

Optical aberrations and alignment of the eye with age

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We explored the relative changes in ocular, corneal, and internal aberrations associated with normal aging with special emphasis in the role of ocular alignment and lens shape factor in the balance of aberrations. Ocular and corneal aberrations together with the angle kappa were measured for a 5-mm pupil diameter in 46 eyes with low refractive errors and ages ranging between 20 and 77 years. The root mean square (RMS) of the higher order ocular and corneal aberrations increased with age at a rate of $0.0032 \mu\text{m}/\text{year}$ and $0.0015 \mu\text{m}/\text{year}$, respectively. While in young eyes the partial compensation of aberrations by the internal surfaces was clear, no significant difference was found between corneal and ocular RMS in the older group. The ocular spherical aberration ($0.0011 \mu\text{m}/\text{year}$) and horizontal coma ($0.0017 \mu\text{m}/\text{year}$) increased moderately with age. This is not due to changes in the optical alignment, since angle kappa did not vary significantly with age. Age-related variations in the radii of curvature of the crystalline lens modify slightly its shape factor, reducing the compensation of lateral coma. This suggests that geometrical changes in the crystalline lens with age contribute to modify its aberration structure, reducing the compensation mechanism and explaining most of the measured increment of ocular aberrations with age.

Keywords: optical aberrations, human eye, age, alignment

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Introduction

The optical system of the human eye is affected by aberrations that limit the quality of the retinal image and visual perception. It is well known that the natural process of aging induces changes in the ocular optics that tend to increase the amount of higher order aberrations (Applegate, Donnelly, Marsack, & Koenig, 2007; Artal, Berrio, Guirao, & Piers, 2002; Atchison & Markwell, 2008; Brunette, Bueno, Parent, Hamam, & Simonet, 2003; Calver, Cox, & Elliot, 1999; Fujikado et al., 2004; Guirao et al., 1999; McLellan, Marcos, & Burns, 2001). This contributes to degrade the overall retinal image quality in older subjects in combination with other optical factors like intraocular scattering (Ijspeert, de Waard, van den Berg, & de Jong, 1990; Pérez, Manzanera, & Artal, 2009) and causes a larger decline in spatial vision than the senescent neural losses (Elliott et al., 2009). It is important to understand the causes of the optical deterioration of the eye with age, not only for the fundamental scientific interest

but also for the development of improved optical solutions for older patients.

The young eye is, in general, less affected by higher order aberrations than any of its optical components. This occurs as a result of a mechanism of partial compensation of aberrations between the anterior corneal surface and the internal optics, mainly the crystalline lens (Artal, Guirao, Berrio, & Williams, 2001; Kelly, Mihashi, & Howland, 2004). This mechanism has demonstrated to work systematically well for spherical aberration (Artal & Guirao, 1998; El Hage & Berny, 1973; Millodot & Sivak, 1979; Smith, Cox, Calver, & Garner, 2001) and horizontal coma (Artal, Benito, & Tabernero, 2006; Tabernero, Benito, Alcón, & Artal, 2007), meaning that the young eye approximates to an aplanatic optical system, only affected in general by small amounts of spherical aberration and coma (Artal & Tabernero, 2008).

However, as the eye ages from the young adulthood (20–30 years) to the elderly (60–80 years) it becomes more aberrated on average. In particular, the spherical aberration (SA) of the eye tends to increase in older eyes.

Similarly, a significant increment of horizontal coma and other third-order aberrations has been reported. In a previous work (Artal et al., 2002), we showed that a progressive disruption of the corneal–internal aberrations balance was the primary source of increment of ocular aberrations in older eyes. However, the underlying causes of this mechanism remain unclear. To answer the question, it is necessary to improve our understanding about how ocular aberrations are generated and how the compensation mechanism works. Ocular aberrations may have an intrinsic origin related to the shape of the surfaces or the profile of the refractive index, or an angular origin associated with the alignment of the optical components. The combination of intrinsic factors makes the cornea of a young eye have, in general, small positive SA while the internal surfaces have a similar amount of negative SA, balancing each other to produce an eye with close to zero SA. With aging, variations in these intrinsic factors might be responsible for an SA reduction. Concerning asymmetric aberrations, the degree of compensation of corneal coma by the internal optics increases with the distance between the pupillary reflex and the center of the entrance pupil (Artal et al., 2006; Kelly et al., 2004). This distance is directly related with angle kappa (Le Grand & El Hage, 1980), also referred in the literature as angle lambda (Atchison & Smith, 2000). Since the eye is a non-aligned optical system, angle kappa represents the global rotation performed by the eye to form the image of a fixation point source on the fovea. Tabernero et al. (2007) found that young hyperopic eyes, although typically affected by larger angle kappa induced by their shorter axial length, exhibit similar amounts of lateral coma than young myopic eyes as a consequence of a significantly larger corneal–internal balance. This indicates that horizontal coma has an angular origin. Therefore, a factor to understand an age-related variation in the balance of horizontal coma might be angle kappa. However, to our knowledge, no data of angle kappa as a function of age can be found in the literature. There are different factors that could modify angle kappa during normal aging: for instance, age-related shifts in the position of the center of the pupil, larger fixation errors in older eyes, or age-related variations in the base curvature of the anterior corneal surface. More important, the shape of the crystalline lens is altered by normal aging, and the radii of curvature of both lens surfaces tend to decrease (Dubbelman & Van der Heijde, 2001). Since the coma generated by a tilted lens depends on the curvature of its surfaces, the age-related variation in the lens shape would affect their value and compensation.

In this context, the aim of this study is to further investigate the mechanism of compensation of aberrations as the eye ages, with special attention to lateral coma. For this purpose, we measured angle kappa as a function of age and studied the effect of the age-related variation in the radii of curvature of the crystalline lens. In addition, we provide an assessment of the variation with age of

the main higher order aberrations in near-emmetropic normal eyes, based on a refined experimental procedure and a careful selection of the sample of older subjects, including objective methods to discard incipient states of cataract likely undetected by standard ophthalmological testing.

Methods

Measurement of wave-front aberrations

We measured the wave-front aberrations of the eye using a custom-made Hartmann–Shack (HS) wave-front sensor (Prieto, Vargas-Martín, Goelz, & Artal, 2000) developed in our laboratory. It was especially designed to perform clinical measurements following a protocol that would be easy and comfortable for untrained subjects. Our device included a super-luminescent diode emitting at $\lambda = 780$ nm to illuminate the retina and an array of microlenses with a pitch of 200 μm and an effective focal length of 8.05 mm.

The wave aberrations of the anterior corneal surface were obtained by measuring its shape with a Placido disk videokeratoscope (Atlas, Carl-Zeiss-Meditec, Dublin, CA, USA), then adjusting the elevations data to a surface described in a Zernike polynomial expansion, and finally importing the data into a ray-tracing software (ZEMAX Development, San Diego, CA, USA) to calculate the wave-front aberrations. This procedure is essentially similar to that described previously (Guirao & Artal, 2000).

Ocular and corneal wave-front aberrations were obtained for a 5-mm pupil diameter and expanded up to the sixth order of the Zernike polynomial basis. The average of at least three HS images and three topograms for each subject was used as the nominal value. Aberrations were reported following the OSA standards (ANSI Z80.28, 2004). The sign of the Zernike coefficients with odd symmetry about the vertical axis (e.g., lateral coma C_3^1 and x -trefoil C_3^3) was reversed in all right eyes to avoid the bilateral symmetry between right and left eyes.

All the measurements were performed under natural viewing conditions, except for four older eyes that required pharmacological pupil dilation (1% tropicamide) to reach a pupil diameter of 5 mm. Internal aberrations were directly estimated by subtracting corneal from ocular mean aberration coefficients (Artal et al., 2001), under the assumption that the small variation in the wave aberrations between the corneal vertex and the entrance pupil plane could be neglected. Due to the similarity between the refractive indexes of the cornea and the aqueous humor, the contribution of the posterior corneal surface to the higher order aberrations is comparably smaller than that of the lens. For this reason, the crystalline lens may

be considered as the main source for the ocular–internal aberrations.

To compare corneal and ocular aberrations is not straightforward (Artal, 2004). Topographers and HS systems typically use different reference axis to report the aberration data, which can induce potential errors (Salmon & Thibos, 2002). In the present study, we reported both corneal and ocular aberrations with respect to the *principle line of sight* (i.e., the line connecting the fixation point and the center of the entrance pupil). Since the topographer provides the corneal elevation data relative to the corneal reflex instead, each topographic map was computationally displaced to the pupil center prior to apply the ray-tracing procedure to estimate the corneal aberrations. On the other hand, the illumination conditions during the topography measurements (photopic) differed from those during the HS recording (mesopic level), inducing a pupil centering shift that might alter the aberrations recovered (Tabernero, Atchison, & Markwell, 2009; Wilson, Campbell, & Simonet, 1992). According to Tabernero et al. who measured the pupillary misalignment between corneal topography and HS illumination conditions in 62 eyes from 19 to 69 years, the modulus of the pupil shift is of 0.21 ± 0.11 mm on average and affects primarily the coma of the anterior corneal surface for a 5-mm pupil. To avoid this problem, we estimated the displacement of the center of the pupil from the corneal reflex for each eye using our Purkinje instrument described below (which operated under mesopic illumination conditions similar to those of the HS sensor) and applied this value to recenter the corneal aberrations.

To describe the level of coupling between corneal and internal aberrations, we calculated a parameter referred as the compensation factor, defined as $CF = 1 - (RMS_{eye} / RMS_{cornea})$ by Artal et al. (2002). Since it represents a relative magnitude, it has no dimensions, and the rate of variation of the compensation factor with age will be evaluated in “units of compensation factor” per year (units/year) when we present these results. Positive values of CF indicate that a fraction of the corneal aberrations is balanced by the internal optics, with the unity (maximum value) representing a totally compensated eye, small values of CF indicate a non-compensatory role of the internal surfaces, and negative values of CF (up to $-\infty$) are associated with the internal surfaces adding their aberrations to those of the cornea. We extended the definition of the compensation factor to evaluate the coupling of individual aberration coefficients in magnitude, according to the expression: $CF\{i\} = 1 - (|C_{i_eye}| / |C_{i_cornea}|)$, where the subindex i denotes any Zernike coefficient. Since this parameter evaluates the level of compensation relative to the particular corneal aberration magnitude, the CF may provide misleading values when the corneal contribution is very small. To avoid this undesirable situation, the CF was only considered when the corneal contribution was $\geq 0.05 \mu\text{m}$.

Measurement of angle kappa

The procedure applied to estimate angle kappa is similar to the one described previously (Tabernero, Benito, Nourrit, & Artal, 2006). The angle kappa is defined (Atchison & Smith, 2000) as the angular distance in the object space between the pupillary axis (the line perpendicular to the cornea that intersects the center of the entrance pupil) and the principal line of sight (defined above), as it is shown in Figure 1 (upper panel). These lines may be considered as clinical approximations to the optical axis and the visual axis of the eye, respectively. To estimate the angle kappa, we measured the displacement of the first Purkinje image with respect to the pupil center as a function of the fixation angle of the eye when it observes a target (Phillips, Pérez-Emmanueilli, Rosskothén, & Koester, 1988). To generate the corneal reflex, we projected into the eye a semicircular arrangement of infrared LEDs, placed at a fixed axial distance from the ocular entrance pupil. This was achieved by aligning the line of sight of the eye with the optical axis of the

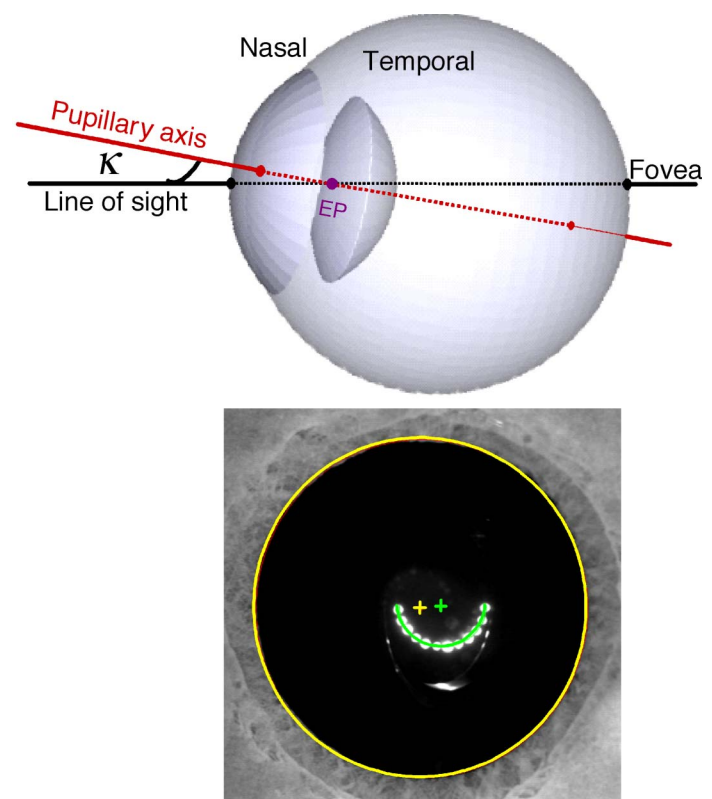


Figure 1. (Upper panel) An example of angle kappa (κ) in the left eye, with the pupillary axis oriented temporal ($\kappa_X > 0$) and superior ($\kappa_Y > 0$) with respect to the line of sight (EP: center of the entrance pupil). (Bottom panel) An image of the entrance pupil adjusted to a full ellipse (yellow line) and of the corneal reflex adjusted to a semiellipse (green line). The yellow cross marks the center of the entrance pupil (EP), and the green cross marks the center of the corneal reflex.

experimental setup, and then focusing the pupil plane (moving axially the head of the subject) on a CCD camera with a telecentric objective. We considered the array of LEDs as a collection of punctual light sources, each subtending a different angular eccentricity with respect to the line of sight. The eye was required to fixate to a single central stimulus and a picture of the anterior pupil plane with the first Purkinje image of the array of LEDs was recorded to estimate angle kappa. This is an improvement with respect to the procedure described by Tabernero et al. (2006), in which the eye had to fixate sequentially to a series of stimulus placed at known angular eccentricities. In the digitalized image, a semiellipse was adjusted to the semicircular corneal reflex and a full ellipse to the pupil edge (Figure 1, lower panel) to measure the longitudinal x - and y -positions of each component of the corneal reflex (LEDs images) with respect to the pupil center. These positions were linearly correlated with the angular positions subtended by the corresponding original illuminating LED, using previously tested fitting constants (Tabernero et al., 2006). Finally, we estimated angle kappa as the extrapolated angle that overlapped the center of the pupil and the corneal reflex.

Subjects

We measured 46 normal eyes of subjects ranging between 20 and 77 years of age. The whole group consisted of 9 young eyes of 20–23 years old, 12 middle-aged eyes of 42–58 years old, and 25 older eyes of 60–77 years old. The mean age and standard deviation for each age group are listed in Table 1. This study adhered to the tenets of the Declaration of Helsinki and informed consent was obtained from the subjects after they were informed of the nature and all possible consequences of the study.

All the eyes included in the study had monocular best-corrected visual acuity $\geq 20/20$ ($\geq 20/25$ for older eyes) and were emmetropic or slightly ametropic, not exceeding ± 2.0 diopters (D) of mean defocus and 1.5 D of astigmatism evaluated by subjective refraction (see Table 1 for averaged data). For each patient, we selected the eye that satisfied the inclusion criteria or the eye closer to emmetropia when both were eligible. None of the eyes measured had a history of ocular surgery, and they all followed a complete ophthalmological exam to discard any disease or abnormality in the ocular media.

In particular, special emphasis was placed on the detection of early stages of cataract in the older eyes.

Those eyes that passed successfully the slit-lamp examination of the crystalline lens underwent two additional measurements. We recorded double-pass retinal images of a point source (Santamaría, Artal, & Bescós, 1987) with a clinical instrument (OQAS, Visiometrics SL, Spain) and discarded those eyes that presented any degradation in the quality of the retinal image that could represent a loss of transparency related to an early cataract. We rejected those eyes with Hartmann–Shack images that exhibited any kind of intensity features (like areas with missing spots) or unusual high levels of the background signal, which could also be related to the initial development of a nuclear or cortical cataract (Thibos & Hong, 1999).

Results

Figure 2a shows the variation of the higher order root-mean-square (RMS) wave-front error as a function of age for the eye (squares) and the cornea (circles). The error bar associated with each data point is the standard deviation in this and the following figures. Solid lines represent statistically significant linear regressions while dashed lines represent statistically non-significant regressions. Both the ocular and the corneal RMS are positively correlated with age (purple line for the eye and blue line for the cornea), although with a faster rate of growth (about two-fold) for the ocular RMS ($0.0032 \mu\text{m}/\text{year}$, $r = 0.60$, $p < 0.0001$) than for the corneal RMS ($0.0015 \mu\text{m}/\text{year}$, $r = 0.39$, $p = 0.008$). To better illustrate this behavior, Figure 2b compares the mean RMS ($\pm SD$) of the eye and the cornea for the three age groups.

While for young eyes the RMS of the cornea is significantly larger than the overall RMS of the eye indicating that part of the corneal aberrations is balanced by the internal surfaces, they do not differ significantly for middle-aged or older eyes. Figure 2c shows the compensation factor. It is positive in all the young eyes and decreases linearly as the eye ages ($-0.0067 \text{ unit}/\text{year}$, $r = 0.45$, $p = 0.002$) reaching zero or negative values in some mature and older eyes. Figure 2d illustrates the RMS of the internal surfaces. It remains statistically stable with age ($p = 0.50$), indicating that age does not affect remarkably the total amount of higher order aberrations of the crystalline lens. We also explored the variation with age of the more relevant higher order aberration coefficients.

Age group	Eyes	Age range (years)	Mean age (years)	Mean defocus (D)	Mean astigmatism (D)
Young	9	20–23	21.0 ± 1.0	-0.29 ± 0.44	-0.17 ± 0.10
Middle-aged	12	42–58	49.2 ± 5.3	-0.04 ± 0.86	-0.50 ± 0.40
Older	25	60–77	67.0 ± 5.2	$+0.75 \pm 0.85$	-0.67 ± 0.33

Table 1. Data of the eyes involved in the study divided in three age groups. Means include standard deviations.

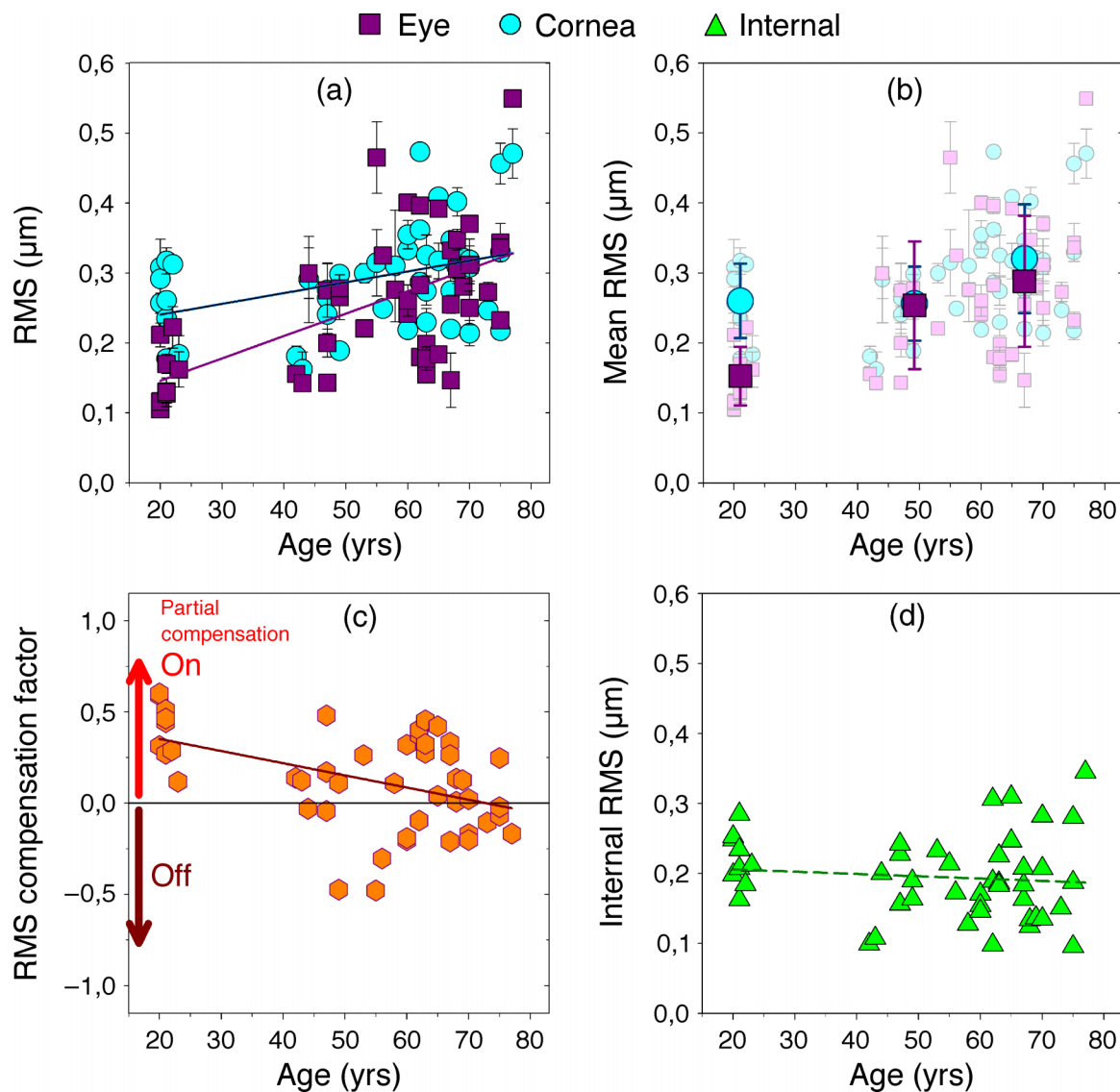


Figure 2. (a) Variation of the ocular (square) and corneal (circle) RMS of the wave-front aberration from the third to the sixth order as a function of age. Error bars represent the standard deviations. Solid lines are significant linear regressions. (b) Comparison of the averaged (\pm SD) higher order RMS of the cornea and the complete eye for the young, middle-aged, and older groups. The size of the mean dots has been enlarged to emphasize the behavior. (c) Variation of the RMS compensation factor with age. (d) Variation of the RMS of the internal surfaces with age. The dashed line represents a non-significant linear regression.

Figure 3a illustrates the behavior of the fourth-order spherical aberration (C_4^0) as a function of age for the eye (squares), the cornea (circles), and the internal surfaces (triangles).

All the eyes under study have positive SA (except for two cases with around zero SA), with small values in young eyes ($\leq 0.1 \mu\text{m}$) and a significant trend to increase slightly with age ($0.0011 \mu\text{m}/\text{year}$, $r = 0.30$, $p = 0.04$) illustrated by the solid red line in Figure 3a. All the corneas are also affected by positive values of C_4^0 that do not show a significant increase along the age interval considered ($0.0005 \mu\text{m}/\text{year}$, $r = 0.24$, $p = 0.10$). The SA of the cornea tends to be larger than the total ocular SA not only in young subjects (as expected) but also in some

middle-aged and older eyes. In fact, the SA of the internal surfaces is negative in all the young eyes but also in 74% of the combined set of middle-aged and older eyes, producing some partial balance of the corneal SA in the majority of eyes irrespective of age. We found that the SA of the internal surfaces tends to decrease smoothly in magnitude with age toward a less negative value that would reduce the compensation effect in the elderly, but the linear correlation with age is not quite statistically significant ($0.0006 \mu\text{m}/\text{year}$, $r = 0.22$, $p = 0.14$). Figure 3b illustrates the variation with age of the compensation factor associated with the magnitude of the SA. It shows a tendency of the SA partial balance to decay linearly along senescence, but it is not significant ($-0.0045 \text{ unit}/\text{year}$,

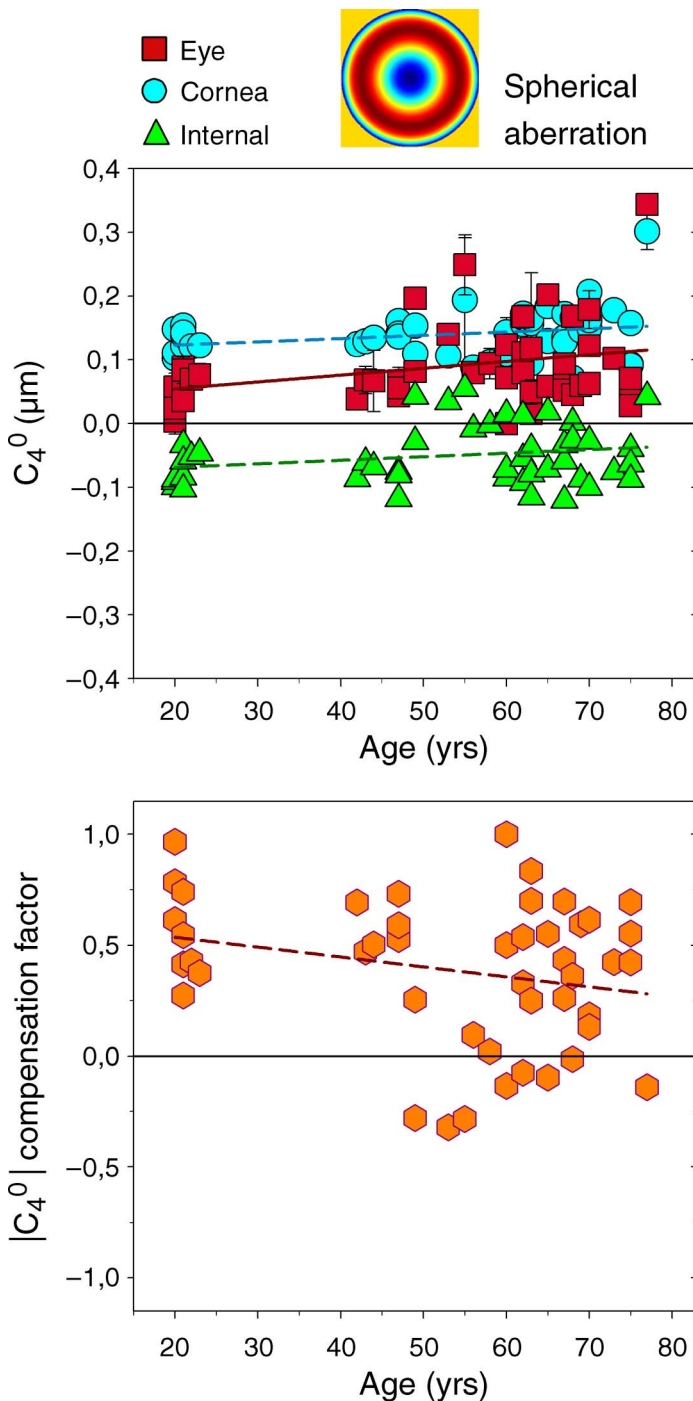


Figure 3. (a) Variation of the fourth-order spherical aberration coefficient, C_4^0 , as a function of age for the eye (squares), the cornea (circles), and the internal surfaces (triangles). The SA of the eye increases significantly with age, while we obtained non-significant linear regressions for the SA of the cornea (blue) and the internal surfaces (green). (b) Age-related variation of the compensation factor associated with the magnitude of the SA.

$r = 0.25$, $p = 0.10$). However, although eyes older than 45 years may fail to compensate the spherical aberration, it is remarkable that positive values of the compensation factor for $|C_4^0|$ prevail at any age, despite the dispersion

of our results, particularly in the older group. Figure 4a shows the age-related variation of the lateral coma coefficient, C_3^1 , for the eye (squares), the cornea (circles), and the internal surfaces (triangles).

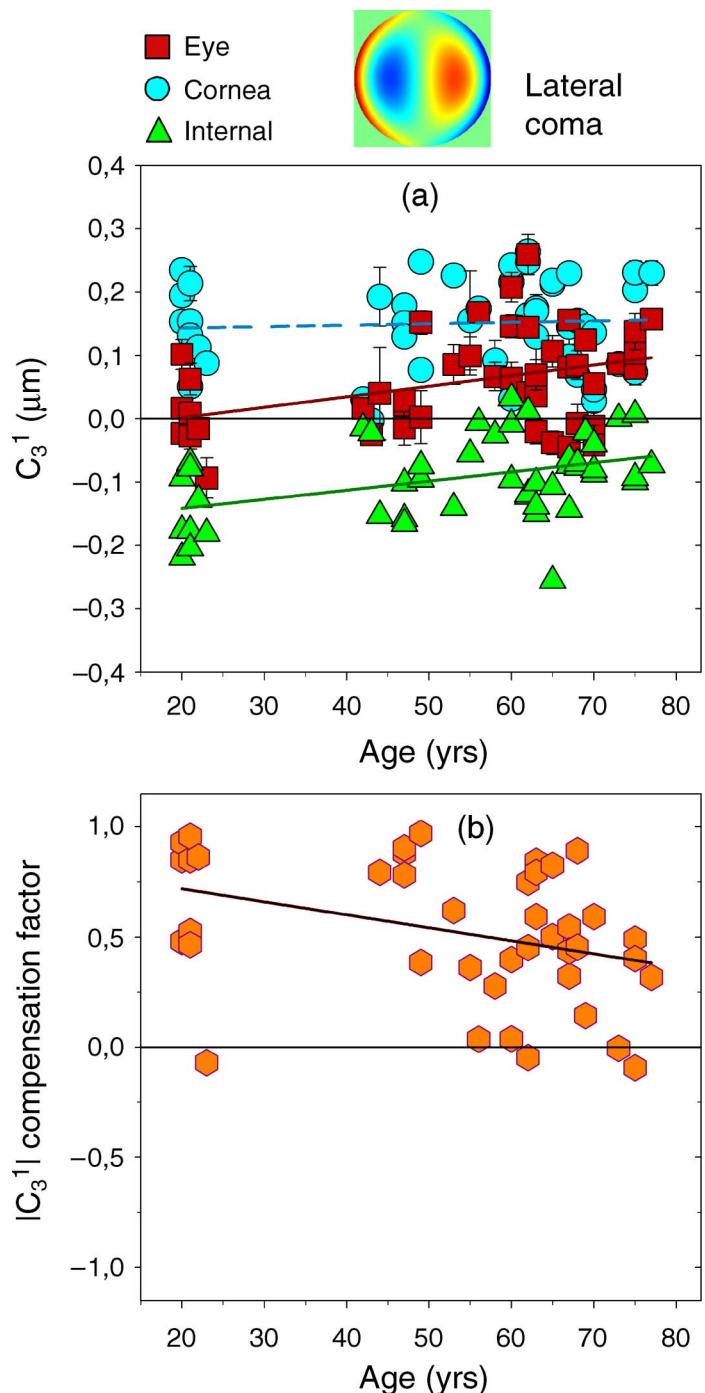


Figure 4. (a) Variation with age of the horizontal coma coefficient, C_3^1 , for the eye (squares), the cornea (circles), and the internal surfaces (triangles). Lateral coma is positively correlated with age in the eye (solid red line) and in the internal surfaces (solid green line) but not in the anterior cornea (dashed blue line). (b) The compensation factor for the modulus of C_3^1 shows a negative linear correlation with age.

There is a significant increment of lateral coma in the eye with age ($0.0017 \mu\text{m}/\text{year}$, $r = 0.41$, $p = 0.005$). The anterior corneal surface has positive horizontal coma (except for one cornea with no coma) that does not show an age-related dependence ($p = 0.70$). However, the horizontal coma of the internal surfaces does vary with age, following a slope close to that found in the eye ($0.0014 \mu\text{m}/\text{year}$, $r = 0.41$, $p = 0.005$): it is negative for all the young eyes and its magnitude decreases linearly with age becoming less negative in the older eyes. The compensation factor we obtained for $|C_3^1|$ as a function of age (Figure 4b) is similar, and even more pronounced, than that found previously for the spherical aberration: the compensation factor is essentially positive for the overall age interval [20–80] years, suggesting that some partial compensation of corneal lateral coma is performed by the crystalline lens at any age but with a significant tendency to decrease in the older eyes ($-0.0059 \text{ unit}/\text{year}$, $r = 0.36$, $p = 0.02$). With respect to vertical coma, C_3^{-1} , the age dependence of the ocular vertical coma is plotted in Figure 5a. It varies significantly with age ($-0.0025 \mu\text{m}/\text{year}$, $r = 0.37$, $p = 0.01$), from small, close-to-zero, values in young eyes (mean \pm SD: $-0.009 \pm 0.073 \mu\text{m}$) to a negative contribution in older eyes (mean \pm SD: $-0.10 \pm 0.12 \mu\text{m}$).

There is a large dispersion of the results for middle-aged and older eyes, i.e., for eyes ≥ 60 years the values are distributed in the range $[-0.33, 0.11] \mu\text{m}$. The vertical coma of the cornea decreases with age following a similar pattern to that of the eye, but the correlation just fails to be statistically significant ($-0.0018 \mu\text{m}/\text{year}$, $r = 0.28$, $p = 0.06$). On the other hand, aging does not seem to affect the vertical coma of the internal surfaces ($p = 0.28$). Besides, corneal coma is highly dispersed at every age group as it occurs for the eye, while the distribution of internal coma is more compact. The compensation factor for the modulus of this aberration term, $|C_3^{-1}|$ (Figure 5b), is clearly more sparse in the middle-aged and older groups, but it declines significantly with age ($-0.0187 \text{ unit}/\text{year}$, $r = 0.45$, $p = 0.006$). The regression line intersects the line of no aberration balance (CF = 0) at around 50 years of age. Vertical coma is compensated in almost all the young eyes, but only in about 50% of the middle-aged and older eyes.

The variation with age of trefoil is illustrated in Figure 6. The upper row exhibits the behavior of the horizontal component (C_3^3) for the anterior cornea and the internal surfaces (left panel) and for the eye (right panel). The lower row shows the corresponding data for the vertical component (C_3^{-3}). The x -trefoil of the cornea tends to spread out on both sides of the zero line so that both orientations (negative and positive values) are possible. Although it exhibits some tendency, it is not significantly correlated with age ($p = 0.10$); however, its magnitude $|C_3^3|$ does increase as the eye ages (solid blue line; $0.0010 \mu\text{m}/\text{year}$, $r = 0.33$, $p = 0.03$). Apparently, this pattern is also followed by the internal x -trefoil, but the variation of its modulus with age does not achieve statistical significance (dotted

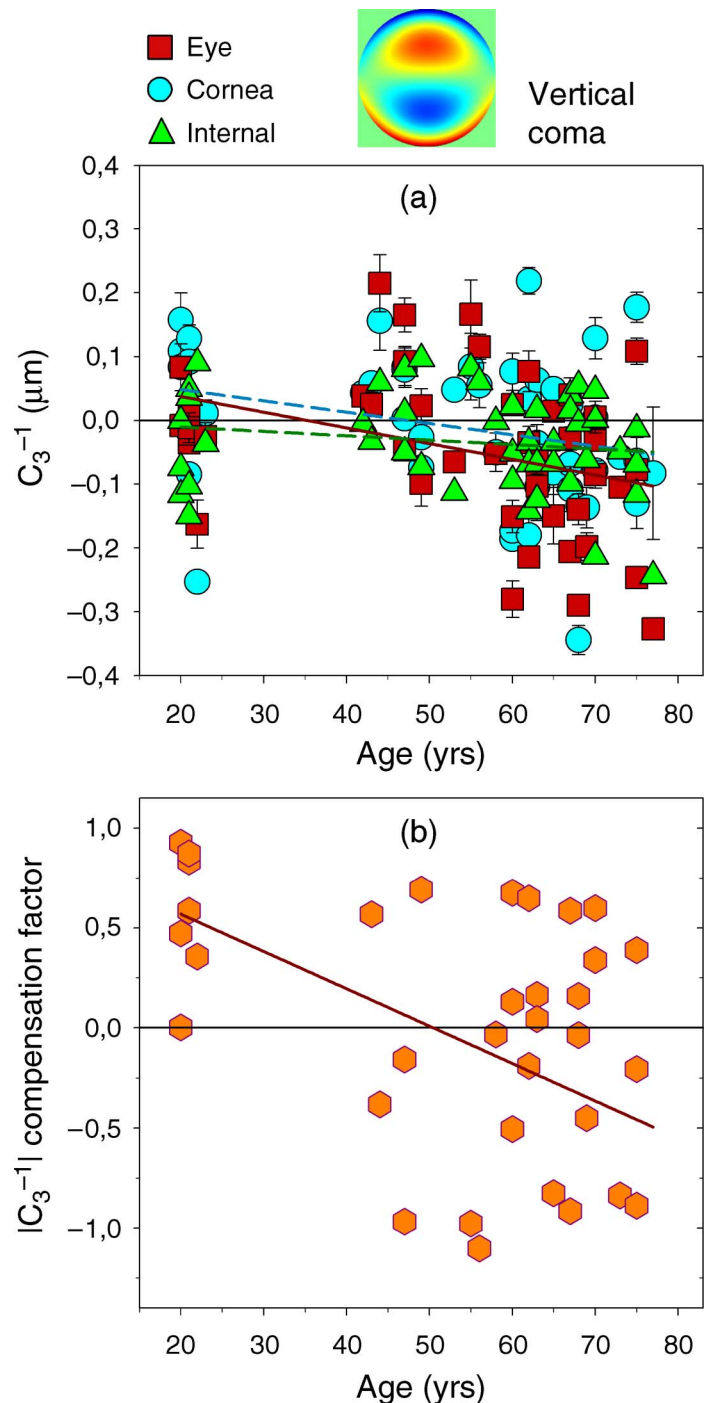


Figure 5. (a) Vertical coma coefficient, C_3^{-1} , for the eye (squares), the cornea (circles), and the internal surfaces (triangles) as a function of age. Vertical coma is negatively correlated with age in the complete eye (red solid line). It follows a similar tendency, though not significant, in the cornea (blue dashed line). (b) In spite of the great dispersion of the data, the compensation factor for $|C_3^{-1}|$ is negatively correlated with age.

green line: $0.0006 \mu\text{m}/\text{year}$, $r = 0.26$, $p = 0.08$). The combined effect is a behavior of the total x -trefoil of the eye along aging (right panel) that resembles that of its main optical components ($0.0008 \mu\text{m}/\text{year}$, $r = 0.27$, $p = 0.06$).

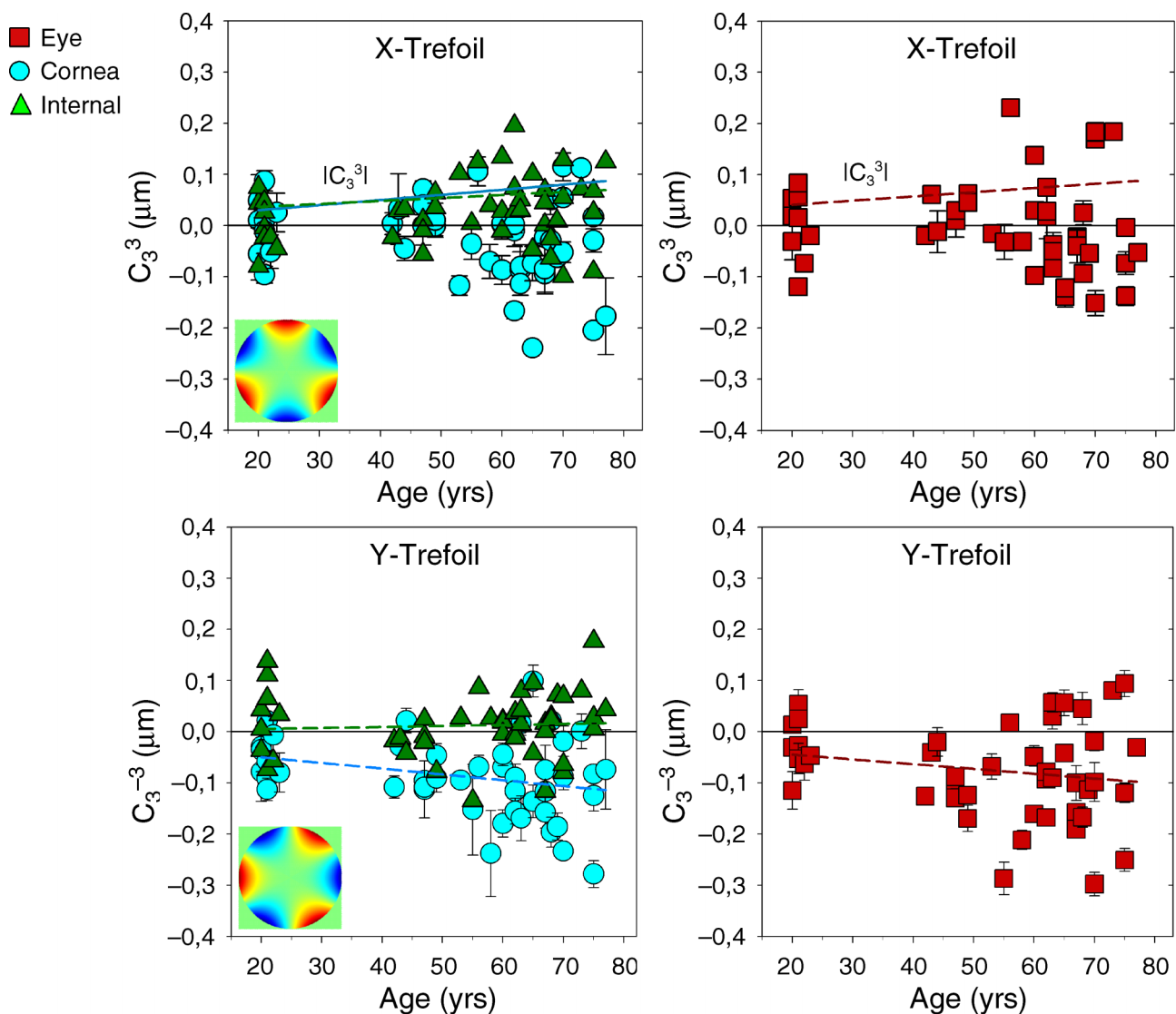


Figure 6. Upper row illustrates the age dependence of the horizontal component of the third-order trefoil in the cornea (circles) and the internal surfaces (triangles) in the left panel and in the eye (squares) in the right panel. All the regression lines in the upper panels correspond to variations with age of the modulus of the x-trefoil. The lower row shows the age dependence of the vertical trefoil component. The corresponding linear fits were calculated for the y-trefoil values with their corresponding sign.

The y-trefoil (lower panels) shows a tendency (not significant) to become more negative in the cornea as the eye gets older ($-0.0011 \mu\text{m}/\text{year}$, $r = 0.27$, $p = 0.07$), while in the internal surfaces it tends to be stable ($p = 0.71$) and small (mean \pm SD = $0.01 \pm 0.06 \mu\text{m}$). Again, the profile of distribution of the ocular y-trefoil follows a similar pattern to that of the cornea: in general, y-trefoil has a small weight in young eyes $\sim [-0.1, 0.1] \mu\text{m}$, but its contribution may be very large in a number of eyes older than 55–60 years (in the range $[-0.2, -0.3] \mu\text{m}$), although the correlation of the ocular C_3^{-3} with age is not statistically significant ($-0.0009 \mu\text{m}/\text{year}$, $r = 0.19$, $p = 0.21$). Since both trefoil coefficients are smaller than $0.05 \mu\text{m}$ in many corneas (particularly the y-trefoil), we do not plot their corresponding compensation factors as a function of age.

With respect to the alignment, we evaluated the distribution of angle kappa for the whole set of subjects (polar plot in Figure 7, upper row: green dots for young, orange for middle-aged, and purple for older eyes). The angle kappa is systematically positive in the horizontal direction (i.e., the pupillary axis on the temporal side of the line of sight) for all the eyes except four, while in the vertical direction it does not show a systematic behavior for any age group. Therefore, no differences in the orientation of angle kappa were found with age. We also explored if there is an age dependence of the angle kappa magnitude (Figure 7, lower row), but the correlation between these two variables is not significant ($p = 0.14$ for the horizontal component, κ_X ; $p = 0.96$ for the vertical component, κ_Y). The error bars for the magnitude of angle

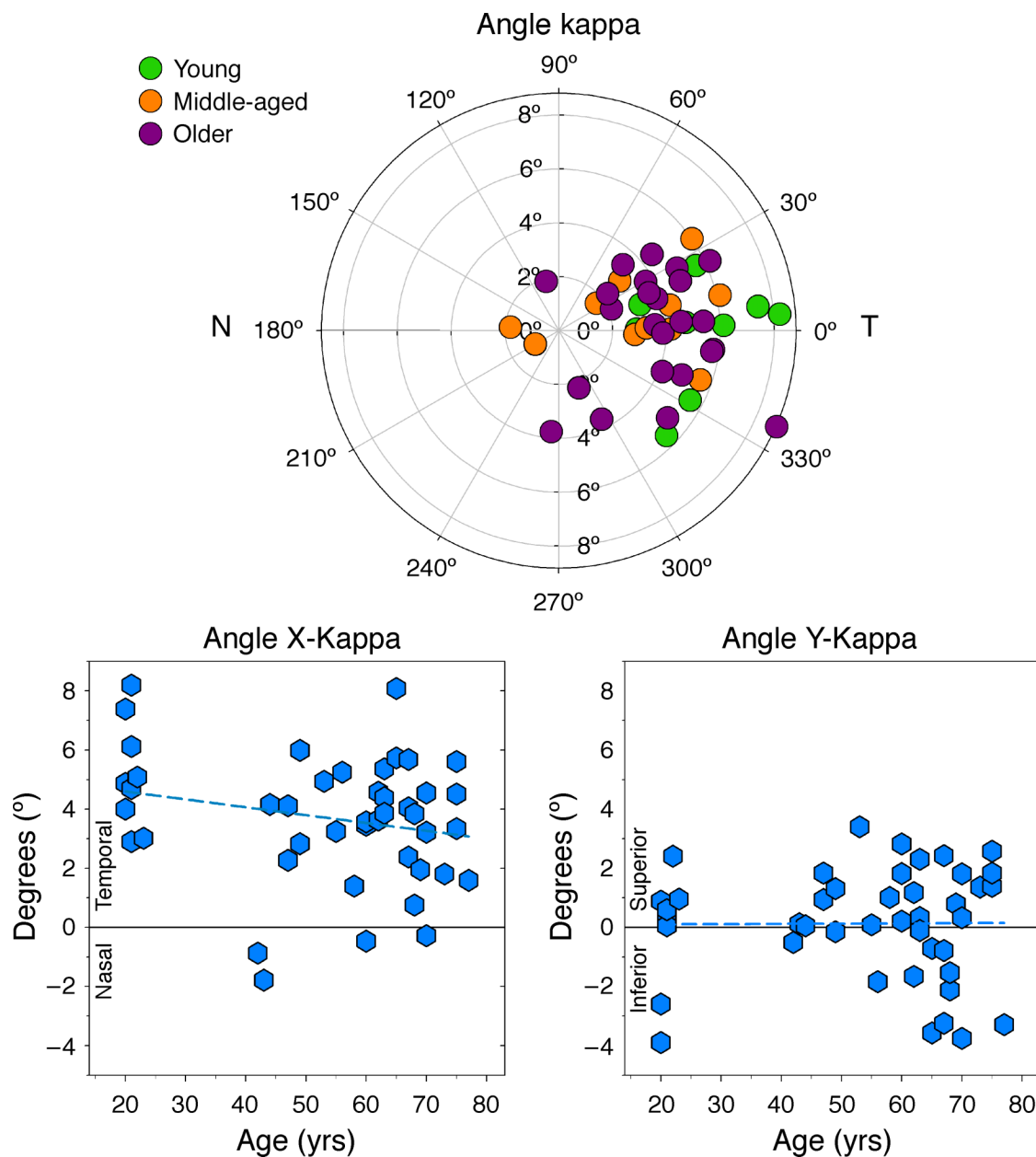


Figure 7. The upper panel represents the angular distribution of angle kappa for all the eyes of the study. Lower panels show the variation of angle kappa as a function of age for both the horizontal and vertical Cartesian components. The linear fit is not significant for κ_X ($p = 0.14$) or for κ_Y ($p = 0.96$).

kappa tend to be small: the averaged standard deviation for all κ_X and κ_Y data corresponding to three estimations of these angles per subject is 0.20 ± 0.15 degrees. Regarding the inter-subjects dispersion, although κ_X varies in a wide range $\sim[-2^\circ, 8^\circ]$ (on average: $3.7^\circ \pm 2.2^\circ$), more than 70% of the eyes have a positive κ_X angle between 2° and 6° . κ_Y varies in the range $\sim[-4^\circ, 4^\circ]$ (on average: $0.1^\circ \pm 1.9^\circ$), with 72% of the eyes concentrated between -2° and 2° .

We also studied the relationship between coma and angle kappa (Figure 8). For the sake of clarity, the group

of young eyes is shown on the left column and the group of older eyes on the right column. In young eyes, higher lateral coma (upper left panel) is correlated with higher horizontal angle kappa in the cornea ($0.028 \mu\text{m}/\text{year}$, $r = 0.85$, $p = 0.004$), while a similar tendency but with opposite sign is found in the crystalline lens, which is not significant ($-0.018 \mu\text{m}/\text{year}$, $r = 0.56$, $p = 0.11$). Thus, in young eyes, horizontal coma does not depend on angle kappa ($p = 0.38$). Similarly, in older eyes the amount of lateral coma of the cornea and of the lens increases with κ_X , with almost identical slopes of opposite sign for the

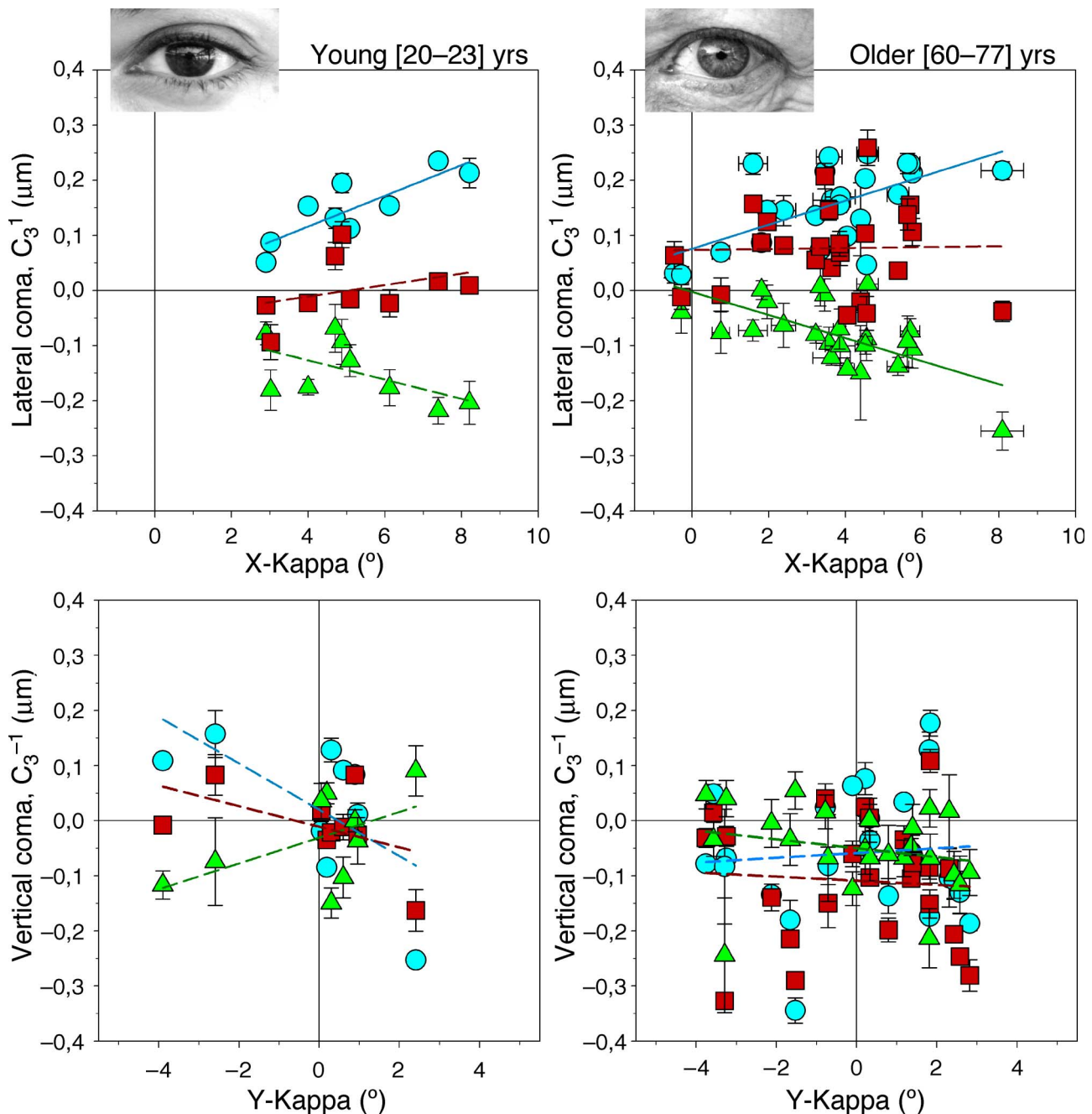


Figure 8. Relationship between the respective Cartesian components of coma and angle kappa measured in young eyes (left column) and in older eyes (right column), for the eye (squares), the cornea (circles), and the crystalline lens (triangles).

cornea ($0.022 \mu\text{m}/\text{year}$, $r = 0.62$, $p = 0.001$) and the lens ($-0.021 \mu\text{m}/\text{year}$, $r = 0.66$, $p = 0.0005$), and no angle kappa dependence of lateral coma is found ($p = 0.92$). However, the situation is different for vertical coma. It is not statistically correlated with age for the cornea, the lens, or the eye in any group of age (young corneas: $p = 0.071$, young lenses: $p = 0.130$, young eyes: $p = 0.176$; older corneas: $p = 0.716$, older lenses: $p = 0.291$, older eyes: $p = 0.750$).

Discussion

Aberrations with age

In agreement with previous studies (Applegate et al., 2007; Artal et al., 2002; Atchison & Markwell, 2008; Brunette et al., 2003; Fujikado et al., 2004; McLellan et al., 2001), our results show that the amount of aberrations of

the eye tends to increase with age beyond the large inter-subject variability. We included in our work a number of improvements to enhance in one or more aspects the reliability of the experimental procedure, i.e., more efficient strategies for wave-front sampling and wave-front recovery, correction of the angular difference between the HS and the topographer axes of measurement for comparison of aberrations, a relatively large sample of older population under study, and especially, a particularly careful criteria of selection of the older eyes to guarantee normal ocular transparency. Since the behavior of young eyes in terms of aberrations and alignment is widely known, we specifically concentrated on eyes of ≥ 60 years old. We verified that in our smaller group of young eyes the averaged ocular higher order RMS ($0.153 \pm 0.042 \mu\text{m}$) was similar to that previously reported for a 5-mm pupil diameter (Applegate et al., 2007; Atchison & Markwell, 2008). For the whole set of subjects we found a similar dependence with age of the magnitudes of the ocular and the corneal higher order RMS than Applegate et al. (2007), but a higher contribution than that provided in Atchison and Markwell's (2008) study. Reanalyzing Applegate et al.'s data in terms of linear regressions with age, they obtained a linear increment of the ocular RMS from the third to the sixth order for a 5-mm pupil of $0.0038 \mu\text{m}/\text{year}$ for the age interval [20, 80] years. This slope is slightly higher but comparable to the one we measured ($0.0032 \mu\text{m}/\text{year}$). It is interesting to note that in Applegate et al.'s study the faster increment of the ocular RMS occurs in the transition from the 60s to the 70s, where undetected early stages of cataract might distort and magnify the internal and ocular aberrations. In general, eyes affected by cataract are more aberrated than normal eyes of similar age. A larger presence of spherical aberration, coma, or trefoil have been reported depending on the intensity and location of the lens opacity (Kuroda, Fujikado, & Maeda, 2002; Lee, Kim, & Tchah, 2008; Rocha et al., 2007; Sachdev, Osmonde, Sherwin, & McGhee, 2004). The standard clinical protocol to assess cataract is based on subjective evaluations of the color and level of opalescence of the crystalline lens (LOCS-III catalog from Chylack, Wolfe, & Singer, 1993) and does not account for forward scattering. This might leave initial phases of this disease undetected. Our protocol was especially designed to discard these artifacts from the older population by applying two objective sets of measurements to those eyes that passed the slit-lamp examination.

On the other hand, Atchison and Markwell obtained a surprisingly low rate of increase of aberrations with age ($0.00093 \mu\text{m}/\text{year}$, $p = 0.05$) for eyes between 18 and 70 years and a 5-mm pupil diameter. The reason they suggested was that all their eyes accomplished very restricted criteria of emmetropia (equivalent sphere <1.00 D and cylinder ≤ 0.50 D). Our groups of young and middle-aged eyes are both emmetropic on average, while the group of older eyes is slightly hyperopic (see Table 1). This could

explain the higher slope with age we found. However, the studies that measured the impact of the refractive error on the higher order aberrations obtained contradictory results and did not find a relevant effect for ametropies as low as the ones involved in our study (Cheng, Bradley, Hong, & Thibos, 2003; Llorente, Barbero, Cano, Dorronsoro, & Marcos, 2004; Paquin, Hamam, & Simonet, 2002; Tabernero et al., 2007).

With respect to the main ocular components, we also confirmed previous results not finding a significant variation with age in the higher order aberrations of the internal optics and only a very small increment of the RMS of the anterior corneal surface (Alió, Schimchak, Negri, & Montes-Micó, 2005; Artal et al., 2002; Atchison & Markwell, 2008; Guirao, Redondo, & Artal, 2000; Oshika, Klyce, Applegate, & Howland, 1999). The increase of aberrations in the elderly is primarily related to the known progressive disruption of the cornea and lens optical coupling (Artal et al., 2002), as it was illustrated by the linear decay of the compensation factor of the RMS (Figure 2c). Nonetheless, it is worth noting that within the large dispersion of the data, around 50% of our sample of older eyes still exhibits some level of partial compensation, even at ages as late as 77 years.

Fourth-order SA is positive in all the eyes (Figure 3) with a magnitude that increases moderately with age ($0.063 \mu\text{m}$ from 20 to 77 years). Our data reproduce well the magnitude and rate of increase of C_4^0 measured by other studies (Applegate et al., 2007; Atchison & Markwell, 2008). In particular, for the whole set of 46 eyes we obtained a mean ocular SA of $0.090 \pm 0.065 \mu\text{m}$, in agreement with that estimated by Atchison and Markwell of $0.061 \pm 0.062 \mu\text{m}$, although these authors did not find a significant variation of the SA in the aging eye. Our data contrast with the steeper increase with age of the ocular SA reported by other previous works (Artal et al., 2002; Glasser & Campbell, 1998). Glasser and Campbell measured positive values of SA in excised older human lenses measured *in vitro*, but the properties of the crystalline lens could be altered outside its natural holder, and they did not account for the oblique incidence of light on the lens after being refracted by the cornea. On the other hand, in our previous work (Artal et al., 2002), a less strict subject selection procedure together with a smaller sample of older eyes could have overestimated the aberrations with age.

The SA of the anterior corneal surface tends to experience a very small increase with age ($0.003 \mu\text{m}$ from 20 to 77 years), likely because of age-related changes in the corneal asphericity (Atchison et al., 2008; Dubbelman, Sicam, & Van der Heijde, 2006), but it is not significant and in any case insufficient to fully justify the total variation of SA in the eye obtained. The crystalline lens presents a progressive reduction of the negative internal SA with aging toward close-to-zero values (although it did not achieve statistical significance) or even small positive

contributions in older eyes (≥ 60 years). This behavior is well known in the literature (Alió et al., 2005; Atchison & Markwell, 2008; Smith et al., 2001). As the negative SA of the aging lens decreases, the cornea–lens coupling loses part of its beneficial effect that explains why the older eye is more affected by positive spherical aberration (Figure 3b).

With respect to the asymmetric aberrations, lateral coma follows a systematic behavior with senescence very close to that found for the SA, maybe even more pronounced: the cornea has an approximately constant value of positive horizontal coma through the life span (mean \pm SD = $0.15 \pm 0.07 \mu\text{m}$ for all the eyes), which is partially balanced by some negative coma in the crystalline lens in all the young eyes and in the great majority of mature and older eyes. As the magnitude of internal coma decreases progressively with age so does the partial compensation. Older eyes tend to have more vertical coma (of negative sign) than young eyes, in some cases as large as $-0.30 \mu\text{m}$, while in young eyes it tends to be smaller than $0.10 \mu\text{m}$ in magnitude. Vertical coma shows a high inter-subject dispersion and does not follow such a well-defined pattern with age as SA or lateral coma does (they exhibit a preferred sign). The result is that in 6 out of 9 young eyes (2/3) the vertical coma of the cornea is almost totally balanced by the crystalline lens, while some balance is only present in 9 out of 25 older subjects (1/3; in a number of older eyes, the lens is even adding vertical coma to the cornea, i.e., CF < 0). The decoupling of vertical coma between the cornea and the lens seems to be more pronounced as the eye ages.

Coupling of aberrations with age and alignment

It is known that the efficient balance of the spherical aberration at young ages and its tendency to decrease at older ages can be formulated in terms of intrinsic parameters, like age-related variations in the asphericity of the crystalline lens surfaces, the curvatures of the anterior and posterior surfaces, and/or in the gradient refractive index (GRIN) profile. Dubbelman and Van der Heijde (2001), using Scheimpflug images of the lens *in vivo*, measured a large variability of the lens asphericity without finding any significant trend with age. The variation in the lens radii of curvature as a function of age reported by different authors (Atchison et al., 2008; Dubbelman & Van der Heijde, 2001) would contribute to a reduction in the magnitude of the spherical aberration. Finally, models of the aging eye to explain the lens paradox by introducing an age-related variation of the GRIN lens have been proposed (Navarro, Palos, & González, 2007), and the most accurate technique to assess the GRIN properties of the lens *in vivo* so far, the MRI technique, also seems to support this variation (Jones, Atchison, Meder, & Pope, 2005).

Another aberration with an origin essentially intrinsic is trefoil, related to the shape of the ocular surfaces (Tabernero et al., 2007). In particular, the larger presence of y-trefoil in the cornea of the older subjects might be associated with the age-related sagging of the eyelids onto the front corneal surface, caused by the stretching of the eyelid skin and to the loss of tone of the muscles that lift the eyelids. The decline of the volume and quality of the tear film as the eye ages (Mathers, Lane, & Zimmerman, 1996; Patel & Farrell, 1989) could be another factor implied in the increment of the measured higher order aberrations in older eyes. To avoid this problem, an artificial tear solution was instilled in the older eyes that exhibited any signs of tear film breaking during the HS image recording.

The coupling of lateral coma between the cornea and the lens has an angular origin (Figure 8): larger horizontal coma correlates with larger angle κ_X , with opposite sign in the cornea and in the lens, producing a partial balance that leaves the young eye approximately free of lateral coma. However, until now it was uncertain whether this angular compensation of lateral coma could be preserved to some extent as the eye ages. We found that the mechanism of angular coupling of lateral coma is still present in older eyes although with a lower level of efficiency. This may be due to a number of factors. We evaluated if there is an age-related variation of angle kappa (Figure 7). Our measurements showed no variation of κ_Y related to age but a tendency of κ_X to decrease with senescence. In young eyes, the mean κ_X measured was $5.1^\circ \pm 1.8^\circ$ while in older eyes it was smaller ($3.6^\circ \pm 2.1^\circ$); however, the regression of κ_X with age did not achieve statistical significance ($p = 0.14$). This indicates that the angle kappa does not vary significantly with age, contributing to maintain some cornea–lens partial compensation of lateral coma in the elderly.

However, coma induced by tilting a lens with respect to some reference axis does not depend only on the angle of rotation but it is also associated with the curvatures of the surfaces under rotation. These curvatures are typically represented by the shape factor (SF), which relates the radii of curvature of the anterior (R_1) and posterior (R_2) surfaces of the lens.¹ In particular, for a lens immersed in symmetrical refractive index media, coma is linearly proportional to the shape factor variable (Hazra & Delisle, 1998). We found that the corneal contribution to the ocular horizontal coma does not vary with age (Figure 4a). This is easy to explain considering that no extra angular coma is generated in the aging cornea: on one hand, we did not find a significant variation in angle κ_X (Figure 7), and on the other hand, changes in the radius of curvature of the front corneal surface associated with age (see, for instance, Dubbelman, Weeber, Van der Heijde, & Völker-Dieben, 2002; Guirao et al., 2000) are not large enough to alter in a significant way the corneal shape factor. In conclusion, we should not expect variations of lateral coma in the cornea as the eye ages. The situation is slightly

different for the crystalline lens. In particular, the aging lens tends to an equiconvex configuration. Dubbelman and Van der Heijde (2001) found that from 20 to 80 years, the radius of the anterior lens surface (of positive sign) decreases linearly at a rate of 0.057 mm/year (Figure 9, upper left panel), while the radius of the posterior lens surface (of negative sign) decreases in magnitude at a rate of 0.012 mm/year. These changes in the radii of curvature of the lens modify its shape factor with age. Figure 9 (upper right panel) depicts this variation for the lens of the Gullstrand unaccommodated theoretical eye model. For this particular case, the shape factor of the crystalline lens varies from -0.25 at 20 years to -0.11 at 80 years, while the shape factor of the cornea will keep an approximately constant value (1.2).

To better illustrate the effects caused by this mechanism, Figure 10 shows the lateral coma of the eye (red solid line) and the cornea (blue solid line) as a function of the shape factor of the crystalline lens in the presence of a field angle of 5° . The eye model used in these ray-tracing calculations took the corneal parameters from the Dubbelman–Norrby model (Norrby, 2005). The crystalline lens was simulated as a lens of 4-mm thickness and 1.42 refractive index. The radius of curvature of the first surface was systematically changed at the same time that the curvature of the second surface was adjusted to maintain a total optical power of the lens of 21.5 diopters. Asphericity in both lens surfaces was incorporated from the same eye model. The arrow along the red line represents the variation of ocular lateral coma induced

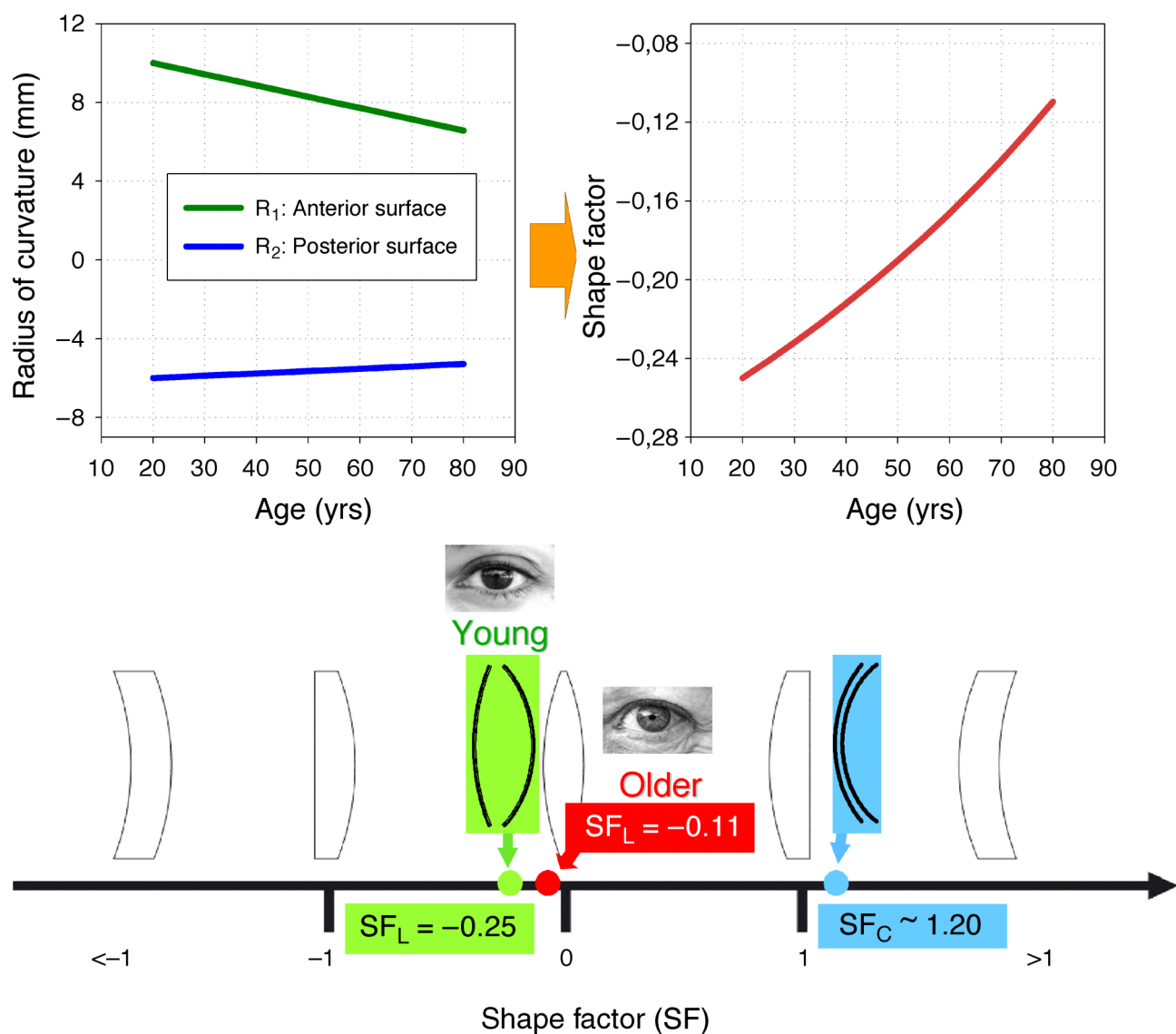


Figure 9. Upper panel on the left shows the variation of the radii of curvature of the surfaces of the Gullstrand lens model based on the ratios given by Dubbelman and Van der Heijde (2001). These variations generate a change in the shape factor of the lens with age as shown on the upper right graph. The lower part of the figure illustrates the different shapes of the young and older crystalline lens together with the corneal shape in a schematic scale of shape factors.

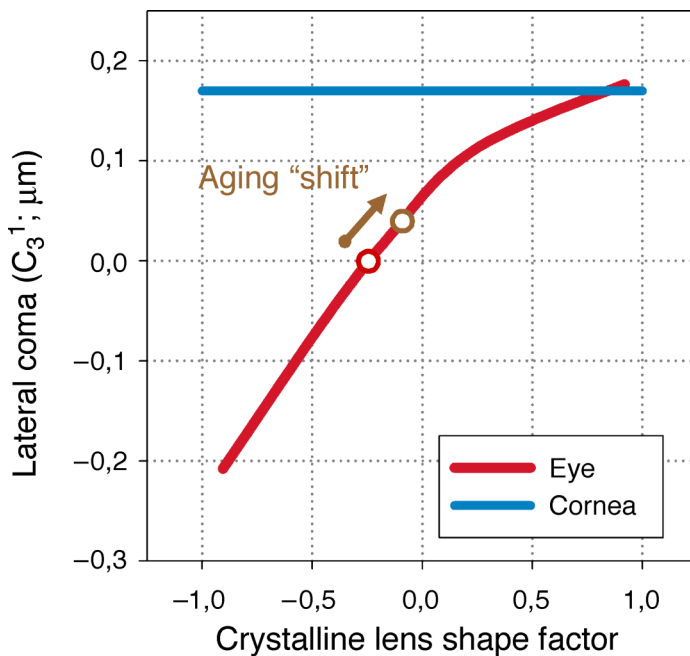


Figure 10. The red solid line represents the lateral coma of the eye as a function of the variation of the crystalline lens shape factor of a model eye (see the text for details). The blue solid line represents the corneal lateral coma of the same model eye. The arrow illustrates the shift of lateral coma in the eye induced by the change in the shape factor of the model crystalline lens from 20 years (red circle: SF = -0.25) to 80 years (brown circle: SF = -0.11).

by the change in the crystalline lens shape factor, due to the aging process from a 20-year-old eye (red circle) to an 80-year-old eye (brown circle).

A shift from -0.25 to -0.11 in the lens shape factor would increase the value of ocular coma around $0.04 \mu\text{m}$. This change is clearly in the direction of the experimentally observed variations although it is not enough to fully explain the changes. Perhaps, there might be other intrinsic factors implied in the generation and decoupling of horizontal coma with aging, like an age-related variation of the asphericity of the crystalline lens (data from the literature do not clearly support this hypothesis, Dubbelman & Van der Heijde, 2001), in the lens thickness (Alió et al., 2005; Dubbelman, Van der Heijde, & Weeber, 2001) and/or in the refractive index profile of the lens (Jones et al., 2005).

Older eyes tend to be more affected by vertical coma (of negative sign) than young eyes. However, Figure 7 shows that the vertical component of angle kappa (κ_Y) does not vary with age, not even in modulus, and according to the polar plot in Figure 7, κ_Y does not exhibit a regular behavior among the population (it may take either positive or negative values). On the other hand, the inferior panels of Figure 8 also show the lack of correlation between the

vertical coma of the cornea, the lens, and the complete eye with angle κ_Y . This seems to indicate that vertical coma is not generated angularly in an eye of any age, but instead, it has an origin basically intrinsic. The explanation for the vertical coma decoupling with age (Figure 5 illustrates how vertical coma in the crystalline lens slightly becomes more negative with age) might be related perhaps to some vertical asymmetry of the lens shape cause by the effect of gravity on to a denser lens (which adds layers with aging). Further studies are needed to clarify this behavior.

Conclusions

We explored the relative changes in ocular, corneal, and internal aberrations in normal aging eyes with special emphasis in the role of the ocular alignment (angle kappa) and the lens shape factor in the balance of aberrations with age. Objective methods were applied to guarantee the selection of older eyes with good ocular transparency. We confirmed that higher order aberrations increase with age due in part to a decoupling of cornea and lens. In particular, lateral coma remains compensated in most of the older eyes due to angle kappa remaining stable with age and the lens shape factor only experiencing small changes. Those slight variations in the geometrical factors of the crystalline lens with age (radii and, perhaps, asphericity) produce modifications in its aberration structure that reduces the compensation mechanism, explaining most of the measured increment of ocular aberrations with age.

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Footnote

$$^1\text{SF} = (R_2 + R_1)/(R_2 - R_1).$$

References

- Alió, J. L., Schimchak, P., Negri, H. P., & Montes-Micó, R. (2005). Crystalline lens optical dysfunction through aging. *Ophthalmology*, 112, 2022–2029. [PubMed] [Article]
- ANSI Z80.28 (2004). *American National Standard for Ophthalmics—Methods for reporting optical aberrations of the eye* (9+ pp.). Washington, DC: American National Standards Institute.
- Applegate, R. A., Donnelly, W. J., Marsack, J. D., & Koenig, D. E. (2007). Three-dimensional relationship between high-order root-mean-square wavefront error, pupil diameter, and aging. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 24, 578–587. [PubMed] [Article]
- Artal, P. (2004). Combining corneal and ocular wave aberrations. In R. Krueger, R. Applegate, & S. MacRae (Eds.), *Wavefront customized visual correction: The quest for supervision II* (pp. 311–316). Thorofare, NJ: Slack.
- Artal, P., Benito, A., & Tabernero, J. (2006). The human eye is an example of robust optical design. *Journal of Vision*, 6(1):1, 1–7, <http://www.journalofvision.org/content/6/1/1>, doi:10.1167/6.1.1. [PubMed] [Article]
- Artal, P., Berrio, E., Guirao, A., & Piers, P. (2002). Contribution of the cornea and internal surfaces to the change of ocular aberrations with age. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 19, 137–143. [PubMed]
- Artal, P., & Guirao, A. (1998). Contribution of cornea and lens to the aberrations of the human eye. *Optics Letters*, 23, 1713–1715. [PubMed]
- Artal, P., Guirao, A., Berrio, E., & Williams, D. R. (2001). Compensation of corneal aberrations by internal optics in the human eye. *Journal of Vision*, 1(1):1, 1–8, <http://www.journalofvision.org/content/1/1/1>, doi:10.1167/1.1.1. [PubMed] [Article]
- Artal, P., & Tabernero, J. (2008). The eye's aplanatic answer. *Nature Photonics*, 2, 586–589.
- Atchison, D. A., & Markwell, E. L. (2008). Aberration of emmetropic subjects at different ages. *Vision Research*, 48, 2224–2231. [PubMed]
- Atchison, D. A., Markwell, E. L., Kasturirangan, S., Pope, J. M., Smith, G., & Swann, P. G. (2008). Age-related changes in optical and biometric characteristics of emmetropic eyes. *Journal of Vision*, 8(4):29, 1–20, <http://www.journalofvision.org/content/8/4/29>, doi:10.1167/8.4.29. [PubMed] [Article]
- Atchison, D. A., & Smith, G. (2000). Chapter 4: Axes of the eye. In *Optics of the human eye* (pp. 30–38). Oxford, UK: Butterworth-Heinemann.
- Brunette, I., Bueno, J. M., Parent, M., Hamam, H., & Simonet, P. (2003). Monochromatic aberrations as a function of age, from childhood to advanced age. *Investigative Ophthalmology and Visual Science*, 44, 5438–5446. [PubMed] [Article]
- Calver, R. I., Cox, M. J., & Elliot, D. B. (1999). Effect of aging on the monochromatic aberrations of the human eye. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 16, 2069–2078. [PubMed]
- Cheng, X., Bradley, A., Hong, X., & Thibos, L. N. (2003). Relationship between refractive error and monochromatic aberrations of the eye. *Optometry and Vision Science*, 80, 43–49. [PubMed] [Article]
- Chylack, L. T., Jr., Wolfe, J. K., & Singer, D. M. (1993). The lens opacities classification system III; The longitudinal study of Cataract study group. *Archives of Ophthalmology*, 111, 831–836. [PubMed]
- Dubbelman, M., Sicam, V. A. D. P., & Van der Heijde, G. L. (2006). The shape of the anterior and posterior surface of the aging human cornea. *Vision Research*, 46, 993–1001. [PubMed]
- Dubbelman, M., & Van der Heijde, G. L. (2001). The shape of the aging human lens: Curvature, equivalent refractive index and the lens paradox. *Vision Research*, 41, 1867–1877. [PubMed]
- Dubbelman, M., Van der Heijde, G. L., & Weeber, H. A. (2001). The thickness of the aging human lens obtained from corrected Scheimpflug images. *Optometry and Vision Science*, 78, 411–416. [PubMed] [Article]
- Dubbelman, M., Weeber, H. A., Van der Heijde, R. G. L., & Völker-Dieben, H. J. (2002). Radius and asphericity of the posterior corneal surface determined by corrected Scheimpflug photography. *Acta Ophthalmologica Scandinavica*, 80, 379–383. [PubMed]
- El Hage, S. G., & Berny, F. (1973). Contribution of the crystalline lens to the spherical aberration of the eye. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 63, 205–211. [PubMed]
- Elliott, S. L., Choi, S. S., Doble, N., Hardy, J. L., Evans, J. W., & Werner, J. S. (2009). Role of high-order aberrations in senescent changes in spatial vision. *Journal of Vision*, 9(2):24, 1–16, <http://www.journalofvision.org/content/9/2/24>, doi:10.1167/9.2.24. [PubMed] [Article]
- Fujikado, T., Kuroda, T., Ninomiya, S., Maeda, N., Tano, Y., Oshika, T., et al. (2004). Age-related changes in ocular and corneal aberrations. *American Journal of Ophthalmology*, 138, 143–146. [PubMed]
- Glasser, A., & Campbell, M. C. W. (1998). Presbyopia and the optical changes in the human crystalline lens with age. *Vision Research*, 38, 209–229. [PubMed]

- Guirao, A., & Artal, P. (2000). Corneal wave aberration from videokeratography: Accuracy and limitations of the procedure. *Journal of the Optical Society of America A Optics, Image Science, and Vision*, 17, 955–965. [PubMed]
- Guirao, A., Gonzalez, C., Redondo, M., Geraghty, E., Norrby, S., & Artal, P. (1999). Average optical performance of the human eye as a function of age in a normal population. *Investigative Ophthalmology and Visual Science*, 40, 203–213. [PubMed]
- Guirao, A., Redondo, M., & Artal, P. (2000). Optical aberrations of the human cornea as a function of age. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 17, 1697–1702. [PubMed]
- Hazra, L. N., & Delisle, C. A. (1998). Primary aberrations of a thin lens with different object and image space media. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 15, 945–953.
- Ijspeert, J. K., de Waard, P. W., van den Berg, T. J., & de Jong, P. T. (1990). The intraocular straylight function in 129 healthy volunteers; dependence on angle, age and pigmentation. *Vision Research*, 30, 699–707. [PubMed]
- Jones, C. E., Atchison, D. A., Meder, R., & Pope, J. M. (2005). Refractive index distribution and optical properties of the isolated human lens measured using magnetic resonance imaging (MRI). *Vision Research*, 45, 2352–2366. [PubMed]
- Kelly, J. E., Mihashi, T., & Howland, H. C. (2004). Compensation of corneal horizontal/vertical astigmatism, lateral coma, and spherical aberration by internal optics of the eye. *Journal of Vision*, 4(4):2, 262–271, <http://www.journalofvision.org/content/4/4/2>, doi:10.1167/4.4.2. [PubMed] [Article]
- Kuroda, T., Fujikado, T., & Maeda, N. (2002). Wavefront analysis in eyes with nuclear or cortical cataract. *American Journal of Ophthalmology*, 134, 1–9. [PubMed]
- Le Grand, Y., & El Hage, S. G. (1980). *Physiological optics, Springer series in optical sciences*. Berlin, Germany/Heidelberg, Germany/New York: Springer-Verlag.
- Lee, J., Kim, M. J., & Tchah, H. (2008). Higher-order aberrations induced by nuclear cataract. *Journal of Cataract and Refractive Surgery*, 34, 2104–2109. [PubMed]
- Llorente, L., Barbero, S., Cano, D., Dorronsoro, C., & Marcos, S. (2004). Myopic versus hyperopic eyes: Axial length, corneal shape and optical aberrations. *Journal of Vision*, 4(4):5, 288–298, <http://www.journalofvision.org/content/4/4/5>, doi:10.1167/4.4.5. [PubMed] [Article]
- Mathers, W. D., Lane, J. A., & Zimmerman, M. B. (1996). Tear film changes associated with normal aging. *Cornea*, 15, 229–234. [PubMed]
- McLellan, J. S., Marcos, S., & Burns, S. A. (2001). Age-related changes in monochromatic wave aberrations of the human eye. *Investigative Ophthalmology and Visual Science*, 42, 1390–1395. [PubMed] [Article]
- Millodot, M., & Sivak, J. (1979). Contribution of the cornea and lens to the spherical aberration of the eye. *Vision Research*, 19, 685–687. [PubMed]
- Navarro, R., Palos, F., & González, L. M. (2007). Adaptive model of the gradient index of the human lens. II. Optics of the accommodating aging lens. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 24, 2911–2920. [PubMed]
- Norrby, S. (2005). The Dubbelman eye model analysed by ray tracing through aspheric surfaces. *Ophthalmic & Physiological Optics*, 25, 153–161. [PubMed] [Article]
- Oshika, T., Klyce, S. D., Applegate, R. A., & Howland, H. C. (1999). Changes in corneal wavefront aberrations with aging. *Investigative Ophthalmology and Visual Science*, 40, 1351–1355. [PubMed]
- Paquin, M. P., Hamam, H., & Simonet, P. (2002). Objective measurement of optical aberrations in myopic eyes. *Optometry and Vision Science*, 79, 285–291. [PubMed] [Article]
- Patel, S., & Farrell, J. C. (1989). Age-related changes in precorneal tear film stability. *Optometry and Vision Science*, 66, 175–178. [PubMed]
- Pérez, G. M., Manzanera, S., & Artal, P. (2009). Impact of scattering and spherical aberration in contrast sensitivity. *Journal of Vision*, 9(3):19, 1–10, <http://www.journalofvision.org/content/9/3/19>, doi:10.1167/9.3.19. [PubMed] [Article]
- Phillips, P., Pérez-Emmanueilli, J., Rosskothén, H. D., & Koester, C. J. (1988). Measurement of intraocular lens decentration and tilt in vivo. *Journal of Cataract and Refractive Surgery*, 14, 129–135. [PubMed]
- Prieto, P. M., Vargas-Martín, F., Goelz S., & Artal, P. (2000). Analysis of the performance of the Hartmann–Shack sensor in the human eye. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 17, 1388–1398. [PubMed]
- Rocha, K. M., Nosé, W., Bottós, K., Bottós, J., Morimoto, L., & Soriano, E. (2007). Higher-order aberrations of age-related cataract. *Journal of Cataract and Refractive Surgery*, 33, 1442–1446. [PubMed]
- Sachdev, N., Osmonde, S. E., Sherwin, T., & McGhee, C. N. J. (2004). Higher-order aberrations of lenticular opacities. *Journal of Cataract and Refractive Surgery*, 30, 1642–1648. [PubMed]

- Salmon, T. O., & Thibos, L. N. (2002). Videokeratoscope—Line-of-sight misalignment and its effect on measurements of corneal and internal ocular aberrations. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 19, 657–669. [[PubMed](#)]
- Santamaría, J., Artal, P., & Bescós, J. (1987). Determination of the point-spread function of human eyes using a hybrid optical-digital method. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 4, 1109–1114. [[PubMed](#)]
- Smith, G., Cox, M. J., Calver, R., & Garner, L. F. (2001). The spherical aberration of the crystalline lens of the human eye. *Vision Research*, 41, 235–243. [[PubMed](#)]
- Tabernero, J., Atchison, D. A., & Markwell, E. L. (2009). Aberrations and pupil location under corneal topography and Hartmann–Shack illumination conditions. *Investigative Ophthalmology and Visual Science*, 50, 1964–1970. [[PubMed](#)] [[Article](#)]
- Tabernero, J., Benito, A., Alcón, E., & Artal, P. (2007). Mechanism of compensation of aberrations in the human eye. *Journal of the Optical Society of America A, Optics, Image Science, and Vision*, 24, 3274–3283. [[PubMed](#)]
- Tabernero, J., Benito, A., Nourrit, V., & Artal, P. (2006). Instrument for measuring the misalignments of ocular surfaces. *Optics Express*, 14, 10945–10956. [[PubMed](#)]
- Thibos, L. N., & Hong, X. (1999). Clinical applications of the Shack–Hartmann aberrometer. *Optometry and Vision Science*, 76, 817–825. [[PubMed](#)]
- Wilson, A., Campbell, M. C. W., & Simonet, P. (1992). Change of pupil centration with change of illumination and pupil size. *Optometry and Vision Science*, 69, 129–136. [[PubMed](#)]