Human Lens Capsule Thickness as a Function of Age and Location along the Sagittal Lens Perimeter

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PURPOSE. To investigate the variation in the thickness of the human lens capsule along the lens perimeter, as well as its changes with age.

METHODS. Altogether, 26 human donor lenses, aged 12 to 103 years, were histologically processed. Sagittal sections were stained for collagen with periodic acid-Schiff (PAS). Serial images of the lens border were taken with a photomicroscope and $25\times$ objective. Capsular thickness was measured every 250 μ m along the entire lens perimeter.

RESULTS. All studied capsules were thicker anteriorly, continuously increasing with age from 11 to 15 μ m in average at the anterior lens pole. Maximum thickness was located at the anterior midperiphery, increasing with age from 13.5 to 16 μ m. In most cases, there was a local thinning at a pre-equatorial zone, recovering to approximately 7 μ m at the equator. The latter value, as well as the minimal thickness at the posterior pole (mean 3.5 μ m), did not change with age, whereas the average thickness at the posterior periphery decreased from 9 to 4 μ m.

Conclusions. The human lens capsule thickness is at its maximum at the anterior midperiphery, which appears to be located central to the zonular insertion. It increases with age, especially at the anterior pole, while the midperipheral zone stabilizes or slightly decreases after the seventh decade. The anterior zonular insertion is actually related to a local preequatorial thinning, which remains unchanged with age. There was no posterior peripheral thickening, except in a few younger patients, with a modest relative maximum roughly at the equator. From here, the posterior capsule becomes progressively thinner and also diminishes with age, except for the thinnest, but stable posterior pole. (*Invest Ophthalmol Vis Sci.* 2006;47:2053-2060) DOI:10.1167/iovs.05-1002

T he lens capsule constitutes a thin, elastic, transparent envelop that encloses the crystalline lens, maintains its shape, and transmits the zonular forces to the lens matter. Although this implies an important role in accommodation, the details are the subject of debate. One possible factor influencing capsular biomechanics is its thickness—thus, the interest of knowing in detail its variations along the lens perimeter and with age.

The lens capsule is formed by the apposition of multiple layers of basal lamina, mainly composed of collagen type IV secreted by the lens epithelial cells. It shows a homogenous appearance on electron microscopy, except for a superficial portion: the pericapsular membrane or zonular lamella, composed of fibrils similar to those of the zonules.¹ Once the lens development is completed, the epithelial cells persist only anterior to the equator, allowing further thickening of the anterior capsule. Their absence at the posterior aspect of the lens explains that the corresponding portion of the capsule does not increase much (if at all) in thickness throughout life,¹ despite some capacity to secrete new basal lamina by the posterior lens fibers.²

During accommodation, the anterior lens surface becomes more curved and hyperbolic centrally, whereas the peripheral zone actually flattens.3 The mechanism responsible for this characteristic anterior conoidal shape is not well understood. Several factors, alone or in combination, have been advocated: (1) the distribution of the zonular forces over the lens surface, (2) the distribution of the elastic forces from the inner lens matter, and/or (3) the influence of the capsular thickness and its local variations. Tscherning⁴ believed that the anterior central surface of the lens bulked forward as a result of being the only "free" region, whereas the periphery was held flattened by the sustained tension from the zonules. Fincham⁵ argued that there was no need for external forces, because he could measure the conoidal form in isolated lenses. The ultimate forces causing the change in lens shape, although set in operation by the contracting ciliary muscle, would therefore reside in the lens matter itself. However, the removal of the lens capsule resulted in the loss of the conoidal accommodated form, indicating a molding effect by the capsule.⁶

Like most biological tissues, the lens capsule has viscoelastic properties. Thus, a considerable part of the applied forces or stress is relaxed within a short time. One theory assigning to the capsule a major accommodative role through the molding of the lens shape⁶ would require low capsular viscoelasticity. If this were true, the local variations of capsular thickness would be relevant. If, according to other theories, the main function of the capsule is merely to distribute the peripherally applied zonular forces over the entire lens, the energy for changing its shape would come mostly from the lens matter itself. The capsular changes in thickness would therefore be of lesser importance.^{7,8}

The ongoing discussion about the role of the lens capsule for accommodation appears based on a limited amount of thickness data. The classic works of Salzmann⁹ and Fincham⁶ (Fig. 1) rely on a few measured locations along the lens perimeter, sometimes from a few human specimens only. The frequently reproduced diagram of capsular thickness by Fincham (Fig. 1) appears to be an artistic representation. The thicknesses, as measured from this graph, give a characteristic bimodal curve that actually appears to be a combination of Fincham's and Salzmann's tabulated data (Fig. 1). More recent studies include detailed topographical information only from isolated cases,¹⁰ or none, apart from the generic anteriorposterior division.¹¹ The present study was undertaken to obtain broader anatomic evidence, especially about the topographical and age-related changes in human capsular thickness.

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FIGURE 1. Comparison of the historical data by Salzmann⁹ and Fincham.⁶ Salzmann's tabulated data are given as the mean of four groups; 10 years (n = 3; ages 7, 9, and 15 years), 23 years (n = 3; ages 19, 23, and 26 years), 37 years (n = 5; age 32, 35, 36, 40, and 41 years), 52 years (n = 3, age 48, 53, and 56 years). Fincham's data are the mean from his Table III (n = 3, age not specified). The data point for the equator comes from Finham's Figure 26 for calibration. The positions at the *x*-axes are defined in Figure 3. *Inset*: the lens sagittal section is Fincham's diagram (his Fig. 3) of the lens capsule with magnified thickness (from Fincham EF. The mechanism of accommodation. *Br J Ophthalmol.* Monograph supplement VIII. 1937:1–80. Reproduced with permission from the BMJ Publishing Group).

MATERIALS AND METHODS

Human crystalline lenses were dissected from fresh donor eyes provided by the Banco de Ojos para Tratamientos de la Ceguera (Barcelona, Spain), after the removal of the corneas for transplantation (mean postmortem time 46 ± 24 hours). In a few cases, they originated from the Cornea Bank Amsterdam (Amsterdam, The Netherlands). The research adhered to the tenets of the Declaration of Helsinki for research involving human tissue. A total of 26 lenses aged 12 to 103 years were thus obtained, fixed in 3.6% buffered formaldehyde, embedded in paraffin, sagittally sectioned, and stained for collagen with periodic acid-Schiff (PAS). Images of the sections passing approximately through the lens poles were taken through a $25 \times$ objective with a digital camera mounted on a photomicroscope (Carl Zeiss, Oberkochen, Germany; Fig. 2).

For each lens, between 80 and 100 serial microscopic images were captured along the section perimeter at a 1200×1600 -pixel resolution, and printed on A4 paper, resulting in a magnification of approx-

imately 780 times, with a total lens size on paper of approximately 3×7.5 m. The actual capsular thickness measured between 12 and 120 pixels in each image, equaling 2 to 20 mm on print. We considered digitally mounting the images for each lens. However, this proved impractical, given the huge size of the resultant files (approximately 980 megapixels). Instead, the complete circumferential series of prints for each lens were registered, aligned, and mounted on the floor of an appropriately sized room. The capsule thickness was measured with a rule on the prints every 20 cm, equaling every 250 μ m along the lens perimeter. Care was taken to distinguish the capsule proper from the zonular lamella and zonular remnants and to include only the former in the measurements.

The thickness data thus obtained were normalized to standard positions (p) in the lens perimeter, with p0 conventionally assigned to the anterior lens pole, p100 to the equator, and p200 to the posterior pole (Fig. 3). For the anterior and posterior portion of the lens, the data from both lateral halves were averaged independently for each lens



FIGURE 2. Sample images of PAS-stained human lens sections (from one lens, age 85 years); *left*: anterior pole; *middle*: equator; *right*: posterior pole. Scale bars, 20 μ m.



FIGURE 3. The lens capsule in sagittal section, illustrating the normalized positions along the lens perimeter. The lens anterior pole is referred to as p0, p100 represents the equator, and p200 the posterior pole. Intermediate positions p45, p80, and p120 in the lens periphery were found to be additional points of interest worthy of analysis.

and fitted to a sixth-order polynomial equation as a function of position along the perimeter.

For statistical analysis of the influence of age, we considered three groups of equal size (n = 7): group A, still with accommodation and a mean age of 36 years (30, 33, 33, 36, 40, 40, and 42 years); group B, presbyopic and a mean age of 65 years (54, 58, 65, 68, 69, 70, and 74 years); group C, advanced age group with a mean age of 92 years (85, 85, 89, 91, 94, 97, and 103 years). The data were evaluated with two-way ANOVA, followed by orthogonal comparison. The significance level was set at 0.05.

RESULTS

The complete data set of each capsule is plotted as a function of the defined normalized position along the lens perimeter: anterior pole set to p0, the equator to p100, and the posterior pole to p200, and so forth. For the sake of clarity, the resultant curves have been divided into six age groups (Fig. 4).

The distribution of capsular thickness in each case, as qualitatively appreciated from these curves, indicated that, apart from the obvious p0, p100, and p200, three additional positions were worthy of analysis: p45 at the anterior midperiphery-45% of the distance between the anterior pole and the equator-was roughly the position of the highest thickness peak; p80 corresponded to a local "valley" just anterior to the equator; and p120, in the posterior periphery, at 80% distance from the posterior pole toward the equator is a location where, according to Salzmann⁹ and Fincham,⁶ there should have been a second thickness peak. Some of the younger lenses, especially in the 40- to 49-year age group, showed both anterior midperipheral and posterior peripheral capsular thickening (at positions p45 and p120, respectively). However, whereas the anterior thickening became more pronounced in the higher age groups, the posterior one seems to diminish until it almost disappears and is "moving toward the equator" itself (Fig. 4). A smaller inflection remains visible, with a "valley" or local minimum just in front of the equator, followed by some equatorial recovery before progressive posterior tapering.

The evolution of capsular thickness at the six selected positions is plotted as a function of age in Figure 5. For clarity, the data points and trend lines (polynomial curve fit) of only three locations are shown in Figures 5A (the basic p0, p100, and p200), and 5B (the intermediate p45, p80, and p120). Figure 5C allows the comparison of all six trend lines without data points. Linear and quadratic regression was performed to find the trend lines as the best-fit-least-order polynomial. The F-value of the best-fit regressions (lowest probability) for each

position and the probability for each of the coefficients is given in Table 1. The best-fit-least-order polynomial for the anterior pole (p0) is a linear function (thickness = $0.093 \cdot \text{age} + 7.530$ μ m) and for the anterior maximum (p45) a second-order polynomial (thickness = $-0.004 \cdot \text{age}^2 + 0.515 \cdot \text{age}$) (capsule thickness expressed in micrometers and age in years). For all other positions, the linear and quadratic regression is not significant, which means that capsule thickness cannot be described with a linear or quadratic function, but only with a line parallel to the *x*-axis (Fig. 5).

Overall, the anterior capsule appeared to thicken with age, as opposed to the posterior portion. The values at the anterior pole (p0) increased clearly and constantly with age from approximately 6 μ m in the 12-year-old specimen to more than 15 μ m in the oldest lenses. In contrast, they remained almost unchanged at $\sim 7.2 \ \mu m$ at the equator (p100), as did the 3.3-µm minimum at the posterior pole (p200; Fig. 5A). In contrast, the intermediate positions showed a different behavior: the anterior midperipheral thickness (at p45) increased only until the seventh decade and then leveled and slightly decreased. The anterior peripheral minimum (at p80) remained unchanged (mean 6.2 μ m). The posterior periphery (at p120) showed, after an initial increase to about the fourth decade, a decrease with age, which, however, cannot be described by a linear or quadratic regression model. The mean thickness was 6.0 µm (Fig. 5B).

These measurements were subjected to a two-way ANOVA for three age groups of approximately 36 (group A), 65 (group B), and 92 (group C) years, on average. This analysis revealed a significant difference between the six positions independent of age (Table 2, source "position") and a significant difference between the positions for different age (Table 2, source "interaction factor age-position"). This means that the effect of position was different in different age groups.¹² Orthogonal comparison between age groups for each position was applied to see where the differences are located. This revealed a significant difference between capsular thickness of groups A and B at the anterior pole (p0), anterior midperiphery (p45), and posterior periphery (p120). However, no significant differences were demonstrated between groups B and C at any of the six positions (Fig. 6).

In summary, mean capsular thickness increased with age from 11 to 15 μ m at the anterior pole and from 13.5 to 16 μ m at the anterior midperiphery (p45, group means). There was a local thinning at the pre-equatorial zone (p80, overall mean 6.5 μ m), which changed little. The equatorial thickness remained constant at 7 μ m (overall mean). At the posterior periphery, thickness decreased with age from 9 to 4 μ m (group mean). There was no change in thickness at the posterior pole (overall mean, 3.5 μ m).

DISCUSSION

The histologic measurements of the human lens capsule thickness date back to early 20 century.^{6,9} The data in the classic paper by Fincham apparently refer to three lenses of unspecified age (Table III, page 18, Ref. 6), with thicknesses averaging 15.5 μ m at the anterior pole, 22.5 μ m at 2 mm from the pole (p45), and 18.5 at 3 mm peripherally (p65). The posterior capsule averaged 2.8 μ m at the posterior pole, 6.3 μ m at 2 mm from it, and 14.8 μ m at 3 mm from it (Fig. 1). Because Fincham states that the latter position was approximately 1 mm from the equator, these lenses must have measured approximately 8 mm in diameter, possibly coming from young individuals. Fincham⁶ also mentions the study of two human lenses of 11 and 68 years of age. An accompanying Figure 26 displays a series of values along the profile of the human lens capsule, possibly



FIGURE 4. Thickness profiles for all lens capsules along the sagittal perimeter (normalized positions, as defined in Fig. 3). Numbers in the keys in the panels represent the donor's age in years.

from those specimens. However, these values do not match those of the previously mentioned Table III. Salzmann's text book⁹ includes data from 17 lenses aged from 14 days to 71 years, which we have plotted in four groups in Figure 1. Both data sets support the concept of the human anterior lens capsule being thicker overall than the posterior and the presence of anterior and posterior peripheral thickenings. Because he found this thickening in other primates but not in lower mammals having little accommodation (rabbit, sheep, pig, and reindeer), Fincham⁶ concluded that the "accommodated form of lens [in humans] is produced by a molding action of the capsule on the soft lens substance," and that the "increased thickness [of the capsule near the equator] would assist in the general equatorial compression." More recently, capsular thickness has been measured in fresh human specimens using the difference in focus between the outer and inner surfaces of the capsule, as marked by the presence of latex microspherules added to a saline medium.^{10,11} The data in Fisher and Pettet¹⁰ came from four neonatal lenses and four additional from each decade until the seventh. Their paper shows tabulated data from the neonatal and second- and seventh-decade groups, with mean thickness, respectively, increasing from approximately 8 to 13 to 15 μ m at the anterior pole, 11 to 17 to 24 μ m at the "zonular insertion," and 10 to 20 to 19 μ m at the equator. These data confirm the progressive thickening of the anterior capsule and the stabilization at the equator after the second decade. Data concerning the posterior capsule are presented only as graphs from isolated "typical" cases. The posterior capsular thickness



FIGURE 5. Evolution of capsular thickness with age at six selected positions. (**A**, **B**) Data points and trend lines for three positions. (**A**) Anterior pole, equator, and posterior pole. (**B**) Anterior midperiphery, anterior peripheral minimum, and posterior periphery. (**C**) All six trend lines without data points, for clarity: anterior pole, anterior midperiphery, anterior peripheral minimum, equator, posterior periphery, and posterior pole.

at 1 mm from the equator was at its maximum in a 37-year-old eye (approximately 22 μ m), diminishing to 14 to 17 μ m in the older lenses. The posterior pole remained stable at approximately 3 μ m (Fig. 6B).¹⁰

Krag and Andreassen¹¹ measured capsular thickness in 25 lenses from donors aged 1 to 94 years, at single positions approximately 1.6 mm (p33) radially from the anterior and posterior poles. They confirmed the thickening with age of the anterior capsule, from approximately 15 μ m at birth to a mean of approximately 28 μ m during the seventh decade, then stabilizing or slightly decreasing. The posterior capsule remained stable around 5 μ m (range, 4-9 μ m, without significant slope; Fig. 6B).

Ziebarth et al.¹³ introduced a new optical technique to measure capsular thickness at the anterior and posterior poles and compared it with histologic measurements. Their noncontact optical system is based on a focus detection technique, in which light from a laser source is focused at various depths in the sample. Intensity changes of the reflected light are recorded that correlate to internal boundaries of the tissue. The optical and histologic results for the posterior pole correspond well with our results, as well as the histologic results for the

TABLE 1. Statistical Results of Curve Estimation for	Capsule Thickness as Function	of Age and for Six Po	sitions along the Lens Perimeter
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	Regression		Coefficient <i>n</i> Constant		Coefficient m1 Age		Coefficient m2 (Age) ²	
	F-value	Р	Value	Р	Value	Р	Value	Р
Anterior pole (p0)	13.791	0.002*	7.530	< 0.001*	0.093	0.002*		
Anterior maximum (p45)	8.769	0.004^{*}	0.219	0.956	0.515	0.002*	-0.004	0.004^{*}
Anterior minimum (p80)	0.980	0.339	8.535	$< 0.001^{*}$	-0.025	0.339		
Equator (p100)	0.000	0.983	7.352	$< 0.001^{*}$	0.000	0.983		
Posterior maximum (p120)	2.434	0.141	8.649	0.001^{*}	-0.046	0.141		
Posterior pole (p200)	0.429	0.523	3.581	0.001*	-0.009	0.523		

Results of best-fit-least-order polynomial: Capsule thickness = $m2 \cdot age^2 + m1 \cdot age + n$ (capsule thickness expressed in micrometers and age in years). Raw data and curves are shown in Figure 5.

*P < 0.05 represents a significant relationship in the regression or a significant contribution by a particular coefficient in the polynomial equation.

anterior pole. The optical results for the anterior pole are somewhat lower (Fig. 6B).

Our data confirm the overall picture of an anterior capsule thicker than the posterior, which is thinnest at the posterior pole, as well the continuous growth with age of the anterior portion, whereas the posterior remains stable or becomes thinner. However, some details of the thickness distribution and their variation with age differ from the previous reports. In the first place, the absolute maximum for each capsule was at the anterior midperiphery (at about p45), except for a few of the older cases in which the anterior pole was thickest (Fig. 4). Second, we consistently found a previously undescribed, anterior peripheral or pre-equatorial thinning at about p80, which appeared to correspond to the area of anterior zonular insertion (Fig. 7). Values at this location were 0.5 to 3 μ m below those at the equator in all lenses. Third, the posterior peripheral "mound" was rather modest and was present only in a few of the younger lenses (aged 30 and 40 years, Fig. 4). Only in the prepresbyopic group A, the mean at p120 was slightly higher than that at the equator. In the older groups, the only feature resembling a (small) second mound would be the relative equatorial thickening itself, compared with the pre-equatorial thinning. Actually, the values at the equator (p100) remained stable with age, whereas the posterior peripheral (p120) diminished (Figures 6). Finally, the thickness of the anterior capsule continues to increase throughout life only at the anterior pole (p0), whereas that of the midperiphery (p45), although significantly greater in group B than in group A, eventually levels and even regresses after the seventh decade, with the p0 and p45 trend lines crossing each other by the ninth decade (Fig. 5C).

For comparison, in Figure 6 we plotted, against position in the lens perimeter, our thickness data summarized for age groups A, B, and C, together with data from Salzmann⁹ and Fincham⁶ (Fig. 6A), and comparable-aged cases of Fisher and Pettet,¹⁰ and Krag and Andreassen¹¹ and the data from Ziebarth et al.¹³ (Fig. 6B). It is noteworthy that Salzmann's data for the posterior periphery (22 μ m) correspond to those for the anterior periphery, in contrast with the more moderate thickness reported by Fincham (14.8 μ m, at approximately p135).

Both Fincham and Salzmann found the anterior maximum (~22 μ m) at 2 mm (p45) and lower thicknesses (13 μ m, 15 μ m) between the anterior and posterior maxima^{6,9} (Fig. 6A). Although they located them at the equator at just over 4 mm from the lens pole), this depression marking the "doublemound" profile could correspond (slightly displaced) to our p80 thinner area (Fig. 6A). In contrast, Fischer and Pettet¹⁰ found the anterior capsular thickening to continue all the way to the equator in the 22- and 37-year-old cases in a "single mound" configuration. However, in the older lenses, the mound apparently moved toward the anterior pole as it continued growing, whereas the equator stabilized and became relatively thinner (see Fig. 3 from Fisher and Pettet¹⁰). The data from Krag and Andreassen¹¹ provide little topographic information, because they were taken from single paracentral positions at approximately 30% radial distance from the lens poles. However, they also support the stabilization or even regression of the thickening of the anterior capsule after the seventh decade¹¹ (Fig. 6B).

Capsule thicknesses from these six studies may not be comparable in absolute terms, because of the different methodologies. The specimens included in our study lacked a representation of the neonatal and childhood period, but otherwise covered the adult age groups including the prepresbyopic and presbyopic periods, and even beyond the eighth decadethe latter not covered by Fisher and Pettet.¹⁰ Our overall lower thicknesses, compared with those using fresh specimens,^{10,11} could be due to tissue shrinkage caused by the histologic processing. In contrast, the saline medium used in the microspherule technique could have induced some tissue swelling, while the storage at minus 80°C may alter tissue properties. In particular, the higher values of the peripheral areas in some studies may represent an overestimation, due to the inclusion of the zonular lamella and zonular remnants in the measurements, which we took care to avoid. Especially the microspherule technique would include any materials attached to the specimens. Fisher and Pettet¹⁰ did not find an appreciable decrease in thicknesses after enzymatic treatment with α -chymotrypsin. However, it is known that this enzyme cleaves the zonular filaments at random positions and not necessarily re-

TABLE 2. Analysis of Variance for Capsule Thickness for Three Age Groups at Six Different Positions along the Lens Perimeter

Source of Variation	Sum of Squares	Degrees of Freedom	Mean Square	F-ratio	Р	
Age	8.392	2	4.196	1.035	0.359	
Position	1916.511	5	383.302	94.543	< 0.001	
Interaction age-position Measurement error	140.427 401.372	10 99	$\begin{array}{r}14.043\\4.054\end{array}$	3.464	0.001	



FIGURE 6. Summarized capsule thickness data along the lens perimeter in the present study, compared with those in the literature. Groups A, B, C: present study, n = 21 (seven lenses per data point); error bars, SE of the predicted value for the mean from ANOVA statistics. Significant difference between groups marked with asterisk (P < 0.05 and orthogonal comparison). *Top*: tabulated data of Salzmann⁹ are given as the mean of two groups: 37 years (n = 5, ages 32, 35, 36, 40, and 41 years) and 52 years (n = 3, ages 48, 53, and 56 years). The data of Fincham⁶ are the mean from his Table III (n = 3, age not specified). The data point for the equator comes from Fincham's Figure 26. Lower part: Fisher¹⁰: one lens per age group. Krag¹¹: n = 25, thickness values from individual cases matching our age groups selected from their graph. Ziebarth¹³: n = 22, mean age, 74 years (range, 40-92), measured histologically and optically.

moves the zonular lamella from the capsule proper, nor all remnants of the zonular insertion footplates. Regarding the localization of measurements along the lens perimeter, we believe our method of full reconstruction of the enlarged lens section from micrographic prints allows a higher precision.

We checked a possible effect of postmortem time on the results of capsule thickness by looking at two small subgroups (n = 3) with different postmortem time (mean, 28 and 74 hours) and similar age (mean, 62 and 66 years). The *t*-test for capsular thickness at all the six positions studied showed a nonsignificant difference.

The authors of the papers cited herein commonly assumed that the peripheral capsular thickenings correspond to the areas of zonular insertion. However, both our data and those of Fincham⁶locate these maxima at approximately 2 mm from the anterior pole (p45; Figs. 1, 7). The common experience of any cataract surgeon indicates that the most anterior insertion of the zonules never reaches 2 mm from the lens pole, and rarely 3 mm from it (p65) in the oldest patients. Farnsworth and Shyne¹⁴ studied the anterior and equatorial zonular insertion and found an increase with age in the distance between the zonular insertion ring and the ciliary body remained rela-



FIGURE 7. Summarized thickness profiles for three age groups (mean of seven lenses per data point), showing a maximum at anterior midperiphery (about p45) and a pre-equatorial minimum (\sim p80) for all age groups. *Vertical lines*: the most anterior location of the zonular insertion.

tively constant. However, their data do not imply that the zonular insertions actually moves toward the anterior crystalline pole. It is rather that the lens grows anteriorly between the equator and the insertion ring. We normalized their data to a standard distance of 100 between anterior pole and lens equator using data of the equatorial lens diameter for different ages from Kuszak and Brown¹⁵ and Al-Ghoul et al.¹⁶ (Fig. 7). The anterior limit of the zonular insertion lies then at about p90 in the young (36 years), relatively advancing to about p82 in the middle ages (65 years), and only reaching p75 (approximately 3.3 mm from the pole) in the elderly (92 years). These positions consistently correlated with the pre-equatorial areas of relative thinning we found for all age groups, being increasingly marked in the older age (Fig. 7).

From the current data we cannot infer directly whether the variations in capsular thickness along the lens perimeter are relevant for accommodation. However, if this were the case, our results would support that these occur almost exclusively at the anterior capsule, and possibly relate to the thickening *anterior* to the limit of zonular insertion. The presence of the pre-equatorial thinning under the zonular insertion could represent an inflection zone facilitating the geometric change from the peripheral flattening.

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References

- Bron AJ, Brown NP. Lens Disorders: A Clinical Manual of Cataract Diagnosis. Oxford, UK: Butterworth-Heinemann; 1996:32–47.
- Parmigiani CM, McAvoy JW. The roles of laminin and fibronectin in the development of the lens capsule. *Curr Eye Res.* 1991;10:501– 511.

- 3. Dubbelman M, Van der Heijde GL, Weeber HA. Change in shape of the aging human crystalline lens with accommodation. *Vision Res.* 2005;45:117-132.
- 4. Tscherning M. H. von Helmboltz et la Théorie de l'Accommodation. Paris, 1909.
- Fincham EF. An experiment on the influence of tension upon the form of the crystalline lens. *Trans Ophthalmol Soc U K*. 1936;56: 138-147.
- Fincham EF. The mechanism of accommodation. Br J Ophthalmol. 1937(suppl 8):1-80.
- Koretz JF, Handelman GH. Model of the accommodative mechanism in the human eye. *Vision Res.* 1982;22:917–927.
- Krag S. Biomechanical measurements of the lens capsule. PhD Thesis. Aarhus, The Netherlands: University of Aarhus; 1998:1–94.
- Salzmann M. Anatomie und Histologie des menschlichen Augapfels im Normalzustande, seine Entwicklung und sein Altern. Leipzig und Wien, Austria: Franz Deuticke; 1912:175-186.
- 10. Fisher RF, Pettet BE. The postnatal growth of the capsule of the human crystalline lens. *J Anat.* 1972;112:207–214.
- Krag S, Andreassen TT. Mechanical properties of the human posterior lens capsule. *Invest Ophthalmol Vis Sci.* 2003;44:691–696.
- Zar JH. Two-factor analysis of variance. In: Zar JH. *Biostatistical Analysis*. Upper Saddle River, NJ: Prentice-Hall International; 1999:231–272.
- Ziebarth NM, Manns F, Uhlhorn SR, Venkatraman AS, Parel JM. Noncontact optical measurement of lens capsule thickness in human, monkey, and rabbit postmortem eyes. *Invest Ophtbalmol Vis Sci.* 2005;46:1690-1697.
- 14. Farnsworth PN, Shyne SE. Anterior zonular shifts with age. *Exp Eye Res.* 1979;28:291–297.
- Kuszak JR, Brown HG. Embryology and anatomy of the lens. In: Albert DM, Jakobiec FA, eds. *Principles and Practice of Ophthalmology*. Philadelphia: WB Saunders; 1994:82-96.
- Al-Ghoul KJ, Nordgren RK, Kuszak AJ, Freel CD, Costello MJ, Kuszak JR. Structural evidence of human nuclear fiber compaction as a function of ageing and cataractogenesis. *Exp Eye Res.* 2001; 72:199–214.