BCLA CLEAR presbyopia: Mechanism and optics

Leon N. Davies [a,*], Sayantan Biswas [a], Mark Bullimore [b], Fiona Cruickshank [c], Jose J. Estevez [d,e],
Safal Khanal [f], Pete Kollbaum [g], Remy Marcotte-Collard [h], Giancarlo Montani [i], Sotiris Plainis [j],
Kathryn Richdale [k], Patrick Simard [h], James S. Wolffsohn [a]

[a] School of Optometry, College of Health and Life Sciences, Aston University, Birmingham, UK
[b] College of Optometry, University of Houston, USA
[c] Division of Pharmacy and Optometry, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, UK
[d] Caring Futures Institute, College of Nursing and Health Sciences, Optometry and Vision Science, Flinders University, Adelaide, Australia
[e] Flinders Centre for Ophthalmology, Eye and Vision Research, Department of Ophthalmology, Flinders University, Adelaide, Australia
[f] Department of Optometry and Vision Science, The University of Alabama at Birmingham, USA
[g] School of Optometry, Indiana University, USA
[h] School of Optometry, Universite de Montreal, Montreal, Quebec, Canada
[i] Centre for Contact Lens Research, University of Salento, Italy
[j] Laboratory of Optics and Vision, School of Medicine, University of Crete, Greece
[k] CooperVision, CA, USA

ARTICLE INFO

ABSTRACT

With over a billion adults worldwide currently affected, presbyopia remains a ubiquitous, global problem. Despite over a century of study, the precise mechanism of ocular accommodation and presbyopia progression remains a topic of debate. Accordingly, this narrative review outlines the lenticular and extralenticular components of accommodation together with the impact of age on the accommodative apparatus, neural control of accommodation, models of accommodation, the impact of presbyopia on retinal image quality, and both historic and contemporary theories of presbyopia.

1. Overall aims

Despite the ubiquitous, global problem of presbyopia [1], the precise mechanism of ocular accommodation and presbyopia progression remains a topic of debate. Therefore, this narrative review aimed to outline the lenticular and extralenticular components of accommodation together with the impact of age on the accommodative apparatus, neural control of accommodation, models of accommodation, the impact of presbyopia on retinal image quality, and both historic and contemporary theories of presbyopia.

2. Mechanism of accommodation

Accommodation is a dynamic process that increases the dioptric power of the eye's optical system to maintain images in sharp focus on the retina as fixation changes from far to relatively near distances. When the eye fixates on a distant (for example at > 6 m) object, the refractive system of the eye is focused at an optical infinity, so parallel rays of light entering the eye form clear images on the retina. As the fixation distance reduces towards the cornea, the diverging rays entering the eye come to a focus behind the retinal plane creating hyperopic retinal image blur, which serves as the primary dioptric stimulus to accommodation [2,3]. In response to this stimulus, the crystalline lens, ciliary body, and zonules undergo various structural alterations to produce an accommodative response that restores image focus and maintains clarity of vision. Collectively, these components constitute the accommodative apparatus [4], and a coordinated response between them is central to the dynamic process of maintaining clear vision at a range of viewing distances.

The accommodative response begins with the contraction of the ciliary body which uses a sphincter-like muscle to fulfil its role of maintaining image clarity. As fixation distance varies, contraction or relaxation of the ciliary muscle produces changes in the tension of

---

https://doi.org/10.1016/j.clae.2024.102185

zonular fibres that are attached to the lens capsule near the equator of the crystalline lens [3]. Alteration of the zonular tension results in modulation of the outward pulling force exerted by the zonular fibres on the crystalline lens [5]. Consequently, the curvature of the lens surface changes, modifying the power of the eye's optical system and restoring image clarity (Fig. 1).

2.1. Crystalline lens

The crystalline lens enables the young human eye to optimize image clarity as the eye modifies its structures to alter fixation between objects at various distances in the visual field. In the absence of accommodation, the crystalline lens contributes approximately one-third (approximately 20 D) of the eye's total dioptric power (approximately 60 D). A remarkable feature of the crystalline lens is that it has a capsular surrounding, and is suspended in fluid (the aqueous humour) by a network of surrounding zonular fibres [6]. The bulk of the crystalline lens is formed by proteins, which play a critical role in maintaining its transparency [7,8]. Indeed, the crystalline lens has the highest protein concentration of any biological tissue (approximately 300 mg/ml) [9,7]. Besides proteins, the crystalline lens is composed of long, thin fibres arranged in concentric orientation giving a flattened (oblate) spheroid shape to the lens [10]. When viewed in cross-section, the crystalline lens has an onion-like structure, containing several layers of fibres surrounding the central core [11]. This arrangement of lens fibres is a consequence of crystalline lens growth as older fibres are located toward the nucleus, surrounded by the younger cortical fibres [12]. The crystalline lens nucleus has no apparent anatomical demarcation with the surrounding cortex. The equator of the crystalline lens separates the anterior and posterior surfaces whose geometrical centres form the anterior and posterior poles, respectively.

On the anterior surface, the crystalline lens has a single layer of epithelial cells which serve as the progenitor for new lens cells [13]. The entire meshwork of lens fibres and the epithelial cells are enclosed within the lens capsule which, near the equator, serves as the attachment site for the zonular fibres extending from the *pars plana* of the ciliary body. This attachment site is not constant, however. While zonular fibres are distributed uniformly from the anterior to the posterior of the lens equator at early stages, the distribution becomes densest anterior to the equator as the crystalline lens ages, and this redistribution continues throughout life [14,15].

With increasing accommodation, the crystalline lens becomes optically stronger to maintain retinal image focus. To facilitate this, several structural changes occur that contribute to the increase in its overall dioptric power [16–18]. The most prominent change is the steepening of the lens surfaces with both anterior and posterior lens surfaces become

more curved with accommodation leading to an increase in dioptric power [19,17,20,21]. The increase in curvature of the anterior surface is greater causing it to become hyperbolic [22,23]. However, the change in curvature is insufficient to account fully for the increase in power required for the accommodative demand. It is hypothesized that changes in the curvature of the interior optical zones of the crystalline lens [24,25] or changes in the refractive index distribution [26,27] account for the remainder of the lens power increment.

Accompanying changes in surface curvatures, the thickness of the crystalline lens also increases along the polar axis with accommodation [19,28,17,29]. This increase in sagittal lens thickness is mainly due to the anterior shift in the position of the anterior pole [30]; however, the displacement of the lens pole appears somewhat dependent on refractive status, as the posterior pole has been found to move backward in myopic eyes [31]. The increase in the thickness of the crystalline lens is produced primarily by the thickening of the lens nucleus [25] that occurs at the same rate in both the anterior and posterior halves [28]. The thickening of the crystalline lens slightly decreases its overall dioptric power, but the forward movement of the lens also causes the anterior chamber (distance between the posterior corneal surface and the anterior lens surface) to become shallower [19]. This reduction in anterior chamber depth increases the effective power of the cornea and lens combination and offsets the slight power reduction brought about by the thickening of the crystalline lens [32]. The net result is a positive increase in the overall dioptric power of the crystalline lens that supplements the increase in power due to changes in the curvature of the lens surfaces. The increase in lens thickness with accommodation is greater than the decrease in anterior chamber depth, suggesting that there is some backward shift in the position of the posterior pole [22,31]. While the lens surface area has been found to decrease with greater accommodative demand, the lens volume appears to remain constant [33,34], although inconsistency exists [18]. It has been suggested that accommodation-induced change in lens shape could be due to redistribution of tissue within the capsular bag without significant compression of the lens contents or fluid exchange through the capsule [33].

The crystalline lens has an internal microcirculation system that creates circulating flow of ions, water and nutrients that maintain the transparency and refractive properties of the lens. Through this active regulation of water content, the microcirculation system controls lens geometry and the gradient of refractive index; together these key parameters determine the refractive properties of the lens. In addition, by delivering antioxidants and nutrients to the lens nucleus, the microcirculation system maintains lens transparency through preventing crystallin aggregation. The ability of crystallin proteins within the lens to dynamically bind water can also modulate their solubility, intramolecular packing and refractive index [8].
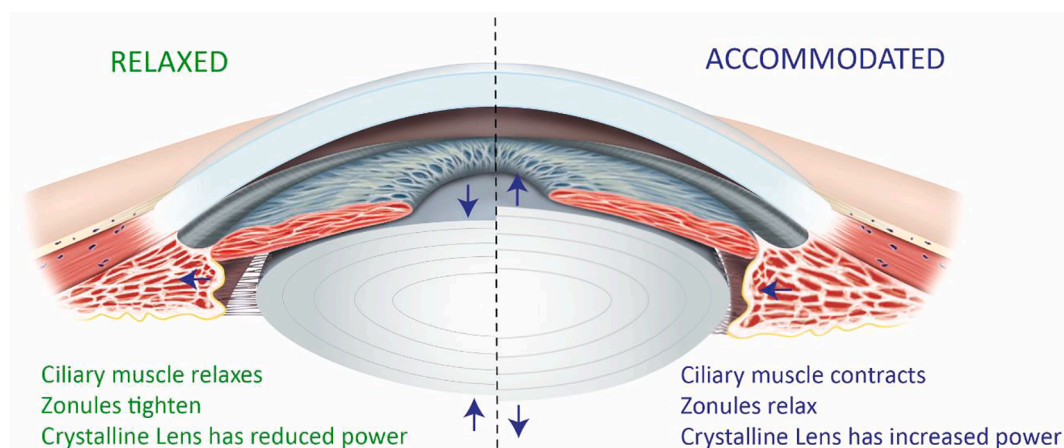

Fig. 1. Schematic outline of the principal structures involved in accommodation. Left, shows the eye in the relaxed state; right, illustrates the accommodated state. Arrows indicate relative movement of structures.

2.2. Lens capsule

The lens capsule is a thin, highly elastic, transparent membrane of 5–30 μm in thickness, that forms a capsular bag and encloses the concentric shells of lens fibres and the anterior epithelium of the lens [35–37]. The capsule serves to maintain the shape of the crystalline lens and transmits forces from the zonular fibres to the lens substance. Since elastin fibrils are absent in the lens capsule, its viscoelasticity is attributed mainly to the flexible, mesh-like arrangement of the collagen fibrils [35,38]. These fibrils are primarily type IV collagen lying within the glycosaminoglycan matrix [39,40]. Owing to its viscoelasticity, the capsule can mould the internal lens during accommodation [41,42].

During embryonic development, the capsule forms as the basement membrane of the epithelium on the lens vesicle [38]. As the lens grows, new material is deposited onto the anterior capsule, which causes a gradual shift of the capsular parts posteriorly. The capsule in the posterior pole, therefore, is the thinnest measuring 2–3 μm [43].

2.3. Zonules

The zonule fibres, 1–2 μm in diameter and thousands in number, originate from the dentate processes of the *pars plana* with the valleys of the ciliary processes on *pars plicata* serving as the anchoring sites of the lens [44]. Adjacent to these anchoring sites are the circular portion of the ciliary muscle. As a result, the force generated by the contraction or relaxation of the ciliary muscle is directly communicated across to the zonules and then to the crystalline lens. The zonular fibres run radially from the valleys of the ciliary processes to extend over the lens capsule and ultimately fuse with the capsular collagen via attachment proteins. This complex system of zonular fibres helps maintain the centration of the crystalline lens within the visual axis and serves physiologically to transmit forces generated by the ciliary muscle to produce changes in lens dimensions during accommodation [45].

Structurally, the zonules are composed of 10–12 nm wide microtubules arranged as long strands [46,47], which collectively form bundles that connect the basement membrane of the unpigmented epithelium of the ciliary body to the crystalline lens capsule [47]. These microtubules are embedded in a polysaccharide matrix with adjacent elastin fibrils, which provide elasticity for the zonules, so they can readily stretch and modify their inherent tension [48]. Because the zonular bundles are transparent in their physiological state, thin and concealed behind the iris, they are visible only with imaging techniques such as ultrasound biomicroscopy [45]. The site of attachment of the zonules on the lens capsule is broadly around the equator of the lens. They attach to the anterior surface, posterior surface, or to the equator of the lens [49,45]. However, the distribution of these zonules changes with age (see section 9.2).

2.4. Ciliary body

The ciliary body is a ring of tissue interfacing outwardly with the sclera's inner surface and extending anteriorly from the uveal tract [50]. Its three principal functions are to produce and secrete aqueous humour via its non-pigmented ciliary epithelium [51], to facilitate accommodation by contracting and relaxing the ciliary muscle contained within [52], and to provide an outflow drainage route for aqueous humour [53].

The ciliary body can be broadly subdivided into: the anterior section or *pars plicata* and the posterior section termed the *pars plana* [54]. The *pars plicata* consists of a series of vascular ridges of non-pigmented ciliary epithelium on its inner surface, which are responsible for aqueous humour secretion against a concentration gradient to maintain intraocular pressure [55]. They are arranged radially around the equator of the crystalline lens, each ridge orientated approximately tangential to the pupil plane. The *pars plana* extends from the ciliary processes to the *ora serrata* and is in contact with the vitreous body. It contains smooth muscle fibres forming the ciliary muscle, which sits beneath the ciliary processes and forms the bulk of the ciliary body [56].

2.4.1. Ciliary muscle

The ciliary muscle is an anulus of smooth muscle cells without spontaneous activity surrounded by connective tissue [57]. The fast multi-unit smooth muscle is primarily involved in accommodation and the regulation of aqueous humour flow into Schlemm's canal [58]. The ciliary muscle differs from other types of smooth muscle cells as it comprises both smooth and striate muscle cells [59]. Ciliary muscle bundles can be histologically delineated into three fibre types: longitudinal, radial and circular. The longitudinal fibres run from the scleral spur to the posterior visible limit of the ciliary muscle, parallel to the sclera. The radial fibres run broadly perpendicular to these longitudinal fibres, while circular fibres encircle the ciliary muscle aperture, lying in the closest proximity to the crystalline lens [60]. Histochemical examination of the primate ciliary muscle suggests that longitudinal fibres are similar to rapid type-II skeletal muscle fibres, whilst radial and circular fibres resemble slow type-I fibres [57].

In its relaxed state, the ciliary muscle's maximum thickness is approximately 0.9 mm [61], thicker temporally than nasally [62], with an overall length of approximately 4.6 mm [62] and a ring diameter of 11.8 mm [61]. Once stimulated, the ciliary muscle's contractile action during accommodation moves the ciliary body forward and inward [63], increasing in thickness at a rate of approximately 0.026 mm per dioptre of stimulus demand at the muscle's thickest point in the horizontal plane [61], whilst the ciliary ring diameter decreases at a rate of between −0.063 and −0.105 mm per dioptre of stimulus demand [64].

2.5. Choroid and axial length

It is well established that the primary correlate of myopia and its progression is an increase in axial length [65], which is typically quantified as the distance between the anterior corneal surface and the retinal pigment epithelium [66]. Similarly, a growing body of evidence suggests that axial length measurements along the visual axis are modified by changes in accommodation [67]; these may be influenced further by differences in an individual's baseline refractive error, with greater accommodation-induced axial length changes detected in both emmetropes [68] and myopes [69], although this phenomenon is often dependent on the level of accommodative demand [70] and it has not been observed universally [71].

In terms of the underpinning mechanism for the increase in axial length as a function of accommodative response, recent studies have converged on the hypothesis that a corresponding decrease in choroidal thickness plays an important role. Indeed, a recent study suggested that choroidal changes account for approximately 60 % of the overall axial length increase observed during active accommodation [72]. Furthermore, studies have shown choroidal thinning with accommodation in the subfoveal [73], macular [74], peripapillary [75], and peripheral regions [72]. It has been suggested that axial elongation during accommodation may be a consequence of the force applied to the equatorial choroid during ciliary muscle contraction, requiring posterior pole elongation to maintain a constant ocular volume [68,70]. It is likely, therefore, that more than one factor produces this axial stretch.

3. Neural control of accommodation

The ciliary muscle is innervated principally by the antagonistic action of the autonomic nervous system [76]. Here, parasympathetic innervation of the ciliary muscle is facilitated by the neurotransmitter acetylcholine on muscarinic receptors [77]. Activation of the parasympathetic system induces contraction of the ciliary muscle, which, in turn, leads to relaxation of the zonular fibres that suspend the crystalline lens, enabling the crystalline lens to assume a more convex shape and, thus, increase the accommodative response [30]. Withdrawal of

parasympathetic innervation reverses this mechanism, leading to a decrease in the overall accommodation response [78]. In parallel, inhibitory sympathetic input to the ciliary muscle is mediated by noradrenaline on adrenoceptors [79].

Since early work elucidated that parasympathetic (cholinergic) innervation to the ciliary muscle facilitates accommodation for near targets [80], much evidence regarding the autonomic control of accommodation has been gathered by measuring accommodative responses to pharmacological [81–83] and physiological [84–86] manipulations of the autonomic nervous system. Additionally, the parasympathetic response has been found to be rapid (1–2 s) when the oculomotor nerve is stimulated via the Edinger-Westphal nucleus in primates [87].

In terms of the sympathetic (adrenergic) nervous system's role in accommodation control, early work showed that stimulation of the pre-ganglionic cervical sympathetic nerves of primates produces a negative accommodative effect [88]. Furthermore, non-selective beta-blockers (e.g., propranolol) eliminate this negative accommodation response, indicating that a beta-adrenergic inhibitory mechanism exists in the control of ciliary smooth muscle. In contrast to the parasympathetic response, the negative sympathetic response is slow, reaching a maximal effect after 10 to 40 s [89], far too slow to have any impact on viewing a dynamic visual environment [90].

Evidence of inhibitory sympathetic input to accommodative control has been demonstrated in both *in vitro* work and functional *in vivo* studies [91]. In addition to the presence of the predominant M3 subclass of muscarinic receptor found in the anterior segment of the human eye [92], studies have also identified the presence of the alpha-1 and beta-2 subclass of adrenoceptors in human ciliary body tissues [93–95].

Functional studies of *in vivo* accommodation have shown that the gain of closed-loop responses to a sinusoidal accommodative stimulus increases following instillation of the alpha-1 adrenoceptor agonist phenylephrine hydrochloride [96]. In terms of sympathetic ubiquity, however, work using the beta-adrenoceptor antagonists timolol maleate and betaxolol hydrochloride showed that only a third of individuals have access to a sympathetic inhibitory facility in accommodation control [82,97]. Since sympathetic inhibition of accommodation may aid relaxation of ciliary smooth muscle following cessation of a near task and, therefore, expedite the distance refocus response, it is conceivable that access to this inhibitory facility may improve accommodative accuracy. To explore this concept further, previous work used the phenomenon of nearwork-induced transient myopia as a measure of post-nearwork relaxation of accommodation [98]. They combined this with manipulation of sympathetic innervation of ciliary muscle using topical timolol maleate to inhibit beta-2 adrenoceptors, together with a betaxolol hydrochloride control agent acting on beta-1 receptors only. Of their 20 participants, 7 (35 % of the cohort) demonstrated access to an inhibitory branch of accommodation control, mediated by the sympathetic autonomic nervous system branch. Those with access to sympathetic facility showed a significant increase in nearwork-induced transient myopia duration following the instillation of timolol maleate; however, no such change was observed following instillation of betaxolol hydrochloride owing to the selectivity of this agent for beta-1 adrenoceptors.

4. Components of the functional accommodative response

A variety of factors influence the accommodative response achieved when the eyes are presented with a near object of interest [99]. It has previously [100] been suggested that the response has several components:

(i) Reflex accommodation, a quasi-automatic involuntary adjustment of refractive state to maintain a sharp retinal focus, of maximal luminance contrast and smallest blur-circle diameter, of

the object of regard [78,101,102]. There are, however, some doubts as to whether a true involuntary reflex is present.

(ii) Proximal or conscious-driven accommodation triggered by knowledge of the distance of the object, without requiring a change in the target size [103,104]. It is considered that voluntary accommodation is a form of proximal accommodation [100], as many individuals can train themselves to deliberately suppress or enhance the normal accommodative response under specific circumstances [105–107].

(iii) Convergence accommodation, driven by fusion disparity vergence, which offers additional cues for accommodation under binocular viewing conditions [108].

(iv) Tonic accommodation, the slightly myopic refractive state of around 1.00 D, to which the system reverts in the absence of an adequate accommodative stimulus [109–113], which has also described as empty-field myopia [114,115], dark focus [116,117] or dark accommodation [118]. A closely related phenomenon is that of instrument myopia, the alternation in focus when viewing a target within or through a measurement system [99,109,119]. These observations lead to the concept that this slightly myopic refractive state, also known as the resting state of response, forms the equilibrium level between parasympathetic and sympathetic innervations to the system [118]. As mentioned previously, this could imply that innervation of the parasympathetic system results in changes in accommodation from this level to view near targets, while innervation of the sympathetic system results in accommodative changes to view distant targets. However, it is more widely believed that sympathetic innervation acts relatively slowly and inhibits existing parasympathetic activity. Thus, its major role may be in the maintenance of sustained responses, rapid response changes being governed by changes in the excitatory parasympathetic activity [120].

Different individuals may use different cues, and they may switch to use other signals in conditions when the cue that they normally use is absent [121]. For example, experiments on monocular accommodation show that although chromatic aberration is useful [122], participants soon learn to use other cues as alternatives, such as small amounts of uncorrected astigmatism or higher order aberrations [122–124]. In real-world situations, binocularity provides disparity cues, while a variety of proximity and other perceptual cues become available [121]. In addition, it has been shown in studies of monocular accommodation that some participants fail to accommodate at all to changes in real space vergence stimuli, despite having clinically normal values of accommodation [124,125]. This suggests that accommodation may demand a voluntary input, and the lack of any true involuntary reflex accommodation.

5. Amplitude of accommodation

Subjective amplitude of accommodation (AoA) is a measure of the maximal focusing range of the eye, the dioptric difference between the far point (optical infinity for emmetropes or fully corrected ametropes) and the near point where an object (usually an optotype) is focused clearly, and there is no noticeable image blur; in other words it is the maximum potential dioptric increase in optical power that an eye can achieve in adjusting its focus. In young eyes, it is usually interpreted as an index of maximum accommodation effort, which declines progressively with age [126,127]. Subjective AoA tend to exceed the corresponding objectively-measured amplitudes (range of the actual accommodative response or change in power of the eye), due mostly to the inclusion of ocular depth of focus (DoF; see section 6.1) [128–132]. This effect is most pronounced beyond the age of 45–50 years, when age-associated pupillary miosis increases DoF [112,133]. The few longitudinal studies of objective accommodative response suggest that, for any individual presbyope, objective amplitudes fall almost linearly with age

to reach zero at about the age of 50–55 years [127,128,134,135].

Since real-world activities are usually performed binocularly, normal proximity cues are expected to allow more natural convergence [104,108]. This is confirmed in Fig. 2, [126], which show that the average difference between binocular vs. monocular conditions is about 0.6 D to 0.7 D for ages up to 18 years, 0.5 D for ages between 18 and 30 years, and 0.4 D for ages between 30 and 50 years. The higher difference in young eyes is possibly due to extra convergence-driven accommodation, when stimuli vergence is quite high. This is not so evident in older eyes, since the target is only clear to about half a meter and there is little convergence demand. Increased demand in convergence may also result in further pupil constriction and a corresponding increased DoF [136].

5.1. Clinical measurements of AoA

Various subjective techniques have been developed to assess AoA. They are not comparable [137–139] and the protocol followed can influence the results, so they need to be carefully conducted (see BCLA CLEAR Presbyopia: Evaluation and diagnosis report [140].

6. Accuracy of the steady-state accommodative response

While AoA is of obvious clinical importance, it gives only partial information on the overall static characteristics of the accommodation system [128,130]. These are more fully illustrated by accommodation response/stimulus curves, which involve measurements of accommodation performance over its full dioptric range, rather than just at the near and far points. Since the accommodative control system generates a signal to minimise retinal image blur [78,121], it would be expected that optimal accommodative performance, resulting in an in-focus retinal image, would automatically be achieved for the full range of distances within the objective AoA. However, the response/stimulus curves typically show steady-state errors in focus (for a review, see [141]), such that the response exceeds the stimulus magnitude for far objects (*accommodative lead*) and is too small for near objects (*accommodative*

lag) [120,142,143]. When the mean steady-state response is plotted as a function of accommodative demand, then a quasi-linear response/stimulus curve is recorded (Fig. 3).

This response/stimulus curve can be divided into four different regions, summarised as: 1) initial non-linear zone characterised by a lead of accommodation (higher accommodative response than stimulus) primarily influenced by tonic accommodation 2) linear manifest zone characterised by a lag of accommodation with response lower, but proportional to the accommodative stimulus and with the slope decreasing with age; 3) soft saturation zone characterised by increasingly smaller changes in accommodative response (increase lag) for progressively greater increases of accommodative stimulus and 4) hard saturation zone that is non-linear and characterised by an accommodative response no longer capable to follow the accommodative stimulus (considered as the limit of AoA) [144,145]. Although the magnitude of the lag of accommodation can be as high as 2.00 D at high stimulus vergences, this error in focus, may not lead to noticeable subjective image blur, since it is within the individual's DoF tolerance [146,147]. This observation also explains the lower levels of the objective AoA compared to the subjective measurement [128–130,132].

Fig. 3 also depicts that the response/stimulus slope varies substantially between individuals of the same age, and is affected by inherent ocular characteristics, such as higher order aberrations (for example spherical aberration [120,148,150]) and pupil size [135,151], and the nature of the stimulus (its contrast, form [such as a letter compared to a Grating], spatial size and colour) [141]. All of these factors are known to influence ocular DoF. Accuracy of accommodative response is also increased with binocular viewing [152]. Increased accommodative lead is associated with small reductions in visual acuity in young adults viewing letters at optical infinity [153]. Likewise, higher levels of accommodative lag lead to small reductions in visual acuity for a 4.00D stimulus.

Active accommodation is less effective at low lighting levels since it depends on cone activity [115,154]. It has been shown that the errors in accommodative response become progressively higher as luminance is decreased, such that the response/stimulus curve becomes flatter; when
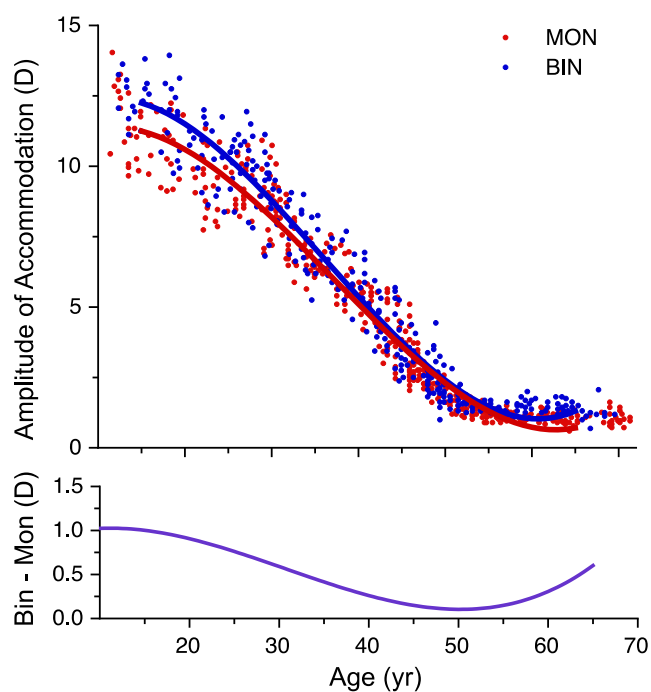
Fig. 2. Comparison of binocular (BIN, blue dots) and monocular (MON, red dots) amplitudes of accommodation (upper) and their difference (lower) as a function of age (replotted data from Duane et al 1922 [126]).
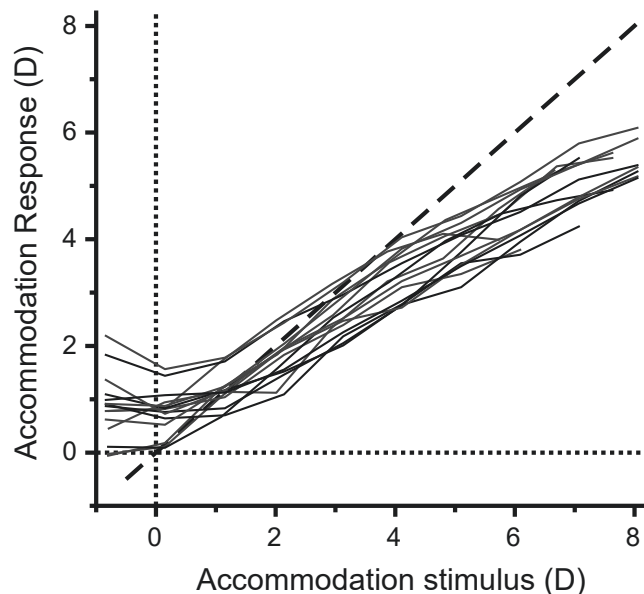
Fig. 3. Accommodation response/stimulus curve from thirteen young participants (age range: 23 to 33 years) under constant photopic conditions. The dashed line represents the ideal one-to-one relationship. Accommodation was measured monocularly using a wavefront analyzer (COAS, Wavefront Sciences Ltd) in conjunction with a purpose-built Badal optometer. Analysis was performed for natural pupils. Note, the high inter-subject variability (data adopted from Plainis et al., 2005 and Plainis et al., 2009) [120,148,149].

only the rods are active, the accommodative system ceases to function [154].

The changes in AoA with age are accompanied by changes in the extent and form of the static response/stimulus curve [128,155]. Fig. 4 presents response/stimulus curves and the associated errors of focus for the same individual at different ages [134]. Here, the slope of the linear portion of the accommodation response/stimulus curve diminishes with age, to reach zero at an age around 50 years [112,155]. Such behaviour appears to result from the ageing accommodation system adapting its characteristics to make optimal use of the available objective AoA, in the form of the effective range of crystalline lens change, pupil diameter miosis [133,156] and DoF, to ensure the retinal image is of satisfactory (rather than perfect) image quality over as large a range of stimulus vergence as possible.

Pupil diameter decreases with accommodative demand (near miosis) and its decrease continues up to the age of 50 years, when true accommodation has declined to near zero, suggesting the existence of a reserve of ciliary effort [135,157,158]. Pupil constriction at near has the advantage of decreasing out-of-focus retinal image blur [129] and improving visual acuity in the presence of accommodation errors in focus [159]. Ocular spherical aberration may also play a role [120,150,156]. Thus, it is thought that the retinal image blur associated with the larger lags of accommodation found at higher stimulus levels is reduced by pupillary constriction and the resultant lower levels of spherical aberration [135].

6.1. Depth of focus (DoF)

As already alluded to, subjective DoF in human vision is a complex, multifactorial concept influenced by various parameters such as test-object characteristics, pupil size, spherical aberration, perceptual discrimination, endpoint criteria, binocular summation and age [112,129,131,132,160,161]. This complexity renders its impact on the measurement of the AoA relatively unpredictable. Fundamentally, DoF is the range of an object's vergence at the eye without any objectionable blur being detected by the observer [162]. Blur is a perceptual phenomenon that can be impacted by neurological and perceived tolerance, while retinal defocus is an optical phenomenon whereby there is a

reduction in the retinal-image contrast gradient [132,163]. Nevertheless, a disparity exists between normative AoA values and those obtained with reduced DoF effects, highlighting the potential for DoF to inflate AoA measurements. Standardisation of AoA measurement methodologies that consider DoF, and its influencing factors could enhance the reliability and comparability of results across studies (see BCLA CLEAR Presbyopia: Evaluation and diagnosis report) [140]. This understanding is vital for accurate clinical refraction and would inform future research into improving refractive error measurements and treatments.

Refractive error impacts DoF because spectacle correction increases the accommodative stimulus for hyperopia compared with emmetropia and myopia [164]. The literature on the critical evaluation or application of this principle in routine clinical work is sparse. Therefore, it is crucial to develop novel methods for AoA measurement that effectively eliminate DoF while being suitable for routine clinical use.

6.2. Pupil diameter

Regulating pupil size is challenging in a clinical setting, as it is highly susceptible to swift alterations due to an array of factors such as ageing [165], the process of accommodation itself [166], and cognitive effort [167].

Accommodation is typically coupled with a reduction in pupil size (miosis) and binocular convergence. Importantly, since the constriction of the pupil diminishes the extent of the blurred image, accommodative miosis is crucial for maintaining satisfactory retinal image quality. This pupillary response also allows for an accommodative response less than the accommodative stimulus [168,169]. Studies have examined age-related changes in accommodative miosis [156].The outcomes of studies on accommodative miosis appear to be inconsistent, contingent on whether the studies were monocular or binocular. On average, the alteration in pupil diameter during accommodation was notably less in infants and children compared to adults and was also significantly less in monocular compared to binocular observations [156]. Accommodative miosis influences the subjective accommodation response by modifying the depth of field and can also impact the objective response through alterations in higher-order aberrations [150]. Pupil miosis also impacts the eye's aberrations, with lower aberration seen with smaller pupil size.
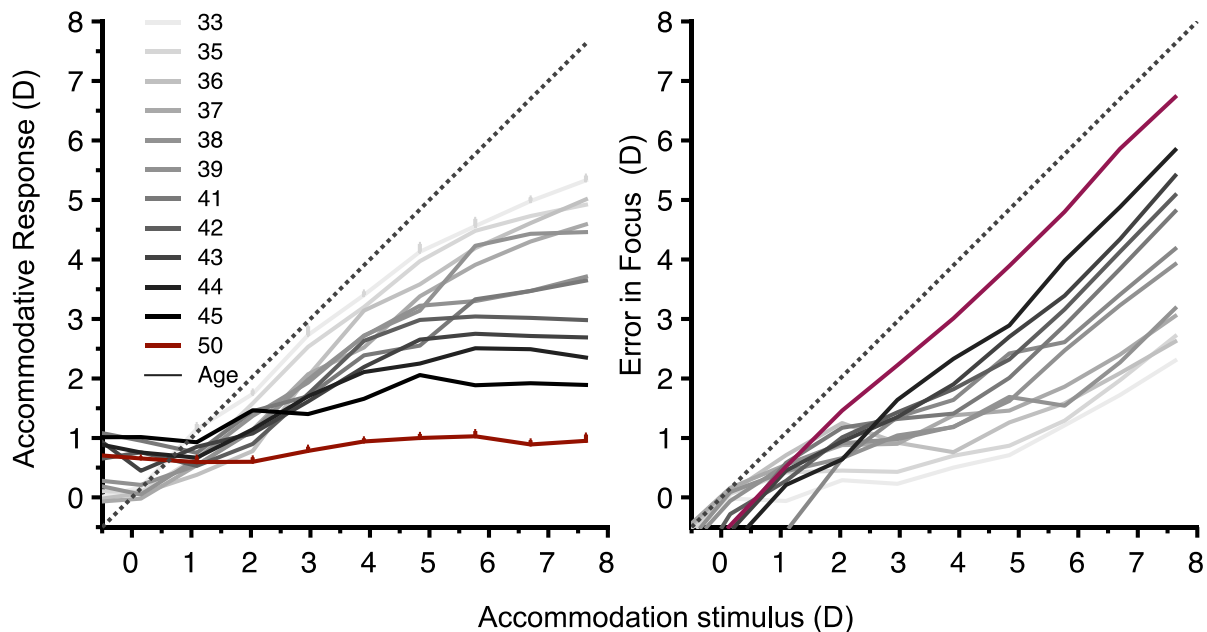
Fig. 4. Age-related changes in accommodative response (left) and errors in focus (right) as a function of stimulus vergence under photopic conditions for a single subject. Accommodation was measured using a wavefront analyzer (COAS, Wavefront Sciences Ltd) in conjunction with a purpose-built Badal optometer, Analysis was performed for a pupil diameter of 3.5 mm [135].

However, these ocular aberrations affect the measure of the eye's objective refractive state, and subsequently the measured accommodative response.

6.3. Spherical aberration

Primary spherical aberration is a refractive error where light rays entering the eye (or optical system) off-centre are refracted more or less than those entering near the optical axis. The presence of primary spherical aberration with a different sign and amount has an effect on the accommodative accuracy and on the slope of the accommodation response curve; negative values improve its accuracy (reducing the lag of accommodation), enhancing the slope of the curve and increasing the subjective AoA [170], while positive values reduce its accuracy (increasing the lag of accommodation) which depress the slope of the curve [171]. In younger eyes, the process of accommodation results in changes in ocular spherical aberration shifting from positive to negative values reducing the lag of accommodation [120] affecting the eye's measured objective refractive state, and subsequently the measured accommodative response. In eyes of individuals older than 40 years, measures of spherical aberration are more variable with some eyes retaining positive spherical aberration, while others even increase in spherical aberration with the reduced AoA available [172]. This different behaviour may be related to changes of the gradients of refractive index within the ageing lens [173].

Meanwhile, other higher-order aberrations are impacted by accommodation and gaze direction. Studies have shown that while horizontal gaze changes minimally affect the eye's optics, downward gaze can increase the eye's total optical power [174,175]. This could be due to biomechanical forces and gravity. Accommodation typically affects astigmatism and comatic aberrations and combined with a downward gaze (i.e., reading), can induce changes in other higher order aberrations such as coma, trefoil, tetrafoil, likely due to eyelid forces on the cornea.

6.4. Ethnicity

Research has shown that the AoA varies among different ethnic groups [176], although it is unclear whether this is a function of study methodologies or ethnicity [177]. For example, some studies did not describe the methods used to obtain or derive AoA, while others also did not describe the selection criteria for participants, nor did they provide information on gender distribution.

Some studies have found that the clinical standard for AoA among Chinese participants in Hong Kong was lower compared to age-matched Caucasian participants, while another noted that presbyopia onset occurred at 35 years and absolute presbyopia by 42 years in Southeast Asian participants, significantly lower than the typical onset at 40 years and absolute presbyopia at 51 years for Caucasians [126,178,179]. Again, issues related to measurement technique may be driving these results, but alternative suggestions have also been made. For example, some have suggested environmental factors to be associated with individuals with lower AoA. Specifically, it has been postulated that individuals residing near the equator and exposed to high solar radiation or temperatures may need near-addition lenses sooner [180]. The dynamics of accommodation have been shown to be greater in those individuals who have been protected from ultraviolet radiation, regardless of global location [181]. However, this result is not consistently found in similar environments, so environmental factors might not explain the observations [182]. An alternative hypothesis which has been proposed is based on the differences in pupil sizes between participants, postulating the role of the iris in accommodation, and different working distances associated with varying arm lengths [183]. However, working distance is not always associated with arm length [184,185], confounding the interpretation of this issue. Additional factors such as the refractive error distribution and correction accuracy are likely important, whereby variations exist even within the same ethnicities [186].

6.5. Direction of gaze

The Hess-Gullstrand theory posits that the AoA should increase in a downward gaze due to gravitational influence on the lens, with this effect being more prominent in older individuals [187]. Early studies investigated the validity of this theory by examining the influence of eye gaze direction and head posture on AoA across two distinct age brackets – 18 to 25 and 35 to 45 years [187]. The study observed minor, yet significant, shifts in near points in the direction of the eye when altering the head position or eye gaze from an upward to a downward orientation, but solely in the younger cohort. The maximum average disparity among test conditions was 1.10 D, compared to a mean accommodation level of 9.80 D in the younger group. Although the changes aligned with the directionality posited in preceding research, they were of significantly lower magnitude. The authors concluded that the variations were sufficiently diminutive to negate the necessity for special attention to head position and eye gaze during clinical appraisals of accommodative amplitude [187].

Given the neural connectivity between the accommodative system and vergence system, and the interplay between them, it should be anticipated that the accommodative function will exhibit variation in multiple gaze positions, notably in the vertical direction. Another study found significant differences in near point of convergence across gaze positions and significant disparities in the AoA between upward, downward, and primary gazes, but not between temporal, nasal, and primary gazes; however, no substantial variations were observed in monocular accommodative facility [188]. The findings demonstrate the existence of variations in convergence and accommodation reflex functions in different gaze positions, with more pronounced changes in the convergence system [188].

6.6. Binocular vision

AoA is larger with binocular vision compared with the monocular condition. These differences, induced by the contribution of convergence accommodation in binocular conditions, have been measured both subjectively and objectively using a binocular Shack-Hartmann wavefront sensor [189,190]. The interaction between the accommodation and vergence systems affects the accommodative response, inducing changes from measurements done in monocular and binocular vision conditions. For example, in exophoric participants, the near accommodative response is higher under binocular compared to monocular visual conditions, while in esophoric participants it was lower [191]. Overall, phoria measurements may impact the near binocular accommodative response [192], with higher levels of vergence accommodation, resulting in differences in lag under monocular and binocular conditions.

7. Stability of the steady-state accommodative response

Under all viewing conditions, the accommodation response is not static. Rather, small oscillations in focus are observed, called micro-fluctuations, having an amplitude of about 0.10 D to 0.50 D [123,193]. Spectrally, they can be classified into a low-frequency component for fluctuations with a frequency between two peaks below 0.6 Hz and in high-frequency component for fluctuations with a frequency between 1 to 2.5 Hz. The low-frequency component has been related to neurological control [194] and the high-frequency component has been associated with factors such as heartbeat and arterial pulse [195,196]. Although a significant inter-subject variability is observed, the magnitude of the fluctuations increases in conditions in which perceived contrast is decreased, such as at low luminance or with low or high spatial frequency targets, and as the target approaches the eye [120,197]. The increased level of micro-fluctuations for very near stimuli may result from the increased instability of the lens as the lens zonules relax during accommodation [120]. In addition, under the same

stimulus conditions, micro-fluctuations are slightly reduced in older as compared to younger eyes, perhaps because of reduced elasticity in the lens zonules and/or capsule [198].

It is thought that the low-frequency component of these fluctuations may have a role in helping to maintain the steady-state response, by providing an essential feedback signal, which is used by the accommodation control system [193,199]. Fluctuations of higher magnitude are expected to maintain the system at higher levels of accommodative response when moderate errors in accommodation are typically present, by producing temporal changes in the contrast of the retinal image [120,142,200]. Note, that oscillations in pupil diameter may also contribute to the micro-fluctuations of accommodation, especially for near targets, as pupil noise is increased for small diameters, while independent of the mean accommodation response level [201].

7.1. Time constant and peak velocity

Dynamic monocular accommodation components (latency, time constant, peak velocity/amplitude relationship, and micro-fluctuations) were objectively assessed using an infrared optometer within the linear accommodation region in 30 visually normal human participants aged 21–50 years [202]. The time constant and the peak velocity/amplitude relationship did not change with age. However, latency progressively increased, and micro-fluctuation amplitude and frequency progressively decreased with age. The invariance in the time constant suggests that the gross biomechanical aspects of the lens and related structures in the remaining linear region are relatively unaffected by age. The time constant and peak velocity/amplitude relationship of accommodation did not change with age in visually normal human participants, but latency increased, and micro-fluctuation amplitude and frequency decreased with age. This suggests that while the gross biomechanics of the lens remain relatively unchanged, there are changes in the dynamic components of accommodation with age [202]. Another investigation revealed age-related changes in the dynamics of accommodation and its relaxation in participants aged 14–45 years. Specifically, the latency of accommodation did not change with age, but the latency of its relaxation increased; while the time constant of accommodation increased, and peak velocity decreased with age, no changes were observed in the time constant or peak velocity of its relaxation [203].

7.2. Dynamics of accommodative response to different stimuli

Under normal conditions, the accommodative response must change from far to near or from near to far to adapt to rapid fixation changes or to follow objects during changes of distances. To evaluate these behaviours, sinusoid stimuli (stimuli with dioptric changes sinusoidally with time), pulse stimuli, step stimuli and ramp stimuli have been used [204–207]. Only studies using step and ramp stimuli will be discussed further because they are more commonly used by the accommodative response in the real world. An example of step stimulus is encountered in situations where accommodation response must change abruptly to focus objects at different distances. The induced step accommodative response is composed of two different components: the first is a fast open-loop component associated with large dioptric changes and the second is a refining component using a slower closed-loop retinotopic system. Using step stimuli the reaction time for far to near conditions has been found to be between 226 to 360 ms [208,209], while for near to far conditions it has generally sound to be higher and ranging from 231 ms to 400 ms [209,210].

Compared with reaction time, the response time, or the time necessary to induce and to reach a stable response, was longer (640 ms to 1060 ms for far to near condition and from 560 ms to for near to far condition) [208,211]. If the required response lies within the available accommodation range (in the linear response region) the response time is unaffected by age, up to approximately 40 years of age [212]. Another characteristic of the dynamic of accommodative response measured

using step stimuli is the peak velocity, which is influenced by the dioptric starting point and by the direction of accommodation [213], and in a lesser way, by the AoA [209]. It reduces roughly linearly with age for the far to near condition [158], although no changes were found for the near to far condition [203]. Ramp stimuli are used to evaluate the characteristic of accommodative response to maintain in focus objects moving smoothly with linearly dioptric changes. The velocity of dioptric change influenced the accommodative response; with slow dioptric change velocities the accommodative response follows the stimulus with a ramp behaviour, but when the velocity increases, the accommodative response presents a step behaviour [214].

8. Fatigue and dynamic accommodative response

Accommodative fatigue related to extended near tasks has been examined through subjective and objective [215–217] methods. Early studies mainly used reduced accommodative amplitude as a subjective measure, while recent studies have objectively analysed different parameters of accommodation. For example, a study found a decrease in the area under the accommodative stimulus/response curve after three hours of near work, indicating a reduction in accommodative accuracy [218]. In contrast, other studies did not find significant differences in the accommodative stimulus/response function between symptomatic and asymptomatic individuals [219,220]. Meanwhile, changes in tonic accommodation following repetitive lens flipping tasks have been observed, suggesting fatigue-induced alterations in baseline neural activity to the ciliary muscle [221].

Further research recorded objective accommodative responses in college students with and without near work-related symptoms. They noted increased accommodative lag at higher dioptric levels in symptomatic individuals, which correlated with the severity of symptoms [222]. Others have highlighted that a high-discomfort group exhibited an accommodative lag comparable to the low-discomfort group in the initial phase, but showed a progressive increase thereafter [223]. The accommodative dynamics in visually normal young adults did not show a reduction in peak velocity, implying no fatigue based on this criterion, during repeated accommodative step tracking across a continuous 30-minute period [224]. Finally, using tasks of differing congruency in terms of the accommodative and vergence stimulus demands, one study found no significant differences in the initial response amplitude, peak velocity and time constant of accommodation across tasks; however, 60 % of study participants reported visual fatigue for the non-congruent task, whereby the accommodation and vergence demands were altered. These findings together suggest that fatigue from repetitive accommodative tasks is mainly reflected as an increase in the steady-state accommodative response level and its variability.

9. Changes to the components of the accommodative system with age

9.1. Crystalline lens and capsule

The lens weighs about 65 mg at birth, then grows to 160 mg by age 10 years. After that, the growth is slow, reaching about 250 mg by age 90 [225]. Male lenses are significantly larger than female lenses [226]. Evolution has maintained this never-ending growth process in multiple species [227].

The crystalline lens grows throughout adulthood by adding new shells from cells produced by the anterior epithelium [228]. This produces a continual change in the dimensions of the crystalline lens with age [10]. As the lens ages, equatorial diameter remains invariant [229] whilst its thickness [229–232] increases at a rate of 2–3 μm per year and the lens becomes thicker and rounder [233–235]. The thickening of the lens cortex is approximately 7 times greater than that of the nucleus [173]. While both anterior and posterior cortices increase in thickness, the thickening is 1.5 times greater in the anterior cortex [173]. The

posterior lens pole moved backward by 0.002 mm, and the lens centre moved forward by 0.0025 mm [232]. With age, the number of lens fibres also increases [233]. This age-related thickening of the lens results in a reduction of the anterior chamber depth causing an increase in the effective power of the cornea and lens combination. However, there is no displacement of the crystalline lens, and the distance between the cornea and lens sulcus (centre of the nucleus) remains constant [173].

The anterior and posterior radii of curvature increase with age, with the anterior increase more significant than the posterior [236]. The steepening of the anterior surface of the lens suggests that an increase in the dioptric power should occur as the lens ages, leading to a progressive myopic shift, but this is not necessarily the case [230,237]. Rather, ageing in general seems to produce a hyperopic shift [238–240]. This discrepancy between changes in lens geometry and refractive power with age, also known as the lens-paradox [230], cannot be explained by changes in corneal power, vitreous chamber depth, or axial length as these components are relatively independent of age [28,241–244]. Changes in the refractive index of the crystalline lens are the likely contributing factor [245]. The gradient refractive index of the lens decreases with age [235,246,247], presumably due to an increase in water content and a decrease in protein content of the lens [8]. This age-related change of the lens refractive index gradient leading to the reduction in its optical power likely compensates for the dioptric power increment caused by the age-related increase in the curvature of the anterior lens surface [248].

The maximum refractive index in the lens centre decreases slightly with age, with considerable scatter in the data and age-related variations in sagittal thickness and equatorial height [249]. Varying concentrations of proteins in successive cell layers create a gradient refractive index (GRIN). The refractive index of the young lens is higher centrally and has a low modulus. Eventually, a tipping point is reached when protein aggregation increases light scatter, inevitably leading to the iconic protein condensation-based disease, age-related cataract [250].

The shear modulus at the lens centre increases with age while it remains nearly constant in the cortex [251–253]. It has been proposed that the stiffness increase of the lens with age is mediated through glycation inter-protein crosslinking promoted by chaperone-client complexes of α-crystallin. This happens through the formation of advanced glycation end products [254]. In a study of post-mortem lenses, all capsules were thicker anteriorly, continuously increasing with age at the anterior lens pole [43]. The mid-peripheral zone stabilises or slightly decreases after the seventh decade. The mechanical properties of an empty lens capsule *ex vivo* show constant stretching properties with age [255]. As the lens capsule ages, the mechanical strength of the capsule decreases [37]. As the lens ages, the lens cortex and nucleus increase in stiffness [38]. The young cortex is stiffer than the nucleus, but near the typical clinical presentation of presbyopia, the nucleus becomes stiffer [256]. The shifting of the capsular parts, as well as the zonular insertions with ageing, causes regional variations in the thickness of the capsule. In early adulthood, the capsule is thickest (approximately 19 μm) at the anterior portion of the lens equator, gradually decreasing in thickness to the anterior (approximately 11 μm) and posterior poles (approximately 3 μm) [43]. With age, the capsule increases in thickness throughout the anterior surface as new material is deposited [43]; this causes an anterior shift in the region of the maximal capsular thickness.

In the seventh decade of life, the thickest capsular region is located halfway between the anterior pole and the equator [257]. Contrary to the change in anterior surface capsular thickness, ageing appears to have little effect on the biomechanical properties of the lens capsule [36,257] as well as its thickness at the posterior pole and much of the posterior lens surface [43,257].

The magnitude of astigmatism in the anterior lens surface decreased with age. Posterior surface astigmatism and lens astigmatism were not age dependent. The presence of GRIN did not significantly alter the magnitude or axis of the lens astigmatism [258,259]. Lens power decreases with age [260–262]. The total refractive power and surface refractive power both showed a biphasic age dependency; up to the age of 50 years, younger participants had lower lens power than older participants, but after age 50 years, older participants had lower lens power [263]. The total lens power decreased at a rate of 0.41D/year between ages 6 and 58 years and increased at 0.33D/year between ages 58 and 82 years; this decrease in power is mainly due to a decrease in the GRIN [260].

9.2. Zonules

Young's modulus of the zonules is approximately 350 kPa [253]. Some researchers have stated that zonular structure and elasticity do not change before the age of 45 years, while others have found that the zonules are thinner, fewer, or less elastic with age [14,48].

The human vitreous zonule and lens equator move forward (anteriorly) during accommodation, and their movements reduce with age [264]. With age, there is a forward shift in the zonule insertion point on the lens [14,265]. In early life, zonular fibres are distributed uniformly from the anterior to the posterior side of the lens equator [14]. As the lens ages, zonular fibres shift anteriorly, and the distribution becomes highest on the anterior surface near the equator [14,15]. This trend of zonular redistribution continues throughout life. However, the separation from the zonular attachment to the anterior and posterior poles remains relatively constant, suggesting that zonular redistribution is likely a consequence of changes in the thickness of the lens capsule over the years [43]. Stiffening of the vitreous zonular system may also contribute to age-related loss of accommodation [266]. This shift in insertion, and the changes in lens size and ciliary apex position with age, mean that the angle, and the amount of force applied to the lens, may diminish with increasing age.

9.3. Ciliary body

9.3.1. Ciliary muscle

Changes in the contraction of the ciliary muscle with age were first examined *ex vivo*, where the results indicated that an increase in maximum ciliary muscle contraction up to about 45 years of age and a decrease thereafter [267]. Other studies have demonstrated that ciliary muscle tissue contracts to pharmacological stimulation well beyond the age of presbyopia [60,268]. Impedance cyclography was used in the first published human *in vivo* study of ciliary muscle [269], but has since been challenged for measuring blood flow, not necessarily muscle contraction [270]. Magnetic resonance imaging (MRI) provides compelling *in vivo* evidence that the ciliary muscle can contract well beyond the onset of presbyopia [64,271]. More recent, higher resolution MRI studies went on to show that the ciliary body ring diameter remained relatively unchanged with age and confirmed ciliary muscle contraction beyond clinical presbyopia [61]. The ciliary muscle ring diameter decreased only 0.015–0.037 mm/year [20,61,271], were linearly correlation with the accommodative response and remained relatively consistent across age groups beyond presbyopia [61,271]. This suggests that ciliary muscle contractile activity remains throughout life [271]. This result supports the Hess-Gullstrand theory of presbyopia, which proposes that the degree of ciliary muscle contraction for each dioptre of accommodative response remains consistent with ageing and that there is an increasing latent amount of ciliary muscle force with age that does not result in accommodative output.

MRI is the only technique that allows visualization of the entire ciliary body ring; however, measurement of fine changes in the ciliary muscle dimensions are limited by the resolution of even ultra-high MRI. Ultrasound biomicroscopy and optical coherence tomography (OCT) allow cross-sectional imaging of the ciliary body. Ultrasound biomicroscopy has been used to demonstrate a shift in the centre of gravity of the muscle with pharmacological stimulation [272,273]. This movement decreased with age but may be restored after cataract extraction. Anterior segment OCT was used to visualize micron level anterior

thickening and posterior thinning of the ciliary muscle with accommodation [62,274]. With age, the ciliary muscle shortens, and the apex is displaced slightly inward [275]. Histological studies reported that, with age, both the longitudinal and radial portions of the ciliary muscle decrease in size while the circular portion increases [276]. This may be the cause of the decrease in length and inward movement of the apical edge [60]. Therefore, the shape and configuration of the ciliary body in older age may resemble that of the young, accommodated eye.

9.3.2. Ciliary body elasticity

While there is no age-related loss of the contractile response, deterioration of the elastic components of the ciliary body and choroid is known to occur throughout adulthood [277–279]. In the posterior region, the elastic tendons appear to become thicker and to have more microfibrils and collagen fibrils with ageing causing a decrease in elasticity [277]. This deterioration can restrict the forward movement of the ciliary muscle, affecting lens thickening and steepening [58]. The limitation can be partially relieved through enzymatic lysis of the posterior vitreous zonule, resulting in enhanced mobility of the ciliary muscle with accommodation [266].

At the ciliary muscle tips, the sheaths of the elastic-like fibres and the elastic-like tendons thicken with age [280]. On the inside, the spaces between the ciliary muscle bundles decrease with time. It is more visible in the reticular portion facing the anterior chamber. The connective tissue in that region of the ciliary muscle increases significantly by the age of 60 years.

9.3.3. Ciliary stroma and epithelium

The ciliary stroma is located between the muscle and the epithelium of the ciliary body. It is composed of highly vascularised, loose connective tissue that form the core of each ciliary processes. There are multiple age-related changes in the stroma. The stromal layer widens in the ciliary processes and in the ground plate between the ciliary valleys and ciliary muscle [281]. Moreover, there is an increase of collagenous fibre diameter accompanied by a decline in stromal cell density [281]. Other changes include a gradual widening of the perivascular space between capillaries and an increase in number of fenestrations in the capillary endothelium [281]. The ciliary process seems to decrease in length and increase in density with age [282].

Significant changes occur in non-pigmented epithelial cells during the ageing process [280]. These include an increase in the number of mitochondria, more fenestrations in capillary endothelium near the ciliary epithelium and an increased presence of vacuoles containing lipid granules within the cytoplasm [280].

9.4. Choroid

The choroid is a tissue located between the retina and the sclera primarily composed of vascular layers supplying the outer retina. It also contains secretory cells that are probably involved in the modulation of vascularization and in the growth of the sclera [50]. The choroid is composed of the Bruch membrane, the choriocapillaris, the Sattler layer, the Haller layer, the choroidal stroma and the suprachoroidal lamina.

9.4.1. Bruch's membrane

Bruch's membrane is the innermost layer of the choroid composed of an acellular extracellular meshwork separating the retinal pigment epithelium from the choriocapillaris. Bruch's membrane is known to increase in thickness with ageing, following a linear correlation with age [283]. This thickening starts earlier in life in the periphery, followed by a macular thickening at around 45 years old [284]. A reduction in Bruch's membrane elasticity accompanies this thickening [285]. The thickening of Bruch's membrane can lead to an increase in hyalinisation spreading into the choroidal intercapillary pillars with age [286]. It has been proposed that a thickened membrane could mechanically compress the choriocapillaris and cause a decrease in choriocapillaris diameter [287].

9.4.2. Choriocapillaris

The choriocapillaris is a dense network of capillaries, bordered by a layer of fenestrated endothelial cells and supported by connective tissue. It nourishes the outer retina composed of the retinal pigment epithelium and the overlying photoreceptors.

In animal and human models, the choriocapillaris decreases in diameter and density with age [288,289]. Ageing is also associated with a decrease of the perfusion of this tissue, where the reduction is higher in the foveal area compared to the parafoveal and perifoveal regions [290]. This decrease of perfusion is explained by a reduced vascular calibre, not by a reduction in the number of capillaries [289,290].

9.4.3. Choroidal thickness

The choroidal thickness decreases with age [75,291,292], particularly in adults older than 40 years of age, with a greater change in the temporal region [293]. When adjusted for axial length, the negative correlation between the macular choroidal thickness and age increases [294], and remains across different ethnicities [295]. The negative correlation is present in the resting and accommodated state [75]. The subfoveal choroidal thickness change per decade is 14 to 20 μm [291,296–298]. It has been proposed that the relation between the decrease in thickness and age is not linear, with a faster decrease noted between 50 and 70 years old [299–303] for the central foveal, parafoveal and the perifoveal regions [302]. The reduction in choroidal thickness is usually related to a decrease in the density and supply of blood, leading to a weakened ability of the choroid to deliver oxygen and nutrients to the retinal pigment epithelium and retina [304,305]. It has been suggested that the reductions in choroidal blood flow and its adaptive control could be explained by the decline in their neural control and the vessel diameter with ageing [306].

Early work on a cohort of incipient presbyopes considered whether transient axial length changes during accommodation attenuate with age [307]. Based on the hypothesis that ciliary muscle contractility and mobility persists into advanced presbyopia [271,275], 20 participants (aged 34–41 years) were recruited and reviewed at 6-monthly intervals over a 30-month period, during which time a range of biometric measures, including axial length, were taken in response to accommodative stimuli up to 4.50 D. A significant axial length elongation with accommodation was observed, proportional to the magnitude of the accommodative stimulus. The change in ocular biometry per dioptre of accommodation exerted remained invariant between the ages of 18 to 44 years; however, beyond the age of 43 to 44 years, the study revealed negligible axial length changes with a concurrent reduction in data variance, perhaps associated with age-related elasticity changes in the choroid and sclera shown elsewhere [58,308].

9.4.4. Choroidal stroma

The choroidal stroma is a loose collagenous tissue composed of elastic and reticulum fibres. It contains pigment and plasma cells. The collagen fibres increase in thickness with age. The elastic fibres lose their elastin core and appear more electron dense with age [309]. In a thick choroid, the network of bundled collagen is loosely packed and separated by cellular elements and ground substance compared to a thin choroid presenting a much higher density of collagen and elastin [310].

9.4.5. Suprachoroidal lamina

The suprachoroidal lamina is a thin membrane located next to the sclera, composed of condensed collagen fibre, melanocytes, and fibroblasts. It contains components of both the sclera and the choroidal stroma. The elastic-like fibres contained in this layer increase in thickness and in cross-linked microfibers. The thickened sheaths of those elastic fibres can merge to form dense plates of cross-linked fibrillar material [311,312].

9.4.6. Change in choroidal biomechanics with ageing

The choroidal tissue increases in stiffness with age. The stability of the choroid is influenced by two key functional aspects: its sponge-like characteristics, and the elastic counterforce during accommodation [313]. The first aspect is explained by a structurally stable network of collagen fibres and nonvascular smooth muscle cells that maintain consistency with ageing [314,315]. The second aspect is supported by elastic fibres within Bruch's membrane and choroidal stroma, with age-related irreversible changes such as calcification of Bruch's membrane elastic fibres [316]. In addition to tissue stiffening, the accumulation of extracellular debris can affect the choroid. While highly vascularized, there is no dedicated lymphatic drainage in this tissue, leading to the accumulation of debris toward Bruch's membrane causing an increase in thickness [317].

9.4.7. Mechanical reciprocal influence of the choroid and the ciliary body

The ciliary body and the choroid form an elastic network influencing each other. The ciliary muscle contraction pulls the entire choroid and retina forward during the accommodative response, creating tension on the posterior pole [318]. With accommodation, the choroid moves forward at the optic nerve head [75]. As individuals age, the elastic choroidal network becomes stiffer [277]. Although there is a decrease in forward muscle movement, centripetal muscle movement remains intact, and the muscle's contractile force is sustained.

The change in elasticity with age can influence the movement of the ciliary muscle and indirectly the accommodative function. As described in section 9.3.1, the elasticity of the ciliary muscle's posterior attachments is crucial for its mobility, as the muscle's forward and inward movement during contraction pulls the elastic network of the choroid forward [268,276,277,319]. The core dynamics of the accommodative mechanism involve the antero-inward movement of the ciliary muscle during contraction, allowing relaxation of the anterior zonula and subsequent lens rounding in concert with other factors [75]. It can be affected by the change in tissue biomechanics with ageing. Age-related thinning of the choroid may result from alterations in the ciliary muscle/lens complex geometry, since the lens thickens with age due to cellular expansion [75]. This increased tension on the zonular/muscle complex results in the stretching and thinning of the choroid to which it is attached. The close relationship between the thickness of the choroid and the lens, in contrast to accommodative amplitude, is accounted for by the connection between the choroid and lens through the zonular/ciliary muscle complex and potential variations in the lens [75]. Notably, while accommodating, the choroid thinning was significant as the lens thickened. The negative correlation between lens and choroidal thickness is not solely due to age-related co-variation. Instead, a direct relationship can be observed, particularly when the lens thickens during accommodation, thus resulting in an additional thinning of the choroid [75].

9.5. Vitreous

The vitreous body is a highly hydrated viscoelastic extracellular matrix. It contains type II collagen, type IX collagen that coats the type II fibrils, type V/XI collagen, and type VI collagen that bind hyaluronan [320]. The concentration of collagen does not vary significantly with ageing [321]; however, the vitreous humour undergoes a natural and irreversible process known as liquefaction, which decreases its viscosity. Liquefaction is thought to result from enzymatic degradation of proteoglycans, resulting in collagen aggregation. The subsequent retraction of the gel-like vitreous leaves spaces within the vitreous known as lacunae, which become filled with liquid [322]. As the vitreous ages, the volume of collagen becomes smaller, and the space is filled with a liquid from depolarizing acid hyaluronic. This process of gradually separating the vitreous into a collagen gel and liquid phase is called vitreous liquefaction [321,323]. At 45 years of age, nearly 95 % of type IX collagen has degraded, exposing type II collagen to the fibril surface and

predisposing the vitreous collagen fibrils to fusion [324]. The vitreoretinal adhesion is weakened with age at the vitreoretinal interface due to biochemical changes.

During accommodation, the vitreous allows or facilitates a small amount of posterior movement of the posterior pole of the lens and the capsule. This movement declines with age [325]. The vitreous may play a role in accommodation. Specifically, the differential pressure between the aqueous and vitreous humours may promote forward movement of the lens during accommodation [326,327]. While accommodation is associated with a decrease in intraocular pressure, the contribution of the vitreous may be trivial, as accommodation still occurs in patients post-vitrectomy [328].

10. Effect of presbyopia on retinal image quality

During the progression of presbyopia there are several factors which collectively interact to drive the attainable image quality of the eye. Among these are AoA, accommodative gain, pupil diameter and primary spherical aberration. All these factors change with age (Fig. 5), but interact.

Although results differ, generally as age increases, the AoA decreases (on average by 0.30 D per year [126]) (Fig. 5a). Related to the AoA is the accommodative gain (Fig. 5d) [172,329], the ratio of the accommodative response to that of the stimulus.

Together AoA and accommodative gain characterise the accommodative response (Fig. 5b) [330]. A typical 10-year-old young eye (solid green line) has an accommodative response that nearly matches that of the stimulus (approximating the 1:1 line), but with only a slight lag at near target vergences. However, as an eye ages it can no longer accommodate to view the target (e.g., solid red line representing a 55-year-old eye) and becomes presbyopic. Any deviation from the 1:1 (stimulus: response) line, introduces defocus which will decrease image quality with larger deviations decreasing image quality more so than the lower deviations seen with young eyes and small accommodative lags.

Age, light level, accommodation, and target vergence affect the size of the pupil (Fig. 5e) [332] which plays a significant role in the image quality of the eye. Pupil miosis occurs with near viewing. The muscles that control the pupil lose elasticity with ageing, causing pupils to not only remain a smaller size and less reactive to light [133,165], but also remain smaller during accommodation in comparison with younger eyes. For example, a typical 10-year-old eye (Fig. 5e, solid green) has at least a 1 mm larger pupil at distance (approximately 5 mm) compared to a 55-year-old (solid red) in photopic conditions. As target vergence increases, near pupil miosis typically occurs [65,332] expanding the eye's DoF [333]. Notice that the 55-year old's pupil remains smaller than the 10-year-old's pupil at all target vergences; however, pupil constriction is limited to approximately 2 mm [165].

Human eyes inherently have many optical defects, including not only defocus (such as myopia) and astigmatism, but also higher order aberrations. Although higher order aberrations only encompass about 3 to 5 % of the eye's total aberration, these aberrations can be visually detrimental to the optical image, with more total aberration corresponding to more visual detriment [334]. The aberration structure of each eye is unique but averaging across the population (across all ages) most higher order aberrations average to 0 µm with some eyes having slight positive or negative magnitude, with one exception. The average unaccommodated eye has around +0.15 µm of primary spherical aberration over a 6 mm pupil [335]. Both positive and negative primary spherical aberration can negatively impact peak image quality, but are known to expand the DoF [336], so are commonly incorporated into contact [337,338] or intraocular lens [339,340] designs. Primary spherical aberration of the eye, however, changes as a function of age, generally becoming more positive with age as the human lens changes in structure (Fig. 5c) [331,341]. A typical unaccommodated 10-year-old eye (Fig. 5c, solid green line) may have close to 0 µm spherical aberration, whereas an equivalent 55-year-old eye (solid red line) may have closer to 0.25 µm.
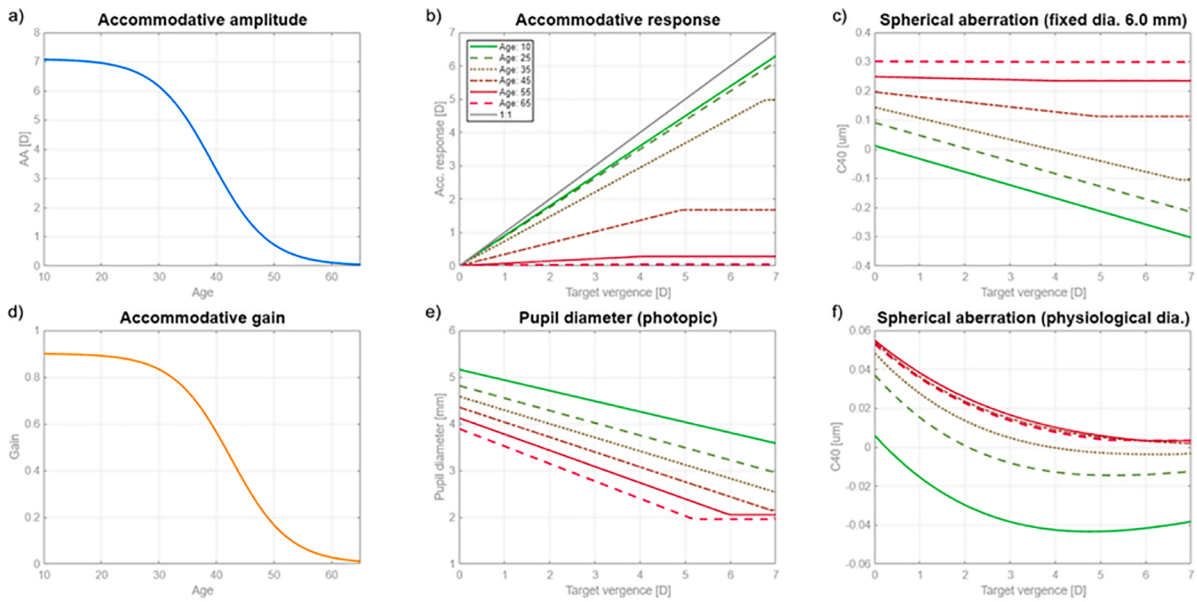
Fig. 5. Summary of several factors which drive image quality as a function of age and target vergence during the emergence of presbyopia. (a) Accommodative amplitude as a function of age [172,329], (b) accommodative response as a function of target vergence for several different ages [330], (c) spherical aberration as a function of target vergence for the same different ages as in (b) for a fixed 6.0 mm pupil diameter [331], (d) accommodative gain as a function of age [329], (e) pupil diameter as a function of target vergence for the same ages as shown in (b)[332], and (f) spherical aberration as a function of target vergence for the same ages as shown in (b) using the physiological pupil diameters shown in (e)[331].

As the 10-year-old eye accommodates (Fig. 5c, solid green line), due to the changing lens shape, the eye gains negative spherical aberration. The 55-year-old eye, which can only minimally accommodate, shows very little change in spherical aberration (Fig. 5c, solid red line). Spherical aberration is also pupil size dependent, so to model what happens to spherical aberration as a function of age, near miosis must also be incorporated (Fig. 5f). Younger eyes always have less spherical aberration, even with larger pupils.

All these factors play an intricate, interrelated role in generating the retinal image of the eye. Through-focus optical modelling systematically demonstrates the impact of each of these factors in isolation and then in combination as occurs clinically. Figs. 6 to 9 each highlight the predicted image quality of three different theoretical eyes (10-year-old in solid green, 35-year-old in dashed dark green, and 65-year-old in dashed red). The normalized mean modulation transfer function (MTF) or image quality at 15 cycles per degree (6/12) is graphed for each theoretical eye
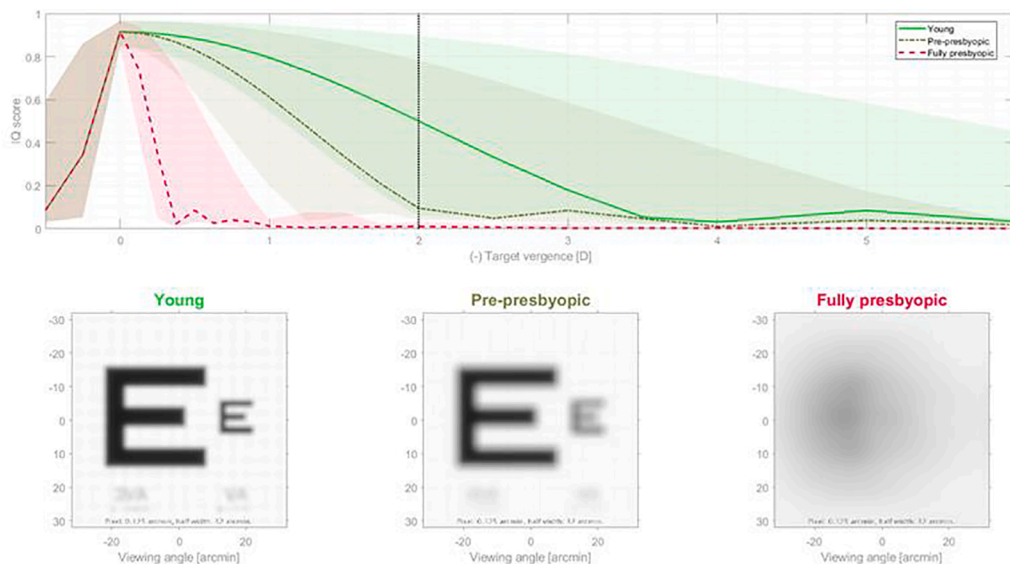
Fig. 6. Top: Through-focus plot with target vergence (D) ranging from 0 (distance) to −6 D (17 cm) on the x-axis and normalized modulation transfer function (MTF) image quality on the y-axis shown for three theoretical eyes (10-year-old in solid green, 35-year-old in dashed dark green, and 65-year-old in dashed red). The lines represent the normalized mean MTF at 15 cycles per degree (6/12). The semi-transparent regions indicate the mean MTF between 30 (6/6) and 5 cycles/degree (6/60) to provide a representation of image quality across a range of target sizes. Bottom: The predicted simulated 6/12 (small) and 6/60 (large) letter image quality for the same young (left), pre-presbyopic (middle), and fully presbyopic (right) eyes when viewing at 50 cm. Data simulated are for age-appropriate aberration-free eyes with their age-appropriate accommodative response, and assuming a 4.5 mm pupil size which remains constant across target vergence (e.g., no near miosis with accommodation).

L.N. Davies et al.
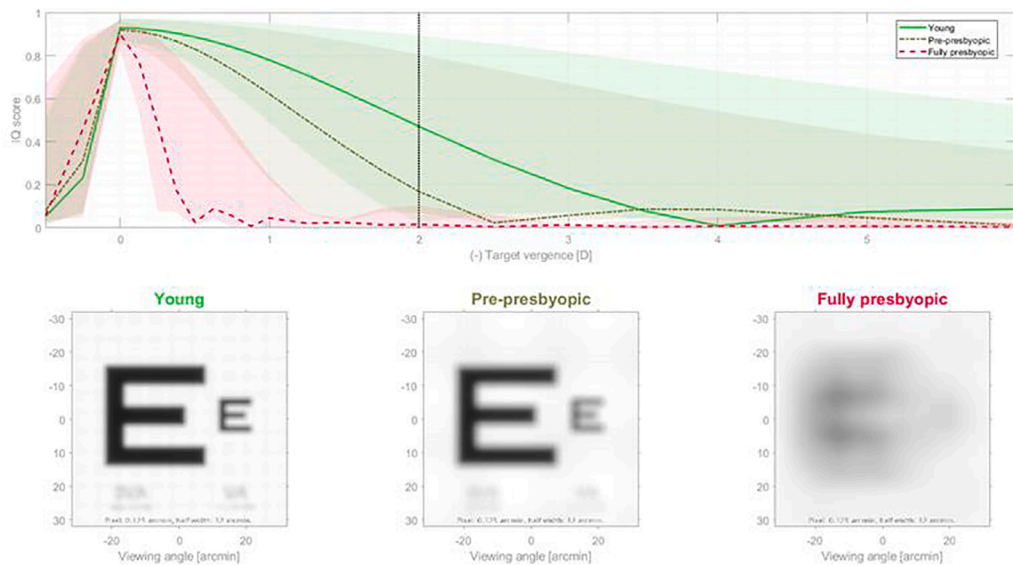
Fig. 7. As shown in Fig. 6, data now represent simulated results of eyes of three different ages, with age-appropriate accommodation, no aberration, now with a pupil size and near miosis appropriate to their age (e.g., no longer fixed at 4.5 mm).
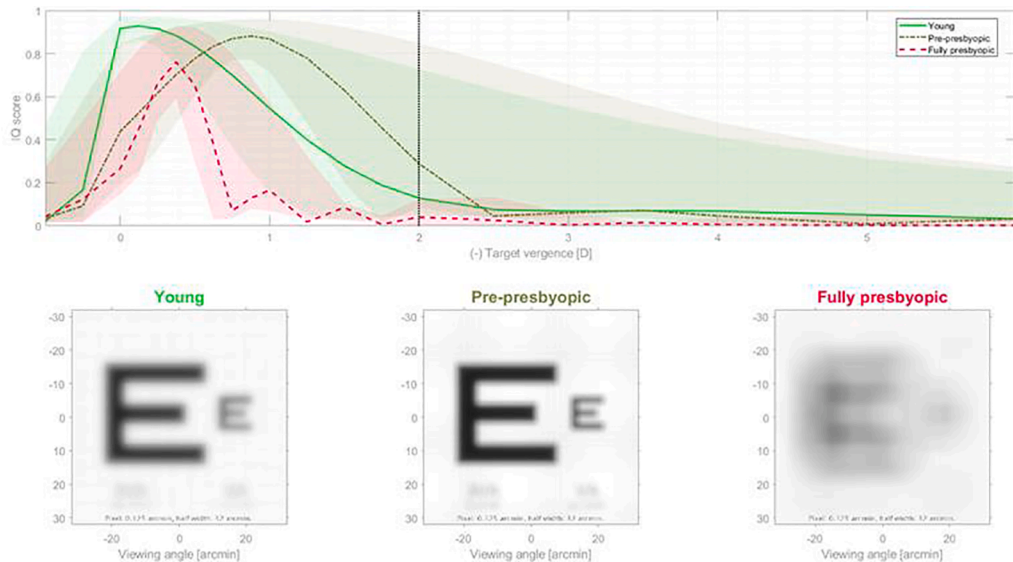
Fig. 8. As shown in Fig. 7, data now represent simulated results of eyes of three different ages, with age-appropriate accommodation, age-appropriate pupil size and pupil miosis, with the addition of age-appropriate primary spherical aberration.

across target vergences ranging from 0 (corresponding to distant viewing) to −6 D (approximately 17 cm focal demand). This type of through-focus approach is commonly used [342] and allows comparison of individuals or optical devices.

Using this graphical approach, Fig. 6 demonstrates the impact of accommodative response on the three theoretical eyes. The accommodative response incorporates both the age-appropriate amplitude (Fig. 5a) and gain (Fig. 5d) of accommodation. To allow comparison across the three eyes with differing accommodative responses, pupil diameter (4.5 mm) and spherical aberration (0 μm) are assumed constant. All eyes exhibit similar image quality at distance (0 D) which decreases with closer viewing distances. As expected, the young eye (solid green line) has little decrease in image quality until very close target vergences, corresponding to an easily distinguishable simulated retinal image (lower left). Alternatively, the fully presbyopic eye (dashed red line) has an immediate drop-off in image quality at only 0.50 D target vergence, and correspondingly the simulated retinal image

is not distinguishable (lower right). The pre-presbyopic eye falls in the middle, with sufficient accommodative response to provide only a somewhat degraded simulate retinal image. It is apparent that decreasing accommodative response leads to the expected decreased image quality at near target vergences, in the absence of the pupil miosis and spherical aberration which typically occur clinically.

Fig. 7 shows the same three eyes with the accommodative responses as shown in Fig. 6, but now with age-appropriate pupil miosis. In all three participants, relative to when no pupil miosis was included there is slight increase in image quality with closer target vergences due to the reduced aberration and increase in DoF a smaller pupil provides. However, only a slight improvement in image quality is attained relative to that shown in Fig. 6. This is largely due to the 4.5 mm pupil size chosen in Fig. 6, as it roughly approximates the average pupil diameter of the eyes modelled.

As highlighted above, spherical aberration also typically changes as a function of accommodation and pupil size. Fig. 8 includes the age-
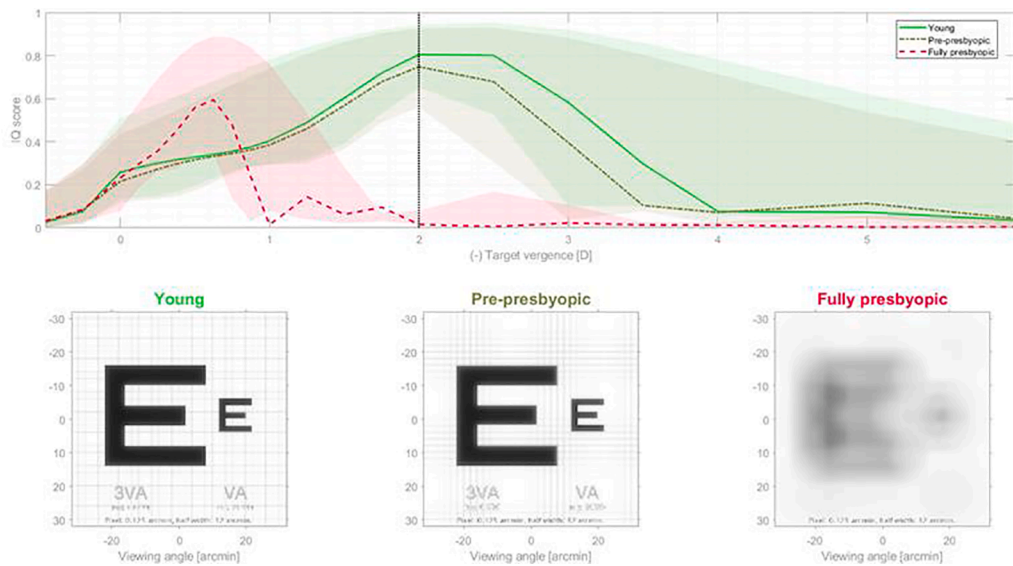
Fig. 9. As shown in Fig. 8, data now represent simulated results of eyes of three different ages, with age-appropriate accommodation, age-appropriate pupil size and pupil miosis, age-appropriate primary spherical aberration, with the addition of pupil size scaled 0.2 μm of primary spherical aberration.

appropriate spherical aberration magnitude and change toward negative spherical aberration with accommodation along with the age-appropriate accommodative response and pupil size change shown in Fig. 7. The age-appropriate positive spherical aberration helps expand the DoF, but does so at the expense of peak image quality. This result is more noticeable on the young eye modelled with a lag of accommodation.

Common presbyopic corrections often utilise spherical aberration to extend the DoF for the wearer. Fig. 9 builds on the analysis presented in Fig. 8, but assumes an additional a pupil-size scaled (from 6 mm) + 0.2 μm of primary spherical aberration added to the eyes shown in Fig. 8. This is a level of primary spherical aberration which may occur from a distance centre multifocal lens. Due to the presence of large amounts of eye and lens primary spherical aberration, there are some reductions in the potential image quality of far objects in all eyes. However, at near, all eyes benefit from the increased primary spherical aberration. At 2D target vergence, there is high quality near vision in the young and pre-presbyopic eyes, and the targets are more, yet not fully, resolvable in the fully-presbyopic individual.

The above sequential analysis at a simplistic level briefly highlights the complex, dynamic situation experienced by all presbyopic eyes both in static and dynamic conditions. Decreased pupil and increased primary spherical aberration can both expand the DoF of an eye with limited accommodative response. However, the situation is more complex in absolute presbyopic eyes with no accommodative reserve. Primary spherical aberration expands the DoF, but at a consequence of reducing peak image quality. This, however, is the current state of many presbyopic designs, providing insight for potential future optimizations leading to enhanced image quality.

11. Presbyopia theories

One longitudinal study of the presbyopic process [307] was conducted on twenty adults aged 34 to 41 years, which were examined every six months for 2.5 years using ocular biometry and measurement of the accommodative responses to various stimuli. The change in anterior chamber depth, crystalline lens thickness and axial length per dioptre of accommodation exerted remained invariant after 2.5 years, consistent with previous cross-sectional studies [343]. Furthermore, the increase in non-accommodated crystalline lens thickness with age was not significantly associated with the reduction in accommodative response, leading to the conclusion that an increase in lenticular stiffness

and not changes in lenticular geometry alone are responsible for the onset of presbyopia.

One characteristic of the proponents of the various geometric theories of presbyopia is their assertion that no other factors play a role, for example, claiming that age-related mechanical changes in the lens material are a consequence, not a cause, of presbyopia [344]. In contrast, others in the field are willing to entertain that several factors may play a role. For example, with ageing, alterations in the geometric alignment between the ciliary muscle and the lens might hasten the decrease in accommodative ability associated with the advancement of presbyopia. This occurs despite the fact that the underlying cause may be lens stiffening [20].

11.1. Lenticular theories

The facility of the crystalline lens to change shape is central to the mechanics of accommodation. It therefore seems obvious to suspect any ageing changes which may alter lens shape, size or structure, or inhibit its pliability, as potential factors in presbyopia development.

One apparent candidate could therefore be the lens capsule, given its role in transmitting zonular force to the lens matter [43] and that its flexibility is known to reduce with age [345]. Nonetheless, lens stretching experiments [255] demonstrated that the age-related changes in capsular elasticity and thickness do not appear to significantly impact its performance.

Senescent stiffening of the crystalline lens itself is a more likely origin, due to lens-fibre sclerosis [346,347] and proliferation in protein cross-linking [348–350]. The increasing rigidity and thickness of the lens means it becomes more resistant to imposed stretching forces with age [267] and more impervious to the moulding forces of the capsule [255,351].

Indeed, presbyopia theories with lenticular bases have evolved to become the most widely accepted. Of these are two classical stances: Hess–Gullstrand presbyopia and Duane–Fincham presbyopia, the key difference being the purported behaviour of the ciliary muscle's contraction and its resulting ability to manipulate lens shape. Each theory has been supported with experimental findings, however, neither is accepted as a definitive explanation.

11.1.1. Hess–Gullstrand model of presbyopia

This model, from works of the 1900s [347,352] is an extension of Helmholtzian accommodation theory and postulates that the ciliary

muscle is not a key factor in presbyopia development as it maintains its contractile strength with age (such that it produces the same contraction force relative to the accommodative stimulus). However, an increasing proportion of this contraction becomes latent: that is, incapable of causing lens shape change [99,202,270,347,352] as a direct result of the lens becoming increasingly inelastic [271].

This theory is supported by contemporary, *in vivo* cross-sectional studies of human eyes using OCT and/or MRI which have found that the anterior [62] and centripetal [61,62,64,271] contractile response of the ciliary muscle is maintained despite the structural changes it undergoes with age [61,62,64,271,344,353]. Although a slight reduction in contractile ability of the ciliary muscle has been observed in early presbyopes, a considerable contraction is still evident in eyes with advanced, established presbyopia where there is no accommodative response [271].

Interesting observations have also arisen from studies of pseudophakic eyes, where ciliary muscle movements resemble those of young pre-presbyopic eyes [273,344]. Additionally, constriction of the ciliary muscle ring diameter is evident during accommodation despite lens exchange, with no significant differences compared to the fellow, phakic eye [64].

Biometric responses of other ocular structures during accommodation have also provided clues. Despite there being significant biometric changes observed in non-accommodating eyes as they age, a longitudinal study of incipient presbyopes found that changes in biometry per dioptre of accommodation exerted did not vary with age [307]. Key amongst these biometric parameters is the transient increase in axial length observed with accommodation, as it is thought to be a structural corollary of ciliary muscle contraction [68–71,354–357]. The invariance with age further supports the notion that lenticular stiffness is likely to be the main factor responsible for the onset of presbyopia, rather than ciliary muscle attenuation [307]. Similarly, continued pupil miosis (an element of the near-vision triad) has been observed when accommodative demand exceeds a patient's maximum AoA [270,358]. This again seems to indicate that the contractile response of the ciliary muscle may continue despite it becoming less capable of instigating changes in crystalline lens shape in advanced presbyopia [270].

11.2. Extra-lenticular theories of presbyopia

The extra-lenticular theories of presbyopia assign the loss of accommodation to parts of the accommodative system other than the crystalline lens. These theories [270] include (a) the ciliary muscle weakened with age [126], and (b) presbyopia is a result of a change in elasticity of the zonules [14] or choroid [359].

11.2.1. Duane–Fincham model of presbyopia
In the 1920s, an alternative theory of presbyopia was produced which, in stark contrast to Hess-Gullstrand, placed the responsibility for presbyopia largely on the ciliary muscle [360,361]. This rooted from observations that older eyes, where the ciliary muscle had been pharmacologically weakened with atropine, showed a much more rapid reduction in maximum AoA [361,362]. This was marked as evidence of a depleted reserve of ciliary muscle contraction at the limit of accommodation in older eyes and therefore a clear sign that it must weaken with age [361]. Indeed, this finding does seem to contradict the Hess-Gullstrand model, given that by the very nature of a latent region there should be a degree of muscle weakening possible without the infliction of corresponding lens shape changes [271].

A modified theory has been offered which proposed that Duane's findings could be justified as in accordance with an essentially Hess–Gullstrandian lenticular mechanism if the latent portion of the ciliary muscle does eventually atrophy due to reduced use [363]. In this scenario muscle weakness remains collateral to, rather than a contributor to lens immobility [270]. Critically, however, this explanation seems contradicted by *ex vivo* experiments that demonstrate that the

ciliary muscle does not attain its maximum force of contraction until the age of 45 years and then declines slowly thereafter [267].

By 1937, a more complex explanation was proposed, reasoning that lenticular and capsular ageing changes are ultimately responsible for presbyopia, but the ciliary muscle contractile strength required to achieve a unit change in accommodation increases throughout life [351]. This works on the assumption that greater capsular pressure, which is needed to mould a more resistant, older lens, can only be achieved by a further release of tension on the capsule [351].

Despite the two concepts discussed fundamentally contradicting each other with regards to whether the lens or the muscle is the origin of presbyopia, what stands in common is the same expected relationship between ciliary muscle contraction and accommodative response. Both postulate a degree of lens response from contraction, and both state the accommodative response is always achieved via the maximum muscle effort, with maximal contraction at the near point of accommodation [270,271]. However, the fact that monocular push-up AoA is generally lower than binocular responses [360,361,364,365] would suggest that the ciliary muscle does not fulfil its potential for contraction when viewing a near target, monocularly. Nonetheless, it has been suggested [270], that the superior binocular response may merely be collateral to a convergence/miosis linked increase in DoF.

Experimental study of accommodative convergence: accommodation (AC/A) ratio was hoped to help elucidate the true mechanism given that the Hess-Gullstrand and Duane-Fincham models should show different characteristics. If Hess–Gullstrand theory applies, the accommodative responses of the manifest region should be unaffected owing to normal accommodative motor processes [270]. The reverse should be true of the latent region as responsiveness is negligible, and the AC/A stimulus ratio should be very large [270]. However, investigations in presbyopic eyes have provided mixed data [366–369], though few studies [370,371] have provided convincing evidence that the response AC/A ratio increases by roughly a tenth of a prism dioptre a year between 30 and 45 years of age, which is suggestive that the ciliary muscle effort required to produce a unit change in accommodation increases with age and most consistent with the Hess–Gullstrand model [270]. These study designs do not account for age-related changes in tonic accommodation and vergence, therefore their use for directly inferring ciliary muscle performance is unclear [112,128,270,370,372–374].

11.3. Geometric theories of presbyopia

The crystalline lens continues to grow throughout life. The primary change is an increase in axial thickness, at a rate of around 0.02 mm per year [29], and a steepening of the anterior radius of curvature [22]. Posterior radius of curvature [20,61] and equatorial diameter are unchanged [61], although authors have reported a small increase in the latter [20]. Furthermore, the increase in lens thickness results in a forward shift in the anterior surface with little or no change in the position of the posterior surface. The axial thickening alone might be expected to play a role in that a thicker elastic band requires more force to stretch it than a thinner band.

The zonules insert into both the anterior and posterior surfaces of the capsule and these insertion points become further apart with age, resulting in the zonular fibres becoming more divergent. Subsequent studies showed that the distance between the lens zonular insertion and the equator increases [14,15], while the distance between the insertion ring and the ciliary body remains relatively constant. These changes are accompanied by a decrease in the circumlental space and are most pronounced in the fifth decade of life [14].

11.3.1. Geometric theory of presbyopia
The development of presbyopia was partially attributed to the change in the geometry of the lens suspensory apparatus and the change the lens curvature [14]. Subsequently, it was proposed that these changes were largely, if not solely, responsible for presbyopia [375].

Their geometric theory of presbyopia proposed that the shift in zonular insertion, associated with crystalline lens thickening with age, changes their angle of insertion such that they apply tension more parallel to the lens capsule, thereby reducing their effectiveness. Consequently, the relaxation of the zonular tension will have a diminishing impact on crystalline lens shape with age and ultimately an immobilisation of ciliary muscle movement.

The theory lost traction based on several observations. First, a scanning laser technique was used to measure focal length of 27 human cadaver lenses (ages 10 to 87 years), while the lenses were subjected to stretching forces applied through the ciliary body-zonular complex [376]. Younger lenses underwent significant changes in focal length with stretching, whereas lenses older than 60 years of age showed no such changes. Thus, no amount of extension or relaxation of the zonule caused a change in power of the older lenses. The authors concluded that changes in zonular insertion angle are unlikely to cause presbyopia [376].

Second, the theory was originally supported by observations in rhesus monkey eyes, where ciliary muscle excursion reduces to zero with age [319], but subsequent studies in humans have shown that ciliary muscle contraction is largely unaffected by age. MRI was used to collect high-resolution images from 25 participants, between 22 and 83 years, while viewing binocular accommodative stimuli of 0.1D and 8D [271]. Muscle contraction was present in all participants and decreased only slightly with age. This result was confirmed in another group of both phakic and pseudophakic individuals [64].

11.3.2. Modified geometric theory of presbyopia

A modified geometric theory was proposed that still attributes presbyopia to a change in the geometric relationship among ocular structures while acknowledging that the ciliary muscle remains capable of contraction [377]. The theory attributes a decrement of zonular tension to thickening and forward movement of the crystalline lens, but considers the influence of the pupillary margin. The anteroposterior movement of the lens causes anterior and inward curvature, and movement of the uvea, with a concomitant reduction in the circumlental space (between the ciliary muscle inner apex and the crystalline lens equator) and thus reduced zonular tension. The observed reduction in the circumlental space in the relaxed eye with age was cited [378], although, ironically, this may be compensated for by the axial movement of the zonular attachments cited in support of the original geometric theory [14,15].

It is unclear whether the asserted reduction in the circumlental space is sufficient to support the modified geometric theory. MRI was first used to measure the human ciliary muscle ring diameter in humans *in vivo*, and an age-related decrease of 0.025 mm per year was found in 40 participants aged 22 to 91 years [64,271]. A higher resolution MRI in 91 adults aged 30–50 years found no statistically significant change in ciliary muscle ring diameter with age [61,229]. The circumlental space can also be impacted by an increase in equatorial lens diameter, but two groups found no change in lens equatorial diameter [61,64,271], while another report reported [20] a slight increase of 0.01 mm per year.

11.3.3. Alternative geometric theory

An alternative geometric theory which is contrary to the widely held Helmholtzian theory, states accommodation is mediated by increased zonular tension which, in turn, causes an increase in lens equatorial diameter and a steepening of the central anterior crystalline lens surface [379]. This theory is opposed to a range of studies that have demonstrated that ciliary muscle diameter decreases during accommodation resulting in reduced zonular tension and a decrease in lens equatorial diameter [20,52,61,64].

In line with the aforementioned geometric theories, it was hypothesised that that presbyopia is a result of normal crystalline lens growth [380,381]. Consistent with the modified geometric theory, this results in a reduction in circumlental space and thus a weakening of zonular

tension rendering them ineffective at imparting the required force to change the shape of the lens.

Based upon this alternative theory, the surgical correction of presbyopia by scleral expansion was devised and championed [380], see BCLA CLEAR Presbyopia: Management with scleral techniques and pharmaceutical therapies report [382], wherein bands are sutured overlying the ciliary muscle to induce a radial outward stretch of the sclera in an attempt to restore zonular tension. Outcome measures were largely based on subjective measures of accommodation and near vision. Evaluation using an objective measure of accommodation in patients who had undergone the procedure found no evidence of objective accommodation [383,384].

Unfortunately, no single theory can fully account for the early onset, almost perfectly linear decline, and complete loss of accommodative function at such a young age. Thus, as suggested, presbyopia is likely to be the additive insult of multiple changes occurring in the human eye with age [385,386]. Nonetheless, the prevailing wisdom is that changes in lenticular elasticity are the dominant cause of presbyopia.

12. Recommendations and future directions

Although great strides have been made in understanding the structure and function of the accommodative system with age, the literature remains fragmented, with researchers focusing on either lenticular or extra-lenticular factors, but failing to provide a comprehensive view of the entire accommodative system with age. The notion that accommodation occurs solely via the lens and ciliary body is an oversimplification of a very intricate system. The lens and ciliary muscle are key players, but the supporting roles of the iris, vitreous, zonules, and choroid should not be ignored. It is certain that there are age-related changes in the entire accommodative system.

The youthful accommodation system allows the eyes to vary their focus to obtain reasonably clear retinal images of objects at different distances. Nevertheless, such focus is rarely exact (lags and leads of accommodation occur), nor is it stable (micro-fluctuations). Accuracy in static accommodation response decreases with age at almost all distances, with the changes being greatest for higher vergences.

The optics of the presbyopic eye and dynamic AoA are complex and multifactorial attributes of the human visual system. Ethnic differences in AoA are acknowledged, although the exact mechanisms remain uncertain, implicating the need for further multi-ethnic population-specific studies. The influence of gaze direction is apparent, yet the practical implications for standard clinical measurements are deemed negligible.

The dynamic nature of the accommodative response is an underexplored domain with evidence pointing towards a myriad of influencing factors including target characteristics, age, task demands, and even fatigue from extensive near work. The understanding of these dynamics is essential for comprehending how the accommodative system maintains clear vision and offers avenues for managing vision-related issues associated with accommodative fatigue. Moreover, studies examining the time constant, peak velocity, and dynamic response of accommodation provide valuable insights into the changes in the accommodative system with age, suggesting a mix of preserved and altered attributes.

In terms of clinical evaluation of AoA, several subjective and objective methodologies exist, each with its strengths and weaknesses. Discrepancies across methods are often observed, emphasizing the need for standardization in measurement techniques and cautious interpretation of results. A reliance on age-expected normative values, although useful, might not capture the full individual or population-specific variability in AoA.

Understanding the various factors influencing accommodation is vital for a comprehensive understanding of the ageing eye, as well as for developing more effective strategies for correcting and better managing age-related vision changes. Future research should continue to delve into the complexities of accommodation dynamics and strive towards enhancing the accuracy and consistency of AoA measurement

techniques.

CRediT authorship contribution statement

Leon N. Davies: Conceptualization, Writing - original draft, Writing - review & editing, validation, project administration. **Sayantan Biswas:** Writing - original draft, Writing - review & editing. **Mark Bullimore:** Conceptualization, Writing - original draft, Writing - review & editing. **Fiona Cruickshank:** Writing - original draft, Writing - review & editing. **Jose J. Estevez:** Writing - original draft, Writing - review & editing. **Safal Khanal:** Writing - original draft, Writing - review & editing. **Pete Kollbaum:** Writing - original draft, Writing - review & editing. **Remy Marcotte-Collard:** Writing - original draft, Writing - review & editing. **Giancarlo Montani:** Writing - original draft, Writing - review & editing. **Sotiris Plainis:** Writing - original draft, Writing - review & editing. **Kathryn Richdale:** Writing - original draft, Writing - review & editing. **Patrick Simard:** Writing - original draft, Writing - review & editing. **James S. Wolffsohn:** Conceptualization, Writing - review & editing, validation, project administration.

Acknowledgement

References

[1] Markoulli M, Fricke T, Arvind A, Frick KD, Garcia-Porta N, Hart KM, et al. BCLA CLEAR Presbyopia: Epidemiology and Impact. Cont Lens Anterior Eye 2024;47 [In press].

[2] Kruger PB, Pola J. Stimuli for accommodation: blur, chromatic aberration and size. Vision Res 1986;26(6):957–71. https://doi.org/10.1016/0042-6989(86)90153-7.

[3] Glasser A. Accommodation: mechanism and measurement. Ophthalmol Clin North Am 2006;19(1):1-12, v. https://doi.org/10.1016/j.ohc.2005.09.004.

[4] Ehrmann K, Ho A, Parel JM. Biomechanical analysis of the accommodative apparatus in primates. Clin Exp Optom 2008;91(3):302–12. https://doi.org/10.1111/j.1444-0938.2008.00247.x.

[5] von Helmholtz H. Mechanism of accommodation. In: Southall JPC, editor Helmholtz's treatise on physiological optics, Vol. 1, Trans. from the 3rd German ed. Rochester, NY, US: Optical Society of America; 1924, p. 143-72. https://doi.org/10.1037/13536-012.

[6] Chen W, Tan X, Chen X. Anatomy and physiology of the crystalline lens. Pediatric Lens Diseases 2017:21–8.

[7] Takemoto L, Sorensen CM. Protein-protein interactions and lens transparency. Exp Eye Res 2008;87(6):496–501. https://doi.org/10.1016/j.exer.2008.08.018.

[8] Donaldson PJ, Chen Y, Petrova RS, Grey AC, Lim JC. Regulation of lens water content: Effects on the physiological optics of the lens. Prog Retin Eye Res 2023; 95:101152. https://doi.org/10.1016/j.preteyeres.2022.101152.

[9] Zinn KM, Mockel-Pohl S. The lens and zonules. Int Ophthalmol Clin 1973;13(3):143–55.

[10] Glasser A, Croft MA, Kaufman PL. Aging of the human crystalline lens and presbyopia. Int Ophthalmol Clin 2001;41(2):1–15. https://doi.org/10.1097/00004397-200104000-00003.

[11] Augusteyn RC. On the growth and internal structure of the human lens. Exp Eye Res 2010;90(6):643–54. https://doi.org/10.1016/j.exer.2010.01.013.

[12] Ruan X, Liu Z, Luo L, Liu Y. The structure of the lens and its associations with the visual quality. BMJ Open Ophthalmology 2020;5(1):e000459.

[13] Bhat SP. The ocular lens epithelium. Biosci Rep 2001;21(4):537–63. https://doi.org/10.1023/a:1017952128502.

[14] Farnsworth PN, Shyne SE. Anterior zonular shifts with age. Exp Eye Res 1979;28 (3):291–7. https://doi.org/10.1016/0014-4835(79)90091-5.

[15] Sakabe I, Oshika T, Lim SJ, Apple DJ. Anterior shift of zonular insertion onto the anterior surface of human crystalline lens with age. Ophthalmology 1998;105(2):295–9. https://doi.org/10.1016/s0161-6420(98)93172-4.

[16] Fincham E. The changes in the form of the crystalline lens in accommodation. Trans Opt Soc 1925;26(5):239.

[17] Garner LF, Yap MK. Changes in ocular dimensions and refraction with accommodation. Ophthalmic Physiol Opt 1997;17(1):12–7.

[18] Sheppard AL, Evans CJ, Singh KD, Wolffsohn JS, Dunne MC, Davies LN. Three-dimensional magnetic resonance imaging of the phakic crystalline lens during accommodation. Invest Ophthalmol Vis Sci 2011;52(6):3689–97. https://doi.org/10.1167/iovs.10-6805.

[19] Koretz JF, Bertasso AM, Neider MW, True-Gabelt BA, Kaufman PL. Slit-lamp studies of the rhesus monkey eye: II. Changes in crystalline lens shape, thickness and position during accommodation and aging. Exp Eye Res 1987;45(2):317–26. https://doi.org/10.1016/s0014-4835(87)80153-7.

[20] Kasthurirangan S, Markwell EL, Atchison DA, Pope JM. MRI study of the changes in crystalline lens shape with accommodation and aging in humans. J vis 2011;11 (3). https://doi.org/10.1167/11.3.19.

[21] Gambra E, Ortiz S, Perez-Merino P, Gora M, Wojtkowski M, Marcos S. Static and dynamic crystalline lens accommodation evaluated using quantitative 3-D OCT. Biomed Opt Express 2013;4(9):1595–609. https://doi.org/10.1364/boe.4.001595.

[22] Dubbelman M, Van der Heijde GL, Weeber HA. Change in shape of the aging human crystalline lens with accommodation. Vision Res 2005;45(1):117–32. https://doi.org/10.1016/j.visres.2004.07.032.

[23] Rosales P, Wendt M, Marcos S, Glasser A. Changes in crystalline lens radii of curvature and lens tilt and decentration during dynamic accommodation in rhesus monkeys. J Vis 2008;8(1):18.1-2. https://doi.org/10.1167/8.1.18.

[24] Weeber HA, van der Heijde RG. Internal deformation of the human crystalline lens during accommodation. Acta Ophthalmol 2008;86(6):642–7. https://doi.org/10.1111/j.1600-0420.2007.01116.x.

[25] Xiang Y, Fu T, Xu Q, Chen W, Chen Z, Guo J, et al. Quantitative analysis of internal components of the human crystalline lens during accommodation in adults. Sci Rep 2021;11(1):6688. https://doi.org/10.1038/s41598-021-86007-6.

[26] Garner LF, Smith G. Changes in equivalent and gradient refractive index of the crystalline lens with accommodation. Optom vis Sci 1997;74(2):114–9. https://doi.org/10.1097/00006324-199702000-00024.

[27] Maceo BM, Manns F, Borja D, Nankivil D, Uhlhorn S, Arrieta E, et al. Contribution of the crystalline lens gradient refractive index to the accommodation amplitude in non-human primates: in vitro studies. J vis 2011;11(13):23. https://doi.org/10.1167/11.13.23.

[28] Koretz JF, Kaufman PL, Neider MW, Goeckner PA. Accommodation and presbyopia in the human eye–aging of the anterior segment. Vision Res 1989;29 (12):1685–92. https://doi.org/10.1016/0042-6989(89)90150-8.

[29] Richdale K, Bullimore MA, Zadnik K. Lens thickness with age and accommodation by optical coherence tomography. Ophthalmic Physiol Opt 2008;28(5):441–7. https://doi.org/10.1111/j.1475-1313.2008.00594.x.

[30] Gibson GA, Cruickshank FE, Wolffsohn JS, Davies LN. Optical coherence tomography reveals sigmoidal crystalline lens changes during accommodation. Vision (Basel, Switzerland) 2018;2(3). https://doi.org/10.3390/vision2030033.

[31] Kaluzny BJ. Anterior movement of the crystalline lens in the process of accommodation in children. Eur J Ophthalmol 2007;17(4):515–20. https://doi.org/10.1177/112067210701700406.

[32] Davies LN, Dunne MC, Gibson GA, Wolffsohn JS. Vergence analysis reveals the influence of axial distances on accommodation with age and axial ametropia. Ophthalmic Physiol Opt 2010;30(4):371–8. https://doi.org/10.1111/j.1475-1313.2010.00749.x.

[33] Marussich L, Manns F, Nankivil D, Maceo Heilman B, Yao Y, Arrieta-Quintero E, et al. Measurement of crystalline lens volume during accommodation in a lens stretcher. Invest Ophthalmol Vis Sci 2015;56(8):4239–48. https://doi.org/10.1167/iovs.15-17050.

[34] Martinez-Enriquez E, Pérez-Merino P, Velasco-Ocana M, Marcos S. OCT-based full crystalline lens shape change during accommodation in vivo. Biomed Opt Express 2017;8(2):918–33. https://doi.org/10.1364/boe.8.000918.

[35] Fisher RF. Elastic constants of the human lens capsule. J Physiol 1969;201(1):1–19. https://doi.org/10.1113/jphysiol.1969.sp008739.

[36] Krag S, Olsen T, Andreassen TT. Biomechanical characteristics of the human anterior lens capsule in relation to age. Invest Ophthalmol Vis Sci 1997;38(2):357–63.

[37] Krag S, Andreassen TT. Mechanical properties of the human lens capsule. Prog Retin Eye Res 2003;22(6):749–67. https://doi.org/10.1016/s1350-9462(03)00063-6.

[38] Danysh BP, Duncan MK. The lens capsule. Exp Eye Res 2009;88(2):151–64. https://doi.org/10.1016/j.exer.2008.08.002.

[39] Hogan MJ, Alvarado JA, Weddell JE. Histology of the human eye: an atlas and textbook. Saunders; 1971, https://books.google.co.uk/books?id=29JqAAAAMAAJ.

[40] Kelley PB, Sado Y, Duncan MK. Collagen IV in the developing lens capsule. Matr Bio: J Inter Soc Matr Bio 2002;21(5):415–23. https://doi.org/10.1016/s0945-053x(02)00014-8.

[41] Fisher RF. The significance of the shape of the lens and capsular energy changes in accommodation. J Physiol 1969;201(1):21–47. https://doi.org/10.1113/jphysiol.1969.sp008740.

[42] Schachar RA, Bax AJ. Mechanism of human accommodation as analyzed by nonlinear finite element analysis. Compr Ther 2001;27(2):122–32. https://doi.org/10.1007/s12019-996-0006-5.

[43] Barraquer RI, Michael R, Abreu R, Lamarca J, Tresserra F. Human lens capsule thickness as a function of age and location along the sagittal lens perimeter. Invest Ophthalmol Vis Sci 2006;47(5):2053–60. https://doi.org/10.1167/iovs.05-1002.

[44] Bornfeld N, Spitznas M, Breipohl W, Bijvank GJ. Scanning electron microscopy of the zonule of Zinn. I. Human eyes. Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie Albrecht von Graefe's archive for clinical and experimental ophthalmology 1974; 192(2): 117-29. https://doi.org/10.1007/bf00410698.

[45] Pan Y, Liu Z, Zhang H. Research progress of lens zonules. Adv Ophthalmol Pract Res 2023;3(2):80–5. https://doi.org/10.1016/j.aopr.2023.02.002.

[46] Farnsworth PN, Mauriello JA, Burke-Gadomski P, Kulyk T, Cinotti AA. Surface ultrastructure of the human lens capsule and zonular attachments. Invest Ophthalmol 1976;15(1):36–40.

[47] Bassnett S. Zinn's zonule. Prog Retin Eye Res 2021;82:100902. https://doi.org/10.1016/j.preteyeres.2020.100902.

[48] Michael R, Mikielewicz M, Gordillo C, Montenegro GA, Pinilla Cortés L, Barraquer RI. Elastic properties of human lens zonules as a function of age in presbyopes. Invest Ophthalmol Vis Sci 2012;53(10):6109–14. https://doi.org/10.1167/iovs.11-8702.

[49] Rohen JW. Scanning electron microscopic studies of the zonular apparatus in human and monkey eyes. Invest Ophthalmol Vis Sci 1979;18(2):133–44.

[50] Nickla DL, Wallman J. The multifunctional choroid. Prog Retin Eye Res 2010;29 (2):144–68. https://doi.org/10.1016/j.preteyeres.2009.12.002.

[51] Michelessi M, Bicket AK, Lindsley K. Cyclodestructive procedures for non-refractory glaucoma. Cochrane Database Syst Rev 2018;4(4):Cd009313. https://doi.org/10.1002/14651858.CD009313.pub2.

[52] Glasser A, Kaufman PL. The mechanism of accommodation in primates. Ophthalmology 1999;106(5):863–72. https://doi.org/10.1016/s0161-6420(99)00502-3.

[53] Costagliola C, dell'Omo R, Agnifili L, Bartollino S, Fea AM, Uva MG, et al. How many aqueous humor outflow pathways are there? Surv Ophthalmol 2020;65(2):144–70. https://doi.org/10.1016/j.survophthal.2019.10.002.

[54] Tamm ER, Lütjen-Drecoll E. Ciliary body. Microsc Res Tech 1996;33(5):390–439. https://doi.org/10.1002/(sici)1097-0029(19960401)33:5<390::Aid-jemt2>3.0. Co;2-s.

[55] Tran TL, Hamann S, Heegaard S. Aquaporins in Eye. Adv Exp Med Biol 2023; 1398:203–9. https://doi.org/10.1007/978-981-19-7415-1_14.

[56] Warjri GB, Senthil S. Imaging of the Ciliary Body: A Major Review. Semin Ophthalmol 2022;37(6):711–23. https://doi.org/10.1080/08820538.2022.2085515.

[57] Wiederholt M, Thieme H, Stumpff F. The regulation of trabecular meshwork and ciliary muscle contractility. Prog Retin Eye Res 2000;19(3):271–95. https://doi.org/10.1016/s1350-9462(99)00015-4.

[58] Croft MA, Lütjen-Drecoll E, Kaufman PL. Age-related posterior ciliary muscle restriction - A link between trabecular meshwork and optic nerve head pathophysiology. Exp Eye Res 2017;158:187–9. https://doi.org/10.1016/j.exer.2016.07.007.

[59] Stahl F, Lepple-Wienhues A, Kuppinger M, Schneider U, Wiederholt M. Measurements of intracellular calcium and contractility in human ciliary muscle. Pflugers Arch 1991;418(6):531–7. https://doi.org/10.1007/bf00370567.

[60] Pardue MT, Sivak JG. Age-related changes in human ciliary muscle. Optom vis Sci 2000;77(4):204–10. https://doi.org/10.1097/00006324-200004000-00013.

[61] Richdale K, Sinnott LT, Bullimore MA, Wassenaar PA, Schmalbrock P, Kao CY, et al. Quantification of age-related and per diopter accommodative changes of the lens and ciliary muscle in the emmetropic human eye. Invest Ophthalmol Vis Sci 2013;54(2):1095–105. https://doi.org/10.1167/iovs.12-10619.

[62] Sheppard AL, Davies LN. In vivo analysis of ciliary muscle morphologic changes with accommodation and axial ametropia. Invest Ophthalmol Vis Sci 2010;51 (12):6882–9. https://doi.org/10.1167/iovs.10-5787.

[63] Wolffsohn JS, Davies LN. Presbyopia: Effectiveness of correction strategies. Prog Retin Eye Res 2019;68:124–43. https://doi.org/10.1016/j.preteyeres.2018.09.004.

[64] Strenk SA, Strenk LM, Guo S. Magnetic resonance imaging of aging, accommodating, phakic, and pseudophakic ciliary muscle diameters. J Cataract Refract Surg 2006;32(11):1792–8. https://doi.org/10.1016/j.jcrs.2006.05.031.

[65] Logan NS, Radhakrishnan H, Cruickshank FE, Allen PM, Bandela PK, Davies LN, et al. IMI Accommodation and Binocular Vision in Myopia Development and Progression. Invest Ophthalmol Vis Sci 2021;62(5):4. https://doi.org/10.1167/iovs.62.5.4.

[66] Zhang Q, Neitz M, Neitz J, Wang RK. Geographic mapping of choroidal thickness in myopic eyes using 1050-nm spectral domain optical coherence tomography. J Innovat Opt Health Sci 2015;8(4):1550012. https://doi.org/10.1142/s1793545815500121.

[67] Hughes RPJ, Read SA, Collins MJ, Vincent SJ. Axial Elongation During Short-Term Accommodation in Myopic and Nonmyopic Children. Invest Ophthalmol Vis Sci 2022;63(3):12. https://doi.org/10.1167/iovs.63.3.12.

[68] Drexler W, Findl O, Schmetterer L, Hitzenberger CK, Fercher AF. Eye elongation during accommodation in humans: differences between emmetropes and myopes. Invest Ophthalmol Vis Sci 1998;39(11):2140–7.

[69] Woodman EC, Read SA, Collins MJ. Axial length and choroidal thickness changes accompanying prolonged accommodation in myopes and emmetropes. Vision Res 2012;72:34–41. https://doi.org/10.1016/j.visres.2012.09.009.

[70] Mallen EA, Kashyap P, Hampson KM. Transient axial length change during the accommodation response in young adults. Invest Ophthalmol Vis Sci 2006;47(3):1251–4. https://doi.org/10.1167/iovs.05-1086.

[71] Read SA, Collins MJ, Woodman EC, Cheong SH. Axial length changes during accommodation in myopes and emmetropes. Optom vis Sci 2010;87(9):656–62. https://doi.org/10.1097/OPX.0b013e3181e87dd3.

[72] Kaphle D, Schmid KL, Suheimat M, Read SA, Atchison DA. Central and peripheral choroidal thickness and eye length changes during accommodation. Ophthalmic Physiol Opt 2023;43(3):311–8. https://doi.org/10.1111/opo.13084.

[73] Ghosh A, Collins MJ, Read SA, Davis BA, Chatterjee P. Axial elongation associated with biomechanical factors during near work. Optom Vis Sci 2014;91(3):322–9. https://doi.org/10.1097/opx.0000000000000166.

[74] Woodman-Pieterse EC, Read SA, Collins MJ, Alonso-Caneiro D. Regional changes in choroidal thickness associated with accommodation. Invest Ophthalmol Vis Sci 2015;56(11):6414–22. https://doi.org/10.1167/iovs.15-17102.

[75] Croft MA, Peterson J, Smith C, Kiland J, Nork TM, McDonald JP, et al. Accommodative movements of the choroid in the optic nerve head region of human eyes, and their relationship to the lens. Exp Eye Res 2022;222:109124. https://doi.org/10.1016/j.exer.2022.109124.

[76] Wu F, Zhao Y, Zhang H. Ocular autonomic nervous system: an update from anatomy to physiological functions. Vision (Basel, Switzerland) 2022;6(1). https://doi.org/10.3390/vision6010006.

[77] McDougal DH, Gamlin PD. Autonomic control of the eye. Compr Physiol 2015;5 (1):439–73. https://doi.org/10.1002/cphy.c140014.

[78] Toates FM. Accommodation function of the human eye. Physiol Rev 1972;52(4):828–63. https://doi.org/10.1152/physrev.1972.52.4.828.

[79] Ooi YH, Oh DJ, Rhee DJ. Analysis of alpha2-adrenergic receptors and effect of brimonidine on matrix metalloproteinases and their inhibitors in human ciliary body. Invest Ophthalmol Vis Sci 2009;50(9):4237–43. https://doi.org/10.1167/iovs.08-2312.

[80] Cogan DG. Accommodation and the autonomic nervous system. Arch Ophthalmol 1937;18(5):739–66. https://doi.org/10.1001/archopht.1937.00850110055004%J Archives of Ophthalmology.

[81] Bullimore MA, Gilmartin B. Tonic accommodation, cognitive demand, and ciliary muscle innervation. Am J Optom Physiol Opt 1987;64(1):45–50. https://doi.org/10.1097/00006324-198701000-00008.

[82] Gilmartin B, Winfield NR. The effect of topical beta-adrenoceptor antagonists on accommodation in emmetropia and myopia. Vision Res 1995;35(9):1305–12. https://doi.org/10.1016/0042-6989(94)00229-f.

[83] Mallen EA, Gilmartin B, Wolffsohn JS. Sympathetic innervation of ciliary muscle and oculomotor function in emmetropic and myopic young adults. Vision Res 2005;45(13):1641–51. https://doi.org/10.1016/j.visres.2004.11.022.

[84] Davies LN, Wolffsohn JS, Gilmartin B. Cognition, ocular accommodation, and cardiovascular function in emmetropes and late-onset myopes. Invest Ophthalmol Vis Sci 2005;46(5):1791–6. https://doi.org/10.1167/iovs.04-0986.

[85] Davies LN, Wolffsohn JS, Gilmartin B. Autonomic correlates of ocular accommodation and cardiovascular function. Ophthalmic Physiol Opt 2009;29 (4):427–35. https://doi.org/10.1111/j.1475-1313.2009.00635.x.

[86] Redondo B, Vera J, Molina R, Davies LN, Jiménez R. Accommodative dynamics and attention: the influence of manipulating attentional capacity on accommodative lag and variability. Ophthalmic Physiol Opt 2020;40(4):510–8. https://doi.org/10.1111/opo.12690.

[87] Ostrin LA, Glasser A. Comparisons between pharmacologically and Edinger-Westphal-stimulated accommodation in rhesus monkeys. Invest Ophthalmol Vis Sci 2005;46(2):609–17. https://doi.org/10.1167/iovs.04-0990.

[88] Törnqvist G. Effect of cervical sympathetic stimulation on accommodation in monkeys. An example of a beta-adrenergic, inhibitory effect. Acta Physiol Scand 1966;67(3):363–72. https://doi.org/10.1111/j.1748-1716.1966.tb03323.x.

[89] Törnqvist G. The relative importance of the parasympathetic and sympathetic nervous systems for accommodation in monkeys. Invest Ophthalmol 1967;6(6):612–7.

[90] Sheppard AL, Wolffsohn JS. Digital eye strain: prevalence, measurement and amelioration. BMJ Open Ophthalmol 2018;3(1):e000146.

[91] Gilmartin B. A review of the role of sympathetic innervation of the ciliary muscle in ocular accommodation. Ophthalmic Phys Opt 1986;6(1):23–37.

[92] Gil DW, Krauss HA, Bogardus AM, WoldeMussie E. Muscarinic receptor subtypes in human iris-ciliary body measured by immunoprecipitation. Invest Ophthalmol Vis Sci 1997;38(7):1434–42.

[93] Wax MB, Molinoff PB. Distribution and properties of beta-adrenergic receptors in human iris-ciliary body. Invest Ophthalmol Vis Sci 1987;28(3):420–30.

[94] Zetterström C, Hahnenberger R. Pharmacological characterization of human ciliary muscle adrenoceptors in vitro. Exp Eye Res 1988;46(3):421–30. https://doi.org/10.1016/s0014-4835(88)80030-7.

[95] Elena PP, Denis P, Kosina-Boix M, Saraux H, Lapalus P. Beta adrenergic binding sites in the human eye: an autoradiographic study. J Ocul Pharmacol 1990;6(2):143–9. https://doi.org/10.1089/jop.1990.6.143.

[96] Culhane HM, Winn B, Gilmartin B. Human dynamic closed-loop accommodation augmented by sympathetic inhibition. Invest Ophthalmol Vis Sci 1999;40(6):1137–43.

[97] Gilmartin B. Sustained near-vision augments inhibitory sympathetic innervation of the ciliary muscle. Clin Vision 1987;1:197–208.

[98] Vasudevan B, Ciuffreda KJ, Gilmartin B. Sympathetic inhibition of accommodation after sustained nearwork in subjects with myopia and emmetropia. Invest Ophthalmol Vis Sci 2009;50(1):114–20. https://doi.org/10.1167/iovs.08-1762.

[99] Charman WN. The eye in focus: accommodation and presbyopia. Clin Exp Optom 2008;91(3):207–25. https://doi.org/10.1111/j.1444-0938.2008.00256.x.

[100] Heath GG. Components of accommodation. Am J Optom Arch Am Acad Optom 1956;33(11):569–79. https://doi.org/10.1097/00006324-195611000-00001.

[101] Phillips S, Stark L. Blur: a sufficient accommodative stimulus. Documenta Ophthalmol Adv Ophthalmol 1977;43(1):65–89. https://doi.org/10.1007/bf01569293.

[102] Sharmin N, Vohnsen B. Monocular accommodation response to random defocus changes induced by a tuneable lens. Vision Res 2019;165:45–53. https://doi.org/10.1016/j.visres.2019.10.002.

[103] Rosenfield M, Gilmartin B. Effect of target proximity on the open-loop accommodative response. Optom Vis Sci 1990;67(2):74–9. https://doi.org/10.1097/00006324-199002000-00002.

[104] Hung GK, Ciuffreda KJ, Rosenfield M. Proximal contribution to a linear static model of accommodation and vergence. Ophthalmic Physiol Opt 1996;16(1): 31–41.

[105] Cornsweet TN, Crane HD. Training the visual accommodation system. Vision Res 1973;13(3):713–5. https://doi.org/10.1016/0042-6989(73)90034-5.

[106] Provine RR, Enoch JM. On voluntary ocular accommodation. Percept Psychophys 1975;17(2):209–12. https://doi.org/10.3758/BF03203888.

[107] Wagner S, Ohlendorf A, Schaeffel F, Wahl S. Reducing the lag of accommodation by auditory biofeedback: A pilot study. Vision Res 2016;129:50–60. https://doi.org/10.1016/j.visres.2016.10.002.

[108] Fincham EF, Walton J. The reciprocal actions of accommodation and convergence. J Physiol 1957;137(3):488–508. https://doi.org/10.1113/jphysiol.1957.sp005829.

[109] Leibowitz HW, Owens DA. New evidence for the intermediate position of relaxed accommodation. Documenta Ophthalmol Adv Ophthalmol 1978;46(1):133–47. https://doi.org/10.1007/bf00174103.

[110] McBrien NA, Millodot M. The relationship between tonic accommodation and refractive error. Invest Ophthalmol Vis Sci 1987;28(6):997–1004.

[111] Rosenfield M, Ciuffreda KJ, Hung GK, Gilmartin B. Tonic accommodation: a review. II. Accommodative adaptation and clinical aspects. Ophthalmic Physiol Opt 1994;14(3):265–77. https://doi.org/10.1111/j.1475-1313.1994.tb00007.x.

[112] Mordi JA, Ciuffreda KJ. Static aspects of accommodation: age and presbyopia. Vision Res 1998;38(11):1643–53. https://doi.org/10.1016/s0042-6989(97) 00336-2.

[113] Liu C, Drew SA, Borsting E, Escobar A, Stark L, Chase C. Tonic accommodation predicts closed-loop accommodation responses. Vision Res 2016;129:25–32. https://doi.org/10.1016/j.visres.2016.08.010.

[114] Otero JM. Influence of the state of accommodation on the visual performance of the human eye. J Opt Soc Am 1951;41(12):942–8. https://doi.org/10.1364/josa.41.000942.

[115] Campbell FW. The minimum quantity of light required to elicit the accommodation reflex in man. J Physiol 1954;123(2):357–66. https://doi.org/10.1113/jphysiol.1954.sp005056.

[116] Leibowitz HW, Owens DA. Night myopia and the intermediate dark focus of accommodation. J Opt Soc Am 1975;65(10):1121–8. https://doi.org/10.1364/josa.65.001121.

[117] Braddick O, Ayling L, Sawyer R, Atkinson J. A photorefractive study of dark focus and refraction. Vision Res 1981;21(12):1761–4. https://doi.org/10.1016/0042-6989(81)90209-1.

[118] Rosenfield M, Ciuffreda KJ, Gilmartin B. Factors influencing accommodative adaptation. Optom vis Sci 1992;69(4):270–5. https://doi.org/10.1097/00006324-199204000-00003.

[119] Rosenfield M, Ciuffreda KJ, Hung GK, Gilmartin B. Tonic accommodation: a review. I Basic Aspects Ophthalmic Physiol Opt 1993;13(3):266–84. https://doi.org/10.1111/j.1475-1313.1993.tb00469.x.

[120] Plainis S, Ginis HS, Pallikaris A. The effect of ocular aberrations on steady-state errors of accommodative response. J vis 2005;5(5):466–77. https://doi.org/10.1167/5.5.7.

[121] Charman WN. Keeping the world in focus: how might this be achieved? Optom vis Sci 2011;88(3):373–6. https://doi.org/10.1097/OPX.0b013e31820b052b.

[122] Wang Y, Kruger PB, Li JS, Lin PL, Stark LR. Accommodation to wavefront vergence and chromatic aberration. Optom vis Sci 2011;88(5):593–600. https://doi.org/10.1097/OPX.0b013e3182112d99.

[123] Campbell FW, Westheimer G. Factors influencing accommodation responses of the human eye. J Opt Soc Am 1959;49(6):568–71. https://doi.org/10.1364/josa.49.000568.

[124] Chen L, Kruger PB, Hofer H, Singer B, Williams DR. Accommodation with higher-order monochromatic aberrations corrected with adaptive optics. J Opt Soc Am A Opt Image Sci Vis 2006;23(1):1–8. https://doi.org/10.1364/josaa.23.000001.

[125] Heron G, Charman WN, Gray LS. Accommodation responses and ageing. Invest Ophthalmol Vis Sci 1999;40(12):2872–83.

[126] Duane A. Studies in Monocular and Binocular Accommodation, with Their Clinical Application. Trans Am Ophthalmol Soc 1922;20:132–57.

[127] Hofstetter HW. A longitudinal study of amplitude changes in presbyopia. Am J Optom Arch Am Acad Optom 1965;42:3–8. https://doi.org/10.1097/00006324-196501000-00002.

[128] Ramsdale C, Charman WN. A longitudinal study of the changes in the static accommodation response. Ophthalmic Physiol Opt 1989;9(3):255–63. https://doi.org/10.1111/j.1475-1313.1989.tb00903.x.

[129] Atchison DA, Charman WN, Woods RL. Subjective depth-of-focus of the eye. Optom Vis Sci 1997;74(7):511–20. https://doi.org/10.1097/00006324-199707000-00019.

[130] Win-Hall DM, Glasser A. Objective accommodation measurements in prepresbyopic eyes using an autorefractor and an aberrometer. J Cataract Refract Surg 2008;34(5):774–84. https://doi.org/10.1016/j.jcrs.2007.12.033.

[131] Burns DH, Allen PM, Edgar DF, Evans BJW. A review of depth of focus in measurement of the amplitude of accommodation. Vision (Basel, Switzerland) 2018;2(3). https://doi.org/10.3390/vision2030037.

[132] Dhallu SK, Sheppard AL, Drew T, Mihashi T, Zapata-Diaz JF, Radhakrishnan H, et al. Factors influencing pseudo-accommodation-the difference between subjectively reported range of clear focus and objectively measured accommodation range. Vision (Basel, Switzerland) 2019;3(3). https://doi.org/10.3390/vision3030034.

[133] Winn B, Whitaker D, Elliott DB, Phillips NJ. Factors affecting light-adapted pupil size in normal human subjects. Invest Ophthalmol Vis Sci 1994;35(3):1132–7.

[134] Hamasaki D, Ong J, Marg E. The amplitude of accommodation in presbyopia. Am J Optom Arch Am Acad Optom 1956;33(1):3–14. https://doi.org/10.1097/00006324-195601000-00002.

[135] Plainis S, Panagopoulou S, Charman WN. Longitudinal changes in objective accommodative response, pupil size and spherical aberration: A case study. Ophthalmic Physiol Opt 2023. https://doi.org/10.1111/opo.13250.

[136] Schäfer WD, Weale RA. The influence of age and retinal illumination on the pupillary near reflex. Vision Res 1970;10(2):179–91. https://doi.org/10.1016/0042-6989(70)90114-8.

[137] Antona B, Barra F, Barrio A, Gonzalez E, Sanchez I. Repeatability intraexaminer and agreement in amplitude of accommodation measurements. Graefes Arch Clin Exp Ophthalmol 2009;247(1):121–7. https://doi.org/10.1007/s00417-008-0938-9.

[138] Momeni-Moghaddam H, Kundart J, Askarizadeh F. Comparing measurement techniques of accommodative amplitudes. Indian J Ophthalmol 2014;62(6): 683–7. https://doi.org/10.4103/0301-4738.126990.

[139] Abu EK, Ocansey S, Yennu J, Asirifi I, Marfo R. Comparing different methods of measuring accommodative amplitude with hofstetter's normative values in a ghanaian population. Curr Eye Res 2018;43(9):1145–50. https://doi.org/10.1080/02713683.2018.1480044.

[140] Wolffsohn JS, Berkow D, Chan KY, Chaurasiya SK, Fadel D, Haddad M, et al. BCLA CLEAR Presbyopia: Evaluation and Diagnosis. Cont Lens Anterior Eye 2024;47 [In press].

[141] Charman W. Optics of the eye. In: Bass M, Enoch I, Lakshminarayanan V, editors. Handbook of Optics: Vision and Vision Optics. New York: McGraw Hill LLC; 2010. p. 1–45. https://books.google.co.uk/books?id=cjXrHLXYKZIC.

[142] Charman WN, Tucker J. Dependence of accommodation response on the spatial frequency spectrum of the observed object. Vision Res 1977;17(1):129–39. https://doi.org/10.1016/0042-6989(77)90211-5.

[143] Seidemann A, Schaeffel F. An evaluation of the lag of accommodation using photorefraction. Vision Res 2003;43(4):419–30. https://doi.org/10.1016/s0042-6989(02)00571-0.

[144] Hung GK, Semmlow JL. Static behavior of accommodation and vergence: computer simulation of an interactive dual-feedback system. IEEE Trans Biomed Eng 1980;27(8):439–47. https://doi.org/10.1109/tbme.1980.326752.

[145] Ciuffreda KJ, Kenyon R. Accommodation Vergence and Accommodation in Normals, Amblyopes and Strabismics. In: Schor CM, Ciuffreda KJ, editors. Vergence Eye Movements: Basic and Clinical Aspects. Boston: Butterworth; 1983. p. 101–73.

[146] Atchison DA, Fisher SW, Pedersen CA, Ridall PG. Noticeable, troublesome and objectionable limits of blur. Vision Res 2005;45(15):1967–74. https://doi.org/10.1016/j.visres.2005.01.022.

[147] Ciuffreda KJ, Selenow A, Wang B, Vasudevan B, Zikos G, Ali SR. "Bothersome blur": a functional unit of blur perception. Vision Res 2006;46(6–7):895–901. https://doi.org/10.1016/j.visres.2005.10.004.

[148] Plainis S, Plevridi E, Pallikaris IG. Comparison of the ocular wavefront aberration between pharmacologically-induced and stimulus-driven accommodation. Ophthalmic Physiol Opt 2009;29(3):272–80. https://doi.org/10.1111/j.1475-1313.2009.00653.x.

[149] Plainis S, Charman WN. Physiology and behaviour of the accommodation system. Thorofare NJ: SLACK; 2012. https://books.google.co.uk/books?id=zuZKYgEACAAJ.

[150] López-Gil N, Fernández-Sánchez V, Legras R, Montés-Micó R, Lara F, Nguyen-Khoa JL. Accommodation-related changes in monochromatic aberrations of the human eye as a function of age. Invest Ophthalmol Vis Sci 2008;49(4):1736–43. https://doi.org/10.1167/iovs.06-0802.

[151] Lara F, Bernal-Molina P, Fernández-Sánchez V, López-Gil N. Changes in the objective amplitude of accommodation with pupil size. Optom Vis Sci 2014;91 (10):1215–20. https://doi.org/10.1097/opx.0000000000000383.

[152] Ibi K. Characteristics of dynamic accommodation responses: comparison between the dominant and non-dominant eyes. Ophthalmic Physiol Opt 1997;17(1): 44–54.

[153] Subbaram MV, Bullimore MA. Visual acuity and the accuracy of the accommodative response. Ophthalmic Physiol Opt 2002;22(4):312–8. https://doi.org/10.1046/j.1475-1313.2002.00037.x.

[154] Johnson CA. Effects of luminance and stimulus distance on accommodation and visual resolution. J Opt Soc Am 1976;66(2):138–42. https://doi.org/10.1364/josa.66.000138.

[155] Kalsi M, Heron G, Charman WN. Changes in the static accommodation response with age. Ophthalmic Physiol Opt 2001;21(1):77–84. https://doi.org/10.1046/j.1475-1313.2001.00546.x.

[156] Radhakrishnan H, Charman WN. Age-related changes in static accommodation and accommodative miosis. Ophthalmic Physiol Opt 2007;27(4):342–52. https://doi.org/10.1111/j.1475-1313.2007.00484.x.

[157] Phillips NJ, Winn B, Gilmartin B. Absence of pupil response to blur-driven accommodation. Vision Res 1992;32(9):1775–9. https://doi.org/10.1016/0042-6989(92)90170-n.

[158] Schaeffel F, Wilhelm H, Zrenner E. Inter-individual variability in the dynamics of natural accommodation in humans: relation to age and refractive errors. J Physiol 1993;461:301–20. https://doi.org/10.1113/jphysiol.1993.sp019515.

[159] Bernal-Molina P, Montés-Micó R, Legras R, López-Gil N. Depth-of-field of the accommodating eye. Optom Vis Sci 2014;91(10):1208–14. https://doi.org/10.1097/opx.0000000000000365.

[160] Benard Y, Lopez-Gil N, Legras R. Subjective depth of field in presence of 4th-order and 6th-order Zernike spherical aberration using adaptive optics technology.

J Cataract Refract Surg 2010;36(12):2129–38. https://doi.org/10.1016/j.jcrs.2010.07.022.

[161] Plainis S, Petratou D, Giannakopoulou T, Atchison DA, Tsilimbaris MK. Binocular summation improves performance to defocus-induced blur. Invest Ophthalmol Vis Sci 2011;52(5):2784–9. https://doi.org/10.1167/iovs.10-6545.

[162] Wang B, Ciuffreda KJ. Depth-of-focus of the human eye: theory and clinical implications. Surv Ophthalmol 2006;51(1):75–85. https://doi.org/10.1016/j.survophthal.2005.11.003.

[163] Alpern M. Variability of accommodation during steady fixation at various levels of illuminance. J Opt Soc Am 1958;48(3):193–7. https://doi.org/10.1364/josa.48.000193.

[164] Rabbetts RB. Bennett & Rabbetts' Clinical Visual Optics. 4th ed. Philadelphia: Elsevier/Butterworth Heinemann; 2007, https://books.google.co.uk/books?id=SyxKPwAACAAJ.

[165] Guillon M, Dumbleton K, Theodoratos P, Gobbe M, Wooley CB, Moody K. The effects of age, refractive status, and luminance on pupil size. Optom vis Sci 2016;93(9):1093–100. https://doi.org/10.1097/opx.0000000000000893.

[166] Yang Y, Huang L, Zhao J, Gu N, Dai Y. Ocular aberration measurement with and without an aperture stop using a Shack-Hartmann wavefront sensor. Appl Opt 2023;62(35):9361–7. https://doi.org/10.1364/ao.505211.

[167] O'Bryan SR, Price MM, Alquist JL, Davis T, Scolari M. Changes in pupil size track self-control failure. Exp Brain Res 2024. https://doi.org/10.1007/s00221-024-06781-3.

[168] Ward PA, Charman WN. Effect of pupil size on steady state accommodation. Vision Res 1985;25(9):1317–26. https://doi.org/10.1016/0042-6989(85)90047-1.

[169] Thibos LN, Bradley A, Lopez-Gil N. Modelling the impact of spherical aberration on accommodation. Ophthalmic Physiol Opt 2013;33(4):482–96. https://doi.org/10.1111/opo.12047.

[170] López-Alcón D, Marín-Franch I, Fernández-Sánchez V, López-Gil N. Optical factors influencing the amplitude of accommodation. Vision Res 2017;141:16–22. https://doi.org/10.1016/j.visres.2016.09.003.

[171] Theagarayan B, Radhakrishnan H, Allen PM, Calver RI, Rae SM, O'Leary DJ. The effect of altering spherical aberration on the static accommodative response. Ophthalmic Physiol Opt 2009;29(1):65–71. https://doi.org/10.1111/j.1475-1313.2008.00610.x.

[172] Radhakrishnan H, Charman WN. Age-related changes in ocular aberrations with accommodation. J vis 2007;7(7):11.1-21. https://doi.org/10.1167/7.7.11.

[173] Dubbelman M, Van der Heijde GL, Weeber HA, Vrensen GF. Changes in the internal structure of the human crystalline lens with age and accommodation. Vision Res 2003;43(22):2363–75. https://doi.org/10.1016/s0042-6989(03)00428-0.

[174] Mathur A, Atchison DA, Kasthurirangan S, Dietz NA, Luong S, Chin SP, et al. The influence of oblique viewing on axial and peripheral refraction for emmetropes and myopes. Ophthalmic Physiol Opt 2009;29(2):155–61. https://doi.org/10.1111/j.1475-1313.2008.00623.x.

[175] Ghosh A, Collins MJ, Read SA, Davis BA, Iskander DR. The influence of downward gaze and accommodation on ocular aberrations over time. J Vis 2011;11(10):17. https://doi.org/10.1167/11.10.17.

[176] Ovenseri-Ogbomo GO, Oduntan OA. Comparison of measured with calculated amplitude of accommodation in Nigerian children aged six to 16 years. Clin Exp Optom 2018;101(4):571–7. https://doi.org/10.1111/cxo.12520.

[177] Majumder C, Afnan H. Amplitude of accommodation among students of a malaysian private university as assessed using subjective and objective techniques. Korean J Ophthalmol 2020;34(3):219–26. https://doi.org/10.3341/kjo.2019.0138.

[178] Ong J. Southeastern Asian refugees' presbyopia. Percept Mot Skills 1981;53(2):667–70. https://doi.org/10.2466/pms.1981.53.2.667.

[179] Edwards MH, Law LF, Lee CM, Leung KM, Lui WO. Clinical norms for amplitude of accommodation in Chinese. Ophthalmic Physiol Opt 1993;13(2):199–204. https://doi.org/10.1111/j.1475-1313.1993.tb00454.x.

[180] Miranda MN. The geographic factor in the onset of presbyopia. Trans Am Ophthalmol Soc 1979;77:603–21.

[181] Wolffsohn JS, Dhallu S, Aujla M, Laughton D, Tempany K, Powell D, et al. International multi-centre study of potential benefits of ultraviolet radiation protection using contact lenses. Cont Lens Anterior Eye 2022;45(6):101593. https://doi.org/10.1016/j.clae.2022.101593.

[182] Vedamurthy I, Lin M, Tong J, Yeh TN, Graham AD, Green H, et al. Does ethnicity influence the short-term adaptation to first reading correction? Optom vis Sci 2012;89(4):435–45. https://doi.org/10.1097/OPX.0b013e318251d2f2.

[183] Weale RA. Chinese and European amplitudes of accommodation. Ophthalmic and Physiological Optics 1993;13(4):431. https://doi.org/10.1111/j.1475-1313.1993.tb00506.x.

[184] Leffler CT, Davenport B, Rentz J, Miller A, Benson W. Clinical predictors of the optimal spectacle correction for comfort performing desktop tasks. Clin Exp Optom 2008;91(6):530–7. https://doi.org/10.1111/j.1444-0938.2008.00288.x.

[185] Soler F, Sánchez-García A, Molina-Martin A, de Fez D, Díaz V, Piñero DP. Differences in visual working and mobile phone usage distance according to the job profile. Curr Eye Res 2021;46(8):1240–6. https://doi.org/10.1080/02713683.2020.1867751.

[186] Raphael J. Accommodational variations in Israel, 1949–1960. Br J Physiol Opt 1961;18:181–5. https://www.ncbi.nlm.nih.gov/pubmed/13739561.

[187] Atchison DA, Claydon CA, Irwin SE. Amplitude of accommodation for different head positions and different directions of eye gaze. Optom Vis Sci 1994;71(5):339–45. https://doi.org/10.1097/00006324-199405000-00006.

[188] Asharlous A, Doostdar A, Ghaemi V, Farzi M, Yekta A, Mortazavi A, et al. Binocular function in different gaze positions. J Ophthalmic Vis Res 2022;17(2):209–16. https://doi.org/10.18502/jovr.v17i2.10792.

[189] Hirota M, Kanda H, Endo T, Morimoto T, Miyoshi T, Fujikado T. Binocular coordination and reading performance during smartphone reading in intermittent exotropia. Clin Ophthalmol 2018;12:2069–78. https://doi.org/10.2147/opth.S177899.

[190] Hirota M, Morimoto T, Kanda H, Endo T, Miyoshi T, Miyagawa S, et al. Objective evaluation of visual fatigue using binocular fusion maintenance. Transl Vis Sci Technol 2018;7(2):9. https://doi.org/10.1167/tvst.7.2.9.

[191] Momeni-Moghaddam H, Goss DA, Sobhani M. Accommodative response under monocular and binocular conditions as a function of phoria in symptomatic and asymptomatic subjects. Clin Exp Optom 2014;97(1):36–42. https://doi.org/10.1111/cxo.12074.

[192] Ong ACH, Cruickshank FE, Sheppard AL, Davies LN. The efficacy of multifocal soft contact lenses for the alleviation of asthenopic symptoms in myopes with accommodative lag. Cont Lens Anterior Eye 2022;45(2):101514. https://doi.org/10.1016/j.clae.2021.101514.

[193] Charman WN, Heron G. Fluctuations in accommodation: a review. Ophthalmic Physiol Opt 1988;8(2):153–64. https://doi.org/10.1111/j.1475-1313.1988.tb01031.x.

[194] Gray LS, Winn B, Gilmartin B. Accommodative microfluctuations and pupil diameter. Vision Res 1993;33(15):2083–90. https://doi.org/10.1016/0042-6989(93)90007-j.

[195] Winn B, Pugh JR, Gilmartin B, Owens H. Arterial pulse modulates steady-state ocular accommodation. Curr Eye Res 1990;9(10):971–5. https://doi.org/10.3109/02713689009069933.

[196] Owens H, Winn B, Gilmartin B, Pugh JR. Effect of a topical beta-adrenergic receptor antagonist on the dynamics of steady-state accommodation. Ophthalmic Physiol Opt 1991;11(2):99–104. https://doi.org/10.1111/j.1475-1313.1991.tb00206.x.

[197] Day M, Gray LS, Seidel D, Strang NC. The relationship between object spatial profile and accommodation microfluctuations in emmetropes and myopes. J Vis 2009;9(10):5.1-13. https://doi.org/10.1167/9.10.5.

[198] Heron G, Schor C. The fluctuations of accommodation and ageing. Ophthalmic Physiol Opt 1995;15(5):445–9.

[199] Walsh G, Charman WN. Visual sensitivity to temporal change in focus and its relevance to the accommodation response. Vision Res 1988;28(11):1207–21. https://doi.org/10.1016/0042-6989(88)90037-5.

[200] Miege C, Denieul P. Mean response and oscillations of accommodation for various stimulus vergences in relation to accommodation feedback control. Ophthalmic Physiol Opt 1988;8(2):165–71. https://doi.org/10.1111/j.1475-1313.1988.tb01032.x.

[201] Stark LR, Atchison DA. Pupil size, mean accommodation response and the fluctuations of accommodation. Ophthalmic Physiol Opt 1997;17(4):316–23.

[202] Mordi JA, Ciuffreda KJ. Dynamic aspects of accommodation: age and presbyopia. Vision Res 2004;44(6):591–601. https://doi.org/10.1016/j.visres.2003.07.014.

[203] Kasthurirangan S, Glasser A. Age related changes in accommodative dynamics in humans. Vision Res 2006;46(8–9):1507–19. https://doi.org/10.1016/j.visres.2005.11.012.

[204] Mathews S, Kruger PB. Spatiotemporal transfer function of human accommodation. Vision Res 1994;34(15):1965–80. https://doi.org/10.1016/0042-6989(94)90026-4.

[205] Kruger PB, Nowbotsing S, Aggarwala KR, Mathews S. Small amounts of chromatic aberration influence dynamic accommodation. Optom vis Sci 1995;72(9):656–66. https://doi.org/10.1097/00006324-199509000-00009.

[206] Heron G, Charman WN. Accommodation as a function of age and the linearity of the response dynamics. Vision Res 2004;44(27):3119–30. https://doi.org/10.1016/j.visres.2004.07.016.

[207] Schor CM, Bharadwaj SR. Pulse-step models of control strategies for dynamic ocular accommodation and disaccommodation. Vision Res 2006;46(1–2):242–58. https://doi.org/10.1016/j.visres.2005.09.030.

[208] Campbell FW, Westheimer G. Dynamics of accommodation responses of the human eye. J Physiol 1960;151(2):285–95. https://doi.org/10.1113/jphysiol.1960.sp006438.

[209] Kasthurirangan S, Glasser A. Characteristics of pupil responses during far-to-near and near-to-far accommodation. Ophthalmic Physiol Opt 2005;25(4):328–39. https://doi.org/10.1111/j.1475-1313.2005.00293.x.

[210] Shirachi D, Liu J, Lee M, Jang J, Wong J, Stark L, et al. Range nonlinearity. Am J Optom Physiol Opt 1978;55(9):631–41. https://doi.org/10.1097/00006324-197809000-00005.

[211] Culhane HM, Winn B. Dynamic accommodation and myopia. Invest Ophthalmol Vis Sci 1999;40(9):1968–74.

[212] Heron G, Charman WN, Schor C. Dynamics of the accommodation response to abrupt changes in target vergence as a function of age. Vision Res 2001;41(4):507–19. https://doi.org/10.1016/s0042-6989(00)00282-0.

[213] Kasthurirangan S, Vilupuru AS, Glasser A. Amplitude dependent accommodative dynamics in humans. Vision Res 2003;43(27):2945–56. https://doi.org/10.1016/j.visres.2003.08.004.

[214] Hung GK, Ciuffreda KJ. Dual-mode behaviour in the human accommodation system. Ophthalmic Physiol Opt 1988;8(3):327–32.

[215] Kajita M, Ono M, Suzuki S, Kato K. Accommodative microfluctuation in asthenopia caused by accommodative spasm. Fukushima J Med Sci 2001;47(1):13–20. https://doi.org/10.5387/fms.47.13.

[216] Wolffsohn JS, Sheppard AL, Vakani S, Davies LN. Accommodative amplitude required for sustained near work. Ophthalmic Physiol Opt 2011;31(5):480–6. https://doi.org/10.1111/j.1475-1313.2011.00847.x.

[217] Kajita M, Muraoka T, Orsborn G. Changes in accommodative micro-fluctuations after wearing contact lenses of different optical designs. Cont Lens Anterior Eye 2020;43(5):493–6. https://doi.org/10.1016/j.clae.2020.03.003.

[218] Takeda T, Ostberg O, Fukui Y, Iida T. Dynamic accommodation measurements for objective assessment of eyestrain and visual fatigue. J Hum Ergol (Tokyo) 1988; 17(1):21–35. https://www.ncbi.nlm.nih.gov/pubmed/3221078.

[219] Ciuffreda KJ, Scheiman M, Ong E, Rosenfield M, Solan HA. Irlen lenses do not improve accommodative accuracy at near. Optom vis Sci 1997;74(5):298–302. https://doi.org/10.1097/00006324-199705000-00026.

[220] Simmers AJ, Gray LS, Wilkins AJ. The influence of tinted lenses upon ocular accommodation. Vision Res 2001;41(9):1229–38. https://doi.org/10.1016/s0042-6989(00)00291-1.

[221] Hasebe S, Graf EW, Schor CM. Fatigue reduces tonic accommodation. Ophthalmic Physiol Opt 2001;21(2):151–60. https://doi.org/10.1046/j.1475-1313.2001.00558.x.

[222] Chase C, Tosha C, Borsting E, Ridder 3rd WH. Visual discomfort and objective measures of static accommodation. Optom vis Sci 2009;86(7):883–9. https://doi.org/10.1097/OPX.0b013e3181ae1b7c.

[223] Tosha C, Borsting E, Ridder 3rd WH, Chase C. Accommodation response and visual discomfort. Ophthalmic Physiol Opt 2009;29(6):625–33. https://doi.org/10.1111/j.1475-1313.2009.00687.x.

[224] Vilupuru AS, Kasthurirangan S, Glasser A. Dynamics of accommodative fatigue in rhesus monkeys and humans. Vision Res 2005;45(2):181–91. https://doi.org/10.1016/j.visres.2004.07.036.

[225] Hejtmancik JF, Shiels A. Overview of the Lens. Prog Mol Biol Transl Sci 2015;134: 119–27. https://doi.org/10.1016/bs.pmbts.2015.04.006.

[226] Mohamed A, Augusteyn RC. Human lens weights with increasing age. Mol vis 2018;24:867. xxx.

[227] Augusteyn RC. Growth of the eye lens: I. Weight accumulation in multiple species. Mol vis 2014;20:410–26.

[228] Augusteyn RC. Growth of the human eye lens. Mol Vis 2007;13:252–7.

[229] Richdale K, Bullimore MA, Sinnott LT, Zadnik K. The effect of age, accommodation, and refractive error on the adult human eye. Optom vis Sci 2016;93(1):3–11. https://doi.org/10.1097/OPX.0000000000000757.

[230] Brown N. The change in lens curvature with age. Exp Eye Res 1974;19(2):175–83. https://doi.org/10.1016/0014-4835(74)90034-7.

[231] Doyle L, Little JA, Saunders KJ. Repeatability of OCT lens thickness measures with age and accommodation. Optom vis Sci 2013;90(12):1396–405. https://doi.org/10.1097/opx.0000000000000080.

[232] Jonas JB, Iribarren R, Nangia V, Sinha A, Pardhi P, Shukla R, et al. Lens position and age: the central India eye and medical study. Invest Ophthalmol Vis Sci 2015; 56(9):5309–14. https://doi.org/10.1167/iovs.15-16796.

[233] Bron AJ, Vrensen GF, Koretz J, Maraini G, Harding JJ. The ageing lens. Ophthalmologica 2000;214(1):86–104. https://doi.org/10.1159/000027475.

[234] Dubbelman M, Van der Heijde GL. The shape of the aging human lens: curvature, equivalent refractive index and the lens paradox. Vision Res 2001;41(14): 1867–77. https://doi.org/10.1016/s0042-6989(01)00057-8.

[235] Kasthurirangan S, Markwell EL, Atchison DA, Pope JM. In vivo study of changes in refractive index distribution in the human crystalline lens with age and accommodation. Invest Ophthalmol Vis Sci 2008;49(6):2531–40. https://doi.org/10.1167/iovs.07-1443.

[236] Mohamed A, Durkee HA, Williams S, Manns F, Ho A, Parel JA, et al. Morphometric analysis of in vitro human crystalline lenses using digital shadow photogrammetry. Exp Eye Res 2021;202:108334. https://doi.org/10.1016/j.exer.2020.108334.

[237] Brown NP, Koretz JF, Bron AJ. The development and maintenance of emmetropia. Eye (Lond) 1999;13(Pt 1):83–92. https://doi.org/10.1038/eye.1999.16.

[238] Fotedar R, Mitchell P, Burlutsky G, Wang JJ. Relationship of 10-year change in refraction to nuclear cataract and axial length findings from an older population. Ophthalmology 2008;115(8). https://doi.org/10.1016/j.ophtha.2007.11.003. 1273-8, 8.e1.

[239] Goldblum D, Brugger A, Haseloff A, Schmickler S. Longitudinal change of refraction over at least 5 years in 15,000 patients. Graefes Arch Clin Exp Ophthalmol 2013;251(5):1431–6. https://doi.org/10.1007/s00417-012-2213-3.

[240] Bomotti S, Lau B, Klein BEK, Lee KE, Klein R, Duggal P, et al. Refraction and Change in Refraction Over a 20-Year Period in the Beaver Dam Eye Study. Invest Ophthalmol Vis Sci 2018;59(11):4518–24. https://doi.org/10.1167/iovs.18-23914.

[241] Ooi CS, Grosvenor T. Mechanisms of emmetropization in the aging eye. Optom Vis Sci 1995;72(2):60–6. https://doi.org/10.1097/00006324-199502000-00004.

[242] Eysteinsson T, Jonasson F, Sasaki H, Arnarsson A, Sverrisson T, Sasaki K, et al. Central corneal thickness, radius of the corneal curvature and intraocular pressure in normal subjects using non-contact techniques: Reykjavik Eye Study. Acta Ophthalmol Scand 2002;80(1):11–5. https://doi.org/10.1034/j.1600-0420.2002.800103.x.

[243] Dubbelman M, Sicam VA, Van der Heijde GL. The shape of the anterior and posterior surface of the aging human cornea. Vision Res 2006;46(6–7):993–1001. https://doi.org/10.1016/j.visres.2005.09.021.

[244] Atchison DA, Markwell EL, Kasthurirangan S, Pope JM, Smith G, Swann PG. Age-related changes in optical and biometric characteristics of emmetropic eyes. J vis 2008;8(4):29.1-0. https://doi.org/10.1167/8.4.29.

[245] Navarro R, López-Gil N. Impact of internal curvature gradient on the power and accommodation of the crystalline lens. Optica 2017;4(3):334–40. https://doi.org/10.1364/OPTICA.4.000334.

[246] Koretz JF, Cook CA. Aging of the optics of the human eye: lens refraction models and principal plane locations. Optom Vis Sci 2001;78(6):396–404. https://doi.org/10.1097/00006324-200106000-00011.

[247] Moffat BA, Atchison DA, Pope JM. Age-related changes in refractive index distribution and power of the human lens as measured by magnetic resonance micro-imaging in vitro. Vision Res 2002;42(13):1683–93. https://doi.org/10.1016/s0042-6989(02)00078-0.

[248] Moffat BA, Atchison DA, Pope JM. Explanation of the lens paradox. Optom Vis Sci 2002;79(3):148–50. https://doi.org/10.1097/00006324-200203000-00008.

[249] Pierscionek B, Bahrami M, Hoshino M, Uesugi K, Regini J, Yagi N. The eye lens: age-related trends and individual variations in refractive index and shape parameters. Oncotarget 2015;6(31):30532–44. https://doi.org/10.18632/oncotarget.5762.

[250] Quinlan RA, Clark JI. Insights into the biochemical and biophysical mechanisms mediating the longevity of the transparent optics of the eye lens. J Biol Chem 2022;298(11):102537. https://doi.org/10.1016/j.jbc.2022.102537.

[251] Weeber HA, Eckert G, Pechhold W, van der Heijde RGL. Stiffness gradient in the crystalline lens. Graefes Arch Clin Exp Ophthalmol 2007;245(9):1357–66. https://doi.org/10.1007/s00417-007-0537-1.

[252] Chai CK, Burd HJ, Wilde GS. Shear modulus measurements on isolated human lens nuclei. Exp Eye Res 2012;103:78–81. https://doi.org/10.1016/j.exer.2012.08.003.

[253] Wang K, Pierscionek BK. Biomechanics of the human lens and accommodative system: Functional relevance to physiological states. Prog Retin Eye Res 2019;71: 114–31. https://doi.org/10.1016/j.preteyeres.2018.11.004.

[254] Nandi SK, Nahomi RB, Rankenberg J, Glomb MA, Nagaraj RH. Glycation-mediated inter-protein cross-linking is promoted by chaperone-client complexes of α-crystallin: Implications for lens aging and presbyopia. J Biol Chem 2020;295 (17):5701–16. https://doi.org/10.1074/jbc.RA120.012604.

[255] Ziebarth NM, Borja D, Arrieta E, Aly M, Manns F, Dortonne I, et al. Role of the lens capsule on the mechanical accommodative response in a lens stretcher. Invest Ophthalmol Vis Sci 2008;49(10):4490–6. https://doi.org/10.1167/iovs.07-1647.

[256] Wilde GS, Burd HJ, Judge SJ. Shear modulus data for the human lens determined from a spinning lens test. Exp Eye Res 2012;97(1):36–48. https://doi.org/10.1016/j.exer.2012.01.011.

[257] Fisher RF, Pettet BE. The postnatal growth of the capsule of the human crystalline lens. J Anat 1972;112(Pt 2):207–14.

[258] Sun M, Birkenfeld J, de Castro A, Ortiz S, Marcos S. OCT 3-D surface topography of isolated human crystalline lenses. Biomed Opt Express 2014;5(10):3547–61. https://doi.org/10.1364/boe.5.003547.

[259] Birkenfeld J, de Castro A, Marcos S. Astigmatism of the ex vivo human lens: surface and gradient refractive index age-dependent contributions. Invest Ophthalmol Vis Sci 2015;56(9):5067–73. https://doi.org/10.1167/iovs.15-16484.

[260] Borja D, Manns F, Ho A, Ziebarth N, Rosen AM, Jain R, et al. Optical power of the isolated human crystalline lens. Invest Ophthalmol Vis Sci 2008;49(6):2541–8. https://doi.org/10.1167/iovs.07-1385.

[261] Jongenelen S, Rozema JJ, Tassignon MJ. Distribution of the crystalline lens power in vivo as a function of age. Invest Ophthalmol Vis Sci 2015;56(12):7029–35. https://doi.org/10.1167/iovs.15-18047.

[262] Mohamed A, Nandyala S, Ho A, Manns F, Parel JA, Augusteyn RC. Relationship of the cornea and globe dimensions to the changes in adult human crystalline lens diameter, thickness and power with age. Exp Eye Res 2021;209:108653. https://doi.org/10.1016/j.exer.2021.108653.

[263] Iribarren R, Morgan IG, Hashemi H, Khabazkhoob M, Emamian MH, Shariati M, et al. Lens power in a population-based cross-sectional sample of adults aged 40 to 64 years in the Shahroud Eye Study. Invest Ophthalmol Vis Sci 2014;55(2): 1031–9. https://doi.org/10.1167/iovs.13-13575.

[264] Croft MA, McDonald JP, Katz A, Lin TL, Lütjen-Drecoll E, Kaufman PL. Extralenticular and lenticular aspects of accommodation and presbyopia in human versus monkey eyes. Invest Ophthalmol Vis Sci 2013;54(7):5035–48. https://doi.org/10.1167/iovs.12-10846.

[265] Croft MA, Glasser A, Heatley G, McDonald J, Ebbert T, Nadkarni NV, et al. The zonula, lens, and circumlental space in the normal iridectomized rhesus monkey eye. Invest Ophthalmol Vis Sci 2006;47(3):1087–95. https://doi.org/10.1167/iovs.04-1524.

[266] Lütjen-Drecoll E, Kaufman PL, Wasielewski R, Ting-Li L, Croft MA. Morphology and accommodative function of the vitreous zonule in human and monkey eyes. Invest Ophthalmol Vis Sci 2010;51(3):1554–64. https://doi.org/10.1167/iovs.09-4008.

[267] Fisher RF. The force of contraction of the human ciliary muscle during accommodation. J Physiol 1977;270(1):51–74. https://doi.org/10.1113/jphysiol.1977.sp011938.

[268] Poyer JF, Kaufman PL, Flugel C. Age does not affect contractile responses of the isolated rhesus monkey ciliary muscle to muscarinic agonists. Curr Eye Res 1993; 12(5):413–22. https://doi.org/10.3109/02713689309024623.

[269] Swegmark G. Studies with impedance cyclography on human ocular accommodation at different ages. Acta Ophthalmol 1969;47(5):1186–206. https://doi.org/10.1111/j.1755-3768.1969.tb02519.x.

[270] Atchison DA. Accommodation and presbyopia. Ophthalmic Physiol Opt 1995;15 (4):255–72. https://www.ncbi.nlm.nih.gov/pubmed/7667018.

[271] Strenk SA, Semmlow JL, Strenk LM, Munoz P, Gronlund-Jacob J, DeMarco JK. Age-related changes in human ciliary muscle and lens: a magnetic resonance imaging study. Invest Ophthalmol Vis Sci 1999;40(6):1162–9.

[272] Stachs O, Martin H, Kirchhoff A, Stave J, Terwee T, Guthoff R. Monitoring accommodative ciliary muscle function using three-dimensional ultrasound. Graefes Arch Clin Exp Ophthalmol 2002;240(11):906–12. https://doi.org/10.1007/s00417-002-0551-2.

[273] Park KA, Yun JH, Kee C. The effect of cataract extraction on the contractility of ciliary muscle. Am J Ophthalmol 2008;146(1):8–14. https://doi.org/10.1016/j.ajo.2008.02.026.

[274] Lossing LA, Sinnott LT, Kao CY, Richdale K, Bailey MD. Measuring changes in ciliary muscle thickness with accommodation in young adults. Optom Vis Sci 2012;89(5):719–26. https://doi.org/10.1097/OPX.0b013e318252cadc.

[275] Sheppard AL, Davies LN. The effect of ageing on in vivo human ciliary muscle morphology and contractility. Invest Ophthalmol Vis Sci 2011;52(3):1809–16. https://doi.org/10.1167/iovs.10-6447.

[276] Tamm S, Tamm E, Rohen JW. Age-related changes of the human ciliary muscle. A quantitative morphometric study. Mech Ageing Dev 1992;62(2):209–21. https://doi.org/10.1016/0047-6374(92)90057-k.

[277] Tamm E, Lütjen-Drecoll E, Jungkunz W, Rohen JW. Posterior attachment of ciliary muscle in young, accommodating old, presbyopic monkeys. Invest Ophthalmol Vis Sci 1991;32(5):1678–92.

[278] Tamm E, Croft MA, Jungkunz W, Lütjen-Drecoll E, Kaufman PL. Age-related loss of ciliary muscle mobility in the rhesus monkey: role of the choroid. Arch Ophthalmol 1992;110(6):871–6. https://doi.org/10.1001/archopht.1992.01080180143043 %J Archives of Ophthalmology.

[279] Wyatt HJ. Application of a simple mechanical model of accommodation to the aging eye. Vision Res 1993;33(5–6):731–8. https://doi.org/10.1016/0042-6989(93)90193-z.

[280] Gabelt BT, Kaufman PL. Changes in aqueous humor dynamics with age and glaucoma. Prog Retin Eye Res 2005;24(5):612–37. https://doi.org/10.1016/j.preteyeres.2004.10.003.

[281] Schlotzer-Schrehardt U, Wirtz PM, Muller HG, Lang GK, Naumann GO. Morphometric analysis of age-dependent changes of the human ciliary body. Fortschr Ophthalmol 1990;87(1):59–68. https://www.ncbi.nlm.nih.gov/pubmed/2323699.

[282] Ren J, Gao X, Chen L, Lin H, Liu Y, Zhou Y, et al. Characteristics of the ciliary body in healthy chinese subjects evaluated by radial and transverse imaging of ultrasound biometric microscopy. J Clin Med 2022;11(13). https://doi.org/10.3390/jcm11133696.

[283] Rymgayłło-Jankowska B, Szczesny P, Zagórski Z. Morphological analysis of age-related changes in the human choroid. Klin Oczna 2002;104(5–6):327–31.

[284] Newsome DA, Huh W, Green WR. Bruch's membrane age-related changes vary by region. Curr Eye Res 1987;6(10):1211–21. https://doi.org/10.3109/02713688709025231.

[285] Okubo A, Rosa Jr RH, Bunce CV, Alexander RA, Fan JT, Bird AC, et al. The relationships of age changes in retinal pigment epithelium and Bruch's membrane. Invest Ophthalmol Vis Sci 1999;40(2):443–9.

[286] Gupta T, Saini N, Arora J, Sahni D. Age-related changes in the chorioretinal junction: an immunohistochemical study. J Histochem Cytochem 2017;65(10):567–77. https://doi.org/10.1369/0022155417726507.

[287] Pauleikhoff D, Chen JC, Chisholm IH, Bird AC. Choroidal perfusion abnormality with age-related Bruch's membrane change. Am J Ophthalmol 1990;109(2):211–7. https://doi.org/10.1016/s0002-9394(14)75989-6.

[288] Klien BA. Regional and aging characteristics of the normal choriocapillaris in flat preparations. Preliminary Remarks Am J Ophthalmol 1966;61(5 Pt 2):1191–7. https://doi.org/10.1016/0002-9394(66)90243-1.

[289] Ramrattan RS, van der Schaft TL, Mooy CM, de Bruijn WC, Mulder PG, de Jong PT. Morphometric analysis of Bruch's membrane, the choriocapillaris, and the choroid in aging. Invest Ophthalmol Vis Sci 1994;35(6):2857–64.

[290] Sacconi R, Borrelli E, Corbelli E, Capone L, Rabiolo A, Carnevali A, et al. Quantitative changes in the ageing choriocapillaris as measured by swept source optical coherence tomography angiography. Br J Ophthalmol 2019;103(9):1320–6. https://doi.org/10.1136/bjophthalmol-2018-313004.

[291] Wakatsuki Y, Shinojima A, Kawamura A, Yuzawa M. Correlation of aging and segmental choroidal thickness measurement using swept source optical coherence tomography in healthy eyes. PLoS One 2015;10(12):e0144156.

[292] Ruiz-Medrano J, Flores-Moreno I, Peña-García P, Montero JA, García-Feijóo J, Duker JS, et al. Analysis of age-related choroidal layers thinning in healthy eyes using swept-source optical coherence tomography. Retina 2017;37(7):1305–13. https://doi.org/10.1097/iae.0000000000001347.

[293] Ruiz-Medrano J, Flores-Moreno I, Peña-García P, Montero JA, Duker JS, Ruiz-Moreno JM. Macular choroidal thickness profile in a healthy population measured by swept-source optical coherence tomography. Invest Ophthalmol Vis Sci 2014;55(6):3532–42. https://doi.org/10.1167/iovs.14-13868.

[294] Hirata M, Tsujikawa A, Matsumoto A, Hangai M, Ooto S, Yamashiro K, et al. Macular choroidal thickness and volume in normal subjects measured by swept-source optical coherence tomography. Invest Ophthalmol Vis Sci 2011;52(8):4971–8. https://doi.org/10.1167/iovs.11-7729.

[295] Bafiq R, Mathew R, Pearce E, Abdel-Hey A, Richardson M, Bailey T, et al. Age, sex, and ethnic variations in inner and outer retinal and choroidal thickness on spectral-domain optical coherence tomography. Am J Ophthalmol 2015;160(5):1034-43.e1. https://doi.org/10.1016/j.ajo.2015.07.027.

[296] Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. Am J Ophthalmol 2009;147(5):811–5. https://doi.org/10.1016/j.ajo.2008.12.008.

[297] Ikuno Y, Kawaguchi K, Nouchi T, Yasuno Y. Choroidal thickness in healthy Japanese subjects. Invest Ophthalmol Vis Sci 2010;51(4):2173–6. https://doi.org/10.1167/iovs.09-4383.

[298] Fujiwara A, Shiragami C, Shirakata Y, Manabe S, Izumibata S, Shiraga F. Enhanced depth imaging spectral-domain optical coherence tomography of subfoveal choroidal thickness in normal Japanese eyes. Jpn J Ophthalmol 2012;56(3):230–5. https://doi.org/10.1007/s10384-012-0128-5.

[299] Ding X, Li J, Zeng J, Ma W, Liu R, Li T, et al. Choroidal thickness in healthy Chinese subjects. Invest Ophthalmol Vis Sci 2011;52(13):9555–60. https://doi.org/10.1167/iovs.11-8076.

[300] Wei WB, Xu L, Jonas JB, Shao L, Du KF, Wang S, et al. Subfoveal choroidal thickness: the Beijing Eye Study. Ophthalmology 2013;120(1):175–80. https://doi.org/10.1016/j.ophtha.2012.07.048.

[301] Park JY, Kim BG, Hwang JH, Kim JS. Choroidal thickness in and outside of vascular arcade in healthy eyes using spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci 2017;58(13):5827–37. https://doi.org/10.1167/iovs.17-22581.

[302] Xie J, Ye L, Chen Q, Shi Y, Hu G, Yin Y, et al. Choroidal thickness and its association with age, axial length, and refractive error in chinese adults. Invest Ophthalmol Vis Sci 2022;63(2):34. https://doi.org/10.1167/iovs.63.2.34.

[303] Liu X, Chen S, Leng H, Wang Y, Liu Y, Shen Y, et al. New findings on choroidal features in healthy people by ultra-widefield swept-source optical coherence tomography angiography. Sci Rep 2023;13(1):9215. https://doi.org/10.1038/s41598-023-36374-z.

[304] Spaide RF. Age-related choroidal atrophy. Am J Ophthalmol 2009;147(5):801–10. https://doi.org/10.1016/j.ajo.2008.12.010.

[305] Abdolrahimzadeh S, Parisi F, Scavella V, Recupero SM. OPtical coherence tomography evidence on the correlation of choroidal thickness and age with vascularized retinal layers in normal eyes. Retina 2016;36(12):2329–38. https://doi.org/10.1097/iae.0000000000001097.

[306] Reiner A, Fitzgerald MEC, Del Mar N, Li C. Neural control of choroidal blood flow. Prog Retin Eye Res 2018;64:96–130. https://doi.org/10.1016/j.preteyeres.2017.12.001.

[307] Laughton DS, Sheppard AL, Davies LN. A longitudinal study of accommodative changes in biometry during incipient presbyopia. Ophthalmic Physiol Opt 2016;36(1):33–42. https://doi.org/10.1111/opo.12242.

[308] Ugarte M, Hussain AA, Marshall J. An experimental study of the elastic properties of the human Bruch's membrane-choroid complex: relevance to ageing. Br J Ophthalmol 2006;90(5):621–6. https://doi.org/10.1136/bjo.2005.086579.

[309] Alm A, Nilsson SF. Uveoscleral outflow–a review. Exp Eye Res 2009;88(4):760–8. https://doi.org/10.1016/j.exer.2008.12.012.

[310] Sohn EH, Khanna A, Tucker BA, Abràmoff MD, Stone EM, Mullins RF. Structural and biochemical analyses of choroidal thickness in human donor eyes. Invest Ophthalmol Vis Sci 2014;55(3):1352–60. https://doi.org/10.1167/iovs.13-13754.

[311] McBrien NA, Gentle A. Role of the sclera in the development and pathological complications of myopia. Prog Retin Eye Res 2003;22(3):307–38. https://doi.org/10.1016/s1350-9462(02)00063-0.

[312] Zhang W, Kaser-Eichberger A, Fan W, Platzl C, Schrödl F, Heindl LM. The structure and function of the human choroid. Annals of anatomy = Anatomischer Anzeiger : official organ of the Anatomische Gesellschaft 2024;254:152239. https://doi.org/10.1016/j.aanat.2024.152239.

[313] May CA. Chronologic versus biologic aging of the human choroid. Scient J 2013;2013:378206. https://doi.org/10.1155/2013/378206.

[314] Poukens V, Glasgow BJ, Demer JL. Nonvascular contractile cells in sclera and choroid of humans and monkeys. Invest Ophthalmol Vis Sci 1998;39(10):1765–74.

[315] May CA. Non-vascular smooth muscle cells in the human choroid: distribution, development and further characterization. J Anat 2005;207(4):381–90. https://doi.org/10.1111/j.1469-7580.2005.00460.x.

[316] Lütjen-Drecoll E. Choroidal innervation in primate eyes. Exp Eye Res 2006;82(3):357–61. https://doi.org/10.1016/j.exer.2005.09.015.

[317] Piguet B, Wells JA, Palmvang IB, Wormald R, Chisholm IH, Bird AC. Age-related Bruch's membrane change: a clinical study of the relative role of heredity and environment. Br J Ophthalmol 1993;77(7):400–3. https://doi.org/10.1136/bjo.77.7.400.

[318] Croft MA, Nork TM, McDonald JP, Katz A, Lütjen-Drecoll E, Kaufman PL. Accommodative movements of the vitreous membrane, choroid, and sclera in young and presbyopic human and nonhuman primate eyes. Invest Ophthalmol Vis Sci 2013;54(7):5049–58. https://doi.org/10.1167/iovs.12-10847.

[319] Lütjen-Drecoll E, Tamm E, Kaufman PL. Age changes in rhesus monkey ciliary muscle: light and electron microscopy. Exp Eye Res 1988;47(6):885–99. https://doi.org/10.1016/0014-4835(88)90070-x.

[320] Bishop PN. Structural macromolecules and supramolecular organisation of the vitreous gel. Prog Retin Eye Res 2000;19(3):323–44. https://doi.org/10.1016/s1350-9462(99)00016-6.

[321] Le Goff MM, Bishop PN. Adult vitreous structure and postnatal changes. Eye 2008;22(10):1214–22. https://doi.org/10.1038/eye.2008.21.

[322] Mishra D, Gade S, Glover K, Sheshala R, Singh TRR. Vitreous Humor: Composition, Characteristics and Implication on Intravitreal Drug Delivery. Curr Eye Res 2023;48(2):208–18. https://doi.org/10.1080/02713683.2022.2119254.

[323] Luo RH, Tram NK, Parekh AM, Puri R, Reilly MA, Swindle-Reilly KE. The roles of vitreous biomechanics in ocular disease, biomolecule transport, and pharmacokinetics. Curr Eye Res 2023;48(2):195–207. https://doi.org/10.1080/02713683.2022.2033271.

[324] Bishop PN, Holmes DF, Kadler KE, McLeod D, Bos KJ. Age-related changes on the surface of vitreous collagen fibrils. Invest Ophthalmol Vis Sci 2004;45(4):1041–6. https://doi.org/10.1167/iovs.03-1017.

[325] Croft MA, Heatley G, McDonald JP, Katz A, Kaufman PL. Accommodative movements of the lens/capsule and the strand that extends between the posterior vitreous zonule insertion zone & the lens equator, in relation to the vitreous face and aging. Ophthalmic Physiol Opt 2016;36(1):21–32. https://doi.org/10.1111/opo.12256.

[326] Coleman DJ. Unified model for accommodative mechanism. Am J Ophthalmol 1970;69(6):1063–79. https://doi.org/10.1016/0002-9394(70)91057-3.

[327] Coleman DJ, Fish SK. Presbyopia, accommodation, and the mature catenary. Ophthalmology 2001;108(9):1544–51. https://doi.org/10.1016/s0161-6420(01)00691-1.

[328] Win-Hall DM, Ostrin LA, Kasthurirangan S, Glasser A. Objective accommodation measurement with the Grand Seiko and Hartinger coincidence refractometer. Optom vis Sci 2007;84(9):879–87. https://doi.org/10.1097/OPX.0b013e3181559ace.

[329] Ostrin LA, Glasser A. Accommodation measurements in a prepresbyopic and presbyopic population. J Cataract Refract Surg 2004;30(7):1435–44. https://doi.org/10.1016/j.jcrs.2003.12.045.

[330] Buehren T, Collins MJ. Accommodation stimulus-response function and retinal image quality. Vision Res 2006;46(10):1633–45. https://doi.org/10.1016/j.visres.2005.06.009.

[331] López-Gil N, Fernández-Sánchez V. The change of spherical aberration during accommodation and its effect on the accommodation response. J vis 2010;10(13):12. https://doi.org/10.1167/10.13.12.

[332] Gislén A, Gustafsson J, Kröger RH. The accommodative pupil responses of children and young adults at low and intermediate levels of ambient illumination. Vision Res 2008;48(8):989–93. https://doi.org/10.1016/j.visres.2008.01.022.

[333] Tucker J, Charman WN. The depth-of-focus of the human eye for Snellen letters. Am J Optom Physiol Opt 1975;52(1):3–21. https://doi.org/10.1097/00006324-197501000-00002.

[334] Marsack JD, Thibos LN, Applegate RA. Metrics of optical quality derived from wave aberrations predict visual performance. J Vision 2004;4(4):8. https://doi.org/10.1167/4.4.8.

[335] Thibos LN, Hong X, Bradley A, Cheng X. Statistical variation of aberration structure and image quality in a normal population of healthy eyes. J Opt Soc Am A Opt Image Sci Vis 2002;19(12):2329–48. https://doi.org/10.1364/josaa.19.002329.

[336] Yi F, Iskander DR, Collins M. Depth of focus and visual acuity with primary and secondary spherical aberration. Vision Res 2011;51(14):1648–58. https://doi.org/10.1016/j.visres.2011.05.006.

[337] Tilia D, Munro A, Chung J, Sha J, Delaney S, Kho D, et al. Short-term comparison between extended depth-of-focus prototype contact lenses and a commercially-available center-near multifocal. J Optom 2017;10(1):14–25. https://doi.org/10.1016/j.optom.2016.04.003.

[338] Bakaraju RC, Tilia D, Sha J, Diec J, Chung J, Kho D, et al. Extended depth of focus contact lenses vs. two commercial multifocals: Part 2. Visual performance after 1 week of lens wear. J Optom 2018;11(1):21–32. https://doi.org/10.1016/j.optom.2017.04.001.

[339] Marcos S, Barbero S, Jiménez-Alfaro I. Optical quality and depth-of-field of eyes implanted with spherical and aspheric intraocular lenses. J Refract Surg 2005;21(3):223–35. https://doi.org/10.3928/1081-597x-20050501-05.

[340] Fernández J, Rodríguez-Vallejo M, Burguera N, Rocha-de-Lossada C, Piñero DP. Spherical aberration for expanding depth of focus. J Cataract Refract Surg 2021;47(12):1587–95. https://doi.org/10.1097/j.jcrs.0000000000000713.

[341] Berrio E, Tabernero J, Artal P. Optical aberrations and alignment of the eye with age. J vis 2010;10(14). https://doi.org/10.1167/10.14.34.

[342] Kollbaum PS, Bradley A. Correction of presbyopia: old problems with old (and new) solutions. Clin Exp Optom 2020;103(1):21–30. https://doi.org/10.1111/cxo.12987.

[343] Jones CE, Atchison DA, Pope JM. Changes in lens dimensions and refractive index with age and accommodation. Optom vis Sci 2007;84(10):990–5. https://doi.org/10.1097/OPX.0b013e318157c6b5.

[344] Strenk SA, Strenk LM, Guo S. Magnetic resonance imaging of the anteroposterior position and thickness of the aging, accommodating, phakic, and pseudophakic ciliary muscle. J Cataract Refract Surg 2010;36(2):235–41. https://doi.org/10.1016/j.jcrs.2009.08.029.

[345] Glasser A, Campbell MC. Biometric, optical and physical changes in the isolated human crystalline lens with age in relation to presbyopia. Vision Res 1999;39(11):1991–2015. https://doi.org/10.1016/s0042-6989(98)00283-1.

[346] Helmholtz H. Über die Akkommodation des Auges. v Graefes Arch Ophthal 1855;1(2):74.

[347] Gullstrand A. Handbuch der Physiologischen Optik. New York: Dover; 1962.

[348] Roy D, Spector A. Human alpha-crystallin-III isolation and characterization of protein from normal infant lenses and old lens peripheries. Invest Ophthalmol 1976;15(5):394–9. https://www.ncbi.nlm.nih.gov/pubmed/1262170.

[349] Srivastava K, Chaves JM, Srivastava OP, Kirk M. Multi-crystallin complexes exist in the water-soluble high molecular weight protein fractions of aging normal and cataractous human lenses. Exp Eye Res 2008;87(4):356–66. https://doi.org/10.1016/j.exer.2008.07.001.

[350] Michael R, Bron AJ. The ageing lens and cataract: a model of normal and pathological ageing. Philos Trans R Soc Lond B Biol Sci 2011;366(1568):1278–92. https://doi.org/10.1098/rstb.2010.0300.

[351] Fincham E. The mechanism of accommodation. Br J Ophthalmol Suppl 1937;8:5–80.

[352] Hess C. Arbeiten aus dem Gebiete der accommodationslehre. VI. Die relative accommodation. Albr von Graefes Arch Ophthalmol 1901;52:143–74.

[353] Tabernero J, Chirre E, Hervella L, Prieto P, Artal P. The accommodative ciliary muscle function is preserved in older humans. Sci Rep 2016;6:25551. https://doi.org/10.1038/srep25551.

[354] Shum PJ, Ko LS, Ng CL, Lin SL. A biometric study of ocular changes during accommodation. Am J Ophthalmol 1993;115(1):76–81. https://doi.org/10.1016/s0002-9394(14)73528-7.

[355] Maheshwari R, Sukul RR, Gupta Y, Gupta M, Phougat A, Dey M, et al. Accommodation: its relation to refractive errors, amblyopia and biometric parameters. Nepal J Ophthalmol 2011;3(2):146–50. https://doi.org/10.3126/nepjoph.v3i2.5267.

[356] Woodman EC, Read SA, Collins MJ, Hegarty KJ, Priddle SB, Smith JM, et al. Axial elongation following prolonged near work in myopes and emmetropes. Br J Ophthalmol 2011;95(5):652–6. https://doi.org/10.1136/bjo.2010.180323.

[357] Read SA, Fuss JA, Vincent SJ, Collins MJ, Alonso-Caneiro D. Choroidal changes in human myopia: insights from optical coherence tomography imaging. Clin Exp Optom 2019;102(3):270–85. https://doi.org/10.1111/cxo.12862.

[358] Alpern MD, H. Effects of illuminance quantity on accommodation of the eyes. . Ind Med Surg 1958; 27: 551.

[359] Bito L, Miranda O. Accommodation and presbyopia. New York, NY: Raven Press; 1989.

[360] Duane A. Studies in monocular and binocular accommodation with their clinical applications. Am J Ophthalmol 1922;5:865–77. https://doi.org/10.1016/S0002-9394(22)90793-7.

[361] Duane A. Are the current theories of accommodation correct? Am J Ophthalmol 1925;8:196–202. https://doi.org/10.1016/S0002-9394(25)90654-X.

[362] Fincham E. The proportion of ciliary muscular force required for accommodation. J Physiol 1955;128:99–112. https://doi.org/10.1113/jphysiol.1955.sp005293.

[363] Alpern M. Accommodation: evaluation of the theories of presbyopia: in The Eye 2ed. New York: Academic Press; 1969.

[364] Fitch RC. Procedural effects on the manifest human amplitude of accommodation. Am J Optom Arch Am Acad Optom 1971;48(11):918–26. https://doi.org/10.1097/00006324-197111000-00004.

[365] Bruckner R, Batschelet E, Hugenschmidt F. The Basel longitudinal study on aging (1955-1978). Ophthalmo-gerontological research results. Documenta ophthalmologica Advances in ophthalmology 1986;64(3):235-310. https://doi.org/10.1007/BF00161733.

[366] Eames T. Physiologic exophoria in relation to age. Arch Ophthalmol 1933;9:104–5. https://doi.org/10.1001/archopht.1933.00830010115011.

[367] Davis CJ, FW. Further studies on the ACA ratio as measured on the orthorater. Optom Vis Sci 1957;34:16-25. https://doi.org/10.1097/00006324-195701000-00003.

[368] Balsam MH, Fry GA. Convergence accommodation. Am J Optom Arch Am Acad Optom 1959;36:567–75. https://doi.org/10.1097/00006324-195911000-00001.

[369] Eskridge J. The AC/A ratio and age – a longitudinal study. Optom Vis Sci (online) 1983:911–3. https://doi.org/10.1097/00006324-198311000-00007.

[370] Bruce AS, Atchison DA, Bhoola H. Accommodation-convergence relationships and age. Invest Ophthalmol Vis Sci 1995;36(2):406–13. https://www.ncbi.nlm.nih.gov/pubmed/7843910.

[371] Rosenfield M, Cohen AS. Push-up amplitude of accommodation and target size. Ophthalmic Physiol Opt 1995;15(3):231–2. https://doi.org/10.1016/0275-5408(95)90576-n.

[372] Ciuffreda KJ, Ong E, Rosenfield M. Tonic vergence, age and clinical presbyopia. Ophthalmic Physiol Opt 1993;13(3):313–5. https://doi.org/10.1111/j.1475-1313.1993.tb00478.x.

[373] Ciuffreda KJ, Rosenfield M, Chen HW. The AC/A ratio, age and presbyopia. Ophthalmic Physiol Opt 1997;17(4):307–15. https://www.ncbi.nlm.nih.gov/pubmed/9390375.

[374] Baker FJ, Gilmartin B. The effect of incipient presbyopia on the correspondence between accommodation and vergence. Graefes Arch Clin Exp Ophthalmol 2002;240(6):488–94. https://doi.org/10.1007/s00417-002-0483-x.

[375] Koretz JF, Handelman GH. Modeling age-related accommodative loss in the human eye. Mathematical Modelling 1986;7:1003–14.

[376] Glasser A, Campbell MC. Presbyopia and the optical changes in the human crystalline lens with age. Vision Res 1998;38(2):209–29. https://doi.org/10.1016/s0042-6989(97)00102-8.

[377] Strenk SA, Strenk LM, Koretz JF. The mechanism of presbyopia. Prog Retin Eye Res 2005;24(3):379–93. https://doi.org/10.1016/j.preteyes.2004.11.001.

[378] Strenk SA, Strenk LM, Semmlow JL. High resolution MRI study of circumlental space in the aging eye. J Refract Surg 2000;16(5):S659–60. https://doi.org/10.3928/1081-597X-20000901-36.

[379] Schachar RA, Cudmore DP, Black TD. Experimental support for Schachar's hypothesis of accommodation. Ann Ophthalmol 1993;25(11):404–9. https://www.ncbi.nlm.nih.gov/pubmed/8109880.

[380] Schachar RA. Cause and treatment of presbyopia with a method for increasing the amplitude of accommodation. Ann Ophthalmol 1992;24(12):445-7, 52, https://www.ncbi.nlm.nih.gov/pubmed/1485739.

[381] Schachar RA. The mechanism of accommodation and presbyopia. Int Ophthalmol Clin 2006;46(3):39–61. https://doi.org/10.1097/00004397-200604630-00006.

[382] Naroo SA, Woods C, Gil Cazorla R, Ang RE, Collazos M, Eperjesi F, et al. BCLA CLEAR presbyopia: Management with scleral techniques and pharmaceutical therapies. Cont Lens Anterior Eye 2024;47 [In press].

[383] Mathews S. Scleral expansion surgery does not restore accommodation in human presbyopia. Ophthalmology 1999;106(5):873–7. https://doi.org/10.1016/S0161-6420(99)00503-5.

[384] Ostrin LA, Kasthurirangan S, Glasser A. Evaluation of a satisfied bilateral scleral expansion band patient. J Cataract Refract Surg 2004;30(7):1445–53. https://doi.org/10.1016/j.jcrs.2003.12.055.

[385] Weale RA. The ageing eye. Proc R Soc Med 1973;66(2):160–1. https://www.ncbi.nlm.nih.gov/pubmed/4541381.

[386] Weale RA. On potential causes of presbyopia. Vision Res 1999;39(7):1263–72. https://doi.org/10.1016/s0042-6989(98)00238-7.