.

Does iRay make financial sense for retina specialists? Probably, if CMS reimburses for it. There would be an initial machine cost plus a per-procedure disposable cost. Taylor believes the procedure will be cost-effective because it should reduce both diagnostic testing and anti-VEGF injections.

iRay is not being tested in dry AMD – but that might be an area for research in the future.

Other wet AMD therapies in development:

- **Alcon's AL-39324**, a tyrosine kinase inhibitor (TKI).
- **CoMentis's mecamylamine (ATG-003)**, a nicotinic acetylcholine receptor (nAChR) antagonist.
- **GenVec's adPEDF** (pigment epithelial-derived factor). A speaker said this is "very, very potent." A dose escalation study of 28 patients showed "hints of biologic activity."
- **GlaxoSmithKline's pazopanib (GW-786034).** This oral TKI has been tested extensively in oncology at a dose of 800 mg/day and is approved for use in renal cell carcinoma. It is now being tested as a single topical drop in AMD. A 28-day, 71-patient Phase IIa trial in AMD, testing 3 doses (0.5 mg/mL TID, 2 mg/mL TID, and 5 mg/mL QD), just finished. There were no treatment-related adverse events. The trial missed the primary endpoint, showing no statistically significant decrease in central retinal thickness by OCT at Day 29. There were some hypothesis-generating findings in secondary endpoints, so a larger Phase IIb study is being planned, probably at the highest dose tested.
- **Jerini Ophthalmic's JSM-6427**, an α5-β2 integrin.
- **Lpath's iSONEP**, an ocular formulation of humanized sphingomab (sonepcizumab), which is an antibody against S1P This has completed Phase I.
- **MacuSight's Perceiva (sirolimus).** This mTOR inhibitor was described as "a very exciting area of AMD." A Phase II trial in 20 treatment-naïve patients is underway comparing conjunctival and intravitreal administration. This also has the potential to be delivered through a long-term implant.
- **Novartis's vatalanib (PTK-787)**, an oral TKI.
- **Ophthotech's E-10030.** A Phase I study of E-10030 plus Lucentis saw an improvement in visual acuity and a reduction in exudation, but what a speaker said was more interesting was that the combination seemed to result in a reduction in lesion size.
- **Oxigene's Zybrestat (fosbretabulin)**, a vascular disruption agent (combrestatin A4 phosphate). A Phase II trial is underway in Asia looking at polypoidal choroidal vasculopathy.
- **PDL BioPharma/Biogen Idec's volociximab.** In animal studies, this has showed an ability to suppress CNV growth. A Phase I is underway.

- **Pfizer's AG-013958**, a VEGFR inhibitor.
- **Quark Pharmaceuticals/Pfizer's PF-4523655 (RTP-801i-14).** This RNAi agent finished Phase I, and a Phase II is being considered.
- **TargeGen's TG-100801/TG-101095**, TKIs.

DRY AMD

More people have dry AMD than wet AMD, but there currently are no good therapies other than laser photocoagulation. There was great hope for TTT (transpupillary thermotherapy), but in 2004 it failed to show benefits in a rigorous trial. However, a number of therapies are in development for dry AMD, and doctors are cautiously optimistic about several of these. Dr. Larry Singerman, retina specialist from Case Western University, said, "We've made huge progress in wet AMD, and we are just starting to make progress in dry AMD …It is unlikely that any one approach will be the winner. It is likely that a combination approach will be needed." Dr. Rich added, "Dry AMD is the big banana. I'm optimistic that something will work."

Among the therapies in development are:

ACUCELA's ACU-4429. A Phase I trial is ongoing and should be finished in December 2009. Dr. Philip Rosenfeld of Bascom Palmer Eye Institute said, "It appears the drug is safe up to 75 mg."

ALCON's brimonidine back-of-the-eye intravitreal implant, which is being tested at 2 doses in the GAP study.

ALCON/POTENTIA PHARMACEUTICALS' POT-4, a complement inhibitor. This is in Phase I development. With a single intravitreal injection at the 450 µg dose, gel-like deposits can be seen to form consistently, with activity lasting 6 months or longer, slowly releasing drug. Dr. Rosenfeld highlighted this agent, which is expected to start Phase II trials in 2010.

ALCON's tandospirone (AL-8309B), a topical agent that protects against blue light-induced photodamage. A large Phase II/III trial is underway in geographic atrophy (GA), an advanced form of dry AMD, with the drug administered either QD or BID at either of two doses (1% and 1.75%).

ALEXION's Soliris (eculizumab), an infused antibody.

ALIMERA SCIENCES' Iluvien. This partially biodegradable implant that elutes fluocinolone over 2-3 years is being studied in dry AMD as well as DME (*see Iluvien under Posterior Drug Delivery on page 20*). The 956-patient FAME trial conducted in the U.S., Canada, Europe, and India is expected to have results in a couple of months.

ALLERGAN's intravitreal brimonidine. This is moving forward in a trial of GA using the Novadur sustained-release system with a Phase II trial of 200 µg and 400 µg.

NEUROTECH's NT-501, a back-of-the-eye intraocular implant of human cells genetically-modified to secrete ciliary neurotrophic factor (CNTF).

OPHTHOTECH's ARC-1905. An uncontrolled, prospective, multicenter Phase I trial is underway in 30-50 patients with geographic atrophy.

OPTHERION's recombinant complement Factor H (CFH). It was infused in preclinical trials and had a "favorable" PK profile. A Phase I trial is expected to start in 2010.

PFIZER's PF-4382923 (RN6G), an antibody against beta amyloid.

SIRION THERAPEUTICS' fenretinide, an oral vitamin A binding protein antagonist. Data from a pre-specified interim, 1-year analysis of an ongoing study was presented at AAO and looked promising. The results came from a randomized, double-blind, placebo-controlled, parallel assignment trial. In the study, 78% of lesions treated with the 300 mg dose grew less than placebo, and there was an unexpected reduction in the conversion from dry to wet AMD in fenretinide-treated patients. There was also a trend with the higher dose to better dark adaptation.

Sirolimus. The National Eye Institute (NEI) is studying a Phase I/II trial of subconjunctival injections in GA to see if it can help preserve vision.

TEVA PHARMACEUTICALS' Copaxone (glatiramer acetate). New York Eye & Ear Infirmary (not Teva) is testing a weekly Copaxone vaccination.

POSTERIOR DRUG DELIVERY

Dr. William Mieler of the University of Illinois Eye and Ear Infirmary reviewed – rather quickly – the options for drug delivery to the posterior segment. Some of these products were discussed in greater detail in other talks.

Relative Potency of Steroids

Steroid	Potency
Cortisone	0.8
Prednisone	4
Triamcinolone	5
Dexamethasone	25
Fluocinolone	25

ALIMERA SCIENCES' Iluvien, a partially biodegradable implant that delivers fluocinolone over 2-3 years. Two Phase III trials under a single protocol are underway in DME, with results expected later this year or early in 2010. Dr. Baruch Kuppermann of the University of California, Irvine, said the Phase II results in 38 patients showed an apparent dose response curve, but the sample size was small, and baseline differences in the patients made the data hard to interpret.

ALLERGAN's Ozurdex (formerly called Posurdex), a biodegradable implant eluting dexamethasone, which was approved by the FDA in June 2009 for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO). Steroids have been the mainstay of RVO therapy for more than 50 years. Dexamethasone is a more potent steroid than the more commonly used triamcinolone acetonide, but it is too short-acting. Ozurdex solves the dexamethasone delivery problems.

In RVO, Dr. Kuppermann said the efficacy appears durable through 180 days, and the dose response curve is "nice." Importantly, no cataract signal has been seen.

In DME, data from a Phase IIb trial have been published, and a Phase III trial is fully enrolled, though still years away from reporting results.

Dr. Julia Haller of Wills Eye Institute in Philadelphia reviewed the Phase III data from the two identical, randomized, multicenter, prospective, masked, sham-controlled trials in RVO that led to FDA approval. In those trials, which compared two doses of dexamethasone (750 µg and 350 µg) to sham, the implant results in greater and more rapid improvement in visual acuity than sham, with 21% of BRVO and 17% of CRVO patients requiring only one treatment in a year. The implant was well tolerated, with no excess cataract formation, which has plagued other steroid implant devices.

Doctors questioned at AAO about the outlook for their use of Ozurdex offered mixed comments. A few expect to have significant usage, but most either have no plans to use it or predicted very limited, niche use. Three issues were cited as holding back use – cost, concern with long-term safety, and uncertain clinical utility.

- *New York:* "Injections (Avastin, Lucentis, triamcinolone) are so safe. We used to worry about infection, but that worry has decreased. So, when we have to go to the OR (operating room) with Ozurdex, it loses its appeal. It is a big deal bureaucratically to go to the OR, and it adds risk for the patient."
- *New Jersey #1:* "It is very expensive, so I'm not sure if I will use it. I'm not sure the cost is justified."
- *New Jersey #2:* "With all the new drugs, doctors will be very careful not to use drugs this expensive when they are not sure about reimbursement to the practice. It is a huge liability. Lots of practices were burned by Lucentis."
- *Texas:* "Use remains to be seen. The utility is not clear. I'm not sure if I will try it. It is one injection vs. several, but the importance of that remains to be seen. If it is expensive, that will be a big negative."
- *Maryland:* "I still need to figure out what I want to do. I will probably experiment with it, probably treating early."
- *Oklahoma:* "I'm not an early adopter. The cost is more than $1,000. I'll probably wait and see how others do with it. This (RVO) is a common problem that they are trying to treat, but most people will wait."
- *Canada:* "Ozurdex is going to be a disaster."
- *California #1:* "I think I will use it in steroid-responsive patients who need repeated injections, and that is a fairly significant number of patients. I like it because there is a fairly low cataract rate, and IOP (intraocular pressure) doesn't increase too much." Asked why he would use this and not Bausch & Lomb's Retisert (a fluocinolone acetonide intravitreal implant approved for uveitis), he said, "Retisert is ridiculously expensive, and there are fewer patients for whom it is indicated."
- *Michigan #1:* "I'm very excited for 2 reasons: (1) dexamethasone is a more potent and safer drug than triamcinolone, but we couldn't use it because of the short duration of action, and (2) Ozurdex will mean fewer injections with lower and safer doses. We have already ordered it and have quite a few patients who are appropriate. The cost is somewhat prohibitive. Triamcinolone used to be dirt cheap (~$4), but the (Bristol-Myers Squibb) Kenalog label now says that it is not approved for ocular use. Alcon and Allergan have an approved triamcinolone, but it costs more (~$150). RVO patients depend on injections every 3 months, so the cost of Ozurdex may end up not prohibitive."
- *New York:* "The Allergan sales reps are pushing it, but I can't justify the use. Kenalog is cheap, and I don't have to worry about paying for it. I can't justify the cost of Ozurdex."
- *California #2:* "The dilemma is the Lucentis data in RVO, which looked very impressive. What I like about Ozurdex is the safety is better than the older steroid formulation. All of us are contemplating combination strategies. Can we do Lucentis + Ozurdex? That seems a rational strategy…I think a high percent of RVO patients will get it."
- *Michigan #2:* "There are not a lot of patients for any single condition, but when Allergan has multiple indications approved, there should be more use. It is expensive, but the cost is just a fact of life. The story is yet to be told with so many other agents coming. Ultimately, the answer will be combination therapy: an anti-VEGF followed by a steroid, such as Avastin or Lucentis then Ozurdex."
- *Minnesota:* "I may use Ozurdex some in RVO, but even there the results are modest."

The results of a Phase IIIb study of Ozurdex + Lucentis vs. Lucentis + sham are expected at the Macular Society in Tucson AZ in February 2010.

MACUSIGHT's Perceiva (sirolimus) – enrollment completed in 131-patient Phase II trial in DME. The drug was recently granted FDA fast-track status.

NOVAGALI PHARMA's Cortiject – a 21-patient Phase I trial of this corticosteroid prodrug in DME is underway. Results in one patient were shown at AAO, and there was nice resolution two weeks after a Cortiject injection.

RECKITT BENCKISER PHARMACEUTICALS' Atrigel, a thermo-responsive gel that is liquid at room temperature but a gel in the body. Dr. Mieler said this agent, which was licensed from QLT, appears safe.

SURMODICS' I-vation – a triamcinolone acetonide-eluting screw-in implant for DME. The results of a 36-month Phase I trial were reported earlier this year, and they showed that the implant is "easily implanted and removed" and that it is safe and well tolerated. The study wasn't powered for efficacy, but there was a trend toward early and sustained reduction in macular thickness as well as an improvement in visual acuity.

SurModics is currently looking for a development partner. SurModics had a deal with Merck, but Merck backed out in September 2008. A Phase I trial in 31 patients with 3-year follow-up was completed, but a Phase II trial has not yet started.

Dr. Kuppermann called this "interesting technology," with IOP controllable with topical medications, but he noted that there were a number of issues, including:

- The visual acuity data were difficult to interpret.
- Explanation was necessary "on a regular basis."
- There were 2 procedure-related serious adverse events – one postoperative endophthalmitis and one postoperative retinal detachment.

Others

- **Aerosolized nanoparticle delivery.**
- **Encapsulated Avastin and Lucentis** in a thermo-responsive hydrogel.
- **Iontophoresis** – which improves drug delivery but has a questionable long-term effect on the cell membrane.

DIABETIC RETINOPATHY

OD-OS's Navilas

This real-time retinal tracking system is not yet FDA approved, but it looked very interesting. It allows retina specialists to pre-plan where they will do laser photocoagulation and to exclude sensitive areas they don't want to photocoagulate. It combines live fundus imaging and fluorescein angiography with established laser photocoagulation.

IMAGING

One of the hot new technologies in retina is autofluorescence. An imaging panel discussion considered the questions: Is it time to update? Is autofluroescence worth the price? All the panel members said they are currently using both OCT – mostly spectral domain (SD-OCT) but also some time domain (TD-OCT) – along with autofluorescence. The majority of audience members also indicated that they were using SD-OCT, and perhaps a third said they were using TD-OCT.

All of the panel members said they have fundus autofluorescence capability, but only ~15% of audience members currently have autofluorescence. One expert explained how autofluorescence helps him, "In our practice – for dry AMD or even exudative AMD with successful anti-VEGF therapy with poor results – we use autofluorescence to assess disease status …It really gives you an insight at what is going on at the level of the RPE (retinal pigment epithelium) that no other technology available is able to do." A New York retina specialist said, "I'm here to buy a camera. Autofluorescence picks up things that OCT misses."

TD-OCT is still useful, and it is less expensive, but experts insisted that they can see things on SD-OCT that are not seen on TD-OCT. Dr. William Freeman of the University of California, San Diego, said, "SD-OCT is always our primary machine. Sometimes we look at (a patient) in another machine, and…there are things, like vitreous structures, that you just don't see well at all on TD-OCT." The panel agreed that clinically important information is missing 5%-20% of the time with TD-OCT vs. SD-OCT.

Among the companies with SD-OCT: Heidelberg's Spectralis, Topcon's 3-D OCT, OptiGen, Optopol's Copernicus, Optovue's RTVue-100, and Zeiss. Several sources said the Spectralis is currently the top-of-the-line autofluorescence. Zeiss reportedly is working on a new OCT that may lessen or obviate the need for autofluorescence.

The Topcon system is available in Europe, but not yet in the U.S. A Topcon official said the company plans to add a Spade filter to its fundus system in early 2010 as a hardware upgrade. He pointed out that this "will be a lot less expensive than the Spectralis." In a poster at AAO, U.K. researchers showed how they used Topcon's autofluorescence to show that

OptiMedica's laser burn pattern created the burns it claimed to do. Topcon claims to be the only company with the combination of autofluorescence, non-mydriatic fundus, and OCT in the same box.

Heidelberg's autofluorescence is a "blue peak" feature. Heidelberg claims to have the only triple infrared fundus, SD-OCT, blue peak autofluorescence. Kester Nahen, vice president of global marketing and business development for Heidelberg, said, "We use a laser to create autofluorescence – a blue wavelength that selectively targets the lipofuscin with blue light. Then, over a broad spectrum, collects autofluorescent light."

Heidelberg's SD-OCT also has active eye tracking, which adds to its price, but which other SD-OCT don't have. Adding blue peak raises the price about $8,000, but that may be cheaper than buying a whole new system for autofluorescence.

Asked who is buying autofluorescence, Nahen said, "Comprehensive ophthalmologists who shy away from angiography – you don't need that for autofluorescence – and to get a 'health check' of the rating of perceived exertion (RPE)."

LUX BIOSCIENCES' Luveniq (voclosporin, LX-211)

Results of a Phase II/III clinical trial of Luveniq, a calcineurin inhibitor, for the treatment of non-infectious uveitis were presented at AAO, showing that the drug reduces recurrence of inflammation by 50% vs. placebo at the 0.4 mg/kg BID dose of Luveniq ($p<0.05$). The double-masked, placebo-controlled, dose-ranging study looked at 232 patients with clinically inactive uveitis.

Overall, Luveniq was well tolerated at the 0.4 mg/kg BID dose. Adverse effects included renal function (a decrease in the glomerular filtration rate of 8.2% with Luveniq vs. 4.1% with placebo), a 6 mmHg increase in systolic blood pressure, and hair growth or hirsutism in 5% of patients. Triglycerides and cholesterol were not elevated.

The study's principal investigator said that the drug "may… effectively increase the interval between inflammatory relapses to 24 months compared to 10 months with placebo… Given that inflammatory exacerbation is a direct trigger of vision loss, this result…is impressive. In addition to a marked reduction in recurrence of inflammation, visual acuity was preserved...The results suggest the potential for disease modification whereby treatment with LX-211 alters the course of the disease, leading ultimately to improved outcomes in this difficult-to-treat condition."

Lux Biosciences plans to file a New Drug Application (NDA) for Luveniq by the end of 2009 and to submit it to European regulators in early 2010.

POLICY ISSUES IN OPHTHALMOLOGY

The four big issues AAO is focused on are the sustainable growth rate (SGR), physician payment reform, practice expense redistribution, and healthcare reform. The AAO's Dr. Parke offered ophthalmologists an update on the status of each of these.

FINANCIAL ISSUES

SGR

The SGR is used to determine physician Medicare fees. Six times in the last six years, Congress has voted to override the SGR because it would have underpaid doctors. This hasn't been done yet for 2010, and Dr. Parke said SGR reform remains a component of the House bill but is at risk and is not in the Senate bill at all, "The real reason this is getting play is access is the key argument. If physician payment rates fall off the cliff, many physicians would withdraw from Medicare…If SGR doesn't get fixed, we are facing a 21% hit on January 1, 2010."

Physician payment reform

There are currently five bills, and all of them move from a pure payment for unit of service to payment based on "episode of care." Thus, a vitrectomy, for instance, would include drugs, surgery, postoperative, and the procedure – everything together. There are huge issues on the table related to how an episode is defined and how it will be linked to licensure and certification.

AAO health policy medical director Dr. Rich predicted there will be "substantial" payment reform, with substantial cuts in high-end imaging, but also office-based imaging, and that could affect a lot of ophthalmologists because it is likely to include visual fields, fluorescent angiography, etc., "Right now, high-end imaging is under severe attack with substantial cuts. The next goal will be office-based testing."

Asked what he would say to doctors considering the purchase of a new OCT, Dr. Rich said, "*Caveat emptor*. The fastest growth in office-based Medicare imaging is 92135 − optic nerve imaging and OCT…Over the last two years, at the retina and glaucoma meetings I go to, I include warnings about long-term payment for OCT."

A few days after AAO, CMS announced the 2010 Medicare Physician Fee Schedule, and it was much as AAO officials had warned: In cardiology, for example, the cuts range from 10% to 40%+, with a 36% cut in SPECT imaging, a 10% cut in transthoracic echo, a 4% in coronary stenting, and a 5% cut in EKGs.

Practice expense redistribution

This issue is "in play," Dr. Parke said, adding, "If you don't pay attention to anything, pay attention to this. The AAO, in conjunction with 69 other specialty societies, funded and commissioned a new multi-specialty survey – the American Medical Association's Physician Practice Information Survey – to help CMS determine rates. The outcome was that ophthalmology is scheduled to get an 11% increase, while radiology is going down 10%, cardiology down 10%, internal medicine up 4%, etc., and the specialties on the losing end are fighting back…The big losers are now spending big dollars − mostly oncologists and community cancer centers, who are sending cancer survivors to Capitol Hill and saying, 'If you don't prohibit CMS from rapidly and totally implementing this study which, yes, we agreed to, cancer treatment in the U.S. is going away,' and the effort is having an impact…(A number of Senators) have signed a letter urging a delay (in CMS implementation)."

HEALTHCARE REFORM

Dr. Parke called healthcare reform "an ongoing saga, a play of many acts." He told ophthalmologists that nothing is likely to happen until mid-December and perhaps not even until mid-2010, "There is a lot of uncertainty out there…The revenue is more front-loaded and expenses are back-loaded. There are $121 billion in Medicare cuts in 2011, new expenses are phased in from 2015-2017…It assumes every dollar paid in employee healthcare coverage is paid as taxable income…but all of us, as employers, know that is a little bit of a stretch…It also assumes revenue from the 'Cadillac tax' will grow by 10%-15% a year…One thing that is not getting a lot of play is that as Medicare grows, so does Medicaid…and states are on the hook for 47% of that cost …(the public option) may be on life support or undead, but it is not dead."

He urged doctors to give money, develop relationships with legislators, send emails, get personally involved, and thank those that do (get involved).

Dr. Rich warned that if the Senate healthcare reform bill fails, there will be no healthcare reform, "It is over." If there is healthcare reform, he predicted, "Doctors will be the losers… Health plans are still fighting, but they probably will do okay. Hospital and pharmas will be all right, and device companies are okay."

What impact will healthcare reform have on pharma R&D? Dr. Rich said more comparative effectiveness research, patient reported outcomes (PROs), scrutiny of diagnostic testing, and pricing pressure on ASC:

- "I think the biggest impact in R&D is the whole new world of comparative effectiveness research. I think that is going to be part of life, period. You will see more and more studies comparing two drugs, two devices, drugs vs. surgery − studies that have not been done. The biggest threat to industry is comparative effectiveness research."
- "There are also some subtleties that will increase their hurdles and costs – for example, the idea of combining traditional studies with PROs. That will be part of FDA labeling, part of comparative effectiveness research, part of quality metrics. You get a person to see X. What does it mean to their lifestyle, independence, sense of well-being? Those things are going to be measured…The FDA and NEI had a meeting (in October 2009) specifically… saying that PROs are now going to be part of FDA approval and expansion of labeling…It absolutely makes sense."
- "There also is going to be short-term scrutiny on all diagnostic testing. The industry understands that, but I'm not sure doctors understand that."
- "There will also be more pricing pressure on supplies in the ASC…We've seen cuts of 2% in the last few years… We won the battle to get more things covered by Medicare, but revenue per case is going down. So ophthalmologists are looking carefully at ASC costs, and you will see pressure on devices, drugs, disposables in cataract surgery, DSEK, etc…I'm actually renegotiating my contracts right now with my ASC, looking at the costs of everything…A lot of doctors are owners in ASCs; close to 40% of surgeons have some ownership in an ASC based on our last survey."

Public option

Dr. Rich said the Academy has no position on the public option debate, "But if there is a public option, we want to make sure there is choice…We favor the ability of physicians to negotiate…The biggest issue in the House is that doctors can't be deemed to participate, they have to attract physicians to participate. In the current House bill there is no 'deemed' participation. They are not saying that if doctors take Medicare, it is assumed they will take the public plan." But Dr. Rich is not optimistic about the outlook for a public plan, "Even with opt out (where states can opt not to participate), I can't imagine a public plan will get any Republican votes – except maybe Sen. Olympia Snowe (Maine), but she has serious concerns about the public option."

Efficiency measures and pay-for-performance

Dr. Rich said that neither of the two commercial products available for risk adjustment within medicine – Ingenix and Thompson Reuters – successfully differentiate within ophthalmology. For instance, he said the programs can't differentiate between a marginal glaucoma patient treated by a general ophthalmologist and an end stage glaucoma patient treated by a glaucoma specialist, "We think this will create barriers to care…The Senate bill has legislation to cut payments if you are an outlier. That (idea) is not supported by MedPac at the current time. They were going to recommend grouper software, but they looked at it, and tested it, and pointed out the vagaries of financial barriers to care for sicker patients. We need newer commercial products that are risk-adjusted.

Unfortunately, those products don't exist…(Penalizing) resource outliers was proposed for 2011 even though there is no risk adjustment product out there…That would absolutely be onerous."

Relations with Optometry

Asked if the Academy might soften its position about optometry, Dr. Parke said, "The Academy is in favor of co-management but co-management with all the right safeguards in place. At the end of the day, it is not an issue of what letters you have after your name, it is an issue of training and validated competency. For many ophthalmologists and optometrists in this country, there is a pattern of practice that involves mutual respect, working together, and it is ultimately in the patient's best interest."

Dr. Parke said that in Oklahoma, where he practiced before taking the reins of the Academy, he worked with both ophthalmologists and optometrists, "I had optometrists in our group, and they had the same rights and privileges in our practice in terms of status as ophthalmologists, and they were wonderful people and practitioners. We setup a system, however, wherein they practiced to what we mutually agreed on as a level of competency, and that is the way it should ideally be. The Academy is strongly in support of an ophthalmology-led eye care team. The number of ophthalmologists that employ optometrists is growing, and if you look at the optometry literature, the percent of optometrists being employed (by ophthalmologists) has gone up. That reflects, from my perspective, that it is a highly attractive way to practice for both sides. It increases the ability to manage the baby boomers, the volume of care out there, and do it in an efficient and effective fashion. So, the Academy is not in any way anti-optometry."

Will the Academy let optometrists attend the annual AAO meeting again in the future as they did in the past? Dr. Parke said that decision is not his alone, "It is a good question. I can't answer it because it is not a decision I will individually make. Major policy decisions are not made by one person… My sense is that this is an issue that is going to be revisited, and my hope is that whatever structure comes out, it fosters building bridges where they are appropriate."

Practice Issues

Ophthalmology registry

One of the key projects on the AAO agenda is getting a national registry set up, the *Clinical Patient Data Registry*, which will be something like the Society of Thoracic Surgeons' coronary artery bypass graft (CABG) registry. Dr. Parke said, "This registry would be a national databank of clinical and surgical encounters and outcomes, for instance, cataract surgery. One of the things people think about is how to measure complications from surgery…Do patients have to go back to the OR to manage complications? If you asked someone how often that happens, you might get local data or do complex mining of the Medicare charge submission database, but we would like to have, ultimately, a very robust registry that has that information. Then, individual physicians can go in and (see how they are doing against the expected outcome in their region), and if they are not doing well, how to change that."

Dr. Parke said the Academy will be working with the subspecialty associations to get the database up and running. Last year, the Academy spent $600,000 on this initiative, and it hopes to launch it in the next several months.

Setting up a database in ophthalmology is not as easy as in cardiology. Dr. Parke explained, "Cardiology is a much easier nut to crack in terms of design because everything is done in the hospital, and much of the data comes from the hospital database…Much of cataract surgery is done in an ASC, and you would have to involve them in this. Yes, it will be more complex because there are more of them (ASCs), and they don't have the robust IT of hospitals…but everyone realizes this is something that needs to be done."

Dyslexia

In August 2009, the AAO in conjunction with several other medical societies issued a joint policy statement on dyslexia, which basically emphasized that dyslexia is not a visual disorder. At the AAO meeting, this was emphasized again. Dr. Sheryl Handler, a California pediatric ophthalmologist, highlighted several points, including:

1. Dyslexia is not a vision-based disorder. It is a specific learning disability that is ***neurological*** in origin.

2. Word reversals and skipping words and lines are due to linguistic deficiencies and not visual or perceptual disorders.

3. There is no evidence that children who participate in vision therapy are more responsive to educational instruction, and the scientific evidence shows vision therapy does not benefit children with learning disabilities.

4. The scientific evidence does not support the use of tinted lenses and filters in patients with learning disabilities.

5. Primary care physicians (PCPs) do not diagnose learning disabilities. The role of the PCP is to "perform a complete medical history and physical examination…to perform vision and hearing screening…and to refer to the ophthalmologist if vision screening is failed or a vision problem is suspected."

6. Ophthalmologists do not diagnose learning disabilities, but they can assist with a referral to the appropriate educational evaluation, medical, psychological, and other services.

7. Children with learning disabilities should receive individualized, evidence-based educational interventions combined with psychological and medical treatments as needed.

8. Diagnostic and treatment approaches for dyslexia that lack scientific evidence of efficacy, such as behavioral vision therapy, eye muscle exercise, or colored filters and lenses, are not endorsed or recommended. ♦