Injectable accommodative lenses, a preclinical study
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Chapter 1.

INTRODUCTION
Introduction

Accommodation is the ability to change the optical power of the eye for near vision, allowing dynamic focusing of the images of close as well as far-away objects on the retina. Credit for explaining the mechanism of accommodation in the human eye is usually given to Hermann von Helmholtz who presented the results of a series of accommodation experiments to the Berlin Academy of Sciences in February 1853. However, two years earlier, in 1851, Anthony Cramer, a physiologist from Groningen in the Netherlands, had already submitted a treatise to the Dutch Society of Sciences describing the changes of the third Purkinje image in the natural lens during accommodation. The decrease in size and positional changes of the third Purkinje image during accommodation point to an increase in anterior lens curvature and show that the anterior surface of the lens shifts toward the cornea. In other words, Cramer discovered the ocular changes occurring during accommodation a little earlier than Helmholtz, but since his treatise was not printed immediately and because it was in Dutch (and therefore less accessible to the rest of the world), the credit for this discovery is usually given to Helmholtz. Cramer speculated that the increase in lens curvature during accommodation was caused by the force of the iris. Helmholtz, on the other hand, was of the opinion that the increase in lens curvature is caused by contraction of the ciliary muscle, and he established that it is not only the anterior lens surface but also the posterior lens curvature that changes during accommodation. These latter observations added to the description of the changes occurring in the eye during accommodation.

According to Helmholtz, ciliary muscle contraction releases the circumferential tension on the zonules. The elasticity of the lens capsule and the malleability of the lens contents enable the lens curvatures to increase. Relaxation of accommodation occurs when increasing tension of the zonular fibers, inserting into the ciliary body and choroid, pull the lens back into its unaccommodated, flattened state.

Presbyopia

Around 45 years of age, an age-related decrease in accommodative amplitude begins to be expressed symptomatically, an occurrence that is called presbyopia.
Factors that might be responsible for presbyopia are lens hardening\textsuperscript{5}, aging of the ciliary muscle\textsuperscript{6}, aging of the choroid\textsuperscript{7,8}, loss of elasticity of the lens capsule\textsuperscript{9}, or growth of the lens during aging\textsuperscript{10}. The relative importance of these factors is still subject to debate. Several authors performed finite element modeling of the lens capsule, the lens contents, and the zonular fibers in order to determine the contribution of the lens to the development of presbyopia\textsuperscript{11, 12,13}. The values of many parameters at different ages are needed to create a precise model. One of these is Young’s modulus, which describes the elasticity of the lens. However, there are few publications on the age-related material properties of the lens nucleus and cortex; not all of the published results seem to be quite reliable\textsuperscript{14,15}. Presently available models cannot fully describe all aspects of presbyopia. This might result from errors in the parameters used, it might be attributed to a certain lack of knowledge regarding the variability of the parameters, or it could mean that extralenticular factors also contribute to the development of presbyopia. Thus, we cannot be quite sure how accurately these models represent the accommodation of the human eye.

Many investigators consider hardening of the lens nucleus and cortex to be an important factor in the development of presbyopia. It seems to provide a logical explanation, since the lens changes its shape during accommodation. Pau and Krantz\textsuperscript{5} described the simultaneous increase of lens sclerosis and decrease of accommodative ability. Fisher\textsuperscript{9}, by placing lenses on a rapidly rotating table, demonstrated that older lenses are more resistant to deformation than younger lenses. Glasser and Campbell\textsuperscript{16} showed that older lenses, when subjected to equatorial stretching forces, reveal less drastic focal length changes than younger lenses.

**Correction of presbyopia using glasses, contact lenses, or monovision.**

Since presbyopia affects the ability to read and to perform fine manual work, attention has always focused on finding ways of obtaining a focused image of nearby objects. The first vision aids were invented around 1000 AD (inventor unknown). They were referred to as reading stones and consisted of a spherical piece of glass that was placed on top of the reading material in order to magnify the letters. Reading spectacles are described by several texts written between 1268 and 1289. The first known painting featuring someone with eyeglasses was created by Tommaso da
Modena in 1352. One of his frescoes shows a man reading a manuscript with glasses perched on his nose. Benjamin Franklin is credited with the invention of bifocal spectacles around 1780. In 1827, trifocals were patented by John Isaac Hawkins. Multifocal glasses were introduced in 1958 by the Essilor company. Developments in manufacturing techniques have enhanced the comfort of wearing eyeglasses, including bifocal or multifocal ones. Today’s eyeglasses are made of lightweight, thin, strong materials that are also scratch-resistant. Strong, non-corrosive, hypo-allergenic materials are used for the frames. Nevertheless, efforts to eliminate the necessity of wearing glasses have never abated. Eyeglasses, after all, have a number of disadvantages. For one thing, they are considered to be cosmetically unattractive by some. In order to clearly see objects at varying distances, the wearer has to look through different sections of his or her bifocal or multifocal glasses. Glasses will cloud over when moving from a cold to a warm environment. People may be unable to find their glasses unless they are worn continuously. The reading addition in bifocal or multifocal glasses is usually located in the lower section of the glass, which makes it cumbersome to view close or overhead objects.

A second type of reading aid that alleviates some of the above-mentioned problems associated with glasses is a contact lens that includes an addition for near vision. However, few presbyopic persons are actually wearing multifocal contact lenses. Age-related changes in the tear film may affect the comfort of wearing contact lenses. Besides, the fine motor skills necessary for insertion and removal of the contact lenses may be an obstacle for elderly people. Compared to monofocal contact lenses, a reduction in optical performance can occur with multifocal contact lenses.

A third possibility for presbyopia correction is monovision. Monovision means that the person in question uses far vision correction for one eye while the other eye is corrected for near vision. This can be achieved with glasses or contact lenses or by implantation of intraocular lenses after cataract surgery. Despite a certain degree of success, not everyone is ready to accept this way of achieving simultaneous far and near vision. Psychological factors as well as reduced stereopsis have been suggested as factors influencing the acceptance of monovision.
Correction of presbyopia with multifocal intraocular lenses

Since presbyopia is associated with somewhat advanced age, cataract is relatively common in any presbyopic population. Implantation of multifocal intraocular lenses after cataract surgery makes it possible to combine the treatment of cataract and presbyopia. Multifocal intraocular lenses have two focal points, and the incident light entering the eye is distributed over both focal points. On the downside, patients implanted with multifocal intraocular lenses have less contrast sensitivity than patients with monofocal intraocular lenses\(^2\). A second drawback of multifocal lenses is their failure to allow clear vision at intermediate distances. On the other hand, it has been shown that multifocal intraocular lenses can effectively contribute to presbyopia correction by reducing the dependence on reading glasses compared to monofocal intraocular lenses\(^2\).

Refractive surgery

During the past decade, refractive surgical techniques were developed for the treatment of problems such as myopia, hyperopia and astigmatism. Following refractive surgery, most patients find that they possess good visional ability without needing glasses or contact lenses. With the onset of presbyopia, however, they have to revert to using reading glasses once more. This is a disappointment for those who have previously experienced clear vision without glasses. The success and the ready availability of refractive surgical techniques have raised the question of whether presbyopia could be corrected by a surgical procedure. Presbyopia is referred to as being “the final frontier” in refractive surgery\(^2\). In response to these demands, several surgical techniques were developed and are being used now in an attempt to correct presbyopia\(^1,2,3\), for instance by creating a multifocal corneal surface by excimer laser surgery. The disadvantages associated with multifocal intraocular lenses also apply to multifocal corneal surfaces, such as reduced contrast sensitivity and no or limited intermediate vision\(^1\). Other techniques involve scleral expansion surgery\(^2\) and the implantation of accommodative intraocular lenses\(^3\). These methods - as opposed to techniques involving multiple focal points - attempt to increase the amplitude of accommodation.
Objective (true) accommodation versus subjective (pseudo) accommodation

In order to determine whether medical intervention influences the accommodative amplitude, uniform measuring techniques are needed. Unfortunately, there is no agreement on this matter; a variety of measuring techniques for the accommodative amplitude are currently in use. The list includes objective and subjective measuring techniques.

Since accommodation is defined as the ability to change the optical power of the eye so as to allow near vision, it stands to reason that the accommodative amplitude may be determined by measuring the optical power change after presentation of a nearby visual stimulus with a refractometer. Since the results are independent of the subject’s response, this method is considered to be objective. The subjective approach usually involves a push-up method. A reading chart is moved progressively closer until the image begins to blur, as indicated by the subject. The dioptric value of the distance between the eye and the reading chart then represents the subjective accommodative amplitude. Empirically it seems that subjective measurements yield higher values than true objective measuring techniques, an effect that is attributed to the subjective end-point criterium (blur) and the depth-of-field effect which affects the outcome. The depth of field is the range of constant visual acuity and it can be accentuated by accommodative pupil constriction. Besides, optical aberrations of the cornea and the lens, too, may influence the depth of field. Given the different results obtained with subjective as opposed to objective measurements, a clear distinction should be made between both methods when judging the effectiveness of any procedure claimed to improve the accommodative amplitude. Subjective measuring techniques may, in some cases, suggest optical power changes that do not actually exist, or at least not to this extent. Accommodative amplitudes obtained by subjective measuring techniques, not based on true optical power changes, are referred to as pseudo-accommodation.

Scleral expansion surgery, surgical reversal of presbyopia.

One of the first surgical procedures developed for the correction of presbyopia was surgical correction of presbyopia (SRP). It was introduced by Schachar. This surgery is based on Schachar’s hypothesis of accommodation. It does not involve
lens surgery as opposed to implantation of a multifocal intraocular lens, but extraocular surgery on the sclera. According to Schachar’s hypothesis of accommodation, the ciliary muscle, when it contracts, pulls the equatorial zonules on the lens equator, thus increasing the central lens curvature. This is in contrast with Helmholtz’s theory of accommodation, where the central lens is supposed to flatten out when the zonules pull on the lens equator. According to Schachar’s hypothesis, presbyopia is caused by increasing lens size and consequently increasing lens diameter. Thus, the equatorial zonular fiber tension is relieved, precluding any tension on the lens equator. During surgery, the sclera covering the ciliary body is expanded by creating four intra-scleral tunnels into which four PMMA implants are inserted. In a similar surgical method, a knife or a laser\textsuperscript{31} is used to make radial cuts in the sclera covering the ciliary muscle. This approach, too, would expand the sclera and facilitate accommodation. A 1-3 D increase of accommodative amplitude was attained according to subjective measurements after scleral expansion surgery\textsuperscript{32}. However, objective measurements of the the accommodative amplitude show that there is no change after such a procedure\textsuperscript{33,34}.

**Accommodative intraocular lenses**

Two companies have developed and are selling products referred to as accommodative intraocular lenses. The Crystalens\textsuperscript{tm} lens has received FDA approval for this labelling. The other lens (1CU), made by HumanOptics, is marketed primarily in Europe. The haptics of both lenses swivel around a hinge with the lens optics. This is supposed to cause an antero-posterior movement of the lens optics whenever the ciliary muscle tension changes. Precise interferometric measurements performed with both types of lenses implanted in human eyes, however, were unable to confirm any relevant antero-posterior movement after pilocarpine stimulation of accommodation – which would have been essential in order to achieve the desired accommodative effect\textsuperscript{35,36,37}. Three months after implantation of the 1-CU lens\textsuperscript{38}, the accommodative amplitude, measured with an autorefractor, showed a peak mean value of 0.5 D during induced accommodation. Subjective accommodation measurements reveal an accommodative amplitude of 1-3 D\textsuperscript{39}. Considering the insufficient empirical evidence of intraocular lens movement, revealing minor
movements at most, the subjective accommodative amplitude must be attributed to pseudo-accommodation.

Other types of accommodative lenses have been described in the literature\(^40\). However, in view of the limited availability of peer-reviewed publications describing results of clinical or pre-clinical testing, these lenses will not be discussed in this context.

**Lens refilling**

Since hardening of the lens substance is considered an important factor contributing to the development of presbyopia, surgeons have considered removing the hardened lens substance through a small opening in the lens capsule and replacing the lens contents with a soft refill material in order to restore accommodation.

The principle of refilling the capsular bag was pioneered by Kessler\(^41\) in 1964, who published experimental results obtained with ex-vivo human and rabbit eyes. He extracted the lens through a 2 mm incision at the pars plana by using loops of thin wire to cut the lens in pieces that were then aspirated. Kessler tried out a range of filling materials but finally favored a room-temperature curing silicone. Postoperatively, the eyes were highly hyperopic, due to the low refractive index (1.40) of his material. In a subsequent rabbit study\(^42\), the author found that refilled capsules remained clear for up to two years.

In 1967, Agarwal and co-workers\(^43\) also used a 2-component, low-temperature curing silicone for capsular bag refilling. They were able to measure refraction in rabbit eyes by retinoscopy. Another paper\(^44\), published the same year, described experiments with rhesus monkey eyes. Despite being treated with steroids, the anterior chambers were cloudy due to inflammation for the first three postoperative weeks. During this period the capsule gradually opacified, preventing retinoscopy, and after four weeks the posterior segment was not even visible.

In 1986, Parel and colleagues\(^45\) at Bascom Palmer developed Phaco-Ersatz, as they termed it, a technique that also involves removal of the lens substance and refilling of the capsular bag. Silicone was selected as a refilling material and tested in ex-vivo human eyes; in-vivo testing was performed in rabbit and cat eyes. In a later publication\(^46\) in 1994, the authors described accommodation measurements in owl
monkey eyes. Initial inflammation followed by capsule opacification prevented optical accommodation measurements, but it was possible to measure anterior chamber shallowing and lens thickening by ultrasound A-scan in response to pilocarpine. In one old monkey, which was about 17 years of age at the time of surgery, the accommodative shallowing of the anterior chamber was still detectable four years later. In the year 2000, in partnership with the Vision Co-operative Research Centre in Sydney, Australia, Parel resumed his work on Phaco-Ersatz.

Nishi, too, systematically studied capsular refilling techniques. In his initial rabbit studies in 1992, he inserted a balloon into the capsular bag. The balloon was then filled with silicone. In a series of papers, some of which were published together with Hara, Sakka and other co-workers, the techniques were gradually refined. Ultimately, however, the balloon was abandoned and Nishi started using a plug to seal the capsular opening. He also investigated the capsular bag filling volume and its effect on ex-vivo accommodation. Accommodation reached its maximum if the bag was filled to about two thirds of its original volume, a result that was utilized for subsequent primate studies in 1998. Capsular opacification remained a constant problem in all studies. In a final paper, Nishi reports up to 4.5 D accommodation in primates in response to pilocarpine, compared to 8 D preoperatively. He concludes that lens refilling is no feasible option for the treatment of presbyopia in human eyes until and unless capsular opacification can be prevented.

Eye models for lens refilling studies

Lens refilling procedures can be studied in various experimental eye models, each with its own advantages and disadvantages.

Pig eyes from the abattoir may be used to study surgical techniques. Despite their easy availability, however, these eyes are not known to show any accommodation at all and are therefore unsuitable for accommodation studies. The porcine lens capsule is comparatively thick (59 µm) in relation to the human lens capsule (13 µm). Putting stress on the lens capsule during surgical manipulation may cause capsular rupture. Due to the thicker porcine lens capsule, this aspect of surgery is not reflected adequately in the pig eye model. The lens substance in young pig eyes is soft and easily aspirated with a cannula, a technique that is
impossible in presbyopic human eyes since their lens substance is much harder. Furthermore, the porcine lens is much thicker and more spherical than the human lens, which makes for different optical characteristics in both species.

Ex-vivo human eyes can be used to study lens refilling. The majority of donated eyes are from elderly people, which means that the hardness of the lenses in the donated eyes is representative for a population suffering from cataract. Lens capsular thickness in conjunction with experimental lens refilling is also realistic, but human eyes may not always be easy to come by, depending on local circumstances. Besides, accommodation studies involving donated eyes are only possible in an experimental setting, for instance with a lens-stretching device. In most ex-vivo human eyes, the cornea is more or less opaque and has to be removed, or it has already been removed for transplantation purposes. Lens refilling surgery on an eye without a cornea does not provide an entirely realistic simulation of the human clinical situation.

Rabbit eyes as models offer the possibility of in-vivo studies. Rabbits are relatively quick to develop capsular opacification, which makes it possible to study this aspect of lens refilling surgery. The thickness of the rabbit lens capsule is similar to that of the human lens capsule. Rabbits do not accommodate, and the lens in young animals is relatively soft. The rabbit lens is very thick and more spherically shaped than the human lens. This results in different optical characteristics.

Rhesus monkey eyes, on the other hand, do undergo accommodation and also develop presbyopia in a pattern similar to human presbyopia. Besides, the thickness of their lens capsule is quite similar to that of the human eye. However, monkeys are scarce. The lenses of young animals are soft compared to presbyopic human lenses. As described in the literature, young rhesus monkeys may exhibit inflammatory reactions after lens refilling surgery, resulting in opacification of the lens capsule. This makes it difficult to measure the resulting accommodative amplitude after lens refilling surgery with a refractometer.

**Scope of this thesis**

Due to the growing interest in the possibility of presbyopia correction, industrial and academic research groups have developed new materials that may lend
themselves as replacement materials for lens refilling. Such materials were also developed by Pharmacia Groningen BV in Groningen in the Netherlands. The company was acquired by AMO (Advanced Medical Optics) in 2003 and is now named AMO Groningen BV. Materials developed by Pharmacia were used in the experiments described in this thesis. Initially, both silicone and hydrogel materials were developed by polymer chemists at Pharmacia\textsuperscript{57,60}. Subsequent efforts focused on silicones.

This thesis describes the testing of lens-refilling materials and the development of suitable surgical procedures for lens refilling using different experimental models. Ultimately it is to demonstrate that accommodation may be measured in a living monkey eye after replacing the natural crystalline lens by polymeric lens material.

A surgical lens refilling technique had to be developed first. Hettlich describes a surgical technique\textsuperscript{61} he used to perform lens-refilling experiments in pig and rabbit eyes. According to his technique, two stab incisions are made in the lens capsule, followed by bimanual irrigation and aspiration of the lens material. The capsule is refilled by injecting the refill material through the capsular opening, accompanied by continuous irrigation of the anterior chamber. Hettlich uses no plug to close the openings in the capsular bag. To prevent tears extending from the stab incisions in the lens capsule, we started using a capsulorhexis in the lens periphery, which, after some practice, was made as small as 1-1.5 mm. Besides, we utilized only a single capsular opening in order to protect the integrity of the capsule. Instead of bimanual irrigation, we used a self-retaining anterior chamber maintainer to allow eye infusion during the surgery. The resulting refilled lens thickness was nowhere near the thickness of natural porcine lenses. Only a limited amount of refill material could be injected into the capsular bag of the porcine lens, since injecting more material would cause the material to leak into the anterior chamber. In order to keep the refill material inside the capsular bag, a small plug was developed in collaboration with engineers at AMO Groningen BV. This plug consists of a small circular plate attached to a 10-0 nylon suture. It is inserted through the opening in the lens capsule; the refill material pressure inside the capsular bag then keeps the plug stuck in the capsular opening. This plug, which offers a number of advantages over the capsular bag plugs developed by Nishi and Parel, was described in a patent (chapter 2). With this plug we can now control the amount of refill material to be injected into the capsular bag.
during surgery and also obtain thicker refilled pig lenses than without a plug (chapter 4).

The development of this plug was followed by experiments involving human eyes. The cornea bank of the Dutch Ophthalmic Research Institute (headed by Mrs E. Pels) regularly provided human eyeballs for experimental purposes. Through our collaboration with Dr. Adrian Glasser (College of Optometry, University of Houston, Texas, USA), a mechanical stretching apparatus became available which is used to simulate accommodative changes in ex-vivo human lenses (figure 1).

The mechanical stretching apparatus, capable of applying radial forces to ex-vivo lenses, was used to study accommodative changes in natural as well as refilled human lenses at various ages (chapter 3). Two refill materials with a different Young’s modulus were used in this context. Presbyopic human lenses, refilled with a silicone material with a Young’s modulus comparable to that of 20-year-old human lenses, showed accommodative changes comparable to those of 20-year-old human lenses (Sil 2). Lenses refilled with a silicone material comparable to that of 40-year-old human lenses (Sil 1) showed less drastic accommodative changes. Subsequent experiments utilized only the material that achieved the greatest accommodative change.
Traditionally, cataract surgeons replace the natural lens by an artificial lens with a predetermined optical power. Regular intraocular lenses are available with a lens power between 0 and 33 D. With capsular bag refilling, however, the optical power of the new lens is determined by the final size and shape of the capsular bag and by the surgeon’s technique. Appropriate systems are needed to inform the surgeon of the optimum amount of refill material injected to achieve the desired optical power. The ability to adjust the power of the refilled lens during surgery is essential. In his thesis, Hettlich suggests that the lens power of the refilled lens may be influenced and possibly adjusted by changing the height of the infusion bottle during surgery. We performed these experiments (chapter 4) and confirmed that the height of the infusion bottle does, indeed, influence the lens power of the refill lens (1.8 D) to a certain degree. Although these changes are too insignificant to imply any clinical importance; i.e., for achieving emmetropia under all circumstances, they can be used for fine tuning the lens power.

Figure 2. Change of lens power with age in three groups of lenses. The results were measured at 4 mm increase of the ciliary body diameter. The lens power changed hardly in older natural lenses, whereas the refilled lenses exhibited a more noticeable change in lens power. Lenses refilled with Silicone 2 showed a larger change in lens power than lenses refilled with Silicone 1. Silicone 2 had a Young’s modulus comparable to that of 20-year-old lenses, while Silicone 1 exhibited a Young’s modulus comparable to that of a 40-year-old person.
Since the optical power of the refilled lens depends on the amount of injected material, we performed additional experiments to establish the relationship between the amount of injected material and the optical power of the refilled lens (chapter 5). Our pig eye experiments revealed that an additional 0.04 mL of injected material increased the lens power by 1 D. This result indicates the filling accuracy required during the procedure.

Postoperative opacification of the lens capsule is a problem with pseudophakic eyes today; it is treated by disruption of the posterior lens capsule with NdYag laser pulses - a procedure that is quite impossible with refilled lenses. Since postoperative opacification of the lens capsule affects the optical clarity of the refilled lens and decreases the accommodative amplitude, postoperative opacification must be prevented even before refilling the lens. In a collaborative effort of AMO Groningen BV and the Department of BMSA at Groningen University (Dr. T.G. van Kooten and Prof. Dr. H. Busscher) as well as a similar cooperative project involving AMO Groningen BV and the Department of Biomaterials at Rostock University, attempts were made to develop an appropriate treatment for the capsular bag so as to prevent capsular opacification. This treatment was to kill off all the lens epithelial cells and was supposed to require only a brief period of time during surgery. The research groups in Groningen and in Rostock tried out various chemical substances during their “in-vitro” and “in-vivo” rabbit experiments. The experiments aimed at the prevention of capsular opacification, which were performed in Groningen, are described in chapter 6.

Parallel to the development of suitable lens capsular refill materials, S. Norrby, P. Piers, and others at AMO Groningen BV developed the Tecnis Z9000 intraocular lens\textsuperscript{62}. This lens reduces the amount of spherical aberration for most patients, compared to standard intraocular lenses; it also enhances the mesopic contrast sensitivity\textsuperscript{63}. Stimulated by the interest in spherical aberration measurements, we hypothesized that refilling of the lens capsule with a material showing a homogeneous refractive index might significantly change the spherical aberration. In our seventh series of experiments, we measured the optical changes caused by lens refilling in a pig lens model (chapter 7). We detected changes due to a varying lens curvature as well as changes caused by the transition of the gradient refractive index into a homogeneous refractive index. It was found that refilling resulted in a more positive spherical aberration than in a natural pig lens. The effect of lens refilling on
the spherical aberration of the human lens remains to be elucidated and might be an interesting topic for further research.

Since primates are the only species showing accommodation similar to the human eye, this animal model was used to study accommodation after in-vivo lens refilling, mostly in collaboration with Dr. Adrian Glasser in Houston, Texas, USA. In a group of four animals, surgery was successful. However, postoperative inflammation and capsular opacification precluded optical accommodation measurements. Ongoing experiments regarding capsular opacification in rabbits resulted in an effective preventive method, which was then also utilized in the monkey experiments. Treating the capsular bag with a chemical substance prevented capsular opacification. In five animals that were treated according to a new protocol involving more intense postoperative treatment with steroid eyedrops, accommodation was measured as an optical power change during the 37-week follow-up period. These experiments are described in chapter 8.

![Figure 3. Refilled rhesus monkey lens capsule. Total iridectomy was performed several weeks before lens surgery. The circular disk is the plug that closes the capsulorhexis.](image)

The experiments described in this thesis are preclinical experiments, aiming at the development of an injectable accommodative lens.

An important outcome was that we succeeded in implanting this lens into human donor eyes and were able to measure accommodative changes while similar
changes were not measurable in presbyopic natural human lenses. A second important outcome was that, in contrast to studies published earlier, the accommodation of an injectable accommodative lens in rhesus monkey eyes was not only measured as an optical power change, but also as a change in lens thickness during a 6-month follow-up period.

Many more questions remain to be answered before the injectable accommodative lens can be used for human eyes. Permanent prevention of capsular opacification is a major aspect. Another challenge is the question of how to measure and control the power of the injected lens during surgery. In the context of the experiments described in this thesis, the natural lens was removed by simple aspiration. A practical solution is needed for the removal of the hard, stiff natural lens material found in older cataract patients through a 1 to 1.5 mm opening in the lens capsule. However, given the worldwide interest in the correction of presbyopia, the prospects for further research and development of accommodating lenses are excellent.
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