Restoration of accommodation

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Purpose of review

This review examines the current status of accommodation restoration concepts with reference to the recent, published peer-reviewed literature with an emphasis on physiological aspects of accommodation and presbyopia.

Recent findings

The mechanisms of accommodation and the causes of presbyopia are described. The physiological amenability of the accommodative structures in the presbyopic eye to accommodation restoration is discussed. General theoretical concepts of accommodation restoration are introduced. The methods that have been used to assess accommodation restoration, including the use of animal models, drug stimulated accommodation, subjective near-vision tests and objective measurements, are reviewed.

Summary

While physiological and clinical evidence supports the notion that accommodation can be restored to the presbyopic eye, progress in this potentially exciting area is hindered by the scarcity of good, large-scale clinical studies using objective measurement techniques to evaluate the outcomes of accommodation restoration concepts.

Keywords

accommodative intraocular lenses, objective measurement, presbyopia, scleral expansion

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The author wishes to disclose that he has served and currently does serve as a consultant to many companies with interests in accommodation and presbyopia and accommodation restoration concepts.

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Introduction

The purpose of this review is to consider the recent literature relating to restoration of accommodation. Accommodation is a dynamic optical change in the eye as a consequence of a ciliary muscle contraction. Optical factors other than accommodation, such as astigmatism, high-order aberrations and pupil constriction, increase the depth of field of the eye to aid near vision. While these are beneficial for alleviating symptoms of presbyopia, they constitute pseudoaccommodation and not accommodation. Multifocal intraocular lenses or multifocal corneal refractive procedures also alleviate the symptoms of presbyopia by providing some functional near vision through increased depth of field of the eye; this, however, is also not accommodation. Published peer-reviewed papers from 2004 and 2005 are reviewed in the context of ongoing studies of accommodation restoration. Much recent information is available in the form of conference abstracts and non-peer-reviewed articles, which are not considered here. This is also not intended to be a review of accommodative intraocular lenses or new intraocular lens designs as this has been addressed elsewhere [1••,2•,3,4•,5].

Accommodation

Accommodation is defined as a dynamic optical change in power of the eye [6,7]. The accommodative mechanism as originally described by Helmholtz [8] has been reconfirmed [9]. In the young phakic eye, contraction of the ciliary muscle moves the apex of the ciliary body forward and inward to release resting zonular tension around the lens equator to allow the elastic lens capsule to mold the lens into an accommodated form [8–10]. With accommodation in the young phakic eye, the lens undergoes a decrease in equatorial diameter, an increase in axial thickness, and a steepening of the anterior and posterior surface curvatures [9,11,12••]. The increase in lens thickness results in a decrease in anterior chamber depth and an increase in anterior segment (anterior chamber and lens thickness) length [11,12••,13]. The increased lens surface curvature results in an increase in optical power of the lens and eye that constitutes accommodation.

Causes of presbyopia

Presbyopia has been attributed to loss of compliance of the posterior attachment of the ciliary muscle [14,15], growth and geometric changes in the lens [16] and hardening of the lens with increasing age [17••,18,19]. While the root cause(s) of presbyopia may be debated, it is generally accepted that hardening of the lens represents the limiting factor for accommodation in the presbyopic eye. Nonconformist theories of presbyopia suggest that accommodation is lost owing to an age-related increase in lens diameter and the resultant slackening of zonular fibers [20]. In-vivo MRI measurements in living human eyes, however, show that lens equatorial diameter does not increase with age [21].

Restoration of accommodation to the presbyopic eye

For accommodation to be restored to the presbyopic eye, the physiology of accommodative structures must remain viable. The ciliary muscle still contracts in presbyopic eyes even in the absence of accommodative changes in the lens [21]. This is not surprising given that the ciliary muscle is a striated intraocular muscle that, like the iris sphincter muscle, receives parasympathetic stimulation when the eyes converge to look at near objects because of the neural coupling of accommodation, pupil constriction and convergence (the accommodative triade) – even in a presbyopic eye. The elastic capsule that molds the young lens during accommodation [10,22,23] should remain viable in a presbyopic eye for accommodation to be restored. With increasing age, Young's modulus of the capsule, for low strains relevant to accommodation, increases with age until about age 35 and thereafter remains constant, thus becoming increasing effective at producing forces required to accommodate the lens and possibly even counteracting the presbyopic progression to some extent [24–26]. The important anatomical accommodative structures appear to remain functional and viable in the presbyopic eye [27].

How much is enough?

The eye generally has approximately 1.5–2.0 D of pseudoaccommodation when focused for near objects owing to ocular aberrations and the increased depth of field because of the pupil constriction that accompanies accommodation [28,29]. This can be as much as 4 D in phakic presbyopes [29]. Restoring as little as 1 D of true accommodation to a presbyopic eye in conjunction with the available pseudoaccommodation would benefit many. Restoring 3–4 D of true accommodation would be considered successful and would probably satisfy most presbyopes [30]. Striving to restore up to 7 D of true accommodation, while a laudable goal, may not be necessary. To understand how much accommodation is available or indeed if accommodation is restored in a presbyopic eye, it is necessary to effectively stimulate accommodation and to measure the response objectively. Clinically, accommodation is often measured subjectively by asking a distance corrected subject to move a near reading target towards the eyes until it can no longer be held in clear, sharp focus. The distance from the eyes to the near target expressed in diopters is used to represent accommodative amplitude. While this is an easy and appropriate clinical test for functional near vision, it does not unequivocally measure the accommodative optical change in power of the eye because it includes the pseudoaccommodative factors, such as depth of field, that also aid near vision. The appropriate way to measure accommodation is to measure the optical change in power of the eye with an objective optical instrument such as a refractometer, autorefractor or wavefront aberrometer as the eye views from far to near.

Scleral expansion

Scleral expansion accommodation restoration concepts are directed at reversing a theorized age-related slackening of zonular fibers at the lens equator. Scleral expansion restoration of accommodation is based on revisionist theories of accommodation [20,31,32] that are untenable [9], and has been shown to be ineffective [33–37]. Surgical manipulations of the sclera cannot reverse lens hardening or restore the accommodative capacity to the lens.

Laser of chemical treatment of the lens

If lens hardening restricts accommodation in the presbyopic eye, theoretically, modification of the presbyopic lens to either beak bonds or soften the lens may restore accommodation. Lens laser modification has been proposed, but is in its infancy and awaiting in-vivo proof of principle [38,39]. Chemical modification of the lens would probably require long-term, sustained therapeutic compliance and so is unlikely to be viable unless short-term treatments are developed.

Accommodation restoration with accommodative intraocular lenses

Theoretically, accommodation could be achieved with intraocular lenses through a forward shift of a single-optic intraocular lens, through an increased separation of the optics in a dual-optic intraocular lens or through an increase in surface curvatures of a deformable lens. Accommodative intraocular lenses of these three types have been developed and are undergoing laboratory and/or clinical studies. With accommodation, the young primate lens increases its axial thickness by about 50–60 μm D^{-1} [11,12••,40,41]. In humans, this results in an increase in lens thickness of about 300 μm for 6 D of accommodation. This suggests that a single-optic intraocular lens may shift forward, or the separation between the optics in a dual optic intraocular lens may increase with an accommodative effort. A 1 mm anterior movement may produce about 1 D of accommodation in a single-optic intraocular lens [42–45] and

2.5–3.0 D in a dual-optic intraocular lens [44,46]. The magnitude of the accommodative effect depends on a number of factors including the power of the optic(s) and the position of the optic(s) within the capsular bag. Deformable lenses that undergo a change in surface curvature may produce about 4–7 D of accommodation [47].

Developing an accommodative intraocular lens that allows accommodation yet retains long-term refractive stability is challenging. When placed in the capsular bag, the intraocular lens must have the correct position, power and configuration to achieve an emmetropic refraction, and yet must also yield to intraocular forces from the ciliary muscle and capsule to produce accommodation. The intended, inherent instability of accommodative intraocular lenses to allow them to move in the eye renders them especially susceptible to tilting [48], deconcentration or other undesirable changes over time. This increases the possibility of undesirable postoperative refractive shifts, astigmatism, other aberrations or surprises due to capsular bag contraction and fibrosis, for example. Thus, while new potentially accommodative intraocular lenses have intriguing new designs, these may present significant new challenges to achieving targeted refractions and long-term postoperative stability. If accommodation is achieved in the immediate postoperative period, proliferation of lens epithelial cells and postoperative fibrotic changes could result not only in secondary cataract, but also secondary presbyopia over a period of months. Natural variations in the dimensions of the eye and capsular bag also present challenges. Accommodative intraocular lenses that rely on a fine balance of forces between the intraocular lens and the physiological accommodative structures are susceptible to variability of postoperative refraction and accommodative amplitudes dependent on how well the intraocular lens fits in the capsular bag.

For accommodative intraocular lenses that rely on the integrity and elasticity of the capsule to perform their accommodative function, YAG laser capsulotomy may be contraindicated. A soft polymer injected into the capsular bag would probably bulge or leak out of a posterior capsulotomy with potentially devastating visual consequences. The clinical performance, however, of a single-optic accommodative intraocular lens based on the forward-shift principle appears not to be affected by YAG capsulotomy, at least as assessed with subjective accommodation testing [49]. Accommodative intraocular lenses that do not rely on elasticity of the capsule or are designed to take advantage of postoperative fibrosis in the capsule [1••,50,51] may circumvent a secondary loss of accommodation. Stability of refraction, anterior chamber depth and subjectively measured accommodative amplitude up to 1 year has been reported with such an intraocular lens [52].

Testing accommodative intraocular lens designs

Other than *in vivo* in humans, relatively few options are available for testing accommodation restoration concepts. Surgical techniques have been evaluated in rabbit, monkey and enucleated pig eyes [53–62]. Postoperative capsular opacification of accommodative intraocular lenses has been studied in rabbits and monkeys [55,63,64]. Mechanical stretching of human donor eyes, used previously to study accommodation and presbyopia in phakic human donor eyes [18], has been used to investigate accommodation restoration with polymer refilling techniques [27] or accommodative intraocular lenses in an artificial capsule [65•].

Limited options for animal testing are available. Rabbits and dogs do not accommodate. Cats do to a limited extent [66], but by translation of the lens [67–69] as with raccoons [70]. Birds accommodate by changes in corneal curvature and the iris sphincter muscle and ciliary body squeezing the lens [71,72]. Monkeys are the only animal species with an accommodative mechanism similar to humans [9]. While polymer refilling techniques can be tested *in situ* in monkey eyes [58,64,73,74], it would be of limited value to test other intraocular lens designs in monkey eyes. Intraocular lenses would have to be specifically designed for the relatively small monkey eye, and material thicknesses and mechanical properties would have to be scaled down, thus making it unclear how applicable the results would be to human intraocular lenses.

Early prototype testing in living human eyes is challenging because of the limited testing that can be done and the time commitment and level of cooperation required from the patients for this testing. If an intraocular lens fails to accommodate in a human eye, it may not be possible to understand why. It may be owing to poor sizing of the intraocular lens for the capsular bag, postoperative fibrotic changes in the capsule, an inability of the subject to elicit accommodation or an ineffective intraocular lens design. An inability to differentiate between these factors makes it difficult to improve the performance of the accommodative intraocular lenses.

Evaluation of accommodation restoration concepts

Providing functional distance and near vision to presbyopes through any means possible is of value if it is safe and effective. The myriad of approaches available or under investigation attest to the clinical need. Many approaches rely on multiple factors to achieve functional distance and near vision. For example, multifocal or diffractive intraocular lenses rely on the optics of the intraocular lens in conjunction with the dynamic pupil changes to provide functional near and distance vision. Functional near vision in the phakic eye is also achieved through a combination of active, dynamic accommodation and static pseudoaccommodative influences as is demonstrated by the difference between subjectively and objectively measured accommodative amplitudes [28,29]. There is little debate that testing of accommodation restoration concepts can and should include standardized, subjective near-vision tests such as distance-corrected near-visual acuities. These tests include the many factors that may improve near vision. This is important clinically to understand the benefits for the patients. The use of subjective tests alone, however, permits no definitive conclusions regarding the ability of accommodation restoration procedures to restore accommodation.

Several recent studies of accommodative intraocular lenses only utilize subjective outcome measures [49, 75•,76,77]. Comparable near-vision performance was reported with multifocal or accommodative intraocular lenses that was better than that achieved with standard, control monofocal intraocular lenses [75••,77]. Another study found better near-visual performance with a multifocal than an accommodative intraocular lens [76]. Studies using subjective tests such as distance-corrected near-visual acuity and dynamic retinoscopy, however, provide no evidence of whether active accommodation is present with the accommodative intraocular lenses. Only the use of objective measures can settle the debate over whether or not accommodation is restored with accommodation restoration procedures including scleral expansion [33–37] or accommodative intraocular lenses [78•,79,80].

Pharmacological stimulation of accommodation

Accommodation can be stimulated by topical application of 2–6% pilocarpine. This produces an involuntary accommodative response that does not rely on the subject's ability to respond to visual, blur or proximal cues. The time course of drug stimulation, however, is slow and it produces a rapid and strong pupil constriction that makes objective accommodative refraction measurements difficult. The amplitude of the accommodative response varies with iris color owing to the extent to which drugs are absorbed by the ocular pigment epithelium [28,29]. The pharmacological stimulated accommodative response results in a net anterior shift of the lens in the phakic eye that does not normally occur with natural accommodation [12••,81]. Pilocarpine stimulated accommodation produces a forward intraocular lens movement that does not occur with a voluntary accommodative effort [82•]. Pharmacological stimulation of accommodation may therefore be inappropriate for evaluating the clinical performance of accommodative intraocular lenses that rely on a forward-shift principle. It may be desirable or appropriate in some cases, however, to use pharmacological stimulation to evaluate the possibility or presence of an axial shift in an intraocular lens that is designed to perform that way.

A number of studies have stimulated accommodation pharmacologically in pseudophakic eyes and measured intraocular lens movement with slit-beam photography, scanning slit topography, ultrasound biomicroscopy or partial coherence interferometry [65•,78•,82•,83]. While these studies are to be lauded for the use of objective measurements of intraocular lens movement, the use of pilocarpine to stimulate accommodation leaves doubt as to whether the movements observed are due to accommodation or due to secondary effects of the pilocarpine.

Accommodative movements of an accommodative intraocular lens have also been assessed with ultrasound biomicroscopy. Anterior chamber depth was measured, first while subjects fixated a near target at 30 cm with the contralateral eye and then subsequently after the measured eye was cyclopleged with 1% cyclopentolate [84•]. A 0.33 mm decrease in anterior chamber depth was reported that was attributed to accommodation. Another study using slit-beam photography attributed an increase in anterior chamber depth of 0.43 mm from the unaccommodated to the cyclopleged state to the accommodative movement of the intraocular lens [75•]. These movements may not be due to anterior movement with accommodation, however, but rather posterior movement with cycloplegia, as has been demonstrated to occur in the normal phakic eye [12••]. Measuring intraocular lens movements with cycloplegia is inappropriate to assess how an intraocular lens may move with accommodation.

Objective measurement of pseudophakic accommodation

Objective measurements during volitional accommodation with forward-shift accommodative intraocular lenses have been reported. One study (evidently the same data reported twice) measured a mean of 1 D (range 0.75–2.13 D) of accommodation with an infrared refractometer [42,85]. Forward movement of an intraocular lens has been demonstrated in one patient with Purkinje image analysis [86]. The accommodative amplitude was measured with an objective infrared autorefractor in 14–66% of 22 subjects followed over 1 year with a peak mean of 0.5 D of accommodation at the 3-month interval [87••].

Conclusion

There is incontrovertible, objective evidence that accommodation can be restored in the pseudophakic eye. Such data are sparse, however, and success in restoring accommodation is limited and variable. The objective clinical data available to date include only studies on forward-shift-principle intraocular lenses. The accommodative amplitude theoretically achievable and clinically measured with such intraocular lenses is small. The current status of accommodation restoration is disappointing because of the lack of sound clinical studies that have used appropriate objective methods to measure accommodation (either the optical response or the physical movement) with voluntary accommodation. Subjective clinical outcomes are important. If restoration of accommodation is to evolve from theory to practice, however, objective measurements are essential. Objective accommodation measurement has, for a long time, been routine practice in accommodation studies in phakic eyes. Many objective instruments exist that are routinely used on pseudophakic eyes that are appropriate for objective accommodation measurement. These instruments can and should be used for objective accommodation measurements in pseudophakic eyes to understand the capabilities of the instruments and to evaluate the efficacy of the intraocular lenses. The current status of this field is exciting for what the future may hold. Preliminary results suggest that accommodation can be restored, and new intraocular lens designs may lead to improved performance and clinical outcomes in the future.

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