Graefe's Arch Clin Exp Ophthalmol (2007) 245:473–489
DOI 10.1007/s00417-006-0391-6

REVIEW ARTICLE

Accommodating intraocular lenses: a critical review of present and future concepts

R. Menapace · O. Findl · K. Kriechbaum · Ch. Leydolt-Koeppl

Received: 2 June 2006 / Accepted: 7 June 2006 / Published online: 30 August 2006
© Springer-Verlag 2006

Abstract
Background Significant efforts have been made to develop lens implants or refilling procedures that restore accommodation. Even with monofocal implants, apparent or pseudoaccommodation may provide the patient with substantial though varying spectacle independence. True pseudophakic accommodation with a change of overall refractive power of the eye may be induced either by an anterior shift or a change in curvature of the lens optic.
Materials and methods Passive-shift lenses were designed to move forward under ciliary muscle contraction. This is the only accommodative lens type currently marketed (43E/S by Morcher; 1CU by HumanOptics; AT-45 by Eyeonics). The working principle relies on various hypothetical assumptions regarding the mechanism of natural accommodation. Dual-optic lenses were designed to increase the dioptric impact of optic shift. They consist of a mobile front optic and a stationary rear optic which are interconnected with spring-type haptics. With active-shift lens systems the driving force is provided by repulsing mini-magnets. Lens refilling procedures replace the lens content by an elastic material and provide accommodation by an increase of surface curvature.

The author has no proprietary interest in any of the materials or equipment mentioned in this study.

O. Findl · K. Kriechbaum · C. Leydolt-Koeppl
Department of Ophthalmology, Medical University of Vienna,
Vienna, Austria

R. Menapace (✉)
Department of Ophthalmology,
University of Vienna Medical School,
Währinger Gürtel 18-20,
Vienna 1090, Austria
e-mail: rupert.menapace@meduniwien.ac.at

Results Findings with passive-shift lenses have been contradictory. While uncorrected reading vision results were initially reported to be favorable with the 1CU, and excellent with the AT-45 lens, distant-corrected near vision did not exceed that with standard monofocal lenses in later studies. Mean axial shift from laser interferometric measurements under stimulation with pilocarpine showed a moderate anterior shift with the 1CU, while the AT-45 paradoxically exhibited a small posterior shift. With the 1CU, the shift-induced accommodative effect was calculated to be less than +0.5 D in most cases, while +1 D was achieved in a single case only. Ranges and standard deviations were very large in relation to the mean values. Under physiological near-point stimulation, however, no shift was seen at all. Prevention of capsule fibrosis by extensive capsule polishing did not enhance the functional performance. Dual optic lenses are under clinical investigation and are reported to provide a significant amount of accommodation. However, possible long-term formation of interlenticular opacifications remains to be excluded. Regarding magnet-driven active-shift lens systems, initial clinical experience has been promising. Prevention of fibrotic capsular contraction is crucial, and it has been effectively counteracted with a special capsular tension ring, or lens fixation technique, together with capsule polishing. Lens refilling has been extensively studied in the laboratory and in primates. Though it offers great potential for fully restoring accommodation, a variety of problems must be solved, such as achieving emmetropia in the relaxed state, adequate response to ciliary muscle contraction, satisfying image quality over the entire range of accommodation and sustained functioning. The key problem, however, is again after-cataract prevention.
Conclusions As opposed to psychophysical evaluation techniques, laser interferometry measures what shift lenses

are designed to provide: axial shift on accommodative effort. While under pilocarpine some movement was recorded, no movement at all was found under near-point stimulation with any of the lenses currently marketed. In contrast, magnetic-driven active-shift lens systems carry the potential of sufficiently topping up apparent accommodation to provide for clinically useful accommodation while using conventional lens designs with proven after-cataract performance. Dual optic implants significantly increase the impact of axial optic shift. The main potential problem, however, is delayed formation of interlenticular regenerates. Lens refilling procedures offer the potential of fully restoring accommodation due to the great impact of increase in surface curvature on refractive lens power. However, various problems remain to be solved before clinical use can be envisaged, above all, again, after-cataract prevention. The concept of passive single-optic shift lenses has failed. Concomitant poor capsular bag performance makes these lenses an unacceptable trade-off. Magnet-assisted systems potentially combine clinically useful accommodation with satisfactory after-cataract performance. Dual optic lenses theoretically offer substantial accommodative potential but may allow for interlenticular after-cataract formation. Lens refilling procedures have the greatest potential for fully restoring natural accommodation, but will again require years of extensive laboratory and animal investigations before they may function in the human eye.

Keywords Accommodative intraocular lenses · Working principle and clinical performance of current lenses · Future concepts

Introduction

Due to advances in material and design, excellent visual and morphological results may be achieved with modern intraocular lenses (IOLs). With laser interferometry for biometry and third-generation formulae a postoperative refraction close to emmetropia can be reached in most cases. One last frontier remains the restoration of true accommodation, the ability of the young eye to focus objects on the retina at any distance between far and near when corrected for its refractive error. This paper critically reviews recent and future concepts with regard to their potential to restore accommodation.

What is true accommodation?

Accommodation is the ability of the eye to continuously change the focal length in order to create a sharp retinal image of objects at any distance between far and near. In the young human eye, this is provided by an increase of lens curvature, and, to some extent, by a forward shift of the lens itself. Presbyopia is mainly due to a decrease in lens elasticity [14], but also an increase in its equatorial diameter, a loss of Bruch's membrane elasticity, and a reduction of ciliary muscle contractility [4].

In a pseudophakic eye with a monofocal IOL, myopic astigmatism [28, 78] may allow for significant reading capability. Even with emmetropia, increase of depth of field through miosis [54, 55], and corneal aberrations or multifocality [13, 67] and cortical mechanisms that enhance visual perception [23] may provide a significant though varying amount of uncorrected near vision. This is also true for the aphakic eye and is generally referred to as apparent accommodation, or pseudoaccommodation. Pseudoaccommodation with monofocal IOL ranges between 0.7 to 5.1 D depending on the method of assessment used, with a mean amount of about 2 D [7, 13, 23, 55, 67, 81].

How can the loss of accommodation be compensated by an IOL?

One way of compensating the loss of accommodation by means of an IOL is to provide the visual system with two simultaneous images. This can either be done binocularly (monovision) or monocularly ("multifocal" IOLs).

Monovision One eye is corrected for far, while the other is corrected for near. Surprisingly good results have been reported [15]. However, the amount of tolerated refractive offset varies significantly among patients, and diplopia may ensue. Stereopsis is reduced or lost. This approach may offer good results in patients with preexistent or cataract-induced myopia in one eye.

"Multifocal" IOLs "Multifocal" IOLs (MIOLs) distribute the incoming light onto two or more foci depending upon the optic principle and the particular optic design. Thereby, part of the light is lost, and the brightness of the various foci is reduced to a varying degree. In fact, these IOLs are bifocal IOLs. This is also true for refractive MIOLs, since only two of the foci produced are intense enough to be perceived. A major drawback of MIOLs is that the image of the object in focus is superimposed by the second image of the object not in focus, resulting in reduced contrast sensitivity and disturbing optical phenomena [43]. This still applies to the most advanced MIOL systems [53]. MIOLs may be considered for young patients with unilateral cataracts, or elderly people asking for greater spectacle independence in daily life.

"Accommodative" IOLs In contrast, "accommodative" IOLs (AccIOLs) are designed to transmit ciliary muscle contraction into a change of dioptric power of the eye. As mentioned, the human crystalline lens provides for that mainly by an increase of curvature, and to some extent by an anterior movement of the lens. The latter is mediated by the change in ciliary body configuration, or its anterior apex [30, 76].

Current AccIOL approaches are based on the "focus shift" principle: Through various, essentially hypothetical mechanisms, contraction of the ciliary muscle should cause the optic to move anteriorly, thereby increasing the dioptric power of the eye. Depending upon the absence or presence of a well-established driving force, these types of AccIOL may be addressed as passive- and active-shift IOL, and as dual-optic IOL when a second optic is incorporated.

Currently marketed accommodating IOLs: design and hypothetical working principle

Currently marketed AccIOLs are all passive-shift IOLs: The moving force of these IOLs is based on a hypothetical working mechanism.

Ring-haptic IOL BioComFold® (H. Payer [68])

This was the first AccIOL on the market (1996, by Morcher GmbH, Stuttgart, Germany). It is a one-piece IOL made of foldable hydrophilic acrylic with a 5.8-mm optic and a total diameter of 10.2 mm. The three broad-based anteriorly angulated haptics (opposite to the usual haptic angulation) are relatively rigid and feature a perforated transition zone and a bulging discontinuous ring at their ends. In 1998, model 43A was followed by model 43E, which differs slightly in the number of perforations and the amount of angulation (Fig. 1a).

The hypothetical working mechanism was circumferential compression of the haptics by the contracting sphincter-like ciliary muscle, resulting in a forward movement of the optic due to the anteriorly angulated haptics, and backward movement upon relaxation due to the material's inherent elasticity.

1CU Accommodative IOL® (K.D. Hanna)

This AccIOL (Fig. 1b) is being marketed since 2001 by HumanOptics AG, Erlangen, Germany. The one-piece construction features a 5.5-mm optic and an overall diameter of 9.8 mm. It is also made of foldable hydrophilic acrylic and features four broad-based delicate haptics with a very flexible optic junction ("transmission element") and a bent-up end. The working principle is based on the hypothesis that the capsular bag retains sufficient residual elasticity to circumferentially compress the haptics upon zonular relaxation, which moves the optic forward. The original concept was based on a finite-element model and included a second component of an ultrathin sheet of elastic material designed to internally line the capsular bag ("2CU": two-component unit), but this was never implemented.

AT-45 CrystaLens® (S. Cumming)

This third AccIOL (Fig. 1c) has been marketed in Europe since 2002 by C&C Vision (now Eyeonics) in Aliso Viejo, California and attained FDA approval in 2003 [5]. This three-piece construction is derived from silicone-plate IOLs. It consists of a silicone body with a 4.5-mm optic and two plate haptics with an anterior groove close to the optic junction (hinge) and a pair of laterally extending polyimide eyelets at their ends. The long-axis length is 10.5 mm and the diagonal loop-tip to loop-tip length is 11.5 mm. The working principle is based on the assumption of "mass redistribution" as presumed by D.J. Coleman [2, 3]: When the ciliary muscle contracts, it bulges into the vitreous cavity, causing the incompressible vitreous body to dislodge anteriorly and push on the capsule-IOL diaphragm. When appropriately designed, this would produce a forward movement of the IOL optic.

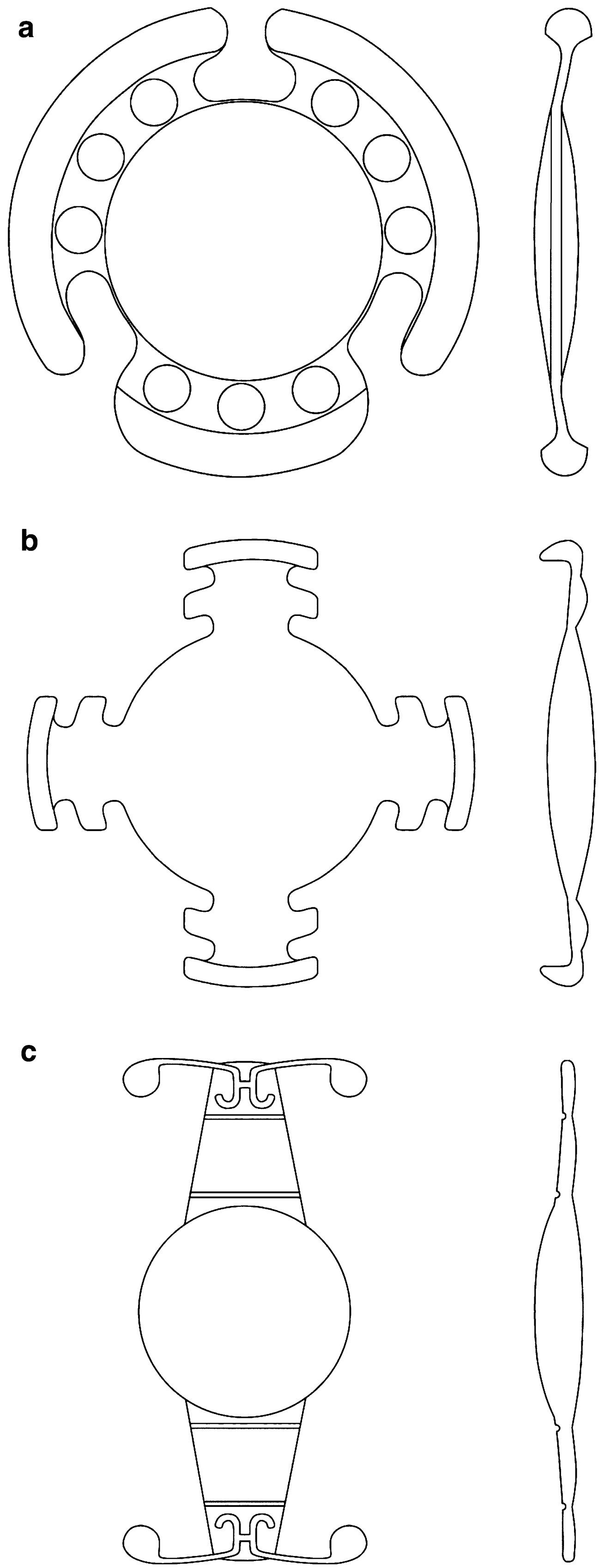
Functional ("accommodative") performance of marketed optic-shift IOLs: clinical results

Reported clinical performance

While Payer published modest functional results with his ring-haptic IOL [69], very favorable results were reported in the initial studies that were initiated by the companies for both the 1CU and the AT-45 IOLs:

Langenbucher et al. [39, 40] found better distance-corrected near visual acuity (DCNVA) and refractive change results with the 1CU than with monofocal IOLs, and the performance was stable through 1 year postoperatively [38]. However, the study was not randomized. In another study by Kuechle et al. [37], a mean anterior shift of 0.63 mm was found measured with a photographic technique. However, the operating manual of the instrument used for measurements explicitly states that the device is inaccurate for measuring anterior chamber depth (ACD) in pseudophakic eyes due to poor optic reflectivity and especially iris artefacts. Another study by Mastopasqua et al. [46] reported an accommodative amplitude as high as 1.9 D with the 1CU at 6 months postoperatively. However,

Fig. 1 **a** Ring-haptic IOL by Payer, **b** 1CU IOL by Hanna, **c** At-45 "Crystalens" by Cumming



in the control group with a standard monofocal IOL the accommodative amplitude was 0.0 D, which is very unlikely due to pseudoaccommodation. Therefore, these results need to be interpreted with caution.

Cumming et al. reported excellent uncorrected distance and near visual acuity results for the AT-45 [5]. However, as pointed out by Werblin in a pertinent paper commentary [79], no randomized internal control group was included in the study. Instead, results were compared with data from other studies using different reading charts and performed under non-comparable conditions.

Vienna results

At the Department of Ophthalmology, Medical University of Vienna, all three above-mentioned AccIOLs were investigated in clinical studies. Laser interferometry, which has a reproducibility of measurement of pseudophakic ACD in the order of 3–4 µm, more than a factor 10 better than other current measurement techniques, such as ultrasound or dedicated photographic set-ups, was used to measure axial shift [1, 9]. Using 2% pilocarpine as a pharmacological stimulus, the ring-haptic IOL exhibited a mean forward shift of −170 µm, with a range between 0 and −750 µm (n=22) (Fig. 2). In a randomized bilateral study with intra-individual comparison, the 1CU IOL showed a mean forward movement of −370 µm as opposed to a slight backward movement of +63 µm with an open-loop monofocal IOL serving as control. This results in an increase in refractive power of less than +0.5 D in most cases, as calculated by ray-tracing, with only one single case achieving +1 D. Extensive anterior capsule polishing with a dedicated suction curette, which results in a marked reduction in capsule fibrosis [72], did not enhance the movement [12].

Paradoxically, the AT-45 IOL moved slightly backwards by a mean of +151 µm corresponding to some amount of desaccommodation. Again, movement was not influenced by extensive anterior capsule polishing [31].

With both lenses, standard deviations (SD) and ranges were large in relation to the mean values of movement: With the 1CU IOL (mean −370), the SD was 290 µm and the range was −592 µm to −148 µm (Fig. 2). Similar findings have been recently reported by Haigis at al. They found a mean forward optic shift of 31±48 µm (−88 to +227 µm) upon optical and 80±146 µm (−16 to +600 µm) upon pharmacological stimulation, equivalent to a refractive change of 0.0–0.85 D [18]. With the AT-45 IOL (mean +151 µm), the SD was 84 µm and the range from +9 to +319 µm (Fig. 2). Axial shift and thus true accommodative

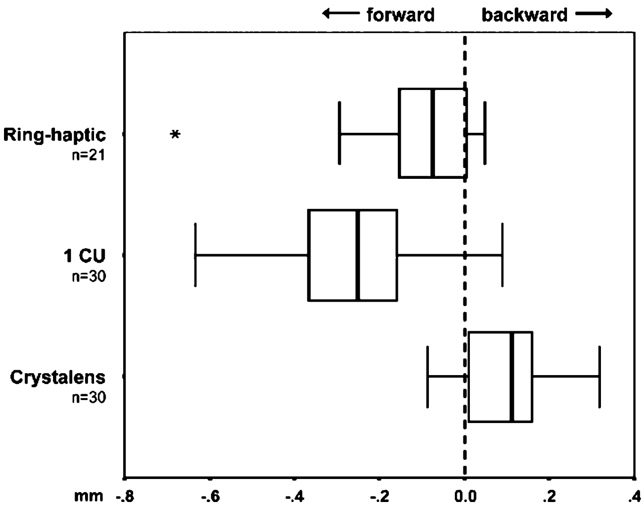


Fig. 2 Axial movement of the various accommodative IOL models following pharmacological stimulation with 2% pilocarpine

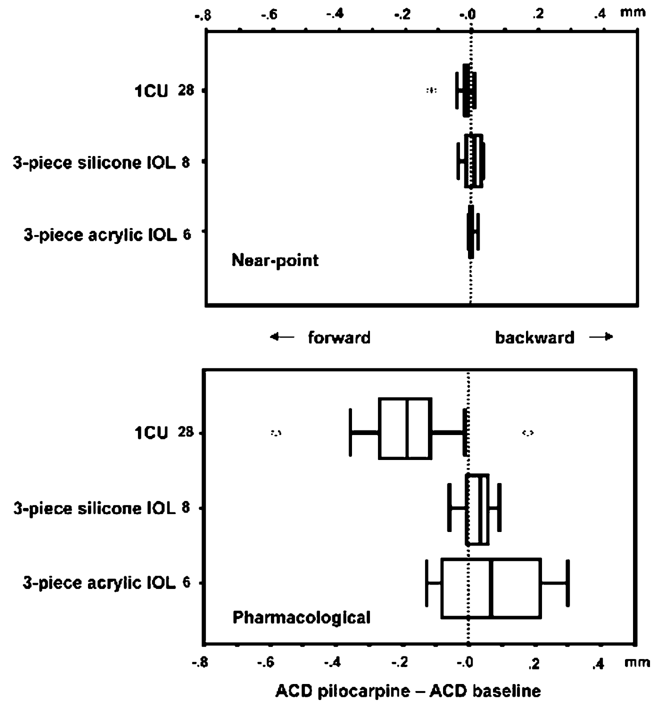


Fig. 3 Axial movement of the various accommodative IOL models under near-point stimulation

effect were small or even absent, and also very variable, making an individual prediction impracticable. When using near-point stimulation, none of the AccIOLs demonstated any significant movement [36] (Fig. 3). Obviously, pilocarpine represents an unphysiological superstimulus which is useful for determining the maximum accommodative potential of an IOL, but overestimates that obtained under near-point stimulation. Not surprisingly, DCNVA was not significantly better than that obtained with the monofocal IOL. No statistically significant correlation was found between axial shift and DCNVA (Fig. 4). Thus, DCNVA essentially resulted from pseudoaccommodation. Only when using a sophisticated setup for DCNVA evaluation under standardized illumination and thus constant pupil size at various distances were slightly better results obtained with the 1CU than with a monofocal open-loop IOL at distances between 50 and 25 cm (Pieh S, Schmidinger G, Italon C, Simader C, Kriechbaum K, Menapace R, Skorpik C. Comparing visual acuities at different distances of an accommodative IOL and a monofocal IOL. Abstract, XXI Congress of the European Society of Cataract and Refractive Surgeons, 2003, Munich, p 104) (Fig. 5).

Why are there such discrepancies among studies concerning functional performance?

The main source of discrepancy is the method used for clinically assessing functional IOL performance. Due to the high inter-patient variability in apparent accommodation, the only means to objectively evaluate the functional performance of a shift AccIOL is to reliably measure the axial shift upon accommodative stimulation. Dual-beam laser interferometry has been adapted for biometry of the eye [8, 9] and is most appropriate for measuring axial intraocular distances for three reasons. Firstly, laser interferometry allows for reliable fixation of the eye to be measured. Most other techniques, such as ultrasound or photography, require fixation of a target with the contralateral eye, resulting in varying convergence movements and, therefore, off-axis measurements of ACD. Secondly, in laser interferometry, reflexes from intraocular interfaces will only be obtained with exact alignment along the optical axis, Thirdly, the peaks produced are slim and high due to the high resolution and signal-to-noise ratio of the technique, allowing for precise measurement of distances. This results in unsurpassed precision of 3 µm and a reproducibility of 4 µm. Resolution is 10 µm, more than 10 times better than what can be obtained with standard ultrasound.

Instead of biometric measurements, most investigators have used distance-corrected near visual acuity as the main or even only outcome parameter. However, DCNVA also mirrors the depth of field as provided by the great variety of sources of apparent accommodation. Also, it strongly depends upon patient and investigator motivation. Differences in the size of optotypes on different reading cards [27] and illumination during examination further reduce comparability. Therefore, DCNVA is a rather poor method for assessing true accommodation in pseudophakic eyes. Uncorrected reading acuity is an inappropriate parameter for judging accommodation since it is critically dependent on postoperative refractive outcome [5].

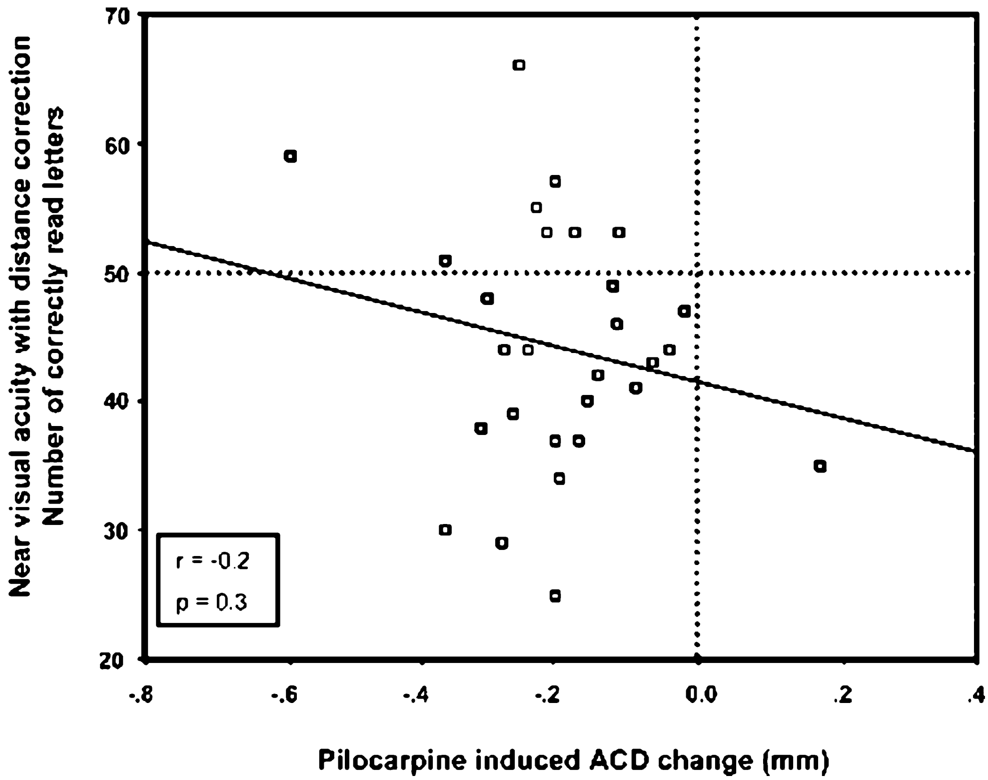


Fig. 4 Lacking correlation between axial optic movement and distance-corrected near visual acuity

Some investigators have used various techniques to directly measure the change in refraction [73]. However, difficulties arise from miotic pupils and from the bright Purkinje reflexes produced by artificial IOL optics. These difficulties have resulted in a poor reproducibility for the pseudophakic eye.

Some investigators have made efforts to measure the change in central ACD and thus axial optic position by ultrasound or various optical techniques: Though it may be enhanced by sophisticated high-frequency devices, the reproducibility of standard ultrasound systems is no greater than 0.15 mm. In addition, echoes from the iris and the IOL itself may be difficult to discriminate. The main difficulty, however, is proper axial alignment of the ultrasound beam. As the ultrasound probe covers the eye to be measured, proper fixation cannot be monitored. Thus, the contralateral

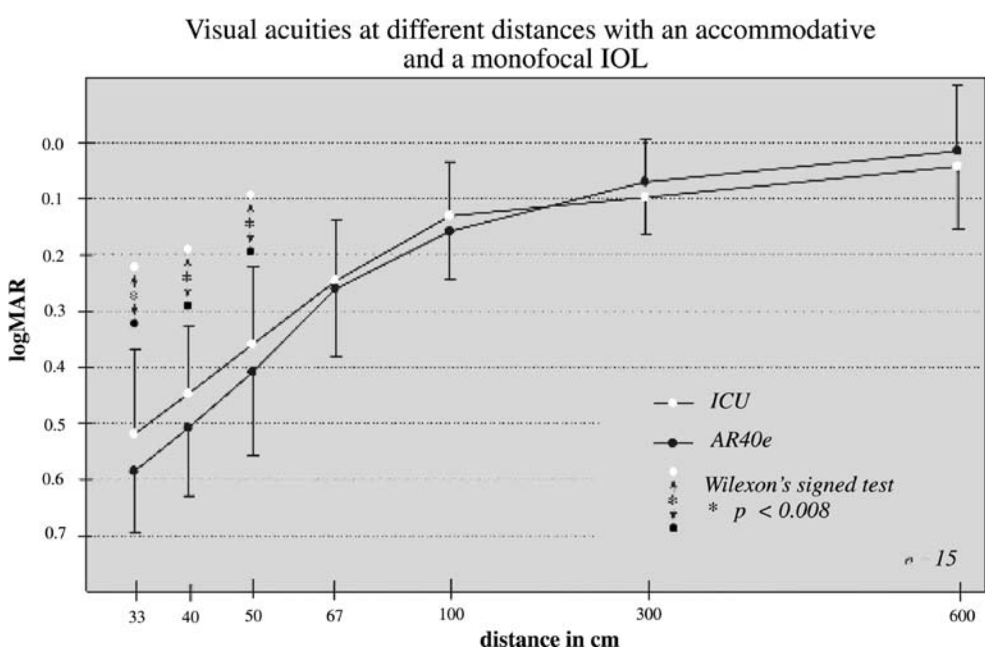


Fig. 5 Accommodative performance of the 1CU as assessed by "dynamic near-point evaluation"

eye must be resorted to. Globe convergence under accommodative effort leads to incremental misalignment between the visual axis and measuring beam which is difficult to compensate for. Differing results have been published with both A- and B-scan devices [1, 41, 42]. More consistent results have been recently reported with a special laboratory set-up [57].

Some investigators have used optical or photographic techniques: For the Jaeger pachymeter mounted on a Haag–Streit slitlamp, reproducibility was found to be 0.1 mm when used for ACD measurements with IOLs of various materials under cyclopegia [22]. However, the reflex from the IOL optic is difficult to identify with small pupils, and reproducibility has not been determined under these conditions. Similarly, measurements with various devices based on Scheimpflug slit-lamp photography (Anterior Segment Analyser by Nidek, Tokyo, Japan; Orbscan by Bausch&Lomb, Rochester, NY; IOL-Master by Carl Zeiss Meditec, Jena, Germany) suffer from inaccuracies caused by misleading reflexes from the iris when the pupil is small [1, 35].

Morphological or "capsular bag" performance of currently marketed shift IOLs

Payer reported a high incidence of regeneratory after-cataract formation with the ring-haptic IOL due to the optic–capsule interspace that results from the anteriorly angulated haptics. In view of the modest accommodative performance, he therefore suggested reverse implantation to reduce the retrolental interspace. Pertinent information regarding the 1CU and AT-45 IOLs is still scarce. The reported Nd:YAG capsulotomy rate for the 1CU was 24% at 2 years, and for the AT-45 29% and 45% after 2 and 4 years (personal communications by G. Sauder, and J. Alió). Almost all eyes of the Vienna series seen between 3 and 4 years postoperatively already had or required YAG-laser capsulotomy (unpublished data; Fig. 6a,b). With both IOL styles the broad optic–haptic junction interferes with circumferential capsular fusion and bending along the posterior optic edge (Fig. 6c). Due to the fibrotic encasement of the floppy haptics, cases of severe haptic deformation and fold-over were seen with the 1CU (Fig. 6d). Not surprisingly, Nd:YAG capsulotomy was shown not to positively affect the accommodation ability of the 1CU [56]. With the 1CU, occasional haptic deformation and folding over onto the optic was a particularly troublesome complication, necessitating IOL exchange in 4 of 74 cases (5.4%) due to significant optic shift or tilt resulting in severe hypermetropization or astigmatism (Menapace R. Nachstarperformance und Kapselsackverhalten accommodativer IOLs [Capsular bag performance and after-cataract with accommodative IOLs]. Abstract 18th Annual Meeting of the DGII, 2004, Heidelberg, p 36). With the AT-45, we occasionally observed partial buttonholing of the small optic within the anterior capsulorhexis opening with fibrosis consecutively encroaching upon the central posterior capsule, and persistent capsular stress folds between the foot plates interfering with complete capsular fusion. Surprisingly, although the optic measures only 4.5 mm in diameter, no case of decentration or edge glare occurred. In summary, the capsular bag performance of the 1CU must be considered inapproriate, while that of the AT-45 may be considered acceptable, though far from optimal.

Why did passive-shift AccIOLs finally fail?

Failure as accommodative implants

The assumptions made regarding the hypothetical working principles were obviously inappropriate: Firstly, capsular fibrosis, which essentially develops during the first 3 months, stretches and thus immobilizes the capsule–IOL diaphragm. The variable diameter between the ciliary body apices will not always tightly fit a fixed-diameter ring-haptic IOL [75], and the compression forces may be insufficient, which both will result in an inconsistent and generally inadequate anterior optic movement. The presumed residual elasticity of the lens capsule that should compress the 1CU upon zonular relaxation, if present at all after removal of the anterior capsule, will be lost due to fibrotic tightening. The forces exerted by mass redistribution as hypothesized for the AT-45, if at all present, will vary in extent and generally be insufficient to move the AT-45 or any other implant immobilized by fibrosis anteriorly. Also, such an effect would quickly decay, since the pressure gradient between the posterior and anterior segments would level out with a detached and liquified vitreous body as the aqueous would escape through the zonules. Failure of extensive anterior capsule polishing to enhance the response in shift must be interpreted as a final proof that the inferred hypothetical working mechanisms are in fact based on erroneous assumptions.

Failure as capsular bag implants

By designing the IOLs according to the hypothetical working principles, established criteria for optimum capsular bag performance were violated [49]: The posterior sharp edge, even when circumferential, will not be functional if capsular bending is obviated along broad optic–haptic junctions. Fibrotic capsular contraction may result in deformation and foldover of overly flexible plate haptics

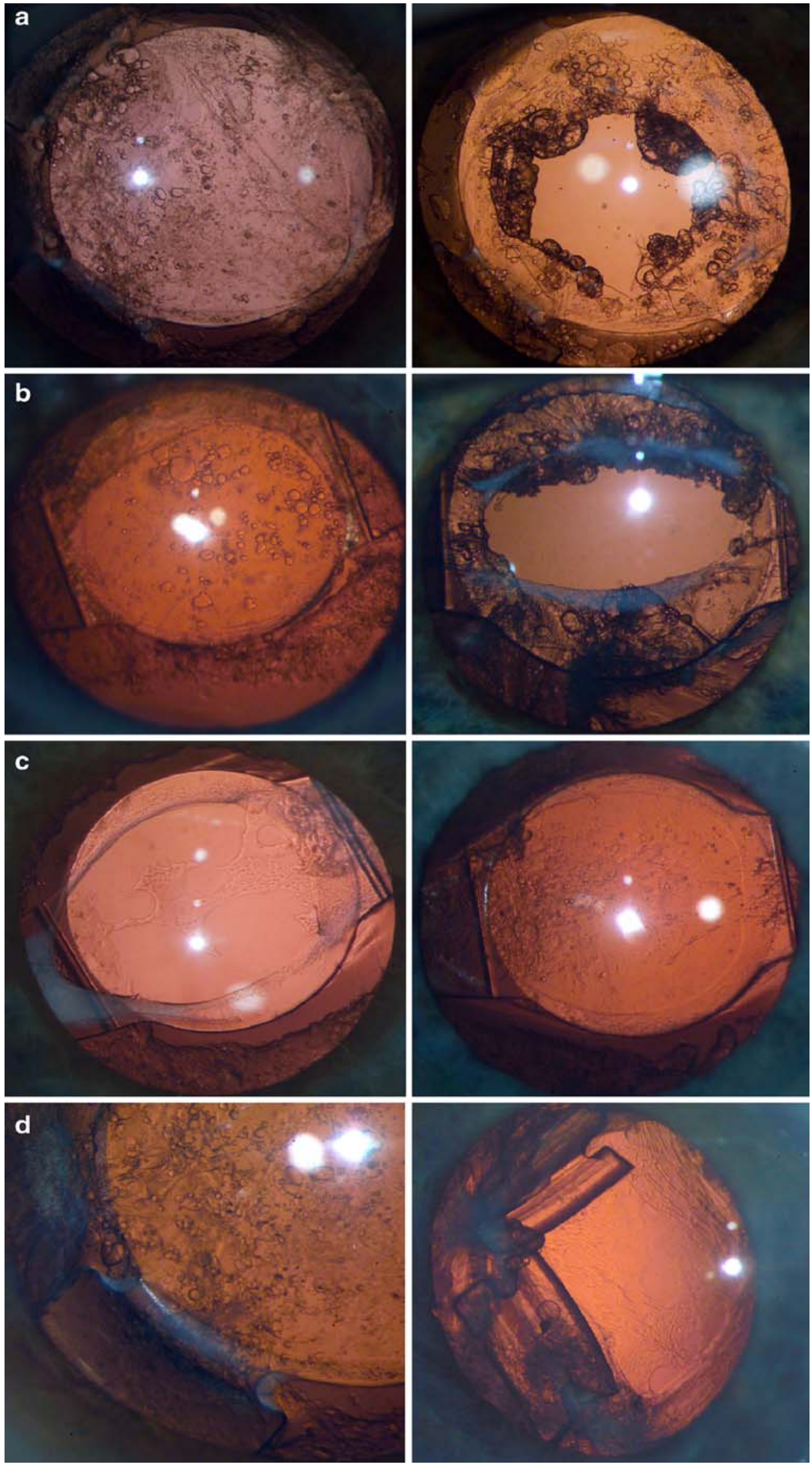


Fig. 6 Regeneratory after-cataract with the 1CU (**a**) and AT-45 "CrystaLens" accommodative IOLs (**b**). Poor capsular performance is due to plate haptics (**c**, **d**)

as occurred with the 1CU. Small optics as used with the AT-45 may lead to optic buttonholing with severe posterior capsule fibrosis.

What amount of maximum anterior shift can be expected with passive-shift IOLs?

Provided that fibrotic distension of the capsule diaphragm is avoided, an IOL may move anteriorly along with the apex of the ciliary body, which has been shown to move in the order of between 0.10 and 0.15 mm during accommodation [30, 76] (Fig. 7). In addition, some shift may be induced by direct compression of an anteriorly angulated lens by the contracting ciliary muscle. The variation in amount of such movement may be explained by the great variety of ciliary body diameters and possible locations of the lens haptics. While the ring-haptic and 1CU IOLs generally moved forward as intended, the AT-45 paradoxically tended to move backwards. This may be explained by the large span of the footplates of the haptics, which results in a posterior vault of the IOL, as also indicated by the high IOL-constant for power calculation. When further compressed by the ciliary muscle, the optic is pushed even more posteriorly, similar to a flat spring. This finding is in good agreement with the axial movement observed with various lens designs [11]: Standard silicone plate lenses, which are smaller and more rigid, exhibited some amount of anterior shift. Seemingly, they were dragged along as the constricting ciliary body apex moved forward. Of the angulated open-loop lenses, those with soft modified C-loops showed almost no movement at all. However, one lens type with overly large and rigid modified J-loops (AcrySof MA60BM, Alcon, Fort Worth) moved posteriorly by a significant amount. Similar to the AT-45 IOL, the optic was obiously pushed posteriorly by the rigid J-loops under compression, while the forces were absorbed by the softer C-loops. Regardless of the IOL concept, the mobility of passive-shift IOLs is obviously not enhanced by avoiding capsular fibrosis through capsular polishing [12, 31]. At best, only a small amount of forward shift can be expected that will be variable depending on factors as the haptic location with regard to the ciliary body apex and the relationship between lens haptic and ciliary sulcus diameter, which cannot be anticipated.

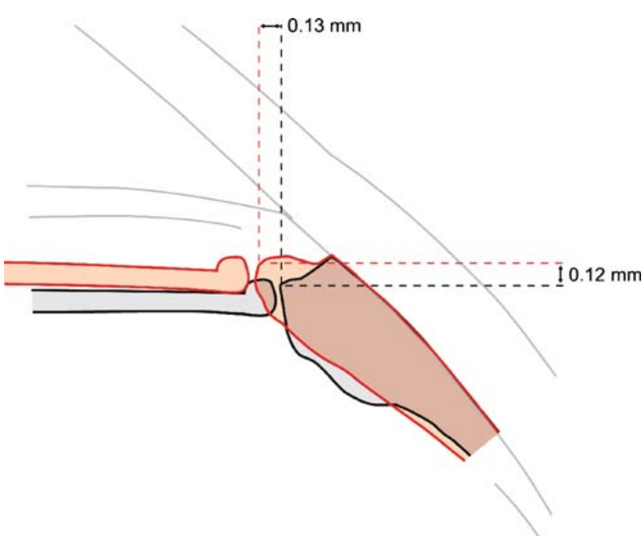


Fig. 7 Upon accommodation, the apex of the ciliary body moves anteriorly by 0.10–0.15 mm

How can the optic shift be enhanced, or: is there a future for shift IOLs?

The concept of optic-shift IOLs may still be considered promising. However, the following requirements must be met:

1. A driving vector force must be implemented that actively moves the implant anteriorly as the zonules are released under ciliary muscle contraction.
2. Capsular fibrosis and its immobilizing effect on the implant must be avoided or neutralized, and regeneratory after-cataract formation counteracted as much as possible.
3. The optic should be positioned as far posteriorly as possible to allow for maximum clearance to the iris and thus space for shift-induced accommodation.

Spring-driven single-optic IOLs

In an attempt to provide for an anteriorly directed vector force, Müller designed a lens with non-angulated rigid loops to be fixated in the sulcus, whereas the optic is secondarily buttonholed posteriorly through the capsulorhexis opening to reside in in the capsular bag [K. Müller. Mögliche Modellansätze zur Realisierung des akkommodativen Fokus-Shift-Prinzips. XIIIth AMO Meeting, January 14th 2004, Zermatt]. According to his hypothesis, the optic would be progressively pulled backwards by the anterior capsule as it is distended by fibrotic contraction. As a result, a spring force would build up at the junction of the sulcus-fixated loops. When the zonules relax under ciliary muscle contraction, this spring force pulls the optic anteriorly, thereby increasing its refractive power. In a pilot study, however, the concept failed. This was explained by the fact that the spring forces of the loops were obviously too strong to allow the optic to be pulled sufficiently backwards by the fibrosing anterior capsule (K.A. Müller, personal communication).

Magnet-driven active-shift IOLs

Preussner proposed using repulsing micro-magnets as a driving force [70]. Two magnets are placed at 3 and 9 o'clock within the capsular bag periphery, while a pair of repulsing twin magnets are sutured under the superior and the inferior rectus muscle insertions (Fig. 8a). In order to prevent immobilization of the capsular diaphragm, a special capsular tension ring (CTR) was developed (Fig. 8b), which carries paddles at its ends that are welded together with argon laser burns shortly after implantation, thereby preventing capsular shrinkage and zonular distension. The paddles also carry the mini-magnets. A standard open-loop IOL is used as the dioptric implant. Since the paddles rest on top of the optic periphery, the latter is pushed posteriorly, thereby increasing its clearance to the iris. As the zonules relax, the entire capsule–CTR–IOL complex would be pushed anteriorly due to the repulsing magnetic forces.

In a phase-1 clinical trial, eight eyes were implanted with this CTR together with an acrylic open-loop IOL (R. Menapace. Vorgespannte Linsensysteme: Konzepte und erste klinische Ergebnisse [Pre-loaded shift IOL systems: Concepts and first clinical experiences]. Abstract 19th Annual Meeting of the DGII, 2005, Magdeburg, p 21). Surgery was uneventful in all cases. The CTR was inserted with an injector directly into the capsular bag fornix, and the paddles positioned on top of the IOL optic. The paddles were laser-welded the day after surgery at the slit lamp using a gonioscope (Fig. 8c). At 1 month postoperatively, ACD was 5.1 mm, which exceeded that with the IOL alone by about 1 mm. Fibrosis-induced contraction was blocked in five of eight cases. In three cases, however, the welding points were too weak to withstand the contraction forces. As the optic is pressed posteriorly by the paddles, circumferential capsular bending was observed also beneath the paddles in spite of the lacking capsular fusion. In two of the five Vienna cases, however, this barrier has meanwhile been overcome by centrally migrating lens epithelial cells (LECs). Additional polishing of the anterior capsule, however, may consistently solve the problem of fibrotic contraction, and primary posterior capsulorhexis (PPCCC) may avoid central opacification of the visual axis by pearls in case of optic edge barrier failures.

Menapace has forwarded a modified surgical approach [51]. By creating a PPCCC and buttonholing the optic of a primarily bag-placed open-loop IOL posteriorly into Berger's space, the posterior capsule is sandwiched between the anterior capsule and the optic, thereby preventing the direct contact of the anterior LEC layer to the optic that usually initiates the process of fibrosis. Contact and consecutive fibrosis thus remain restricted to the small triangular area adjacent to the haptic–optic junction where the rim of the posterior capsule undercrosses the haptic base (Fig. 9). Mobility of the capsule–lens diaphragm should thereby be sufficiently preserved, and may be further enhanced by anterior capsule polishing if found necessary. Since migrating equatorial LECs are deviated to the front of the optic, the retrolental space will be kept clear from LEC pearls. Other than with any bag-fixated IOL [50], adjunctive capsule polishing will therefore have no negative impact on regeneratory after-cataract. With this concept, no additional CTR would be required. Instead, a standard open-loop IOL with a slightly modified design adapted to the particular requirements of the technique described, and with the magnets integrated into the optic periphery, would be used (Fig. 9). The surgical technique of PPCCC and posterior optic

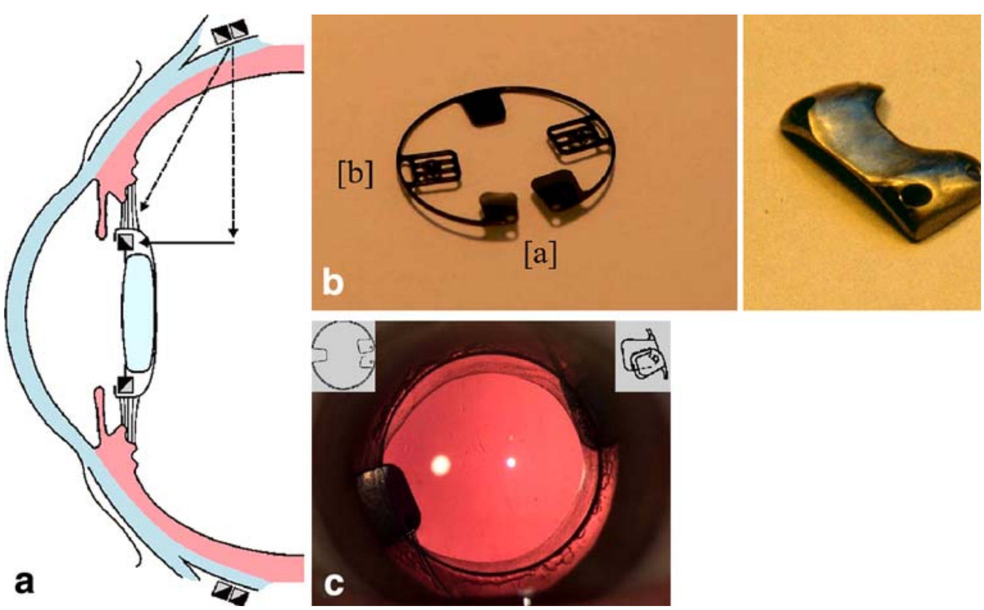


Fig. 8 Magnet-driven active-shift concept as put forward by Preussner. **a** Working principle. **b** Weldable capsular tension ring with paddles. **c** Capsular tension ring with paddles on top of IOL optic in situ; note laser burns that weld paddles together. Paddles will carry magnets that may be removed if required later on

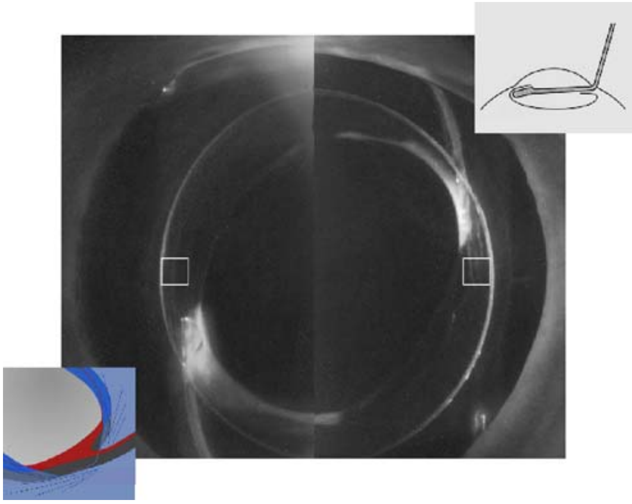


Fig. 9 Posterior optic buttonholing through PPCCC preserves capsular elasticity and thus axial optic mobility by precluding contact-mediated capsular fibrosis. With this concept, a pair of magnets would be integrated into the optic periphery, and the IOL rotated to place the magnets horizontally and thus at right angles with the external pair of repulsing magnets

buttonholing has been used in over 500 cases with very promising results [51].

When comparing the two approaches, the latter has the following advantages. No additional special implant (CTR) or procedure (laser welding) is required. Fibrosis is largely reduced by the technique itself, and may be completely avoided by additional anterior capsule polishing if this should turn out to further enhance capsular mobility [52, 72]. Since no fibrotic and regeneratory after-cataract forms, the full optic diameter is kept clear.

With both approaches, longer follow-up must be awaited before the second phase of clinical trails with magnet-loaded implants can be initiated. A practical drawback of the implanted magnets may be that patients would need to avoid magnetic resonance imaging. However, magnet embedding has recently been modified as to allow easy removal in the rare case such imaging should be required.

Can single-optic shift IOLs provide clinically sufficient accommodative power?

The optic shift principle suffers from two limitations: First, the potential change in dioptric power is limited by the amount of possible forward shift that is defined by the optic–iris clearance. Otherwise, the optic would cause iris bulging and pigment chafe. Second, the resulting increase in dioptric power depends on the optic power. Compared with a 20-D IOL, a 30-D IOL will provide for about double the increase in power with movement, against only about half the increase when a 10-D IOL is implanted [26].

Considering the additional effect of the various mechanisms of apparent accommodation that have been reported to provide as much as 2 D of accommodation on average, a consistent anterior shift in the order of 1 mm should suffice as an add-on to attain full spectacle independence. This may be achieved by magnet-driven active-shift systems as described above.

Alternative concepts: working principle, accommodative potential, and problems to be solved

Dual-optic IOLs

This IOL concept dates back to Hara in 1990 [19, 20]. One type is being developed under the name "Synchrony" [48] by Visiogen Inc., Irvine, California. The implant consists of two separate optics that are interconnected by a spring-type haptic mechanism (Fig. 10a). The posterior 6-mm minus-powered optic is designed to remain stationary during ciliary muscle contraction and its dioptric power is varied according to the biometric requirements. The anterior optic has a fixed dioptric power of +32 D and is supposed to move forward during attempted accommodation. The implant is designed to fully occupy the bag, with the haptics conforming to the capsular bag fornix. As it is circumferentially compressed or allowed to extend within the elastic capsular bag according to the changing zonular tension, the anterior optic is pushed anteriorly or moves backwards, thereby increasing or decreasing the overall dioptric power (Fig. 10b). Distance holders secure a fixed minimal distance between the optics and thus baseline refraction under zonular relaxation. For an IOL with a front lens of +32 D and a rear lens of −12 D, an increase in distance from 0.5 mm to 1.5 mm would result in an increase in power of 2.2 D, which would be about twice as much as achieved with a single-optic design (Fig. 10c). The implant is made of silicone and can be injected through a small incision, though it has so far been implanted with forceps, requiring a 4.0–4.5 mm incision width. Promising clinical results with dual-optic IOLs have been reported concerning safety in primate [47] and human eyes (I.L. Ossma–Gomez, A. Galvis, V. Galvis. Synchrony dual-optic accommodative IOL: 1-year results; A. Galvis. How the Synchrony dual-optic accommodating IOL works: in-vivo ultrasound biomicroscopy. Symposium on Cataract, IOL, and Refractive Surgery, 2005, Washington). However, detailed functional data are not yet published. After-cataract results in the rabbit eye were favorable [80]. This may be partially due to the spring design which actively presses the rear optic against the posterior capsule. In the living eye, the constant movement of the anterior optic may provide an additional preventive effect. The design has been recently

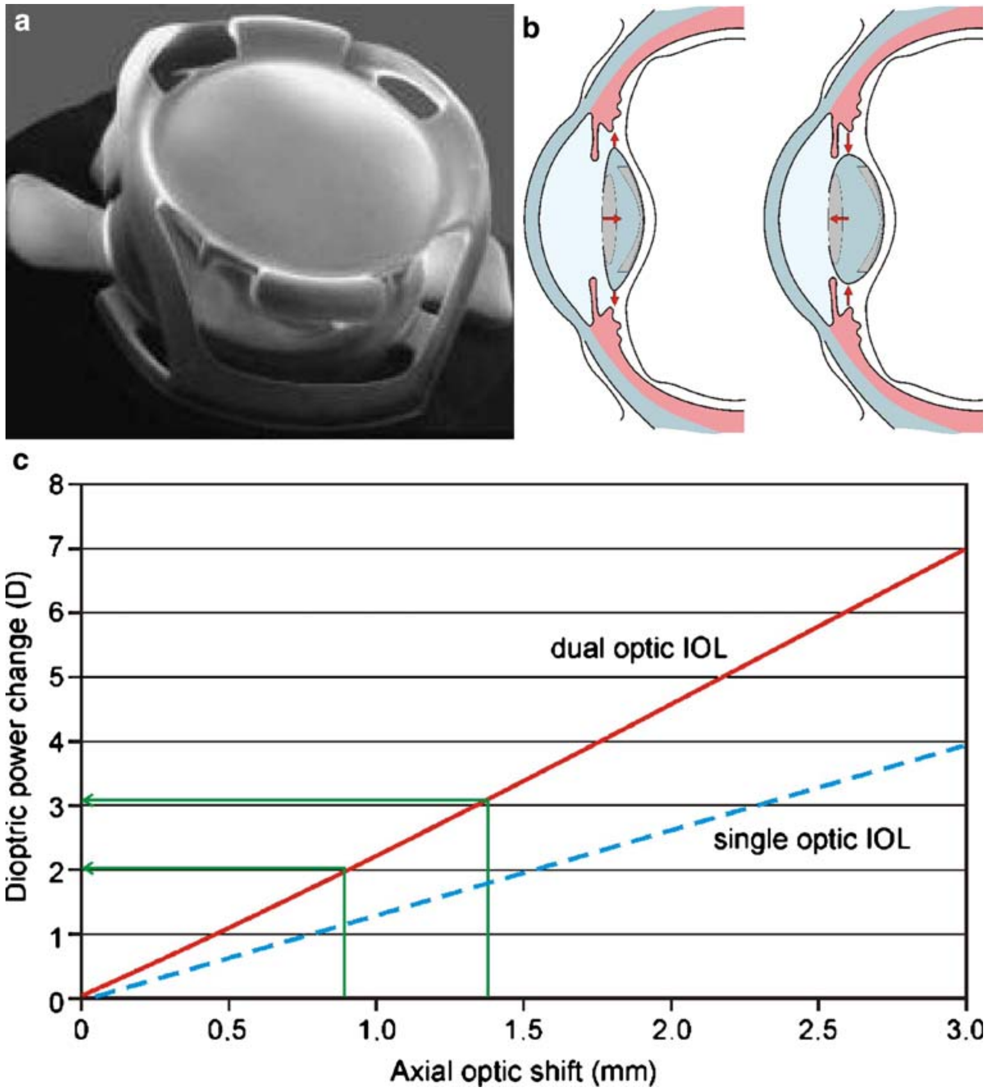


Fig. 10 The Synchrony dual-optic IOL concept by Visiogen, USA. **a** SEM of IOL; **b** working principle; **c** increase in shift-induced dioptric power change

modified, including the implementation of channels to enhance interlenticular aqueous circulation. However, long-term formation of interlenticular opacities is still a major concern as the construction offers ample pathways and interspaces for LEC immigration and pearl formation [10].

More recently, a two-component device was presented with a piston-like central lens that is moved along the axis of the eye as the zonule–capsule diaphragm stretches or relaxes ("NuLens" ®, Fig. 11; R. Hofman, M. Packer, H. Fine. Technology generates IOL with amplitude of accommodation. Ophthalmology Times, March 2005). As opposed to the natural mechanism, the first model provided near focusing under ciliary muscle relaxation, while far focusing required ciliary muscle contraction. A more recent model has again reversed this working mechanism. Clinical results have not yet been presented.

"Lens refilling"

This concept was investigated as early as 1964 by Kessler [29]. In 1987 Haefliger et al. [16] took up the concept under the name "Phaco-Ersatz," which has since been further developed at various institutions. In a study published in 1994, the aforementioned group proved the efficacy of the concept to restore accommodation in the senile primate eye [17]. With this technique, the capsular bag is evacuated through a small capsular opening to be then refilled with an elastic polymer that responds with an adequate change in surface curvature according to the varying zonular tension (Fig. 12). Ideally, the material should be cytotoxic upon direct contact in order to prevent after-cataract, but should not release toxic substances to the surroundings and should not leak into the anterior chamber before polymerization. The surgical technique and instrumentation were adapted to

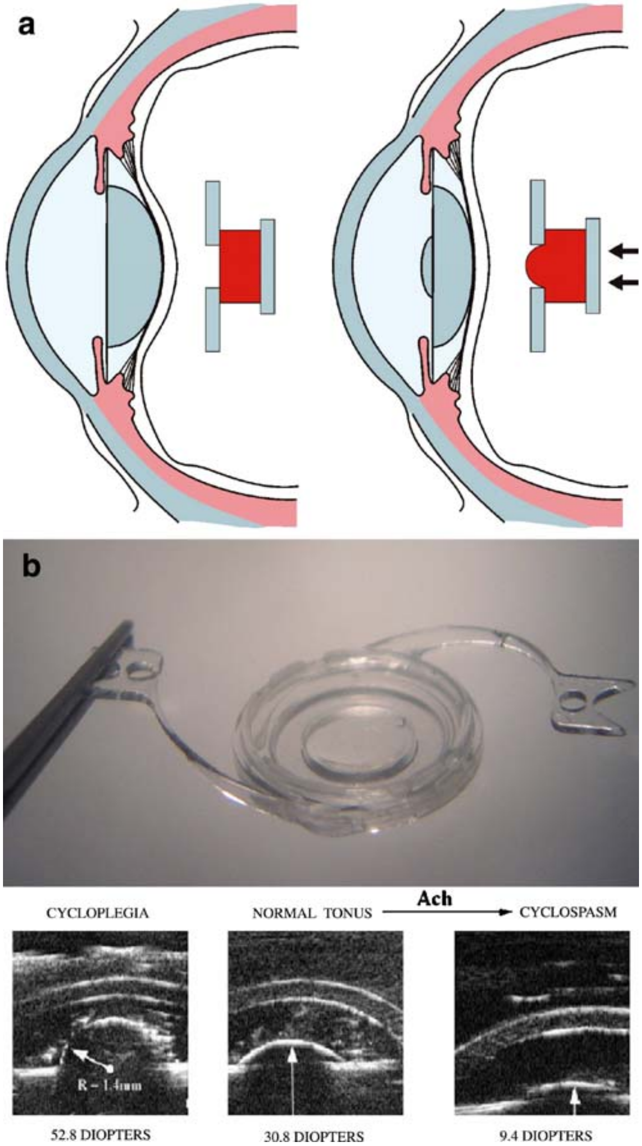


Fig. 11 The "NuLens" concept: Haptic settled in sulcus, while optic rests on capsular diaphragm. Upon axial compression, soft central component bulges anteriorly. **a** Schematic; **b** prototype of IOL

the needs of ultra-small cataract surgery [44], and various materials tested that polymerize either spontaneously or under light exposure. Various alternative approaches have

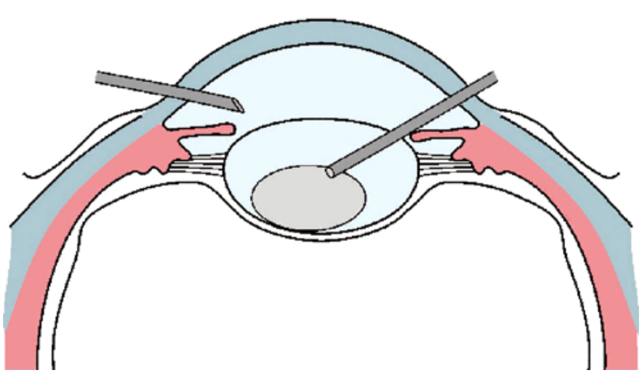


Fig. 12 Lens refilling technique

been presented for capsular bag refilling: Nishi and co-workers (Osaka, Japan) designed an inflatable balloon made of a thin silicone membrane that is filled with a liquid silicone polymer through a delivery tube after being placed in the emptied bag [59]. They investigated the influence of the shape of the balloon [60] and the volume of injected silicone [61, 62] on the accommodative amplitude. In primates, Sacca et al. reported a mean ACD change of 0.5 mm and a maximum refractive change of +6.7 D [71]. While Hara et al. reported an acceptable complication profile [21], Hettlich et al. found no advantage of using balloons over other filling techniques because of the difficulty of insertion [25]. In order to prevent leakage after direct filling of the capsular bag, Nishi et al. introduced a silicone plug for sealing the mini-capsulorhexis [64]. With both the balloon and plug approaches, however, the accommodative amplitude achieved was only a fraction of the values determined before surgery [60, 63] and decreased over time. This was attributed to the loss of lens fiber cells, which actively contribute to the mechanism of natural accommodation ("intracapsular accommodation") [63]. Another problem was again after-cataract formation. After 3 months, thick opacification of the central posterior capsule was regularly observed [63]. Though a capsulotomy does not lead to polymer leakage, it may annihilate the accommodative potential [64]. Though reduced by LEC removal and plump filling, formation of after-cataract could not be completely inhibited [65]. Hettlich and coworkers investigated the safety and efficacy of a monomer that polymerizes under light exposure [24]. More recently, reactive hydrogel polymers have been shown to be promising [6]. Koopmans and co-workers (Groningen, Netherlands) created a laboratory set-up that allows study of the shape and refraction response of natural and refilled lenses under circumferential stretching through the ciliary body and zonular complex and found the power changes of refilled lenses to be comparable with the young natural lens [32]. They found that an increase in thickness of the relaxed lens by 0.54 mm resulted in a 1-D increase in power in refraction, whereas overfilling decreased the amount of lens power change [34]. They also learned that when using an adequate bottle height during refilling and a plug for capsulorhexis closure, lens dimensions similar to the natural lens could be achieved [33].

Though lens refilling carries significant potential, many problems remain to be solved, e.g., achieving emmetropia in the relaxed state, adequate accommodative reponse upon zonular relaxation, appropriate image quality throughout the full range of accommodation, and sustained functionality. The major problem, however, remains after-cataract. Recently, a suction device has been introduced that hermetically seals off the capsular bag, thus allowing for closed-system irrigation of the bag with LEC-destroying

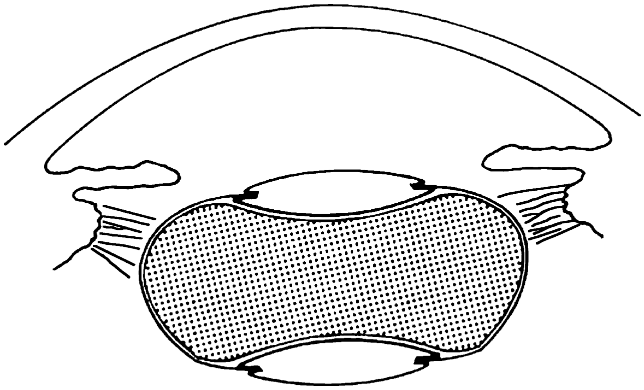


Fig. 13 Concept by Nishi using two grooved optics fixated within an anterior and posterior capsulorhexis opening

agents [45]. A multicenter trial has been initiated to elucidate the efficacy and safety of this approach (M. Tetz, C.S. Siganos, I.G. Pallikaris, G. Auffarth. [European multicenter trial with the Sealed Capsule (Perfect Capsule) irrigation system: 6-months results]. 102nd Annual Meeting of the DOG, 2004, Berlin). However, long-term results from clinical trials are lacking. Cases of LEC regrowth have been reported, which has been attributed to residual cortex material protecting LECs from being accessed by the agent. Though sophisticated, this approach has two major technical drawbacks: firstly, the device is costly and cumbersome to introduce. Secondly, the profuse leakage of toxic agents into the extracapular environment in the case of an inadvertent vacuum loss, which can never fully be excluded, carries the potential risk of severe damage to susceptible ocular tissues and structures. For these reasons, others have incorporated the toxic agent into a viscoelastic agent which is injected into the evacuated capsular bag. After the desired time of exposure, the viscoelastic is aspirated. Also with this appraoch, however, a significant amount of capsular fibrosis has been observed (T. Terwee, S. Koopmans. Wiederherstellung der Akkommodationsfähigkeit durch Injektion künstlicher Linsenmaterialien in den Kapselsack [Restitution of accommodation by injection of artificial lens materials into the capsular bag.] Abstract, 20th Annual Meeting of the DGII, 2006, Heidelberg, p 15).

Due to the seemingly unsurmountable problems with after-cataract formation, Nishi has recently modified an earlier concept which encomprizes both the lens refilling and optic shift principles [58] (Fig. 13). In order to keep the central capsule clear he suggested performing standard well-centered capsulorhexis openings in both the anterior and posterior capsules which are then hermetically sealed by IOLs with optics that carry a circumferential groove to accommodate the capsulorhexis rim similar to the lens design marketed by Morcher for the bag-in-the-lens technique porposed by Tassignon [77]. Implementing a front IOL would potentially allow to postoperatively correct for refractive errors when using an "adjustable" optic materials [74]. This concept is no longer based on the

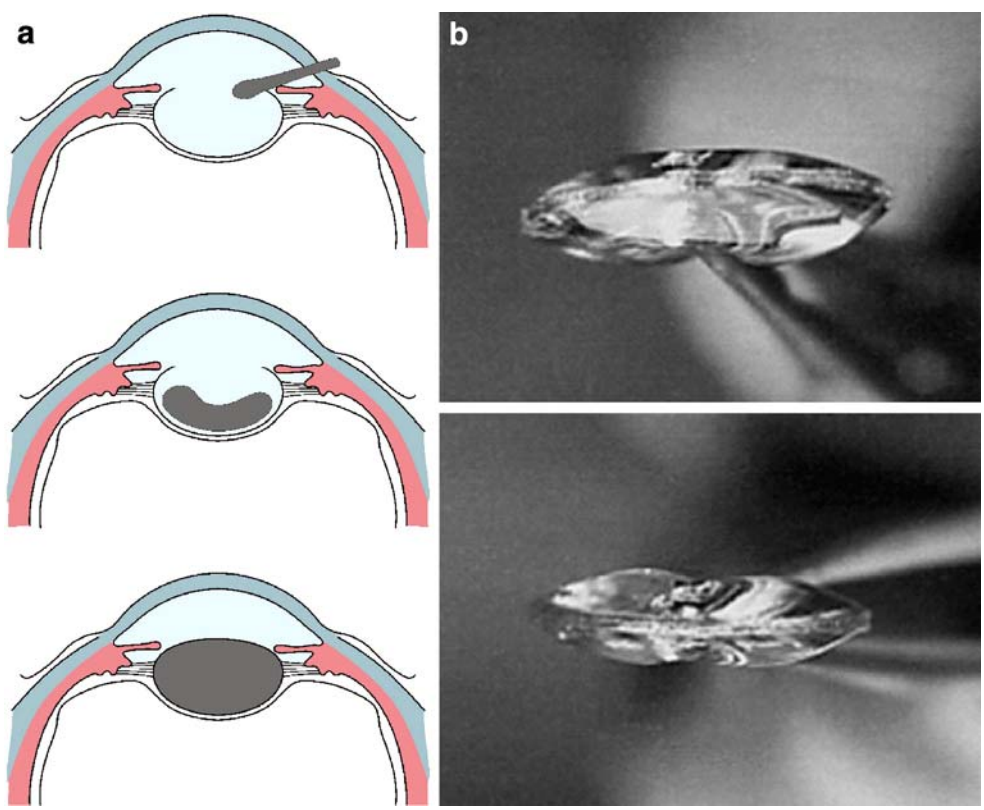


Fig. 14 The "SmartLens" concept: upon hydration, the rod swells to a disc lens 9.5 mm in diameter and 2–4 mm thick within approximately 30 s. **a** Schematic; **b** soft and compressible disc lens

change in surface curvature, but may provide some accommodative effect by the axial shift of the anterior optic when the central thickness increases upon ciliary muscle contraction. In essence, this is another variant of the shift lens concept. As two optics are used, a combination of dioptric powers similar to that of the Synchrony IOL may be implemented to maximize the dioptric effect resulting from an axial movement.

The above-mentioned requirements of achieving emmetropia in the relaxed state and appropriate image quality may be met by the SmartLens® IOL concept (H. Fine. The SmartLens: A fabulous new IOL technology. EyeWorld Oct 2002; 7/4:24-25). This IOL is a small rod when dehydrated and may be inserted into the capsular bag through a very small capsulorhexis opening. Upon hydration, the rod expands to finally take up the shape of a full-size disc lens filling up the capsular bag (Fig. 14a). After-cataract is again a major problem, though it may avoided by adding non-leaking toxic agents to the surface. The optic material is soft and elastic (Fig. 14b) and may be modulated to provide an adequate accommodative response upon zonular relaxation (S. Masket, personal communication). To date, no experimental or clinical results have been presented in this respect.

Conclusions and future perspectives

Passive-shift IOLs have generally failed. Though the ring-haptic and 1CU IOLs have provided some amount of anterior shift, it was generally too small and variable to provide clinically useful accommodation. Other than intended, the AT-45 IOL moved backwards and thus paradoxically tended to induce slight desaccommodation under pilocarpine-induced ciliary muscle contraction. On the other hand, capsular performance was negatively affected by violating approved design criteria. While it may still be acceptable with the AT-45, the cases of fibrotic deformation with consecutive hyperopic refractive surprise caused by the axial posterior optic displacement and tilt-induced astigmatism observed with the 1CU make this lens inappropriate for capsular bag fixation. Magnet-driven active-shift IOLs have a potential to provide clinically useful accommodation, as do dual-optic IOLs. However, clinical data are lacking or still preliminary. Lens refilling carries the potential of fully restoring accommodation due to the great impact of changes in optic curvature on the refractive power. Also, light-adjustable devices may potentially be designed that allow for fine-tuning of the residual refractive error following polymerization [66]. Apart from appropriate filling materials and techniques, however, after-cataract prevention is still the major problem. Dual-optic IOLs and magnetic-assisted active-shift IOLs may possibly be functional in the near future, to be replaced by lens refilling systems in the longer run.

References

1. Auffarth GU, Martin M, Fuchs HA, Rabsiber TM, Becker KA, Schmack I (2002) Validity of anterior chamber depth measurements for the evaluation of accommodation after implantation of an accommodative HumanOptics 1CU intraocular lens. Ophthalmologe 99:815–819
2. Coleman DJ (1986) On the hydraulic suspension theory of accommodation. Trans Am Ophthalmol Soc 84:846–868
3. Coleman DJ, Fish SK (2001) Presbyopia, accommodation, and the mature catenary. Ophthalmology 108:1544–1551
4. Croft MA, Glasser A, Kaufman PL (2001) Accommodation and presbyopia. Int Ophthalmol Clin 41:33–46
5. Cumming JS, Slade SG, Chayet A (2001) Clinical evaluation of the model AT-45 silicone accommodative intraocular lens: results of feasibility and the initial phase of a food and drug administration clinical trial. Ophthalmology 108:2005–2008
6. De Groot JH, van Beijma FJ, Haitjema HJ, Dillingham KA, Hodd KA, Koopmans SA, Norrby S (2001) Injectable intraocular lens materials based upon hydrogels. Biomacromolecules 2:628–634
7. Elder MJ, Murphy C, Sanderson GF (1996) Apparent accommodation and depth of field in pseudophakia. J Cataract Refract Surg 22:615–619
8. Fercher AF, Roth E (1986) Ophthalmic laser interferometer. Proc SPIE 658:48–51
9. Findl O, Drexler W, Menapace R, Hitzenberger CK, Fercher AF (1998) High precision biometry of pseudophakic eye using partial coherence laser interferometry. J Cataract Refract Surg 24:1087–1093
10. Findl O, Menapace R (2000) Piggyback intraocular lenses. J Cataract Refract Surg 26:308–309
11. Findl O, Kiss B, Petternel V, Menapace R, Georgopoulos M, Rainer G, Drexler W (2003) Intraocular lens movement caused by ciliary muscle contraction. J Cataract Refract Surg 29:669–676
12. Findl O, Kriechbaum K, Menapace R, Koeppl C, Sacu S, Wirtitsch M, Buehl W, Drexler W (2004) Laserinterferometric assessment of pilocarpine-induced movement of an accommodating intraocular lens: a randomized trial. Ophthalmology 111:1515–1521
13. Fukuyama M, Oshika T, Amano S, Yoshitomi F (1999) Relationsship between apparent accommodation and corneal multifocality in pseudophakic eyes. Ophthalmology 106:1178–1181
14. Glasser A, Campbell MC (1999) Biometric, optical and physical changes in the isolated human crystalline lens with age in relation to presbyopia. Vision Res 39:1991–2015
15. Greenbaum S (2002) Monovision pseudophakia. J Cataract Refract Surg 28:1439–1443
16. Haefliger E, Parel JM, Fantes F, Norton EW, Anderson DR, Forster RK, Hernandez E, Feuer WJ (1987) Accommodation of an endocapsular silicone lens (Phaco-Ersatz) in the nonhuman primate. Ophthalmology 94:471–477
17. Haefliger E, Parel JM (1994) Accommodation of an endocapsular silicone lens (Phaco-Ersatz) in the aging rhesus monkey. J Refract Corneal Surg 10:550–555
18. Haigis W, Auffarth GU, Limberger IJ, Rabsilber TM, Reuland AJ (2005) [Precision measurements of accommodative shift of the 1CU-lens for assessment of resulting refractive changes.] Proceedings 19th Congress of the German-speaking Society of Intraocular Lens Implantation and Refractive Surgery, Magdeburg pp241–255

19. Hara T, Yasuda A, Yamada Y (1990) Accommodative intraocular lens with spring action. 1. Design and placement in an excised animal model. Ophthalmic Surg 21:128–133
20. Hara T, Yasuda A, Mizumoto Y, Yamada Y (1992) Accommodative intraocular lens with spring action. 2. Fixation in the living rabbit. Ophthalmic Surg 23:632–635
21. Hara T, Sakka Y, Sakanishi K, Yamada Y, Nakamae K, Hayashi F (1994) Complications associated with endocapsular balloon implantation in rabbit eyes. J Cataract Refract Surg 20:507–512
22. Hardman Lea SJ, Rubinstein MP, Snead MP, Haworth SM (1990) Pseudophakic accommodation? A study of the stability of capsular bag supported, one piece, rigid tripod, or soft flexible implants. Br J Ophthalmol 74:22–25
23. Hayashi K, Hayashi H, Nakao F, Hayashi F (2003) Aging changes in apparent accommodation in eyes with a monofocal intraocular lens. Am J Ophthalmol 135:432–436
24. Hettlich HJ, Lucke K, Asiyo-Vogel MN, Schulte M, Vogel A (1994) Lens refilling and endocapsular polymerization of an injectable intraocular lens: in vitro and in vivo study of potential risks and benefits. J Cataract Refract Surg 20:115–123
25. Hettlich HJ, Asiyo-Vogel M (1996) [Experimental experiences with balloon-shaped capsular sac implantation with reference to accommodation outcome in intraocular lenses] Ophthalmologe 93:73–75
26. Holladay JT (1993) Refractive power calculations for intraocular lenses in the phakic eye. Am J Ophthalmol 116:63–66
27. Horton JC, Jones MR (1997) Warning on inaccurate Rosenbaum charts for testing near vision. Surv Ophthalmol 42:169–174
28. Huber C (1981) Planned myopic astigmatism as a substitute for accommodation in pseudophakic eyes. Am Intraocular Implant Soc 3:244–249
29. Kessler J (1964) Experiments in refilling the lens. Arch Opthalmol 71:412–417
30. Kirchhoff A, Stachs O, Guthoff R (2001) Three-dimensional ultrasound findings of the posterior iris region. Graefes Arch Clin Exp Ophthalmol 239:968–971
31. Koeppl C, Findl O, Menapace R, Kriechbaum K, Wirtitsch M, Buehl W, Sacu S, Drexler W (2005) Pilocarpine-induced shift of an accommodating intraocular lens: AT-45 Crystalens. J Cataract Refract Surg 31:1290–1297
32. Koopmans SA, Terwee T, Barkhof J, Haitjema HJ, Kooijman AC (2003) Polymer refilling of presbyopic human lenses in vitro restores the ability to undergo accommodative changes. Invest Ophthalmol Vis Sci 44:250–257
33. Koopmans SA, Terwee T, Haitjema HJ, Barkhof J, Kooijman AC (2003) Effect of infusion bottle height on lens power after lens refilling with and without a plug. J Cataract Refract Surg 29:1989–1995
34. Koopmans SA, Terwee T, Haitjema HJ, Deuring H, Aarle S, Kooijman AC (2004) Relation between injected volume and optical parameters in refilled isolated porcine lenses. Ophthalmic Physiol Opt 24:572–579
35. Kriechbaum K, Findl O, Kiss B, Sacu S, Petternel V, Drexler W (2003) Comparison of anterior chamber depth measurement methods in phakic and pseudophakic eyes. J Cataract Refract Surg 29:89–94
36. Kriechbaum K, Findl O, Koeppl C, Menapace R, Drexler W (2005) Stimulus-driven versus pilocarpine-induced biometric changes in pseudophakic eyes. Ophthalmology 112:453–459
37. Kuechle M, Nguyen NX, Langenbucher A, Gusek-Schneider GC, Seitz B, Hanna KD (2002) Implantation of a new accommodative posterior chamber intraocular lens. J Refract Surg 18:208–216
38. Kuechle M, Seitz B, Langenbucher A, Martus P, Nguyen NX (2003) Erlangen Accommodative Intraocular Lens Study Group. Stability of refraction, accommodation, and lens position after implantation of the 1CU accommodating posterior chamber intraocular lens. J Cataract Refract Surg 29:2324–2329
39. Kuechle M, Seitz B, Langenbucher A, Gusek-Schneider GC, Martus P, Nguyen NX (2004) The Erlangen Accommodative Intraocular Lens Study Group. Comparison of 6-month results of implantation of the 1CU accommodative intraocular lens with conventional intraocular lenses. Ophthalmology 111:318–324
40. Langenbucher, Langenbucher A, Huber S, Nguyen NX, Seitz B, Gusek-Schneider GC, Kuechle M (2003) Measurement of accommodation after implantation of an accommodating intraocular lens. J Cataract Refract Surg 29:677–685
41. Legeais JM, Werner L, Abenhaim A, Renard G (1999) Pseudoaccommodation: BioComFold versus a foldable silicone intraocular lens. J Cataract Refract Surg 25:262–267
42. Lesiewska-Junk H, Kaluzny J (2002) Intraocular lens movement and accommodation in eyes of young patients. J Cataract Refract Surg 26:562–565
43. Leyland M, Ziniola E (2003) Multifocal versus minifocal intraocular lenses in cataract surgery: a systematic review. Ophthalmology 110:1789–1798
44. Lucke K, Hettlich HJ, Kreiner CF (1992) A method of lens extraction for the injection of liquid intraocular lenses. Ger J Ophthalmol 1:342–345
45. Maloof AJ. Selective targeting of lens epithelial cells during human cataract surgery using sealed-capsule irrigation with distilled water. ARVO 2004, Fort Lauderdale, Abstract B291
46. Mastropasqua L, Toto L, Nubile M, Falconio G, Ballone E (2003) Clinical study of the 1CU accommodating intraocular lens. J Cataract Rferact Surg 29:1307–1312
47. McDonald JP, Croft MA, Vinje E, Glasser A, Heatley GA, Kaufman P, Sarfarazi FM (2003) Sarfarazi elliptical accommodating intraocular lens (EAIOL) in rhesus monkey eyes in vitro and in vivo. Invest Ophthalmol Vis Sci;44: Abstract 256
48. McLoed SD, Portney V, Ting A (2003) A dual optic accommodating foldable lens. Br J Ophthalmol 87:1083–1085
49. Menapace R (2004) Prevention of after cataract. In: T Kohnen, DD Koch (eds) Cataract and refractive surgery, Series Essentials in Ophthalmology. pp 101–122
50. Menapace R, Wirtitsch M, Findl O, Buehl W, Kriechbaum K, Sacu S (2005) Effect of anterior capsule-polishing on posterior capsular opacification and neodymium-YAG capsulotomy rate: a three-year randomized trial. J Cataract Refract Surg 31:2067–2075
51. Menapace R (2006) Primary posterior buttonholing for eradication of after-cataract: report of 500 cases. J Cataract Refract Surg 32:929–943
52. Menapace R (2006) “Aspiration Curette”: an instrument for efficient and safe anterior capsule polishing: laboratory and clinical results. J Cataract Refract Surg, in press
53. Mester U, Dillinger P, Anterist N, Kaymak H (2005) Functional results with two multifocal intraocular lenses (MIOL). Array SA40 versus Acri.Twin] Ophthalmologe 102:1051–1056
54. Nakazawa M, Ohtsuki K (1983) Apparent accommodations in pseudophakic eyes after implantation of posterior chamber lenses. Am J Ophthalmol 96:435–438
55. Nakazawa M, Ohtsuki K (1984) Apparent accommodation in pseudophakic eyes after implantation of posterior chamber lenses: optical analysis. Invest Ophthalmol Vis Sci 25:1458–1460
56. Nguyen NX, Seitz B, Reese S, Langenbucher A, Kuchle M (2005) Accommodation after Nd: YAG capsulotomy in patients with accommodative posterior chamber lens 1CU. Graefes Arch Clin Exp Ophthalmol 243:120–126
57. Niessen AGJE, de Jong LB, van der Heijde GL (1992) Pseudo-accommodation in pseudophakia. Eur J Implant Refract Surg 4:91–94
58. Nishi O, Sakka Y (1990) Anterior capsule-supported intraocular lens. A new lens for small-incision surgery and for sealing the capsular opening. Graefes Arch Clin Exp Ophthalmol 228:582–588

59. Nishi O, Hara T, Hara T, Sakka Y, Hayashi F, Nakamae K, Yamada Y (1992) Refilling the lens with a inflatable endocapsular balloon: surgical procedure in animal eyes. Graefes Arch Clin Exp Ophthalmol 230:47–55
60. Nishi O, Nakai Y, Yamada Y, Mizumoto Y (1993) Amplitudes of accommodation of primate lenses refilled with two types of inflatable endocapsular balloons. Arch Ophthalmol 111:1677–1684
61. Nishi O, Nishi K, Mano C, Ichihara M, Honda T (1997) Controlling the capsular shape in lens refilling. Arch Ophthalmol 115:507–510
62. Nishi O, Nakai Y, Mizumoto Y, Yamada Y (1997) Capsule opacification after refilling the capsule with an inflatable endocapsular balloon. J Cataract Refract Surg 23:1548–1555
63. Nishi O, Nishi K (1998) Accommodation amplitude after lens refilling with injectable silicone by sealing the capsule with a plug in primates. Arch Ophthalmol 116:1358–1361
64. Nishi O, Nishi K, Mano C, Ichihara M, Honda T (1998) Lens refilling with injectable silicone in rabbit eyes. J Cataract Refract Surg 24:975–982
65. Nishi O (2005) [After-cataract prevention and the restitution of accommodation—A new lens-refilling procedure. PPCCC+PBH: Proceedings 19th Congress of the German-speaking Society of Intraocular Lens Implantation and Refractive Surgery, Magdeburg 2005, pp247–250
66. Olsen R, Mamalsi N, Haugen B (2006) A light-adjustable lens with injectable optics. Curr Opin Ophthalmol 17:72–79
67. Oshika T, MimuraT, Tanaka S, Amano S, Fukuyama M, Yoshitomi F, Maeda N, Fujikado T, Hirohara Y, Mihashi T (2002) Apparent accommodation and corneal front aberration in pseudophakic eyes. Invest Ophthalmol Vis Sci 43:2882–2886
68. Payer H (1997) Ringwulstlinse mit Zoomwirkung zur Verstärkung einer Pseudoakkommodation und deren Erklärung aus erweiterter Akkommodationstheorie. [Posterior chamber lens allowing cases of pseudoaccommodation]. Spektrum Augenheilkd 11:81–89
69. Payer H, Reiter J (2003) Five years of experience with the Annular Ring Lens In: Guthoff R, Ludwig K (eds) Current aspects of human accommodation II. Kaden, Heidelberg, pp 179–192
70. Preussner PR, Wahl J, Gerl R, Kreiner C, Serester A (2001) Accommodative lens implant. Ophthalmologe 98:97–102
71. Sacca Y, Hara T, Yamada Y, Hara T, Hayashi F (1996) Accommodation in primate eyes after implantation of refilled endocapsular balloon. Am J Ophthalmol 121:210–212
72. Sacu S, Menapace R, Wirtitsch M, Buehl W, Kriechbaum K (2004) Effect of anterior capsule polishing on fibrotic capsule opacification: three-year results. J Cataract Refract Surg 30:2322–2327
73. Schaeffel F (2003) Optical techniques to measure the dynamics of accommodation. In: Guthoff R, Ludwig K (eds) Current aspects of human accommodation II. Kaden, Heidelberg, pp 71–94
74. Schwartz DM (2003) Light-adjustable lens. Trans Am Ophthalmol Soc 101:417–436
75. Smith SG, Snowden F, Lamprecht EG (1987) Topographical anatomy of the ciliary sulcus. J Cataract Refract Surg 13:543–547
76. Stachs O, Martin H, Kirchhoff A, Stave J, Terwee T, Guthoff R (2002) Monitoring accommodative ciliary muscle function using three-dimensional ultrasound. Arch Clin Exp Ophthalmol 240:906–912
77. Tassignon MJ, De Groot V, Vrensen GF (2002) Bag-in-the-lens implantation of intraocular lenses. J Cataract Refract Surg 28:1182–1188
78. Verzella F, Colossi A (1993) Multifocal effect of against-the-rule myopic astigmatism in pseudophakic eyes. Refract Corneal Surg 1:58–61
79. Werblin TP (2003) Discussion of article "Clinical evaluation of model AT-45 silicone accommodative intraocular lens: results of feasibility and the initial phase of a food and drug administration clinical trial". Ophthalmology 108:2010
80. Werner L, Pandey SK, Izak AM, Vargas LG, Trivedi RH, Apple DJ, Mamalis N (2004) Capsular bag opacification after experimental implantation of a new accommodating intraocular lens in rabbit eyes. J Cataract Refract Surg 30:1114–1123
81. Yamamoto S, Adachi-Usami E (1992) Apparent accommodation in pseudophakic eyes as measured with visually evoked potentials. Invest Ophthalmol Vi Sci 33:443–446