An eye to the future of IOLs and cataract surgery

At a EuroTimes Roundtable which took place at the ASCRS Congress in San Diego earlier this year four ophthalmologists and an optical physicist met to discuss current trends and innovations in cataract surgery. ESCRs President Marie-Jose Tassignon MD chaired the session.

Tassignon: Today we are discussing new IOLs and the future of cataract surgery. I would like to begin with a question about PCO: how close is modern cataract surgery to conquering PCO? What are the challenges that remain?

Fine: I think that if we look at the data and the work that came out of David Apple’s lab there has been a dramatic reduction in PCO from a percentage of about 50% perhaps a decade ago down to a capsulotomy rate of 15% or maybe less the for at least the first three years. We have achieved that reduction partially as a result of changes lens design and lens material. The most important aspects of lens design are sharp edge and a bending of the capsule with that edge. Materials also have an impact; hydrophobic acrylics adhere to the capsule and are a further barrier. That adherence is because they become coated with fibronectin which is a biological glue.

Another factor in the decreasing incidence of PCO is surgical technique. We know that accurate cortical clean-up is an important component and we’ve recently learned from well-designed studies in Europe and America that avoiding polishing the anterior capsule is associated with a smaller rate of YAG laser capsulotomy. I think the most important new development is Anthony Maloof’s perfect capsule which is a device that allows us to seal the intracapsular environment and irrigate with something that will probably just wash off the lens epithelial cells from the capsule and out of the eye. So PCO is much less of a problem than it was.

Holladay: David Apple’s studies show that the square posterior edge had the most significant impact in terms of impeding lens epithelial cell migration, but it also requires some tension on the bag capsule so that that right angle is actually pushing and so there is an actual impediment to the migration of the cells. Although the idea of not cleaning off the anterior capsule is sort of counterintuitive, in fact Randy Olson’s work shows that as those cells on the anterior capsule undergo that metaplasia they are actually a part of the force that creates the contraction in the peripheral part of the bag. That actually adds to the force pulling on the posterior capsule which ends up trapping cells in the space peripheral to the lens so they can’t get out to proliferate somewhere else.

The problem is not how to delay PCO but how to make the peripheral capsule transparent forever after lens removal. If we preserve the lens capsule probably we shall open the next stage of cataract surgery with new methods to remove and replace the lens and restore accommodation.

Tassignon: If we want to get a kind of accommodation, I think we need a capsular bag that is very elastic and I think the only way to do that is to put the lens epithelial cells in their normal physiological situation. That means, entrapped in a really closed system where they can proliferate just enough to cover again the remaining capsular bag and that’s it. Then there is a kind of autoregulation within the lens epithelial cells that stops the proliferation as soon as everything is filled. We were able to confirm this in our laboratory experiments and due to this knowledge we developed a bag-in-the-lens system where, in fact, the lens epithelial cells are entrapped in a very closed area. The only problem is that when we evaluate these cases we have only a slight improvement in the range of accommodation compared to the normal classical intraocular lens implantations.

Accommodation of course is another question that we will have to answer. The Holy Grail of cataract surgery is to restore physiological accommodation so what is your opinion about how soon we will get to that point?

Fine: I think there’s no doubt that accommodative lenses that work and work well will be available.

Holladay: With the currently available focus-shift accommodating lenses, the most we’ve really seen from actual OCT measurements is about 1.8 dioptres of accommodation which is the equivalent of about 0.6-0.8 mm of anterior focus-shift.

Alio: Yes, we’re taking part in that research and while as yet the company do not want to say how the lens works, it’s a scientific fact that monkeys implanted with the new lens get from 8.0 to 55 dioptres of accommodation.

Alio: Well in my opinion we know more and more how to delay PCO, but not how to eliminate PCO. The problem is not how to delay PCO but how to make the peripheral capsule transparent forever...
movement ... the average is much less. My concern is that the mediation of accommodation is the contraction of the ciliary muscle tending on the zonules which then causes that lens to go forward and that is why we believe these motions are mostly mediated by the elasticity of the bag. It took us 3-5 years to find that change in elasticity of the bag and the myofibril of the epithelial cells with foldable lenses. My concern is that it may take 3-5 years to detect that in eyes with accommodating lenses. The lens of a patient may shift forward to the point that they end up at the ~2.0 D with no accommodation.

**Fine:** We have four years of experience with the CrystaLens and that's not really been our experience. We have had to YAG a certain number of those and they appear to lose some accommodative amplitude during the process of opacification and their distance vision goes down as well. But I think in every instance following YAG laser they regain their amplitude of accommodation. The other thing that I think you may want to consider is that the bag fibres and the optic is forced forward there may be a compensatory phenomenon with the reduction in the diameter of the capsule which is pushing on the haptics and forcing the optic backward so these may be competing forces which neutralise each other.

**Alio:** From our initial attempts to solve the problem of accommodation I see clearly that we have two directions we might take. One is multifocality and the other is the restoration of physiological accommodation. Accommodation is a change of power related to the ciliary muscle contraction - this is real accommodation. At this moment we are in the initial steps and from the behaviour of the lenses inside the eye we have discovered that we know much less than we expected. I have never seen lenses working not because of displacement, but because of the induction of coma aberration when the ciliary muscle is contracted. Probably we will gain a lot more insight over the next couple of years about why there is this contradiction between the minimal displacement of the lenses and the clinical findings.

**Holladay:** I think that we can explain the accommodation with the CrystaLens optically, because 50% of the patients with monofocal lenses get J2 and J3 vision and still have 2/020 at distance and remember again that’s with the 5.5 to 6.0 mm diameter aperture because we have a 5.5 to 6.0 mm pupil. An accommodating lens is 4.5 mm, so it’s as if we’ve cut the F-stop of a camera down to 4.5 from 6.0, so you get a 25% better depth of field. In the Crystal Lenses study 80% could read J2 compared to 50% with the monofocal control. The smaller aperture (primary factor) and the forward movement (secondary minimal factor) do explain very clearly why you get better vision at near with an accommodating lens compared to the monofocal lens with the larger aperture.

**Alio:** The main problem for me and for my patients is that we cannot promise anything with this technology. We can promise better accommodation than that achieved with a monofocal, but we cannot promise 1.51 or 0.5 of accommodation because all of these ranges are possible. At the moment I prefer multifocal technology, especially the ReSTOR lens from Alcon with the new apodisation. My outcomes with these lenses are much better than they are with accommodative lenses and probably this is part of the future. In the mean time we can continue our research until we know how to restore real accommodation, which is the one of the focuses of our current research.

**Haigis:** I have no experience with the CrystaLens but some experience measuring eyes with ICL lenses. We have applied high precision immersion ultrasound, the UBM and real time high resolution ultrasound to measure the change in position and we found there is no movement. With optical biometry what we see is of the order of 0.2 mm to 0.3 mm, equivalent to 0.5 dioptres of accommodation. But lens movements will cause different changes in refraction for different eyes. In short eyes, a change of 1.0 mm results in a refractive change of 2.0 dioptres. This means that, if it works at all, it would work in hyperopes. There are some very individual cases where we can show that there is a considerable movement but in general it is not more than 0.3 mm.

**Holladay:** As you point out, the stronger the powers of the lens the more accommodative effect you achieve for the same amount of forward movement and therefore in the hyperope we should see a bigger lens-related effect. But if you have two patients, one with an anterior chamber lens and one with a posterior chamber lens, both patients emmetropic and both patients have a good distance image, and you run a ray trace, the image of a near source is further away from the anterior chamber lens than it is from the posterior chamber lens. So the idea that the more posterior the lens the greater will be the depth of field is just wrong, it’s the opposite, the more anterior the lens is in the eye, if they’re both equal for emmetropia, the better chance you have to see up close.

**Alio:** At the same time, with all current accommodating lenses we’re fighting for one dioptre of accommodation - this is not the solution. The real solution is to make something that changes the index of refraction or the radius of curvature in response to ciliary body contraction. Until we do that we won’t have real accommodation.

**Tassignon:** The problem is up to now that we don’t understand the mechanism of accommodation in the eye completely. We know that a curvature of the lens plays a role and changes in the refractive index probably also plays a role. The most important drawback for all intraocular lens devices implanted in the capsule is the healing process of the capsular bag comparable to a foreign body reaction against the IOL.

**Haigis:** I guess it was Gullstrand who actually got the Nobel prize for this internal mechanism of accommodation which he attributes to a rearrangement of the fibres inside the lens such as to change the distribution of proteins and thus the refractive index. There are ultra sound measurements - because the ultra sound velocity depends on the protein content – confirming this and all these measurements indicate that the Helmhotlz picture, which includes a re-distribution of the index, is on a pretty firm scientific basis.

**Holladay:** I think that we’ll end up doing is a 1.0 mm capsulorhexis at the equator of the lens.

**Tassignon:** Gradient refractive index lenses exist in communication technology but so far it has never been used in ophthalmology.

**Holladay:** The biggest use of the gradient index lenses was in the military for making single lenses and in communications for making the connection in fibre optics to where you need a gradient to bend the light without the light loss. But ophthalmology just so low on the totem pole for the utilization of gradient optics. It’ll be a while before we get to integrate gradient index into intraocular lenses and glasses.

**Tassignon:** We have calculated that we can build up a gradient of refractive index easily over 2.5 cm of 3 dioptres, no problem with that. We have asked a Japanese company to help us develop such lenses but they are not interested because they say that the market is too small. They also would have to gain approval for the
products because the refractive index gradient is built up by thallium and lithium, but you can encapsulate it and I don’t think it’s a big problem, but nevertheless it will require a lot of biocompatibility testing.

Now we have emphasised the very big importance of the contraction and the healing of the capsular bag. We know because of that healing process the current intraocular lenses that we put in the bag will change position with time, they will induce aberrations due to changes in the position, and so concerning the quality of vision what will you expect as ideal profile of intraocular lens?

Fine: It would seem to me that there is going to have to be some sequential light adjustability or some other form of adjustability in order to compensate for the changing characteristics of the optics as the bag changes conformation and loses its elasticity and alters the position of the lens over a period of time.

Holladay: If we talk about the movement of the lenses, I think that the lenses that we have today with graduated C-loops have been shown pretty conclusively to have very little tilt and de-centration from day to day. But as long as we’ve got surgeons that use different techniques putting lenses in the eye we’re never going to be able to absolutely predict the position and orientation of the lens in the bag. That’s why Howard’s comment on having an adjustable lens to make it better the next day will eliminate the surgeon variability.

Atio: I think that the idea of customising the lens according with the cornea is feasible because actually there is one German company that is offering this and definitely this is a way to improve the results and the visual outcome of our patients and so this idea that was futuristic at this moment is real.

Tassignon: Another question we can address in this round table is, do we need other technologies to calculate intraocular lens powers?

Holladay: There are three variables in IOL calculation that I think we are improving. The first is retinal thickness. This was not accounted for when we measured with ultrasound because it measures to the internal limiting membrane and you have to add an average retinal thickness figure. The IOLMaster on the other hand provides an accurate measurement of the axial length which includes the thickness of the retina. The second biggest problem has to do with the posterior radius of the cornea which there is a physiological variability. Not everybody’s posterior radius is 82% of their front curve not everybody’s asphericity is the same. The next leap forward will be measurements with machines like the Pentacam from Oculus and Artemis because it measures the angle, the sulcus, the zonular insertions and all the dimensions. Then we need to find out whether we can get a better prediction of the lens postoperatively from internal measurements of the eye rather than the ACD. But as long as we’ve got surgeons that use different techniques putting lenses in the eye we’re never going to be able to absolutely predict the position and orientation of the lens in the bag. That’s why Howard’s comment on having an adjustable lens to make it better the next day will eliminate the surgeon variability.

Haigis: It’s going to be necessary to have new concepts but even with today’s formulas if some basic principles are followed it is possible to improve the outcomes. One example is personalisation of constants. Even with the IOLMaster there are differences in personalised constants. They definitely help to give you more correct predictions.

Holladay: Well I think Wolfgang has made an excellent point and he has a website that has beginning constants for sums for the new IOL s. If we walk away with one message today it is that every surgeon should personalise his constant for every lens that he is using because that variation from surgeon to surgeon can be eliminated if he’ll take the time to put that postoperative information into his calculations. I think we all agree with that.

Tassignon: Well I think we have had a very fascinating discussion. Thank you all very much.