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EXTENDED REPORT

Insights into the age-related decline in the amplitude of accommodation of the human lens using a non-linear finite-element model

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Aim: To understand the effect of the geometric and material properties of the lens on the age-related decline in accommodative amplitude.

Methods: Using a non-linear finite-element model, a parametric assessment was carried out to determine the effect of stiffness of the cortex, nucleus, capsule and zonules, and that of thickness of the capsule and lens, on the change in central optical power (COP) associated with zonular traction. Convergence was required for all solutions.

Results: Increasing either capsular stiffness or capsular thickness was associated with an increase in the change in COP for any specific amount of zonular traction. Weakening the attachment between the capsule and its underlying cortex increased the magnitude of the change in COP. When the hardness of the total lens stroma, cortex or nucleus was increased, there was a reduction in the amount of change in COP associated with a fixed amount of zonular traction.

Conclusions: Increasing lens hardness reduces accommodative amplitude; however, as hardness of the lens does not occur until after the fourth decade of life, the age-related decline in accommodative amplitude must be due to another mechanism. One explanation is a progressive decline in the magnitude of the maximum force exerted by the zonules with ageing.

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The aetiology of the age-related decline in accommodative amplitude is not established.^{1–5} Mathematical modelling offers the opportunity of evaluating some of the lens parameters responsible for presbyopia. This study uses the non-linear finite-element method (FEM) in parametric assessment^{6–16} to determine the effect of varying the geometric and material properties of the lens on the ability of zonular traction to change central optical power (COP).

MATERIALS AND METHODS

Non-linear finite-element model

A non-linear FEM of the lens was constructed using ABAQUS, V.6.5. Standard^{17,18} (ABAQUS Inc, Pawtucket, RI, USA) and hybrid¹⁹ quadrilateral elements were used for the capsule and stroma, respectively (fig 1A). The number of stromal elements was varied, and 2113 stromal and 118 capsular mesh elements were found to consistently result in a converged solution.^{20,21}

Geometry

The baseline anterior and posterior profiles of the lens were given by^{22,23}

$$y(x) = \left[b + c \left(\sin^{-1} \left(\frac{x}{a} \right) \right)^2 + d \left(\sin^{-1} \left(\frac{x}{a} \right) \right)^4 \right] \times \cos \left(\sin^{-1} \left(\frac{x}{a} \right) \right) \quad (1)$$

This equation is a continuous function and meets the following essential requirements:

1. The radii of curvatures at any point on the lens surface are smoothly varied.
2. The radii do not change abruptly near the optical axis.

Abbreviations: COP, central optical power; FEM, finite-element method

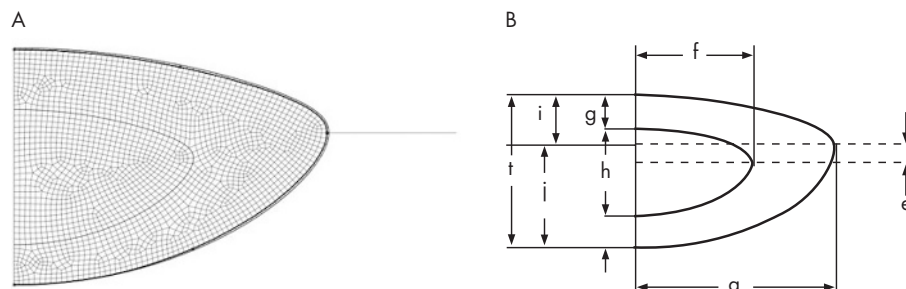


Figure 1 (A) Finite-element model mesh of the capsule, cortex and nucleus. (B) Outline of the lens and nucleus. The dimensions of the outline for each profile are given in table 1 under the third subheading.

Table 1 Geometric properties of the lenses

		40 years old _{unacc}	40 years old _{acc}	60 years old _{unacc}	~20 years old _{unacc}	~20 years old _{acc}	Idealised 20 years old _{unacc}
Coefficients for the anterior profile, equation 1 (mm)	a	4.485	4.282	4.5	4.5	4.3	4.3
	b	1.209	1.464	1.555	1.440	1.751	1.9
	c	-0.267	-0.167	-0.329	-0.096	-0.130	0.180
	d	0.117	-0.021	0.081	0.113	0.117	-0.385
Coefficients for the posterior profile, equation 1 (mm)	a	4.485	4.282	4.5	4.5	4.3	4.3
	b	2.167	2.260	2.270	2.378	2.628	2
	c	-0.369	-0.260	-0.633	-0.589	-0.964	-0.193
	d	0.001	-0.114	0.087	0.158	0.311	-0.25
Dimensions for the outline, fig 1B (mm)	a	4.485	4.282	4.5	4.5	4.3	4.3
	e	0.357	0.394	0.405	0.404	0.463	0.405
	f	2.557	2.441	2.385	2.79	2.666	2.85
	g	0.877	1.023	1.135	0.951	1.129	0.971
	h	1.924	2.123	2.027	2.367	2.715	2.418
	i	1.209	1.464	1.555	1.440	1.751	1.9
	j	2.167	2.260	2.270	2.378	2.628	2
	t	3.377	3.724	3.825	3.817	4.379	3.9

acc, accommodated; unacc, unaccommodated.

- The radii are identical at the equator, where the anterior and posterior surfaces meet.
- The functions have a positive Gaussian curvature everywhere on the surface.

The profiles were derived from published magnetic resonance images of the lenses of a 60-year old,²⁴ a 40-year old²⁵ and a mid-20-year old.²⁶ The two lens images of the 40- and the mid-20-year old were available in both the unaccommodated (unacc) and accommodated (acc) states. The lens of the 60-year old was unaccommodated.

The normal variation in capsular thickness²⁷⁻²⁸ was represented by fifth-degree polynomials.²² The lens nucleus was modelled as a percentage of the total central thickness of the lens²⁹ (fig 1B; table 1).

Central optical power

$$\text{COP} = \frac{n_1 - n_a}{r_a} + \frac{n_1 - n_a}{r_p} - \frac{t(n_1 - n_a)^2}{r_a r_p n_1} \quad (2)$$

where $n_1 = 1.42$ ³⁰ and $n_a = 1.336$; t = central lens thickness, r_a = the anterior radius of curvature and r_p = the posterior radius of curvature.³¹ The r_a and r_p were obtained by determining the radii of the spheres that best fit the central 1.6-mm diameter aperture of the centre of each lenticular surface.³¹ The lens has a varying index of refraction.³² However, the use of a fixed refractive index minimally alters the validity of using equation 2 to calculate the COP.³² In addition, the central refractive index of the lens does not seem to change markedly with age.³⁰

Baseline material properties

The capsule Poisson's ratio is $\nu = 0.47$.³³ Consistent with the in vivo mean speed of ultrasound through the lenses of 15–45-year-old people,³⁴ the bulk modulus of the young lens stroma is $K = 2.8$ GPa.³⁵⁻³⁶

The mean shear modulus of the young human lens stroma is $G = 50$ Pa.³⁷ The Poisson's ratio of the lens stroma is³⁸

$$\nu = \frac{3K - 2G}{6K + 2G} \cong 0.5$$

The baseline values for the elastic moduli of the anterior capsule,²⁷⁻²⁸ posterior capsule,²⁷⁻²⁸ cortex, nucleus and zonules

were 1.5, 0.75, 1.7×10^4 , 2×10^4 and 1.5 MPa, respectively. The baseline capsular thicknesses were 24 μm for the central anterior capsule and 5 μm for the central posterior capsule.²⁷⁻²⁸

Parametric assessment

Each parameter was varied below and above its baseline value to determine its critical value. The change in COP in response to zonular traction was the outcome determinant. The 40-year-old unaccommodated model lens had the median response and was used for the parametric study. The effect of the strength of the attachment between the capsule and its underlying cortex and between the cortex and nucleus was evaluated by altering the stiffness and frictional coefficient of contact elements placed between these interfaces.

Idealised young_{unacc} lens

Baseline lens shape seems to be a major determinant of the response of COP to zonular traction.²³ As none of the lenses studied showed changes in COP comparable with the young in vivo human lens, an idealised lens was modelled (table 1). For this lens, the elastic modulus values of the cortex, nucleus, anterior and posterior capsules, and zonules were 170 Pa, 220 Pa, 0.5 MPa, 1.5 MPa and 1.5 MPa, and the central thickness values of its anterior and posterior capsules were 24 and 5 μm , respectively. Contact elements between the capsule and cortex had a stiffness of 0.1 N/mm and a frictional coefficient of 0.005. The idealised lens was also modelled with the elastic modulus of both the cortex and nucleus equal to 1.7×10^4 MPa.

RESULTS

Effect of baseline lens shape

The baseline lens shape affected the magnitude of the COP in response to zonular traction; however, all lenses, independent of baseline shape, showed an increase in COP in response to zonular traction, starting at zero (fig 2).

Effect of strength of attachment between the capsule and cortex and cortex and nucleus

A weak attachment between the capsule and cortex, ratio of stiffness to frictional coefficient >10 , improved the increase in COP associated with zonular traction. Varying the strength of the attachment of the cortex to the nucleus had almost no effect.

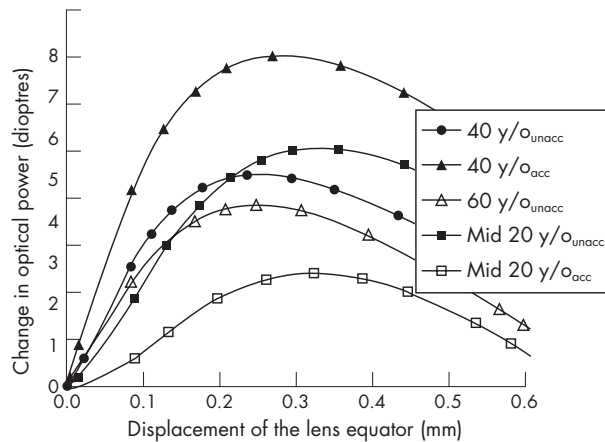


Figure 2 Effect of baseline shape on the change in central optical power associated with zonular traction. acc, accommodated; unacc, unaccommodated; y/o, years old.

Effect of changing stiffness

1. *Capsule*: Increasing the elastic modulus of the lens capsule increased the change in COP associated with zonular traction (fig 3A).
2. *Total lens stroma (cortex and nucleus assigned the same elastic modulus)*: Increasing the elastic modulus of the lens stroma decreased the change in COP associated with zonular traction (fig 3B).
3. *Cortex and nucleus*: Independently increasing the elastic modulus of either the cortex or the nucleus was associated with a decrease in the change in COP during zonular traction (fig 3C,D)

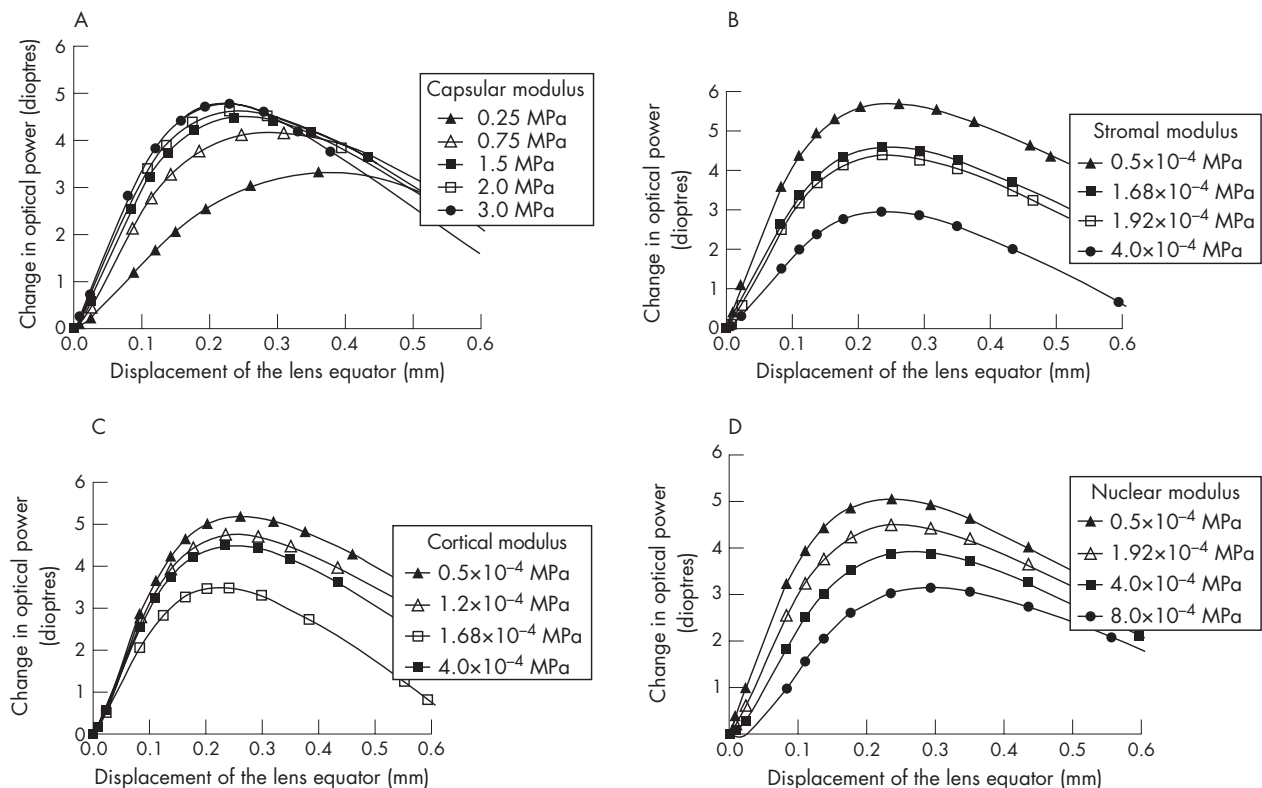


Figure 3 Effect of changing stiffness of the (A) capsule, (B) lens stroma, (C) cortex and (D) nucleus associated with zonular traction.

4. *Zonules*: Zonular stiffness did not affect the change in COP associated with zonular traction.

Effect of changing Poisson's ratio of the lens stroma

The increase in COP associated with zonular traction was observed for all values of ν between 0.38 and 0.5. However, the magnitude of the change in COP in response to zonular traction considerably declined when $\nu < 0.499$.

Effect of changing thickness of the capsule and lens

Increasing the central thickness of the anterior capsule increased the change in COP. Changing lenticular thickness, without changing central or peripheral curvatures, had little effect on the increase in COP associated with zonular traction.

Idealised young_{unacc} lens

With the optimisation of the values of the parameters in this idealised lens, minimal zonular force ~ 15 mN/dioptr, and minimal outward displacement ~ 10 μ m/dioptr were associated with the maximal increase in COP (fig 4A) while simultaneously increasing the central thickness (fig 4B), steepening the anterior and posterior central surfaces (fig 4C) and flattening the peripheral surfaces (fig 4D).

With additional zonular traction, the COP decreased. However, this required considerably more force, ~ 30 mN/dioptr, and considerably more outward displacement of the lens equator, ~ 200 μ m/dioptr.

The same magnitude of these responses to zonular traction occurred when the nucleus and cortex had elastic moduli of 1.7 and 2.2×10^{-4} MPa, respectively, and when their moduli were both equal to 1.7×10^{-4} MPa (fig 4A).

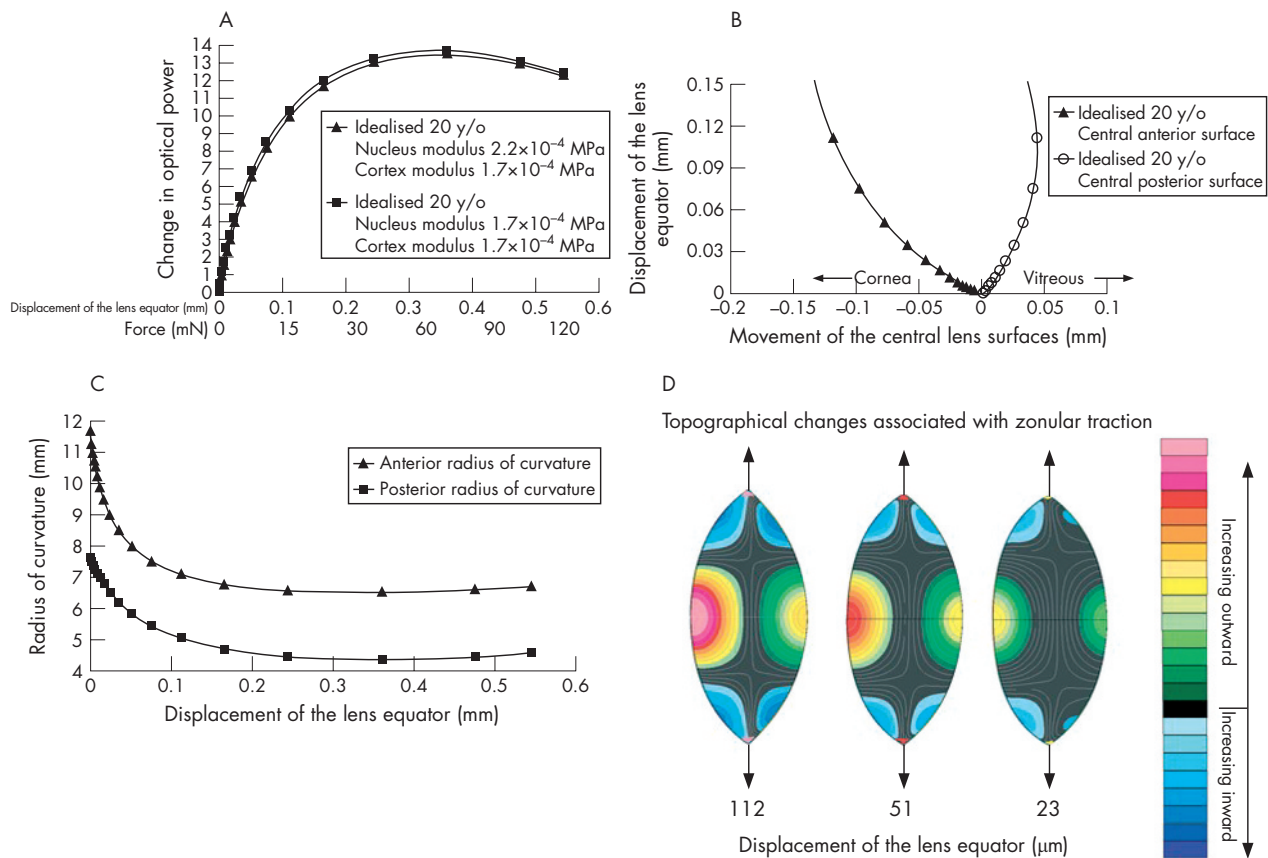


Figure 4 (A) Outward displacement of the lens equator and force required for zonular traction to change the central optical power of the idealised 20-year-old unaccommodated (y/o_{unacc}) model lens when the elastic modulus of the nucleus is greater than the cortex and when it is the same. (B) Movement of the anterior and posterior surfaces of the idealised 20 y/o_{unacc} model lens in response to outward displacement of the lens equator induced by zonular traction. (C) Change in the radii of curvatures of the central anterior and central posterior surfaces of the idealised 20 y/o_{unacc} model lens in response to outward displacement of the lens equator induced by zonular traction. (D) Topographical changes of the lens surfaces of the idealised 20 y/o_{unacc} model lens in response to outward displacement of the lens equator induced by zonular traction.

DISCUSSION

FEM constraints

The following anatomical, physiological and topographical constraints were used to confirm that the model of the idealised lens represented in vivo human lenticular accommodation.

- The lens model must simulate the well-documented and non-controversial shape changes that the crystalline lens undergoes during in vivo human accommodation. These in vivo changes are an increase in central thickness, steepening of its anterior central surface, flattening of its anterior peripheral surface, and a large increase in COP in response to a change in zonular traction.
- The total force required to induce a large change in COP must be less than the maximum force capacity of the ciliary muscle. An upper estimate for the maximum force capacity of the human ciliary muscle is 50 mN. This estimate was based on:
 - estimation from the deformation of the surfaces of spinning human lenses, which is 16 mN³⁹ and
 - the maximum force exerted by a 6-mm-wide strip of monkey ciliary muscle in response to pilocarpine, which is 3.2 mN⁴⁰; that is, the load and the force of contraction (tables 1 and 2 of this reference). As the circumference of the monkey ciliary ring is approximately 48 mm, the total force capacity of the monkey ciliary muscle is approximately 26 mN.
- The change in the equatorial radius of the lens model must be less than the maximum 1.3-mm space between the lens equator and the ciliary sulcus.⁴¹

Accuracy of the FEM

When zonular traction was applied to the idealised lens to induce a 10-dioptre increase in COP, its r_a and r_p decreased from 11.7 to 7.1 mm and from 7.75 to 5.0 mm, respectively. During 10 dioptres of in vivo human accommodation, r_a and r_p similarly decreased from 11.7 to 7.6 mm and from 7.6 to 5.4 mm, respectively.⁴²

One third of the increase in the central thickness of the idealised lens that occurred in response to zonular traction was due to an outward movement of the centre of the posterior lenticular surface towards the retina. This corresponds to in vivo measurements obtained during human accommodation, using partial coherence interferometry⁴³ and an A-scan ultrasound probe designed to track the eye.⁴⁴ These high-resolution in vivo techniques support the validity of our mathematical model of the lens.

In the idealised lens, when zonular traction reached 15 mN, the equatorial radius increased by 112 μ m and the COP increased by 10 dioptre. The magnitude of the force and the displacement required to obtain this increase in COP were within the anatomical constraints of the circumlenticular equatorial space and the physiological force capacity of the ciliary muscle.

Once the lens is maximally accommodated, the FEM predicts that there are two ways to reduce its COP. Zonular traction could simply be decreased. Under this scenario, COP is decreased within the constraints of the accommodative system. Alternatively, zonular traction could be applied to the maximally accommodated lens to reduce COP. Under this option, the FEM model predicts that to decrease the COP of the lens from its maximally accommodated state, a mechanism proposed by von Helmholtz,⁴⁵ a 4-mm increase in the equatorial diameter of the lens and a zonular force of >300 mN would be required. This would exceed the physiological force capacity of the ciliary muscle and the anatomical limitation of the equatorial circumlental space. Other FEM models^{30 46 47} of human accommodation also predict that a non-physiological zonular force would be required to decrease the COP of the maximally accommodated lens.

Zonular attachment

The location of the zonular–capsule attachment was not a variable in this parametric FEM model, and zonular traction was applied by only the equatorial zonules for four reasons. Firstly, it has been shown that a simplified representation of the zonules is sufficient for modelling accommodation.⁴⁸ Secondly, whether zonular traction, beginning at zero, is applied by the equatorial zonules only, the anterior and posterior zonules, or all three sets of zonules, the COP increases.⁴⁷ Thirdly, zonular traction, beginning at zero, increases COP regardless of the location of the attachment of the anterior and posterior zonules.⁴⁷ Fourthly, the closer the location of the attachment of the anterior and posterior zonules is to the lens equator, the greater is the increase in COP.⁴⁷

Effect of capsule stiffness and thickness

From birth to 35 years of age, the lens capsule becomes thicker and stiffer.^{27 28} The FEM model predicts that an increase in capsular thickness or stiffness would enhance the amplitude of accommodation. For this reason, the normal age-related increase in capsular thickness and stiffness cannot be the basis for the decline in the amplitude of accommodation with age.

Effect of the strength of the cortex–capsule and cortex–nucleus attachments

No published evidence suggests that there is a change in the strength of the capsular–cortical or cortical–nuclear attachments during the first four decades of life. The FEM model predicts that weak capsular–cortical attachments, as observed in vivo⁴⁹ and in vitro,⁵⁰ increase the magnitude of the change in COP associated with zonular traction. The strength of the cortical–nuclear attachment has almost no effect on the change in COP. Thus, a change in the strength of the attachment between the cortex and capsule or between the cortex and nucleus is probably not the aetiology of presbyopia.

Effect of zonular stiffness

Actual zonular stiffness has not been directly measured. However, from in vitro stretching experiments, the elastic modulus of the zonules has been calculated to be 1.5 MPa.⁵¹ In the model, varying zonular elastic modulus from 0.5 to 3 MPa does not affect the change in COP associated with zonular traction. Consequently, a change in zonular stiffness does not seem to be the basis for presbyopia.

Effect of lens stromal stiffness

The FEM model predicts that an increase in the elastic modulus of the entire lens stroma, cortex or nucleus would

decrease the maximum change in COP associated with zonular traction. Although stiffness measurements of the cortex and nucleus of thawed lenses frozen in liquid nitrogen^{52 53} seem to be markedly higher than those from fresh intact lenses,⁵⁴ even these measurements show very little difference between the elastic moduli of the lens stroma, cortex or nucleus of 14 and 25-year olds.⁵⁵ Furthermore, there seems to be no change in the optical density, a surrogate marker for sclerosis,⁵⁴ of lenses of <39-year olds.⁵⁶ Therefore, lens sclerosis is probably not the aetiology of the 10-dioptre decline in accommodative amplitude that evolves from birth to 40 years of age.

Effect of lens thickness

Changing lens thickness without changing the central and anterior peripheral curvatures of the model lens had only a minimal effect on the change in COP associated with zonular traction. In agreement with this FEM prediction, the pattern of in vivo change in central lenticular thickness, decreasing from birth until the second decade^{57–60} and increasing thereafter,^{59 60} does not seem to relate to the linear decline in accommodative amplitude.

Effect of lens shape

The FEM model shows that baseline lens shape affects the magnitude of the increase in COP associated with zonular traction. As the changes in COP of the ~20-year-old accommodated and 40-year-old unaccommodated model lenses respond similarly to zonular traction (fig 2), it is improbable that baseline shape is a major aetiological parameter of the age-related decline in the amplitude of accommodation. Consistent with this conclusion, the central lenticular anterior radius of curvature measured by Scheimpflug photography,⁶¹ and peripheral lens curvature inferred from wavefront aberrometry,^{62 63} change minimally between 20 and 40 years of age.

In summary, the FEM model predicts that the age-related changes in capsular stiffness, capsular thickness, strength of the capsular–cortical attachment, strength of the cortical–nuclear attachment, zonular stiffness, lens thickness and lens shape are not responsible for presbyopia. The model predicts that an increase in stiffness of the entire stroma, its cortex or nucleus will cause a decrease in the amplitude of accommodation. However, a progressive increase in lens stiffness does not occur until after the fourth decade.^{54 56} Therefore, lens stiffness cannot be the cause of the 10-dioptre decline of accommodative amplitude that occurs from birth to 40 years of age.^{64 65} One explanation is a progressive decline in the magnitude of the maximum force exerted by the zonules with ageing.⁶⁶

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Competing interests: RAS has a financial interest in the surgical reversal of presbyopia.

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