28

LENS REFILLING

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During recent decades, demands made on cataract surgery have rapidly increased. Axial eye length abnormalities, corneal astigmatism, and, to some extent, higher-order aberrations can all be corrected with modern IOLs. However, it is still not possible to restore accommodation after cataract surgery. Therefore, patients must decide whether they wish to wear spectacles for distance or for near work. Alternatively, spectacle dependence can be reduced by choosing either monovision or multifocal IOLs. Both of these alternatives have potential disadvantages; monovision reduces stereopsis and causes irritation due to anisometropia, and multifocal IOLs can induce loss in contrast vision, halos, and glare.

So-called "accommodative" intraocular lenses (A-IOLs), which are intended to work using the focus-shift principle, thus far have not shown any clinically relevant axial movement of the optic. Any apparent improvement in near vision is therefore probably due only to depth of focus (DOF) pseudoaccommodation, as is also seen with standard monofocal IOLs.[1]

The ultimate option to restore accommodation is lens refilling. An injectable material replaces the nucleus and cortex of the lens in the presence of capsular and zonular integrity and ciliary muscle function. This arrangement imitates the situation with the prepresbyopic crystalline lens. Ideally, the lens refilling creates an emmetropic eye, yields reasonable amplitude of accommodation, and remains viable over the several decades of presbyopic life.

This chapter presents an overview of the existing knowledge about lens-refilling techniques and their effects on accommodation and capsular bag transparency, as well as discussing the outstanding issues that need to be resolved before the techniques can become clinically useful.

THE BASICS OF ACCOMMODATION AND PRESBYOPIA

As discussed in Sections II to IV of this book, many details of the nature of accommodation and the age-related changes leading to presbyopia remain imperfectly understood. Nevertheless, there is general agreement that a major role in presbyopia development is played by changes in the crystalline lens, particularly the progressive loss in its elasticity. In contrast, the ciliary muscle retains its ability to contract, although some changes in its structure and function may occur.[2-6]

Pallikaris IG, Plainis S, Charman WN.
Presbyopia: Origins, Effects, and Treatment (pp. 233-238).

PSEUDOPHAKIC EYES AND (PSEUDO)ACCOMMODATION

The residual extralenticular accommodative function in patients at the age of about 45 years has led to the development of so-called A-IOLs. Unfortunately, there is no evidence that any of the currently available A-IOLs offer reproducible and clinically relevant optical shift (see Chapter 19). In addition, near vision performance with A-IOLs is no better than that with monofocal IOLs.[7]

It has been shown that some patients who have undergone cataract surgery have good distance and near vision and do not need spectacles for either distance. They attain this mainly through the possession of a large DOF of the eye, or pseudoaccommodation. This is influenced by various factors such as small pupil size, myopic astigmatism, corneal multifocality, and higher-order aberrations. Macular and cortical function related to perception are also known to play a role in extracting information from a defocused image, such as deciphering optotypes from a reading chart. Therefore, visual perception also contributes to psychophysically assessed pseudoaccommodation. These effects can result in good uncorrected distance and near vision.[8]

LENS REFILLING

An alternative to A-IOLs, as a way of exploiting the continuing activity of the ciliary muscle, is lens refilling. This idea was mentioned in the early 1960s by Kessler[9] who suggested that the lens capsule might be refilled after the removal of the relatively rigid presbyopic crystalline lens. The refilled capsule would then mimic the mechanical properties of the youthful capsule and natural lens. However, at that time, this idea could not be realized due to the technological constraints of existing surgical technique and instruments.

Injectable Materials

During experimental studies and modifications in capsular bag refilling techniques, several issues have persistently hampered success. One of these problems is that the injectable matter can leak from the anterior capsule opening through which lens matter is removed. Ideally, therefore, the material for injection in lens refilling should be fluid enough to allow smooth injection but yet be viscous enough to reduce the risk of leakage. Once injected, the viscoelastic properties should imitate those of the young crystalline lens. The injected material must be safe in relation to toxicity and must be durable while also being optically transparent.

To prevent leakage of injected material from the lens, several methods have been developed.[10] One of these methods is that of endocapsular polymerization, where an injectable fluid material is polymerized inside the capsule using a short ultraviolet light exposure.[11] Another innovative strategy is that of injecting a polymer in a fluid state, which then becomes more viscous in the capsule. Although the concept of modifying the density of the polymer worked well, difficulties occurred in attaining complete filling of the lens capsule.

Surgical Procedures

In the first attempts, when the lens capsule was refilled directly (Figure 28-1A), the main problem during lens refilling was leakage. To solve this problem, several different methods were developed, such as the endocapsular balloon by Nishi[10] (Figure 28-1B), which prevented silicone leakage with reasonable preservation of accommodation. Other methods included a specially designed sealing plug (Figure 28-1C) and later, an optic plug (Figures 28-1D and 28-1E).

The endocapsular balloon method was considered to be far too complicated for standard clinical applications. To improve the technique, a plug to seal a continuous curvilinear capsulorrhexis (CCC) was developed by Nishi and Nishi (Figure 28-1F).[12] This newer technique was shown to be feasible, with a good outcome for centration and only a little posterior capsule opacification.

Historically, however, the approaches used to prevent leakage of injected fluid did not prove effective, reproducible, simple, or safe for human application.[10] Recently, a new method using an innovative foldable silicone IOL and a thin plate-disc haptic has been developed by Nishi et al.[13] The novelty of this technique is during the polymer injection, the CCC edge is slightly pulled aside, and the silicone is injected through the delivery hole into the capsular bag and beneath the IOL. A small delivery hole in the haptic and a small, round, cave-like dent at the optic margin serves as a positioning pocket. This technique allows the anterior capsule to then cover the injection hole

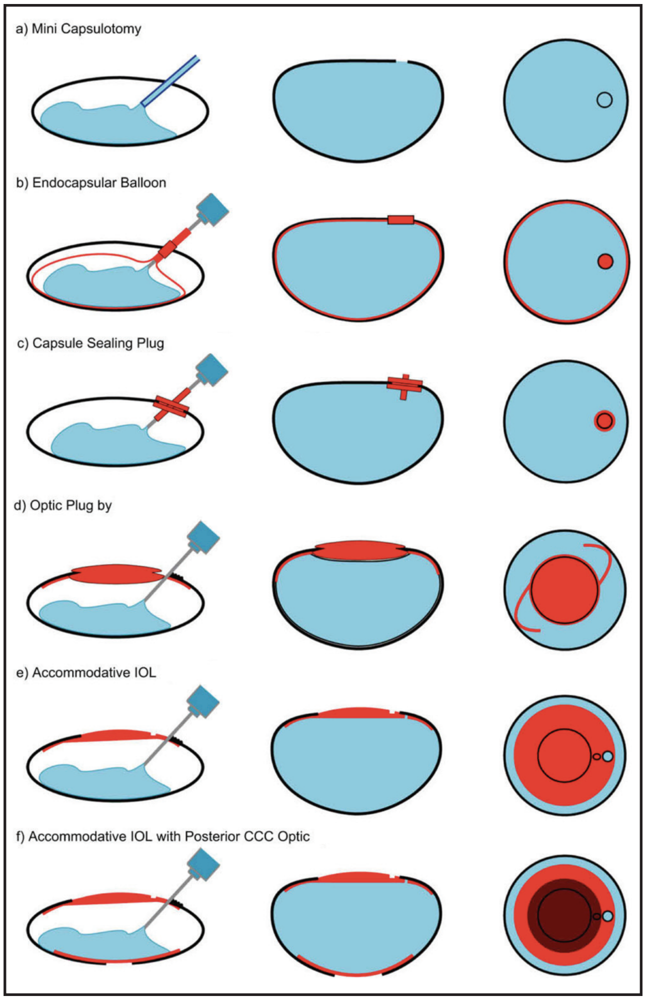

Figure 28-1. Schematic representation of lens refilling techniques used in animal experiments. The diagrams depict the filling techniques (left) and sagittal (middle) and frontal (right) views of the filled capsular bag with injectable polymers (blue) and implanted devices (red). CCC indicates continuous curvilinear capsulorrhexis. (Reprinted from *J Cataract Refract Surg*, vol 35(2), Nishi Y, Mireskandari K, Khaw P, Findl O, Lens refilling to restore accommodation, pp 374-382, Copyright 2009, with permission from Elsevier.)

to prevent leakage of the silicone. The 2 additional advantages of this technique are that the cohesive silicone polymer with its high molecular weight does not leak through the space between the anterior capsule and the IOL, and the injected liquid silicone polymerizes 2 hours after injection so that postoperative leakage is unlikely to occur.[10]

The Accommodative Potential of Lens Refilling

Haefliger et al[14] showed that owl monkeys with an endocapsular implant (Phaco-Ersatz) could accommodate; pilocarpine produced an increase in the curvature of the lens surface and a decrease in the anterior chamber depth, just as that which occurs with the untouched natural lens. In the Haefliger et al[14] experiments, an accommodative potential of up to 6.00 D, as judged from the changes in anterior chamber depth and anterior lens curvature, was observed, but the accommodative amplitude was not measured directly.

The main problem was the extent to which the lens capsule should be refilled because this affected the amplitude of accommodation and the residual unaccommodated refractive error. Findings by Nishi et al suggested that refilling the implant with 60% to 70% of the possible volume leads to the highest accommodative amplitude.[15]

It should be kept in mind that these exploratory studies showed that the accommodative amplitude achieved decreased significantly at the time point when capsule fibrosis developed, suggesting the importance of capsular elasticity in the accommodation mechanism. Also, the importance of the volume of the injected material for obtaining appropriate postoperative refraction was demonstrated.

Two different shapes of endocapsular balloons were developed: one to compare the accommodative effects of an implant with the shape of a unaccommodated lens and one with the shape of an accommodated lens.[16] It was shown that the implant having the shape of a unaccommodated lens resulted in a higher amplitude of accommodation. Thus, the feasibility of lens refilling with an inflatable balloon to achieve some degree of accommodation was successfully demonstrated, at least in monkeys. However, when refilling the lens using a plug to seal the capsule, the amplitude of accommodation achieved was only a small fraction of that prior to surgery.[10] Furthermore, problems occurred because the rhexis-capturing IOL that was developed to seal the capsule and prevent anterior capsule opacification often caused iris capture.

To compare the likely influence of different polymers for lens refilling on the achievable amplitude of accommodation, Young's modulus can be used. Young's modulus indicates the stiffness of a given material and is experimentally determined from the slope of a stress/strain curve of tensile tests conducted on the sample of the material.[10] As expected, the nature of the silicone polymers used for lens refilling was found to influence the lens power change.

REMAINING PROBLEMS

Capsule elasticity and transparency are necessary for a successful outcome after lens refilling. After-cataract appears to be the main problem of lens refilling because it can compromise both the elasticity of the capsule and visual acuity and, therefore, the accommodative function and optical clarity. Clinically, after-cataract has 2 different components: a fibrotic and a regeneratory component. Fibrotic after-cataract is more common and is the main reason for the decrease in visual function as it mainly results in the loss of elasticity of the capsule due to the laying down of collagen by myofibroblasts. Regeneratory after-cataract results in compromised visual function due to inhomogeneities caused by regenerating equatorial lens epithelial cells (LECs) and Elschnig pearls. In the case of lens refilling, fibrotic after-cataract can severely compromise accommodative function due to decreases in capsule elasticity. Furthermore, regeneratory after-cataract may be difficult or impossible to treat due to the risk of leakage of the refilling material into the posterior segment.[10] These difficulties have made after-cataract the main hurdle to be tackled in achieving successful lens refilling.

In all in vivo animal lens refilling experiments mentioned, after-cataract was seen to be a major obstacle in achieving success in lens filling, but only a few of these studies analyzed opacification of the capsule quantitatively.[10]

The accommodation-reducing effect of posterior capsule opacification (PCO) was also shown in a recent study.[17] Some accommodation was restored in adolescent rhesus monkeys that had the lens capsule refilled with a silicone polymer using a plug. However, those monkeys that did not receive anti-inflammatory or after-cataract inhibiting treatment showed essentially no accommodation. In 5 other monkeys, which were intraoperatively treated with a sodium hyaluronate solution containing cycloheximide and actinomycin-D in demineralized water to inhibit after-cataract formation, refraction measurements were successful in all cases. Although refraction measurements were still possible 37 weeks after surgery, reduced optical quality due to opacification of the posterior capsule, as well as fibrotic changes in the midperiphery of the posterior capsule, were reported. Only in 2 cases could pharmacologically induced accommodation still be measured after 37 weeks. In these 2 cases, the accommodative amplitude (±4.00 D) could be considered to be sufficient for reading purposes in humans.

In standard cataract surgery, the introduction of IOLs with a sharp optic edge has resulted in a significant decrease in PCO rates, probably due to contact inhibition at the capsule bend created by the optic edge.[10] However, other factors, such as IOL optic material and overall design of the IOL, also influence PCO development,[18] and it should be taken into account that PCO shows highly active changes and spontaneous disappearance.[19]

PREVENTION OF AFTER-CATARACT

Different techniques to prevent after-cataract have been evaluated. From the mechanical point of view, minimally traumatic surgery and the removal of LECs were found to be the most important factors for PCO prevention. Capsule polishing, hydrodissection, simple aspiration, ultrasound aspiration, cryocoagulation, and osmolysis have been tested, but it has been shown to be very difficult, or impossible, to completely remove all LECs.[18]

To ensure long-term efficacy of the lens-refilling procedure, complete eradication of LECs during surgery will be necessary, whether by pharmacological, genetic, or mechanical means. However, it is not entirely clear whether the lens capsule is viable without resident LECs, which are thought to support the capsule. The LECs may be essential for the long-term integrity of the capsular bag after surgery, and their total eradication might lead to as yet unrecognized complications, such as a delayed onset of zonular disinsertion, leading to subluxation or dislocation of the refilled bag into the vitreous cavity.[10] Furthermore, it is also unknown whether the capsular bag can maintain its long-term biomechanical integrity so that it can continue to permit accommodation. Further in vitro and in vivo models to investigate capsule bag eradication (under conditions of LEC) over a long period need to be conducted.[10]

Rather than eliminating LECs, an alternative approach is to attempt to control LEC behavior, both in growth and in morphological appearance. Attempts at controlling regrowth of a crystalline lens in nonhuman eyes indicate that this may be a promising route to pursue. Currently, we may need to accept that lens refilling will be achievable only with some degree of concomitant after-cataract.

Two models recently suggested by Nishi et al[10] may lead to a future clinical application, although some important issues remain to be resolved. One of the suggested models is the implantation of thin anterior and posterior IOLs with sharp-edge design between which silicone can be injected.[10] Another model uses a posterior IOL to seal a primary posterior CCC made surgically to maintain a visual axis free from LEC proliferation. However, with this design, the necessary changes of curvature of the anterior lens surface (now replaced with an IOL optic) may not be achievable.

These techniques need further investigation to assess the attainable accommodative amplitudes, the elasticity and the integrity of the entire capsule, the calculation of the lens power of both the posterior and anterior IOLs, and a long-term follow-up to evaluate potential complications. In addition, the development of an intraoperative monitoring device to measure refraction during lens refilling must be developed.[10]

SUMMARY

Although the accommodative process is not yet fully understood, animal experiments with lens refilling from the past 3 decades have shown that lens shape changes are indeed attainable in the early postoperative period. Thereafter, after-cataract remains the main obstacle, resulting in both a decrease in lens capsule elasticity and a loss of optical clarity of the capsule. Attempts to eradicate LECs during surgery have not yet been fully successful, and a depletion of all LECs may also result in long-term decay in lens capsule integrity. Thus, lens refilling remains, as yet, an unproven method for the long-term restoration of useful levels of active accommodation in humans.

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