Contributions to Accommodative Loss of Ageing Human Lens by Shape and Stiffness: An Assessment using Finite Element Models

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Abstract: Ageing changes to the various components of the accommodative system of the eye lens contribute to the loss of focusing power. The relative contributions of each ageing component, however, are not well defined. This study investigates the contribution of geometric parameters and material properties on accommodation simulated using models based on human lenses aged 16, 35 and 48 years. Each model was tested using two different sets of material properties and a range of zonular fibre angles and compared to results from *in vivo* measurements. The geometries and material parameters of older and younger lens models were interchanged to investigate the role of shape and material on accommodative capacity. Results indicate that geometry has the greater role in accommodation.

1. Introduction

Presbyopia is a ubiquitous process that manifests in loss of near focusing capacity in the fifth to sixth decade of life. The gradual decrease in accommodation with age follows a well-recognised trend [1,2] although rates are known to vary with individuals. Reading glasses remain the common method of dealing with presbyopia; a number of attempts have been and continue to be made to develop accommodative intraocular lenses [3,4]. Success is limited because of a lack of understanding of how presbyopia develops and how different ocular components involved in accommodation may contribute to the process, as well as difficulties in determining a suitable material model of the eye lens and current limitations in surgical techniques.

Possible causes of presbyopia include changes in geometry [5,6] and in material properties of the lens [7-10] and its capsule [11-13] with age, as well as morphological changes to the ciliary muscle associated with alterations in zonular angles [6,14]. The lens grows throughout life such that both its thickness and equatorial diameter increase with age [15]. With the concomitant thickening of the ciliary body [16,17], there may be insufficient space left between the lens equator and ciliary body for the lens to alter its shape. Whilst varying techniques have resulted in a diverse range of values, even on lenses at similar ages, the consistent finding is that the lens becomes less pliable with age [7-10] while the lens capsule becomes more flaccid [11,18]. The apparent anterior shift of the zonular fibres [5] and the anterior inward movement of the apex of the ciliary body [16,17] could cause age-related alterations in the angles of the zonular fibres [6,14]. These combined changes would render it harder for the lens to alter its shape.

Although factors that contribute to accommodative loss have been studied (reviewed by [19,20]), an improved understanding of the major or leading causes of accommodative loss and relative importance of these changes are needed. This study presents a sensitivity analysis based on axisymmetric Finite Element (FE) lens models for three different ages: 16, 35 and 48 years.

The effect of age-related changes in geometries and material properties as well as a range of different combinations of zonular angles on the loss of accommodative capacity were investigated.

2. Method

Axisymmetric FE models of three human lenses aged 16, 35 and 48 years (Fig.1) were developed using ANSYS mechanical APDL (ver. 18.2, Canonsburg, Pennsylvania, USA). This is a mechanical simulation software that can be controlled by parametric design language and is mainly used for Finite Element Analysis. Geometries of models were based on optical measurements of human lenses using X-ray interferometric analysis at the SPring-8 synchrotron [21]. Similar to previous studies [21, 22], detailed geometrical parameters used to construct each model were determined by fitting two splines to optical images [21] in SolidWorks (ver. 2017, Waltham, Massachusetts, USA), one for the whole lens shape and the other for the shape of the nucleus. Each spline is defined by three points (Fig. 2a) and three tangents (shown in Fig.2a in blue color with arrows). Coordinates of each point and weightings and radial direction of each tangent are listed in Table 1.

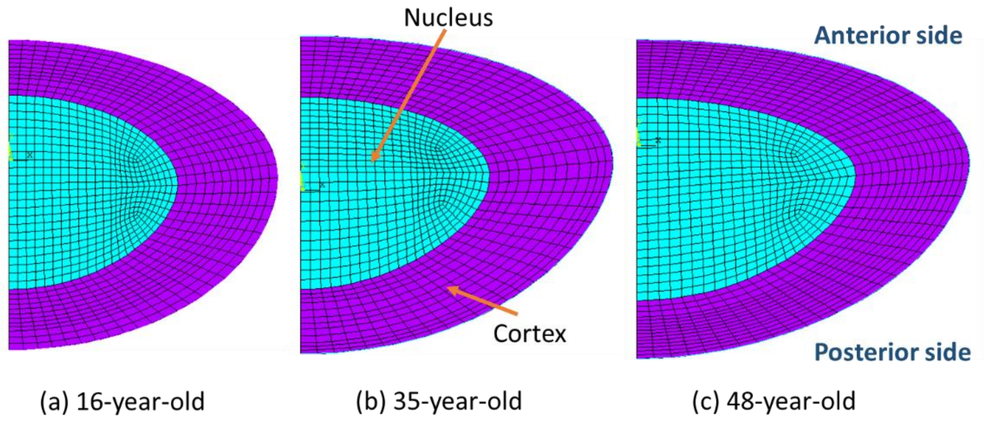


Fig. 1. Representations of Finite Element models based on lenses aged (a) 16 years (b) 35 years and (c) 48 years. Nuclear elements are shown in light blue, cortical elements are shown in purple.

Each model consists of a nucleus, cortex, capsule, anterior, equatorial and posterior zonular fibres (Fig. 2). Capsular thicknesses were 13µm, 15µm and 17µm for the 16, 35 and 48 year old lenses, respectively [11]. The length and thickness of each zonular fibre was 1.5mm [23] and 50µm [24] respectively. Anchorage points of each zonular fibre on the lens capsule (labelled as A, L_2 and P), were coupled to a number of neighboring nodes (Fig. 2b) such that the smooth curvature of lens model could be maintained during simulations. A range of angle combinations of the three zonular fibres (Fig. 2a) using a developed exhaustive search program, as reported in [22], were simulated for each model. The domain of the anterior zonular angle θ_a was [10°, 30°] toward the posterior direction (as indicated in Fig.1c), the domain of the equatorial zonular angle θ_e was [-14°, 14°] (the positive sign denotes the anterior direction) and the domain of the posterior zonular angle θ_p was [24°, 44°] toward the anterior direction of the lens.

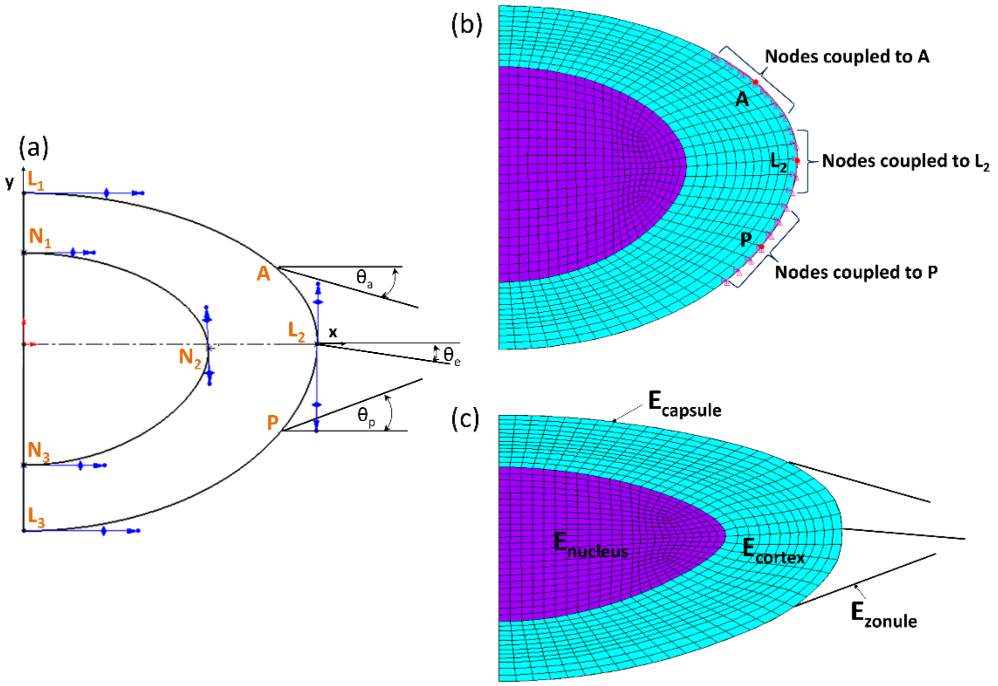


Fig. 2. Using 16-year-old lens as an example showing (a) geometrical parameters used to construct the lens models and zonular fibres, (b) undeformed FE model and (c) deformed FE model.

Table 1. Geometrical parameters used for constructing each lens model

		L1	L2	L3	N1	N2	N3	A	P
16	x-coordinate (mm)	0.00	4.03	0.00	0.00	2.53	0.00	3.46	3.54
	y-coordinate (mm)	2.08	0.00	-2.56	1.26	-0.06	-1.66	1.04	-1.19
	Tangent weighting 1	0.00	3.16	6.51	0.00	2.13	4.56	-	-
	Tangent weighting 2	6.75	4.24	0.00	3.98	1.84	0.00	-	-
	Tangent radial direction	0.00	-90.77	180.00	0.00	-87.31	180.00	-	-
35	x-coordinate (mm)	0.00	4.47	0.00	0.00	2.70	0.00	3.73	3.88
	y-coordinate (mm)	1.78	0.00	-2.76	0.9.	-0.18	-1.84	0.99	-1.26
	Tangent weighting 1	0.00	2.23	8.60	0.00	1.77	4.40	-	-
	Tangent weighting 2	9.61	3.37	0.00	4.62	1.98	0.00	-	-
	Tangent radial direction	0.00	-87.44	180.00	0.00	-83.74	180.00	-	-
48	x-coordinate (mm)	0.00	4.71	0.00	0.00	3.10	0.00	3.92	4.05
	y-coordinate (mm)	1.65	0.00	-2.86	0.82	-0.20	-2.04	0.62	-1.66
	Tangent weighting 1	0.00	2.18	6.56	0.00	1.49	5.59	-	-
	Tangent weighting 2	9.67	5.12	0.00	5.25	2.03	0.00	-	-
	Tangent radial direction	0.00	-82.61	180.00	0.00	-79.54	180.00	-	-

Each material component of the FE model (Fig. 2c) was assumed to be linear elastic, isotropic and homogenous; elastic moduli for nucleus and cortex were taken from previous studies [7,10] and are listed in Table 2. Shear moduli obtained from [10] were converted into Young's moduli using E=3G treating the lens as nearly incompressible [25,26]. Poisson's ratio of 0.49 was used for the lens [22] and 0.47 for the capsule and zonular fibres [11,27]. Young's moduli of the lens capsule [11] and zonular fibres [28,29] are also given in Table 2.

Table 2. Material properties (Young's moduli) of lens nucleus, cortex, capsule and zonular fibres from Fisher [7] and Wilde et al [10] (kPa: kilopascal; MPa: megapascal)

Material set	Fisher [7]			Wilde et al. [10]		
Age	16yo	35yo	48yo	16yo	35yo	48yo
Nucleus (kPa)	0.5	0.6	1.1	0.5	2.7	5.6
Cortex (kPa)	2.4	3.7	4.0	0.5	2.7	5.6
Capsule (MPa)	5.9	4.9	4.2	5.9	4.9	4.2
Zonular fibres (kPa)	350					

The lens nucleus and cortex were meshed using 8-node axisymmetric elements PLANE 183 in ANSYS mechanical APDL. The capsule was treated as a membrane and meshed using 3-node axisymmetric shell elements SHELL 209. The zonular fibres were modelled as 2-node shell elements SHELL 208, with membrane stiffness only. The total number of elements for each examined model was 1131 and the total number of nodes was 5500. Non-linear geometrical analyses were performed for all models. Displacements of 0.6mm by the anterior and posterior zonular fibres and 0.5mm by the equatorial zonular fibre were applied in six equal increments as previously described [22]. Applied displacements were made in accordance with a previous MRI study which showed that the maximal change in ciliary ring diameter during accommodation was 1.0 - 1.2mm [30]. It has been shown that the contractility of the ciliary muscle was retained with age even after the onset of presbyopia [31,32]; hence, constant displacements were applied for models of three different ages.

Fig. 2b and Fig. 2c show the undeformed and fully deformed states of the 16-year-old lens model. The resultant changes in lens surface curvatures and thicknesses for each increment were used to analyse the relationships between radii of curvature of both anterior and posterior lens surfaces, and the changes in Central Optical Power (COP) [22, 33]. Standard statistical t-test analyses for comparing slopes of two independent samples [22] was used to compare responses obtained from models with each zonular angle triplet and *in vivo* measurements [34] and a significance level of 0.05 was used to determine zonular angles that compare with *in vivo* data [34].

Original models were subjected to an interchange between shape and material properties to investigate how the various age-related changes contribute to accommodative loss. In the shape modified model set, the two older lens models, i.e. 35yo and 48yo models, assumed the geometry of the 16yo lens while retaining their original material properties. In the material modified model set, Young's moduli of the lens nuclei, cortices and capsules of the two older lens models were given the values from the 16-year-old lens while retaining their original shapes.

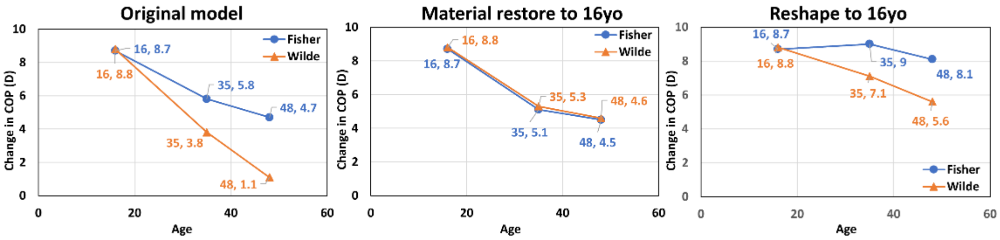
3. Results

The maximum change in COP, i.e. difference in optical powers of each lens model in undeformed and fully deformed states is shown plotted against age in Fig. 3 for the original models, the material modified models and the geometry modified models and for two sets of material properties [7,10]. Each value in Fig.3 was obtained from the corresponding model with a zonular angle triplet that provided the highest change in COP from all simulated zonular angle triplets. For original models, using the material properties of Fisher [7], the maximum change in COP decreases with age from 8.7 dioptres for the 16 year old model to 4.7 dioptres for the 48 year old model. A more pronounced decrease is seen in models with material properties of

Wilde et al., [10] where the maximum change in COP decreases from 8.8 dioptres for the 16 year old model to 1.1 dioptres for the 48 year old model (Fig. 3a).

When Young's moduli of the two older lens models were substituted with the values from the 16 year old model, the decreasing trend with age was reduced. This was predominantly evident for models with material properties of Wilde et al. [10] (Fig. 3b). For these sets of models there was little if any difference between the models with material properties of Fisher [7] or Wilde et al [10].

When the two older lens models were given the geometries of the 16 year old lens, the changes in COP with age is significantly reduced (Fig. 3c) compared to the other sets (Figs. 3a and b). This is particularly clear for the models with material properties of Fisher [7] for which the 35 year old lens shows a higher COP change with accommodation than the 16 year old lens model. (Fig. 3c).



(a) (b) (c)

Fig. 3. Maximum change in Central Optical Power of models with both sets of material properties [7, 10] plotted against age for (a) original lens models, (b) models with material properties replaced with those of the 16year old lens and (c) models with the shape of the 16year old lens.

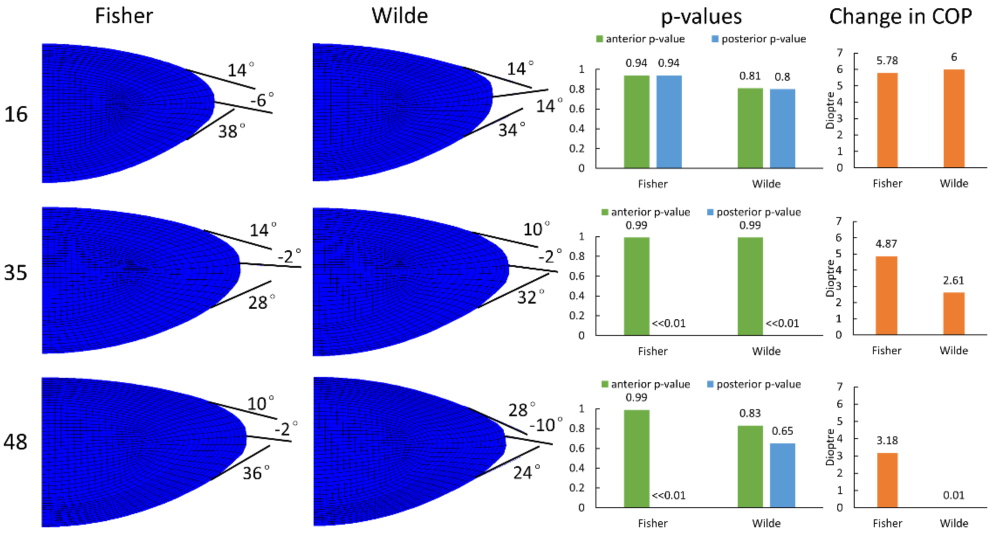
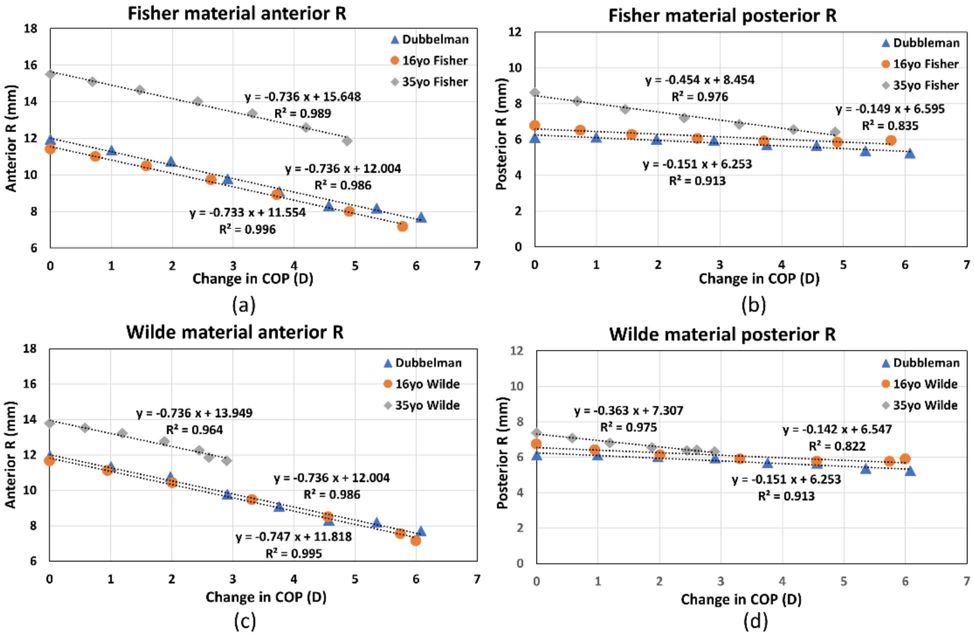


Fig. 4. Zonular angles that provide the closest fits to *in vivo* data [34], p-values used to evaluate the fits and resultant change in COP for all three aged models using two sets of material properties [7,10].

For each model, the optimal fits to the *in vivo* data [34] were determined by selecting the zonular angle combination that produced the maximum p-values for both anterior and posterior lens surfaces. A p-value lower than significance level of 0.05, indicates the existence of a statistical difference between two compared groups while a p-value closer to 1 means that there is no statistical difference found between the two compared groups. The results are plotted in Fig. 4 for the original models and for both sets of material properties. Only the 16 year old model demonstrates good fits to the *in vivo* data [34] for both anterior and posterior lens surfaces: no statistically significant differences were found between models with plotted zonular angle combinations (Fig. 4) and *in vivo* data [34] (p=0.94 for anterior and posterior surface fitting for the model with material properties of Fisher [7]; p=0.81 and 0.80 for anterior and posterior surface fitting for the model with material properties of Wilde et al. [10]). The two older lens models with either choice of material properties demonstrated good fits to *in vivo* data [34] for the anterior surface only (Fig. 4).

The fits of the 16 and 35 year old models with zonular angle combinations as displayed in Fig. 4 are plotted in graphs in Fig. 5a, b for models with material properties of Fisher [7] and in Fig. 5c, d for models with material properties of Wilde et al. [10]. The 48 year old models are not shown because the resultant changes in COP were too low to be compared with the *in vivo* data [34] for either set of material properties [7,10]. It should be noted the maximum change in COP for each model as shown in Fig. 5 does not translate exactly to the values shown in Fig. 3 as these were obtained from models with different zonular angle triplets.



(a) (b) (c) (d)

Fig. 5. (a) Anterior and (b) posterior radii of curvature (R) plotted against change in Central Optical Power for models with material properties of Fisher [7] and (c) anterior and (d) posterior lens surfaces of models with material properties of Wilde et al. [10]. Model data is compared to *in vivo* measurements obtained from Dubbelman et al. [34]

The optimal fits to *in vivo* data [34] of material modified and shape modified models of the 35 and 48 year old models with two sets of material properties are plotted in Fig. 6. The shape modified models with either set of material properties show good fits for both anterior and posterior lens surfaces (all p-values > 0.05) as well as comparable changes in COP to those of *in vivo* data [34] (Fig. 6). The exception is the 48 year old model with material properties of Wilde et al. [10] as this model only provides 3.47 dioptres of COP change. Material modified models with both sets of material properties all demonstrate good fits for the anterior lens surfaces (p-values = 0.99) but poor fits for the posterior lens surfaces (p-values << 0.01) with the *in vivo* data [34] (Fig. 6).

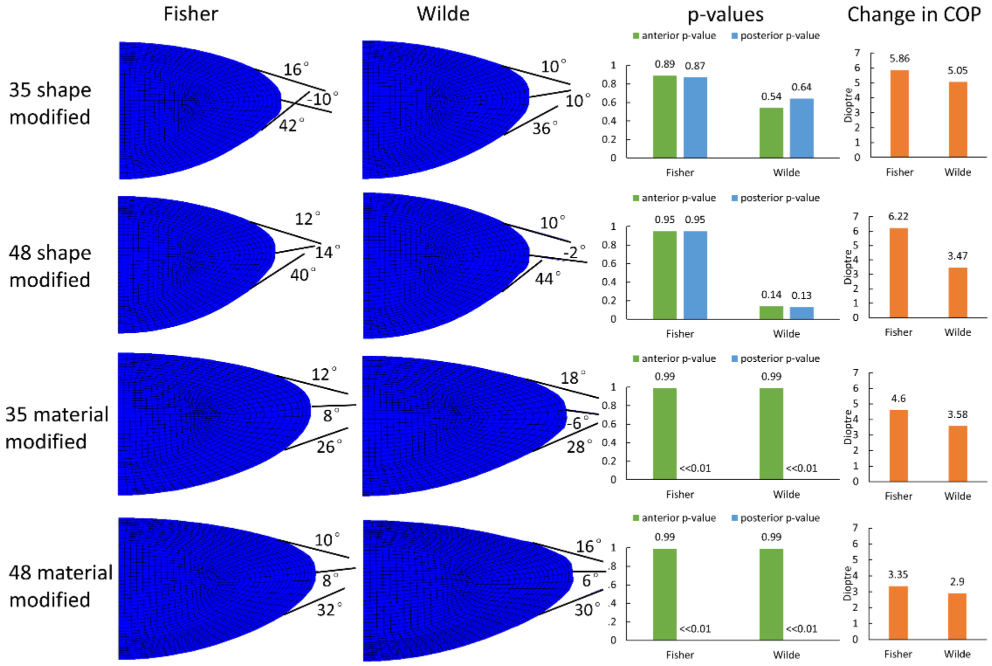


Fig. 6. Zonular angles that provide the closest fits to *in vivo* data [34], p-values used to evaluate the fits and resultant change in COP for modified models assuming either shape or material parameters of the 16-year-old lens.

4. Discussion

Models developed in the present study were based on material properties obtained from two studies using centrifugal forces to calculate lens elasticity [7,10]. The earlier study by Fisher [7] reported a stiffer lens cortex than nucleus at all measured ages. Burd et al. [35] indicated that Fisher [7] used simplified assumptions of lens geometries, and that contributions of capsular elasticity were not excluded. Such assumptions would result in erroneous findings of a greater stiffness in the lens cortex than in the nucleus [35]. To overcome these inaccuracies, Wilde et al. [10] adopted a high-speed camera that was synchronised for lens orientation and developed a hyper-elastic Finite Element model for inversely calculating the elastic moduli of measured lenses. Contrary to the results reported by Fisher [7], Wilde et al. [10] showed that the lens nucleus becomes stiffer than the lens cortex around the fourth to fifth decade of life.

The present study adopts a similar modelling concept as in several previous studies [36-39] by constructing axisymmetric lens models, each with three different sections of zonular fibres. Each developed model was constructed in accordance with geometries of an intact lens rather than an assemblage of parameters from various sources [36,38,39]. In addition, a nodal coupling mechanism was introduced to anchorage points of zonular fibres on the lens capsule, to maintain smooth curvatures at the lens periphery during simulation. Instead of attaching the three zonular fibres to a single stretching point [36-39], the three different zonular fibres were provided with the capacity to move in three independent directions. A range of displacement combinations, of 0.5mm and 0.6mm, to three different sections of the zonule were simulated for the 16-year-old lens model. The combination that provided the closest fits to *in vivo* data [34] was 0.6mm to anterior and posterior zonular fibre, 0.5mm to the equatorial zonular fibre.

Recent studies show that the capsular thickness varies spatially and is thicker at the anterior than the posterior pole and that the thickest part is at the lens periphery [40,41]. A previous study [22] showed that models with spatially varying capsular thicknesses [41], in general, demonstrate a slightly higher change in COP than models with uniform capsular thicknesses [12] but both types of models gave same conclusion with regard to the relative importance of different zonular sections. The choice of uniform capsular thickness for models in this study reduced computational power and simulation time.

The selection of domains of three zonular angles were made according to a previous study [33]: the model with 20 degree anterior zonular angle demonstrated good fits to *in vivo* data [34] for the anterior lens surface; the model with 35 degrees of posterior zonular angle demonstrated good fits to *in vivo* data [34] for the posterior lens surface; the equatorial zonular angle was not found to have make any significant contribution to either the optical powers or to the deformations of lens models [22]. Therefore, a baseline value of zonular angle triplet of [20, 0, 35] was selected for the sensitivity analysis and the angular domain was decided by extending each of three baseline values to 10 degrees on either side. The 16 year old models (Fig. 4) and the shape modified models of both 35 and 48 year old models with two sets of material properties [7,10] (Fig. 6) show good fits to the *in vivo* data [34]. All have relatively flatter anterior zonular angles ranging from 10 to 16 degrees, and a steeper posterior zonular angle, ranging from 34 to 44 degrees. It should be noted that the incremental changes in COP from lens models do not map exactly onto *in vivo* data (Fig. 5) because the latter measured response to an accommodative stimulus [34]. The comparison between models and *in vivo* data [34] were via slopes of linear regression lines of radius of curvature versus change in focusing power; this evaluates the extent to which the lens can alter its surface curvature per dioptre.

The maximum change in COP produced by original models decreases with age and is more pronounced for models using material properties of Wilde et al. [10] (Fig. 3a). This is closer to the *in vivo* results as accommodation is almost lost by the fifth decade [1, 2]. Replacing the material properties and the geometries of the 35 and 48 year old models with those of the 16 year old model, can increase the change in COP as seen in Figures 3b,c. These results confirm that both geometrical and mechanical changes with age play a role in accommodative loss. However, geometric changes seem to have a more important influence as the shape modified models show a higher restoration of COP (Fig. 3c). Such results are consistent with a previous modelling study that reported a restoration of up to 3.7 dioptres of accommodative amplitude in a model based on a 45 year old lens when the model was given the curvatures of a younger lens (29 year old); replacing the material properties of the older lens model with those of the younger lens only restored 0.83 dioptres of optical power [42]. Dimensions of the lens: the thicknesses and equatorial diameters, increase with age [43-45], resulting in anterior and posterior surfaces becoming steeper as the lens grows [46, 47].

Consistent with the previous study [22], altering the zonular angles for the 16 year old model can provide good fits to *in vivo* data [34] for both anterior and posterior lens surfaces. Modifying the shapes of the 35 and 48 year old models gives good fits for both surfaces (Fig. 6). Modifying the material properties only provides good fits of the modelling data to the *in vivo* data [34] for the anterior lens surface (Fig. 6). This further indicates the predominant importance on accommodative capacity of lens geometry over material properties. Efforts at restoring the accommodative ability of implants should focus on techniques and designs that can mimic lens shapes of younger, highly accommodating lenses. This may also apply to lens refilling techniques using elastic polymers [48-51] that behave mechanically and optically as the natural lens; the desired shape should be one that maximizes accommodation for the least effort.

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References

1. F.C. Donders and W.D. Moore, “On the anomalies of accommodation and refraction of the eye: With a preliminary essay on physiological dioptrics,” The New Sydenham Society, (1864).
2. A. Duane, “Normal values of the accommodation at all ages,” J. Am. Med. Assoc. **59**(12), 1010-1013 (1912).
3. J.L. Alio, J.L. Barrio and A. Vega-Estrada, “Accommodative intraocular lenses: where are we and where we are going,” Eye Vis(Lond.). **4**(1), 16 (2017).
4. A.L. Sheppard, A. Bashir, J.S. Wolffsohn and L.N. Davies, “Accommodating intraocular lenses: a review of design concepts, usage and assessment methods,” Clin. Exp. Optom. **93**(6), 441-452 (2010).
5. P.N. Farnsworth and S.E. Shyne, “Anterior zonular shifts with age,” Exp. Eye Res. **28**(3), 291-297 (1979).
6. J.F. Koretz and G.H. Handelman, “How the human eye focuses,” Scientific American. **259**(1), 92-99 (1988).
7. R.F. Fisher, “The elastic constants of the human lens,” The Journal of Physiology. **212**(1), 147-180 (1971).
8. K.R. Heys, S.L. Cram and R.J. Truscott, “Massive increase in the stiffness of the human lens nucleus with age: the basis for presbyopia?” Mol. Vis. **10**, 956-963 (2004).
9. H.A. Weeber, G. Eckert, W. Pechhold and R.G. van der Heijde, “Stiffness gradient in the crystalline lens,” Graefes Arch. Clin. Exp. Ophthalmol. **245**(9), 1357-1366 (2007).
10. G.S. Wilde, H.J. Burd and S.J. Judge, “Shear modulus data for the human lens determined from a spinning lens test,” Exp. Eye Res. **97**(1), 36-48 (2012).
11. R.F. Fisher, “Elastic constants of the human lens capsule,” J. Physiol. **201**(1), 1-19 (1969).
12. S. Krag and T.T. Andreassen, “Mechanical properties of the human lens capsule,” Prog. Retin. Eye Res. **22**(6), 749 – 767 (2003)
13. N.M. Ziebarth, E. Arrieta, W.J. Feuer, V.T. Moy, F. Manns and J.M. Parel, “Primate lens capsule elasticity assessed using Atomic Force Microscopy,” Exp. Eye Res. **92**(6), 490 – 494 (2011).
14. J.F. Koretz and G.H. Handelman, “Modeling age-related accomodative loss in the human eye,” Mathematical Modelling. **7**(5-8), 1003-1014 (1986).
15. A.J. Bron, G.F. Vrensen, J. Koretz, G. Maraini and J.J. Harding, “The ageing lens,” Ophthalmologica. **214**(1), 86-104 (2000).
16. M.T. Pardue and J.G. Sivak, “Age–related changes in human ciliary muscle,” Optom. Vis. Sci. **77**(4), 204–210 (2000).
17. A.L. Sheppard and L.N. Davies, “The effect of ageing on in vivo human ciliary muscle morphology and contractility,” Invest. Ophthalmol Vis. Sci. **52**(3), 1809-1816 (2011).
18. E. Fincham, “The Mechanism of Accommodation,” Br. J. Ophthalmol. **Suppl. 8**, 1–80 (1937).
19. L. Werner, F. Trindade, F. Pereira, and L. Werner, “Physiology of accommodation and presbyopia,” Arq. Bras. Oftalmol. **63**(6), 487 – 493 (2000).
20. W.N. Charman, “The eye in focus: accommodation and presbyopia,” Clin. Exp. Optom. **91**(3), 207-225 (2008).
21. M. Bahrami, M. Hoshino, B. Pierscionek, N. Yagi, J. Regini and K. Uesugi, “Optical properties of the lens: An explanation for the zones of discontinuity,” Exp. Eye Res. **124**, 93-99 (2014).
22. K. Wang, D.T. Venetsanos, J. Wang, A.T. Augousti and B.K. Pierscionek, “The importance of parameter choice in modelling dynamics of the eye lens,” Scientific Reports. **7**(1), 16688 (2017).
23. R.C. Augusteyn, A. Mohamed, D. Nankivil, P. Veerendranath, E. Arrieta, M. Taneja, F. Manns, A. Ho and J.M. Parel, “Age-dependence of the optomechanical responses of ex vivo human lenses from India and the USA, and the force required to produce these in a lens stretcher: the similarity to in vivo disaccommodation,” *Vision Res.* **51**(14), 1667-1678 (2011).
24. L.A. Levin, S.F. Nilsson, J. Ver Hoeve, S. Wu, P. L. Kaufman and A. Alm, “Adler’s Physiology of the Eye E-Book,” Elsevier Health Sciences, (2011).
25. E.A. Hermans, P.J. Pouwels, M. Dubbelman, J.P. Kuijer, R.G. van der Heijde and R.M. Heethaar, “Constant volume of the human lens and decrease in surface area of the capsular bag during accommodation: an MRI and Scheimpflug study,” Invest. Ophthalmol. Vis. Sci. **50**(1), 281-289 (2009).
26. J.F. Koretz and G.H. Handelman, “A model for accommodation in the young human eye: the effects of lens elastic anisotropy on the mechanism,” Vision Res. **23**(12), 1679-1686 (1983).
27. G. Van Alphen, and W.P. Graebel, “Elasticity of tissues involved in accommodation,” Vision Res. **31**(7-8), 1417–1438 (1991).
28. R.F. Fisher, “The ciliary body in accommodation,” Trans. Ophthalmol. Soc. UK. **105**, 208–219 (1986).
29. R. Michael, M. Mikielewicz, C. Gordillo, G.A. Montenegro, L. Pinilla Cortés and R.L. Barraquer, “Elastic Properties of Human Lens Zonules as a Function of Age in Presbyopes,” Invest. Ophthalmol. Vis. Sci. **53**(10), 6109–6114 (2012).
30. S. A. Strenk, J.L. Semmlow, L.M. Strenk, P. Munoz, J. Gronlund-Jacob and J.K. DeMarco, J.K., “Age-related changes in human ciliary muscle and lens: a magnetic resonance imaging study,” Invest. Ophthalmol.Visual Sci. **40** (6), 1162 – 1169 (1999).

31. G. Swegmark, “Studies with impedance cyclography on human ocular accommodation at different ages,” Acta Ophthalmol. **47**(5), 1186‐1206 (1969).
32. A.L. Sheppard, L.N. Davies, “The effect of ageing on in vivo human ciliary muscle morphology and contractility,” Investig. Ophthalmol. Vis. Sci. **52**(3), 1809‐1816 (2011).
33. K. Wang, D. Venetsanos, J. Wang and B.K. Pierscionek, “Gradient moduli lens models: how material properties and application of forces can affect deformation and distributions of stress.” Sci. Rep. **6**, 31171 (2016).
34. M. Dubbelman, G.L. Van der Heijde and H.A. Weeber, “Change in shape of the aging human crystalline lens with accommodation,” Vision Res. **45**(1), 117-132 (2005).
35. H.J. Burd, G.S. Wilde and S.J. Judge, “Can reliable values of Young’s modulus be deduced from Fisher’s (1971) spinning lens measurements?” Vision Res. **46**(8-9), 1346-1360 (2006).
36. H.J. Burd, S.J. Judge and J.A. Cross, “Numerical modelling of the accommodating lens,” Vis. Res. **42**(18), 2235‐2251 (2002).
37. R.A. Schachar and A.J. Bax, “Mechanism of human accommodation as analyzed by nonlinear finite element analysis,” Ann. Ophthalmol. **33**(2), 103–112 (2001).
38. D. Ljubimova, A. Eriksson, and S. Bauer, “Aspects of eye accommodation evaluated by finite elements,” Biomechanics Model. Mechanobiol. **7**(2), 139–150 (2008).
39. H.M. Pour, S. Kanapathipillai, K. Zarrabi, F. Manns, and A. Ho, “Stretch‐dependent changes in surface profiles of the human crystalline lens during accommodation: a finite element study,” Clin. Exp. Optom. **98**(2), 126–137 (2015).
40. R.F. Fisher and B.E. Pettet, “The postnatal growth of the capsule of the human crystalline lens,” J. Anat. **112**(2), 207–214 (1972).
41. R.I. Barraquer, R. Michael, R. Abreu, J. Lamarca, and F. Tresserra, “Human lens capsule thickness as a function of age and location along the sagittal lens perimeter,” Invest. Ophthalmol. Vis. Sci. **47**(5), 2053–2060 (2006).
42. D. Van de Sompel, G.J. Kunkel, P.S. Hersh and A.J. Smits, “Model of accommodation: Contributions of lens geometry and mechanical properties to the development of presbyopia,” J. Cataract Refract Surg. **36**(11), 1960-1971 (2010).
43. N. Brown, “The change in shape and internal form of the lens of the eye on accommodation,” Exp. Eye Res. **15**(4), 441–459 (1973).
44. B.K. Pierscionek, and R.C. Augusteyn, “Shapes and dimensions of in vitro human lenses,” Clin. Exp. Optom. **74**(6), 223–228 (1991).
45. A.M. Rosen, D.B. Deham, V. Fernandez, D. Borja, A. Ho, F. Manns, J.M. Parel and R.C. Augusteyn, “In vitro dimensions and curvatures of human lenses,” Vision Res. **46**(6-7), 1002-1009 (2006).
46. N. Brown, “The change in lens curvature with age,” Exp. Eye Res. **19**(2), 175-183 (1974).
47. M. Dubbelman, and G. Van der Heijde, “The shape of the aging human lens: curvature, equivalent refractive index and the lens paradox,” Vision Res. **41**(14), 1867–1877 (2001).
48. S. Saika, “Relationship between posterior capsule opacification and intraocular lens biocompatibility,” Prog. Retin. Eye Res. **23**(3), 283-305 (2004).
49. O. Nishi, K. Nishi, C. Mano, M. Ichihara, and T. Honda, “Controllling the capsular shape in lens refilling. Archives of Ophthalmology,”Arch. Ophthalmol. **115**(4), 507-510 (1997).
50. J.W. Kwon, Y.K. Han, W.J. Lee, C.S. Cho, S.J. Paik, D.I. Cho, J.H. Lee and W.R. Wee, “Biocompatibility of poloxamer hydrogel as an injectable intraocular lens: a pilot study,” J. Cataract Refract. Surg. **31**(3), 607-613 (2005).
51. O. Nishi, K. Nishi, Y. Nishi and S. Chang, “Capsular bag refilling using a novel accommodative intraocular lens,” J. Cataract Refract. Surg. **34**(2), 302-309 (2008).