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Non-invasive measurements of the dynamic changes in the ciliary muscle, crystalline lens morphology, and anterior chamber during accommodation with a high-resolution OCT

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ABSTRACT

Purpose: To assess non-invasively the changes in the anterior chamber eye, crystalline lens morphology, and ciliary muscle during accommodation by means of an anterior chamber optical coherence tomographer (OCT), and correlate them with vergence.

Methods: Twenty-five eyes of twenty-five healthy subjects, whose mean age was 29.9±7.1 years, were included and measured with an anterior chamber OCT. The central corneal thickness (CCT), anterior chamber depth (ACD), anterior crystalline lens radius of curvature (ALRC), crystalline lens thickness (CLT), and ciliary muscle area (CMA) were measured for each participant at 0, –1, –2, and –3 D of target vergence. A linear model was used to assess the correlation of each eye parameter with the vergence demand.

Results: The mean CCT showed no change for all the accommodative stimuli. The mean ACD and ALRC decreased with the vergence, about 4.5 and 30 % at –3 D, respectively. On the contrary, the CLT and CMA showed an opposite tendency, where the mean CLT was increased by 4.0 % and the mean CMA was done by 26% at –3 D. Statistical significant differences ($p < 0.001$) were obtained among all vergences for each eye metric, except for the CCT ($p = 0.76$).

Conclusion: The ACD and ALRC decreased about 2 and 10 % per dioptre of accommodation, respectively; whereas the CLT and CMA increased about 2 and 9 %, respectively. These results lend to add to the area of knowledge regarding the modern understanding of accommodation biometry and biomechanics.

Key words: Accommodation; Ciliary muscle; lens morphology

INTRODUCTION

The crystalline lens is the ocular structure that undergoes the principal morphological change during accommodation. This structure modifies its thickness and curvature to adjust its refractive power thus focusing the image at the retina. Concretely, during this process the lens' radii of the anterior and posterior surfaces experiences a decrease,[1] and its thickness increase. At the same time, the anterior chamber depth (ACD), anterior chamber angle, and pupil diameter are reduced,[2-4] meanwhile the ciliary muscle area (CMA) increases.[4, 5] Nonetheless, contradictory results regarding corneal changes with accommodation have been reported in the literature. In this regard, several studies reported changes in the corneal keratometry, volume and aberrations;[6-8] whereas another study obtained stable keratometry, thickness and aberrations with accommodation.[9]

All in all, the study of changes in the anterior chamber during accommodation might have two main clinical implications. On the one hand, it might help to better understand the mechanism of accommodation, which could enable the recovery of the accommodation of elderly people through the design of new intraocular lenses (IOLs).[1] On the other hand, it might help clinicians to understand the lens vault and its dynamic changes with accommodation to select the proper phakic lens size and then anticipate and prevent postoperative complications, such as glaucoma or cataract.[10]

The aim of the present study was to assess changes in the anterior chamber eye during accommodation, and correlate them with vergence by means of an anterior chamber optical coherence tomographer (OCT).

METHODS

Patients

This study included 25 subjects with healthy and phakic eyes, and those who used contact lenses were asked to attend the examination without wearing them. Only one eye per participant was included because of the similarity between both eyes in healthy population, which in the end would simply double the number of data points providing the same information as one eye.[11] Each patient was checked to have enough amplitude of accommodation of at least 3.00 D measured monocularly by the Donder’s method, and had all measurements taken during the same session.

The Universitat de Valencia Ethics Committee gave the ethical approval and the study was performed in adherence with the tenets of the Declaration of Helsinki. All patients provided written informed consent after the nature and possible consequences of the study were explained to them.

Optical coherence tomographer

The Visante omni (Carl Zeiss AG, Oberkochen, Germany) is the OCT used for taking all measurements. Basically, this is a non-contact diagnostic system that acquires and analyses detailed cross-sectional tomographic images of the anterior segment. This equipment combines OCT technology with Placido disk topography to obtain measurements of both the cornea and anterior segment, and uses an infrared light of 1310 nm. Furthermore, the vergence of the fixation target can be adjusted through a set of internal lenses, which were used to evaluate changes in the anterior eye with accommodation.

Experimental procedure

The measurement procedure took place at the laboratory of the Grupo de Investigación en Optometría (University of Valencia, Spain), in which one skilled operator acquired all measurements on the right eye of each subject. The ambient lighting conditions were controlled to be stable in order to avoid any significant variations in the pupil diameter. At the same time, no contact in the eye was allowed prior to start the measurements with the OCT.

All measurements were taken with the stimulus fixed at the patient's far point, which is referred as 0.00 D (unaccommodated state), at –1.00, –2.00 and –3.00 D of vergence. Additionally, the order of each vergence was chosen randomly, and each acquisition was taken 4 seconds after the subject's last blink to allow tear film to spread over the cornea along the horizontal meridian.[12] Finally, three different scan modes were used in this study (i.e. "Enhanced anterior segment single", the "Raw Image", and the "Raw Image HR"), and for each one, three measurements were taken for the same vergence.

Anterior eye segment parameters

Figure 1 (panels A and B) illustrates the ocular parameters analysed as a function of the vergence, which were the central corneal thickness (CCT), ACD, anterior crystalline lens radius of curvature (ALRC), CMA, and crystalline lens thickness (CLT). The scan "enhanced anterior segment single", which represents a total area of 16 mm in width and 6 mm in depth, was used to capture the CCT and internal ACD. The 'Raw image', which has the same width and depth as the previous one, captured the images of the whole crystalline lens and were then used to obtained the central CLT. Finally, the 'Raw image HR' mode, which has an area of 10 mm width and 3 mm depth, was used to capture the ALRC, and CMA at the temporal region.

All results at each vergence were reported as relative differences with respect to the unaccommodated state because the OCT images taken in raw mode were not corrected for the refractive indexes of the ocular media. Regarding the image analysis, the Image J software (National Institute of Health, USA) was used to measure all axial lengths, such as the CCT, ACD and CLT. Furthermore, this software was also used to measure the CMA after applying a smooth image processing filter and then enhancing the contrast. Conversely, a custom made MATLAB (MathWorks, USA) program was used to measure the ALRC, which was obtained by adjusting a circumference to the central area moving aside a fixed number of pixels from the centre (corresponding to approximately 1.5 mm taking as a reference a model eye with known dimensions). In this case, smooth and Sobel filters were applied on the image in order to enhance the limits of both surfaces.

Statistical analysis

A repeated measure analysis of variance (rANOVA) was used to study if there were significant differences among the stimulus vergences for each anterior segment biometry. The normality of all data sets was evaluated with the Shapiro-Wilk test. The ANOVA procedure based on the *F* statistic is robust under the breach of the normality assumption, provided that the data samples have no important asymmetries or similar distribution shapes.[13] Prior the rANOVA, the Mauchly's sphericity test was used to check the sphericity assumption. In cases in which sphericity could not be assumed, the Greenhouse-Geisser correction was applied.[14] The Bonferroni procedure was used as a post hoc test for comparisons between data groups when the rANOVA revealed significant differences between measurements. In all cases, the statistical significance limit was set to $p < 0.05$. Finally, the SPSS software v.22 (IBM Corp., Armonk, New York) was used to perform this analysis.

On the other hand, a linear model was used to describe the relationship between the dependent variable (each biometric parameter) and the independent variable (each accommodative stimulus). Then, the coefficient of determination (represented as R^2) was used to assess how well the regression model fits the data, which can be interpreted as the proportion of the variance in the dependent variable that is predicted from the independent variable.[15]

RESULTS

A total of 25 eyes of 25 subjects were included in the study, from which 68 % were men and 32 % women. Their mean age was 29.9 ± 7.1 years (range: 20 to 41 years), and average spherical equivalent refraction was –0.77 ± 1.93 D (range: −6.25 to 2.63 D).

Central corneal thickness

Figure 2 panel A displays the box plot for the relative changes in the CCT as a function of the vergence. According to the results obtained, the mean relative change in the CCT was 0 % at each vergence group, where the difference between the lower and upper quartiles was almost 0 % in each vergence. At the same time, differences among the three vergence groups were not statistically significant ($p = 0.76$).

Figure 2 panel B displays the regression model used to fit the relative change in the CCT as a function of the vergence. The fitted line was practically horizontal, meaning that there was no change in this parameter with vergence. The coefficient of determination was 0.656.

Anterior chamber depth

Figure 3 panel A displays the box plot for the relative changes in the ACD as a function of the vergence. Generally speaking, this plot shows that the larger the vergence, the larger the relative change in the ACD. Concretely, the median change was –0.99 % at 1 D, –2.63 % at 2 D, and –4.47 % at 3 D, where the negative sign denotes that the ACD becomes shallower. Additionally, the relative differences among the three vergence groups were statistically significant ($p < 0.001$). Finally, this plot shows larger variability in the ACD at greater vergences. The difference between the lower and upper quartiles at 1 D was about 2 times smaller than that obtained at the other two vergences.

Figure 3 panel B shows the lineal regression model used to fit the relative changes in the ACD with the accommodation. This plot shows a negative and steep tendency between the relative difference in the ACD and the vergence, in which the slope was –1.80 and the coefficient of determination was 0.997. Furthermore, this graphs also shows that the standard deviation obtained at 1 D of accommodation is about two times smaller than that obtained at larger vergences.

Anterior crystalline lens radius of curvature

Panel A in Figure 4 shows the box plot for relative changes in the ALRC as a function of the vergence. According to this graph, the larger the vergence, the smaller the ALRC, which median relative changes were –10.45 % at 1 D, –23.86 % at 2 D, and –30.24 % at 3 D (where the negative sign denotes that the ALRC is reduced with the vergence). Furthermore, the relative differences in the ALRC among the three vergence groups were statistically significant ($p < 0.001$).

Figure 4 panel B displays the lineal regression model used to fit the relative change in the ALRC with the accommodative demand. This plot shows a negative and steep tendency between both variables, which slope and coefficient of determination were –9.94 and 0.982, respectively.

Crystalline lens thickness

Figure 5 panel A displays the box plot for the relative change in the CLT as a function of the vergence. On the whole, this graph shows that the larger the vergence, the thicker the crystalline lens in which the median relative changes at 1, 2, and 3 D were 0.76 %, 2.61 % and 4.25 %, respectively. Additionally, differences in the relative change in the CLT were statistically significant ($p < 0.001$) among the three accommodative stimulus. Finally, this graph also shows larger variability in the CLT with the vergence, in which the difference between the lower and upper quartiles at 1 D was about three times smaller than that obtained at the other two vergences.

On the other hand, Figure 5 panel B shows the linear regression model used to fit the CLT as a function of the vergence. This graph shows a positive and steep tendency between the vergence and lens thickness, in which the slope was 1.66 and the coefficient of determination was 0.999. Furthermore, this graphs also shows that the standard deviation obtained at 1 D of accommodation is about two times smaller than that obtained at larger vergences.

Ciliary muscle area

Panel A in Figure 6 displays the box plot for the relative changes in the CMA as a function of the accommodative demand. All in all, this graph shows that the greater the accommodative effort, the larger the area of the ciliary muscle is. The median relative changes were 8.64 %, 17.22 %, and 25.53 % at 1, 2, and 3 D, respectively. Furthermore, statistical significant CMA differences were obtained among the three vergences ($p < 0.001$). Finally, it was found that the larger the vergence, the wider variability in the relative changes in the CMA, where the difference between the lower and upper quartiles at 2 and 3 D was about two times bigger than that obtained at 1 D.

Regarding the linear regression model (Figure 6, panel B), a positive and steep tendency was obtained between the CMA and the vergence, in which the slope and coefficient of determination were 8.46 and 0.998, respectively. Furthermore, this graph also shows that the standard deviation obtained at 1 D is two times smaller than that obtained at 2 and 3 D.

DISCUSSION

The aim of the present study was to assess changes in the anterior chamber eye during accommodation, and correlate them with vergence by means of an anterior chamber OCT. Clinically, these results might help clinicians to have objective evidences about all dynamic changes taking place in the anterior segment with accommodation.

Central corneal thickness

Regarding changes in the CCT with accommodation, the results obtained showed almost no changes with the accommodation (Figure 2, panels A and B). On the one hand, the median relative changes were comparable among the vergences ($p = 0.76$), and at the same time the line was flat, which a slope value of 0.03 (Figure 2, panel B). Thus, these results show that the CCT and accommodation are not related. In other words, this reflects that the CCT does not change with the accommodation.

The hypothesis that the cornea might play a role in the accommodation comes from the assumption that the ciliary muscle affects the cornea. Specifically, it has been suggested that this effect occurs mainly in the corneal periphery because of the anatomic proximity of the ciliary muscle to the limbus.[6] With this regard, some studies have assessed the corneal periphery (R>7.0 mm), and reported changes in the corneal curvature, volume and aberrations with accommodation.[6-8, 16] Contrarily, other studies hypothesized that corneal changes with the accommodation are associated to the cyclotorsion produced in the corneal topography.[17, 18] Nevertheless, when that rotation was corrected, corneal changes were reduced considerably and were not significant.

Finally, and in spite of these contradictory results among all previous studies,[6-9, 17-19] it should be taken into account that only three studies assessed corneal changes at different accommodation ranges.[6, 9, 17] Concretely, these studies reported that corneal changes are not statistically significant during accommodation, and are in agreement with those obtained previously. Thus, from all this information seems plausible that the CCT does not change with the accommodation.

Anterior chamber depth

In general terms, the results obtained showed that the mean ACD becomes about 1 % and 5 % shallower at 1 D and 3 D, respectively (Figure 3, panel B). Similarly, the linear regression model showed a slope of –1.80 and a coefficient of determination of 0.997. According to these results, the ACD seems to reduce about 2 % per dioptre of accommodative demand. The equation used to adjust the linear model shows a non-zero y-intercept (Figure 3, panel B), which is not realistic from a clinical point of view because it denotes the ACD changes when the eye is relaxed. In this regard, Table 1 depicts the slope and coefficient of determination when the regression model was forced to be zero with no accommodation effort (i.e. y-intercept equal to zero). In this case, the new slope and coefficient of determination were about –1.5 and 0.953, respectively. In other words, with this model the ACD becomes about 1.5 % shallower per dioptre of accommodative demand. From a physiological point of view, the reduction in the ACD with the accommodation was expected due to changes in the CLT and curvature.[20]

All these results report more evidences about all changes taking place in the eye with accommodation, which could enable the recovery of the accommodation of elderly eyes through the design of new IOLs.[1] At the same time, the vault between a phakic lens and its surroundings is critical to avoid either cataract or glaucoma during the postoperative.[21] Thus, the results obtained in the present study might help clinicians to prevent postoperative complications after a phakic IOL implantation.

Finally, it is worth pointing out that the standard deviation obtained at 1 D was two times smaller than that obtained at 2 or 3 D. This is, the results' variability is larger for large accommodative demands. This behaviour could be related to either the fact that some volunteers were pre-presbyopic and might have some problems to maintain the accommodative effort stable during the measurement, or due to accommodative micro fluctuations, which are greater with the accommodative demand. Further studies with more homogeneous population would be expected to report more homogeneous dispersions measurements among accommodative demands.

Anterior crystalline lens radius of curvature

According to the results obtained for the ALRC, the larger the vergence, the lower the radius of curvature, where the median decrease was about 10 % at 1 D and 30 % at 3 D (Figure 4, panel A). Furthermore, the lineal model used to adjust the results obtained confirmed this tendency (Figure 4, panel B), in which the mean crystalline lens radius of curvature decreased about 10 % per dioptre of accommodation. Nevertheless, the equation used for this adjustment showed a non-zero y-intercept, which is not realistic as was stated previously. When the model was forced to have a zero y-intercept, the slope and coefficient of determination were –10.98 and 0.970, respectively (Table 1). These results reflect that the ALRC is expected to decrease about 11 % per diopter of vergence. From a physiological point of view, the reduction in the ALRC is necessary to increase the refractive power of the crystalline lens,[22] and hence, change the eye focus to near vision.

The results obtained in the present study are in agreement with those obtained previously.[20, 22] One of them used a Scheimpflug camera to measure changes in shape of the crystalline lens during accommodation.[20] According to the results obtained, the anterior and posterior radius of the lens decreased with the accommodation, in which the anterior lens surface becomes more hyperbolic. The other study,[22] used a custom build and dual-focus spectral domain OCT to image the anterior segment of the eye from the cornea to the posterior lens surface. Regarding the crystalline lens, these authors obtained that the anterior and posterior radius of curvatures significantly decreased with accommodation. Although the steepening on the anterior surface was greater than that of the posterior surface, suggesting that changes in the anterior lens might play greater roles than the posterior surface in the accommodation.

These results might help the development of new IOL designs that better fit with all changes taking place in the eye, and then, recover some of the ability to see clear objects at different distances. At the same time, these results could also be used in the preoperative assessment of a phakic surgery to minimize possible postoperative complications due to dynamic changes with the accommodation.

Crystalline lens thickness

Regarding changes in the CLT during the accommodation, the median change at 1 and 3 D was about 1 and 4 %, respectively (Figure 5, panel A). Additionally, the slope of the linear model used to fit the results was 1.66, and its coefficient of determination was 0.999. In other words, this graph reflects that the crystalline lens becomes about 2 % thicker per dioptre of demand (Figure 5, panel B). Nonetheless, it should be pointed out that the linear model used to fit the results showed a non-zero y-intersection, which is not logic from a physiological point of view because the CLT should not change during far vision. To circumvent this limitation, a new linear model was used but in this case it was forced to have a zero y-intersection (Table 1), and the new slope and coefficient of determination were 1.31 and 0.948, respectively. In other words, the new results show that the crystalline thickness increases about 1.3 % per dioptre of accommodation, which was similar to the value obtained with the previous model.

It should be pointed out that the standard deviation obtained at 1 D was about 2 and 2.5 times smaller than that obtained at 2 and 3 D, respectively. In other words, this reflects that the variability in the lens thickness is larger for greater accommodative demands. In this sense, further studies with more homogeneous population would be expected to report more homogeneous dispersions measurements among accommodative demands.

The results obtained in this study show the same tendency as those obtained previously,[1, 4, 22-24] in which the lens thickness increased with vergence. At the same time, it has been reported that the posterior lens surface might move backwards with accommodation, because the increase in lens thickness with accommodation is higher than the decrease in the ACD.[20] Furthermore, the lens thickness has been reported to increase significantly with age, in which the ACD shallows and the anterior lens curvature steeps.[4] Another study assessed the dynamic response of the crystalline lens with a spectral domain OCT as a function of age.[25] That study focused the analysis on the lens thickness and anterior radius, and obtained that the lens reshaping was much slower in aging eyes.

Ciliary muscle area

Generally speaking, the median CMA becomes about 9 % and 26 % bigger at 1 and 3 D of vergence, respectively (Figure 6, panel A). In other words, the larger the vergence, the greater the ciliary muscle area. Additionally, the linear regression model (Figure 6, panel B) used to fit the results showed a slope and coefficient of determination equal to 8.46 and 0.998, respectively. This is, the CMA changes about 9 % per dioptre of accommodation. In spite of these results, and as was reported previously, the equation model used to fit the results shows a non-zero y-intercept value (Figure 6, panel B). As mentioned before, a new linear model was applied, in which the y-intercept was forced to be zero (Table 1). According to the new values obtained, the CMA changes about 9 % per dioptre, which in this case was the same rate as the one obtained with the previous model.

Imaging the ciliary muscle during the accommodation could help to understand the ageing of the accommodative system.[5] Despite all of this, the biggest challenge in imaging these structures is the light attenuation caused by the sclera and ciliary body, which reduce the image contrast, and makes it more difficult to recognize.[26] Nevertheless, OCT with a wavelength of 1300 nm allows deeper visualization of the posterior ciliary muscle boundary and the inner apex,[26, 27] which is important to obtain accurate ciliary muscle thickness measurements.[5] After all this, the OCT used in the present study seems to be an appropriate system to measure the CMA because it works with a wavelength of 1310 nm.

In an attempt to measure the ciliary muscle with high resolution, a previous study synchronized two spectral domain OCTs working at 840 and 1325 nm, and a dual channel accommodation target to image the accommodative system during dynamic accommodation.[5] Concretely, that system enables synchronous recording of temporal images of the anterior segment and the ciliary muscle at 13 frames per second during accommodation, which is sufficient to characterize the dynamics of the response. Furthermore, since the ciliary body inner apex is difficult to visualize due to the attenuation of light by the sclera and ciliary body, consecutive pairs of OCT images were registered and averaged during dynamic acquisition to increase the visibility of the ciliary muscle. Finally, with this new system the authors could quantify the dynamic changes of the crystalline lens and ciliary muscle thickness, and could also characterize the relationship between the ciliary muscle contraction and the resulting changes in the lens thickness during accommodation.

The current study included healthy eyes without any surgery. For this reason, further studies should include eyes with phakic IOL implanted to report evidences about the relationship between the phakic lens and the structures surrounding it with the accommodation. At the same time, the results analysed in this study did not take into account the refractive error, age, gender, etc. Since it is known that the accommodative effort is lost with age, further studies could include several age groups and assess changes in the whole anterior chamber with the accommodation.

Summarizing, the ACD and ALRC decreased about 1.5 % and 11 % per dioptre of accommodation; whereas the CLT and CMA increased about 1.3 % and 9 %, respectively. To know the real effects of accommodation in the biomechanics of the eye could be useful to design optical systems to complement the loss of accommodation maintaining the crystalline lens, or replacing it, when presbyopia appears. In addition, a better understanding of the biomechanics related to accommodation may lead to early detection of individuals at risk for developing myopia, and new treatments to prevent and reduce myopia.

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FIGURE LEGENDS

Figure 1. Parameters measured with the anterior segment optical coherence tomographer. CCT: Central corneal thickness, ACD: Anterior chamber depth, ALR: crystalline lens radius of curvature, CMA: ciliary muscle area, and LT: Lens thickness.

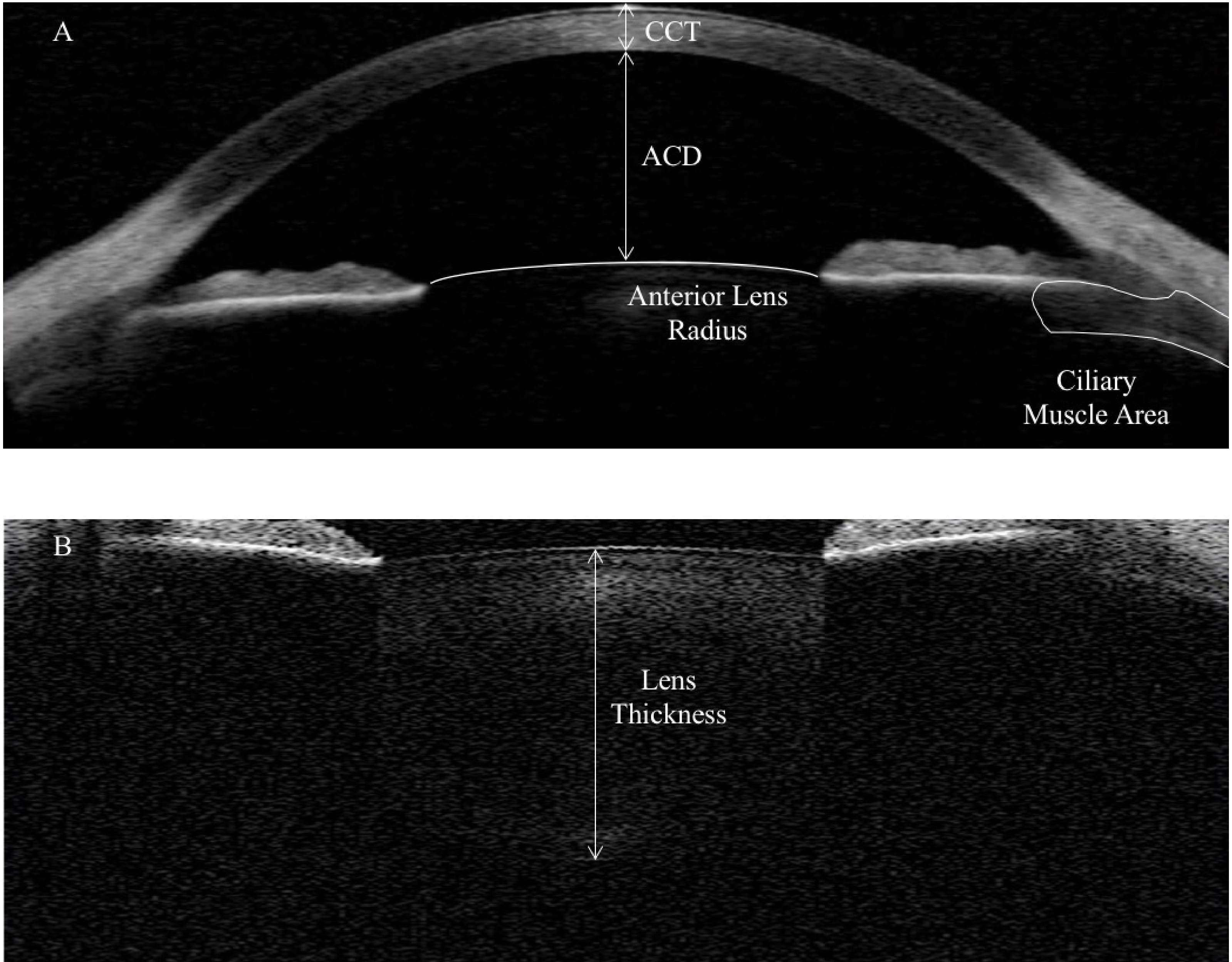
Figure 2. Box plot (panel A) and linear model (panel B) of the relative changes in the central corneal thickness as a function of the vergence.

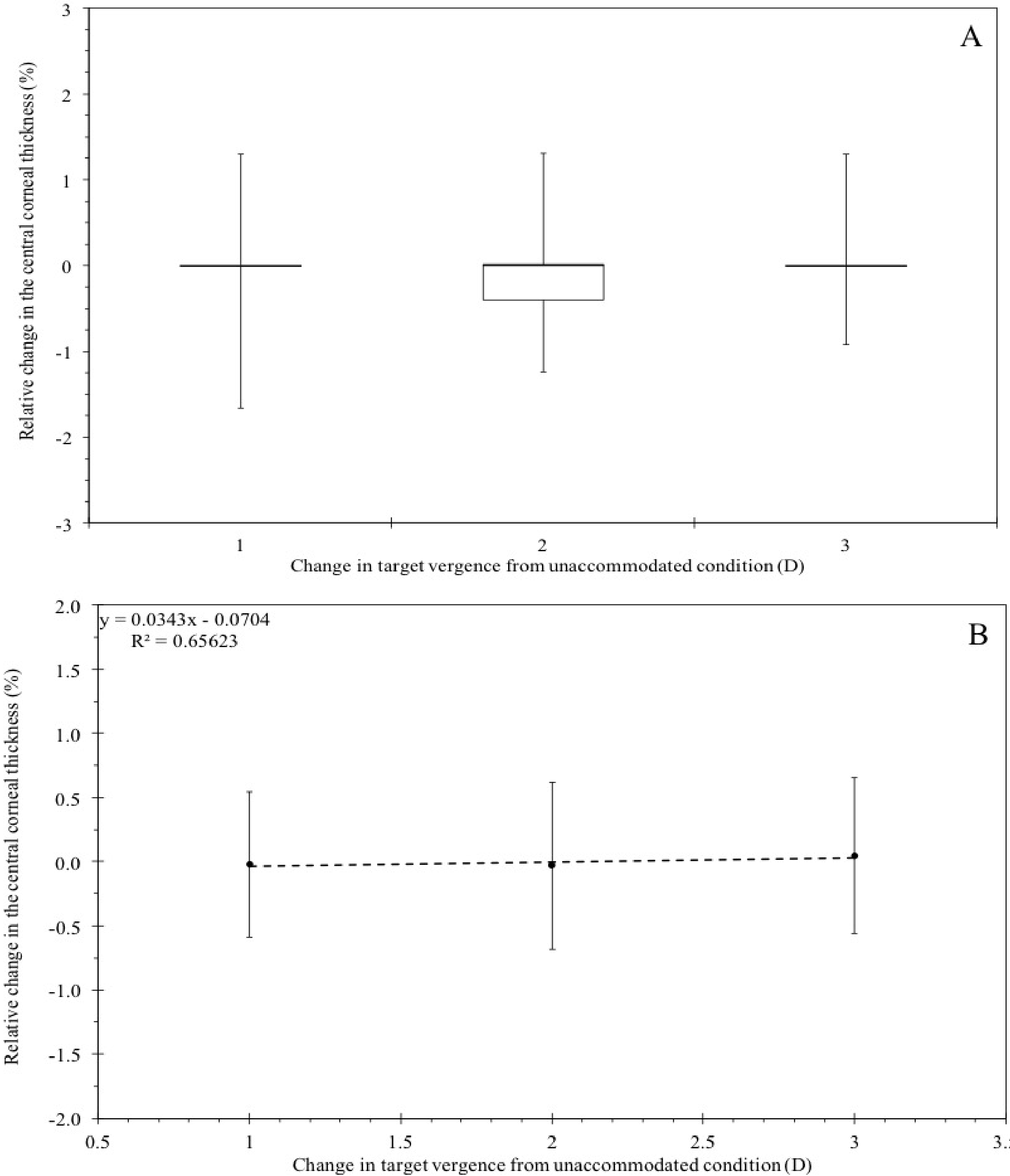
Figure 3. Box plot (panel A) and linear model (panel B) of the relative changes in the anterior chamber depth as a function of the vergence.

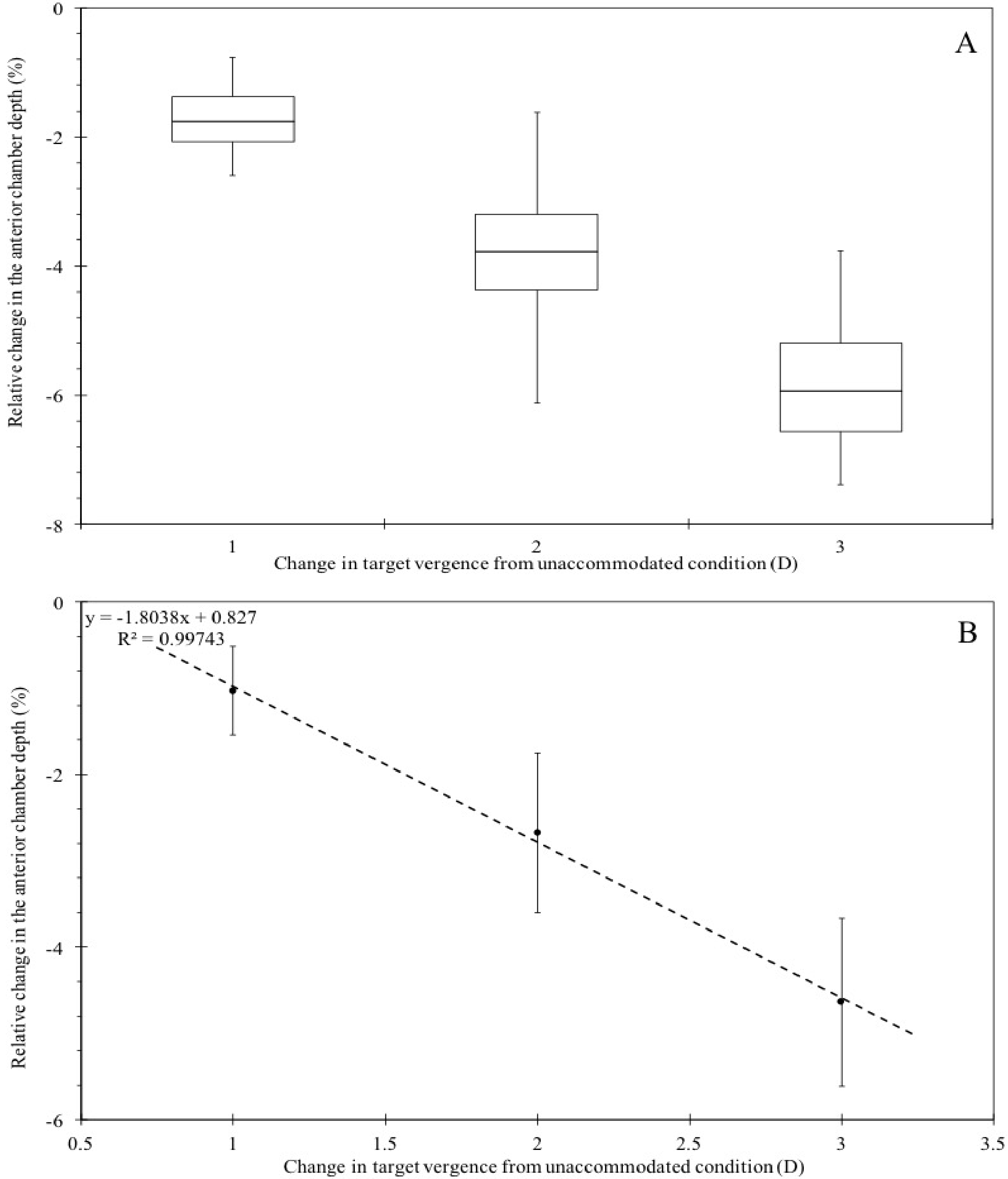
Figure 4. Box plot (panel A) and linear model (panel B) of the relative changes in the crystalline lens radius of curvature as a function of the vergence.

Figure 5. Box plot (panel A) and linear model (panel B) of the relative changes in the crystalline lens thickness as a function of the vergence.

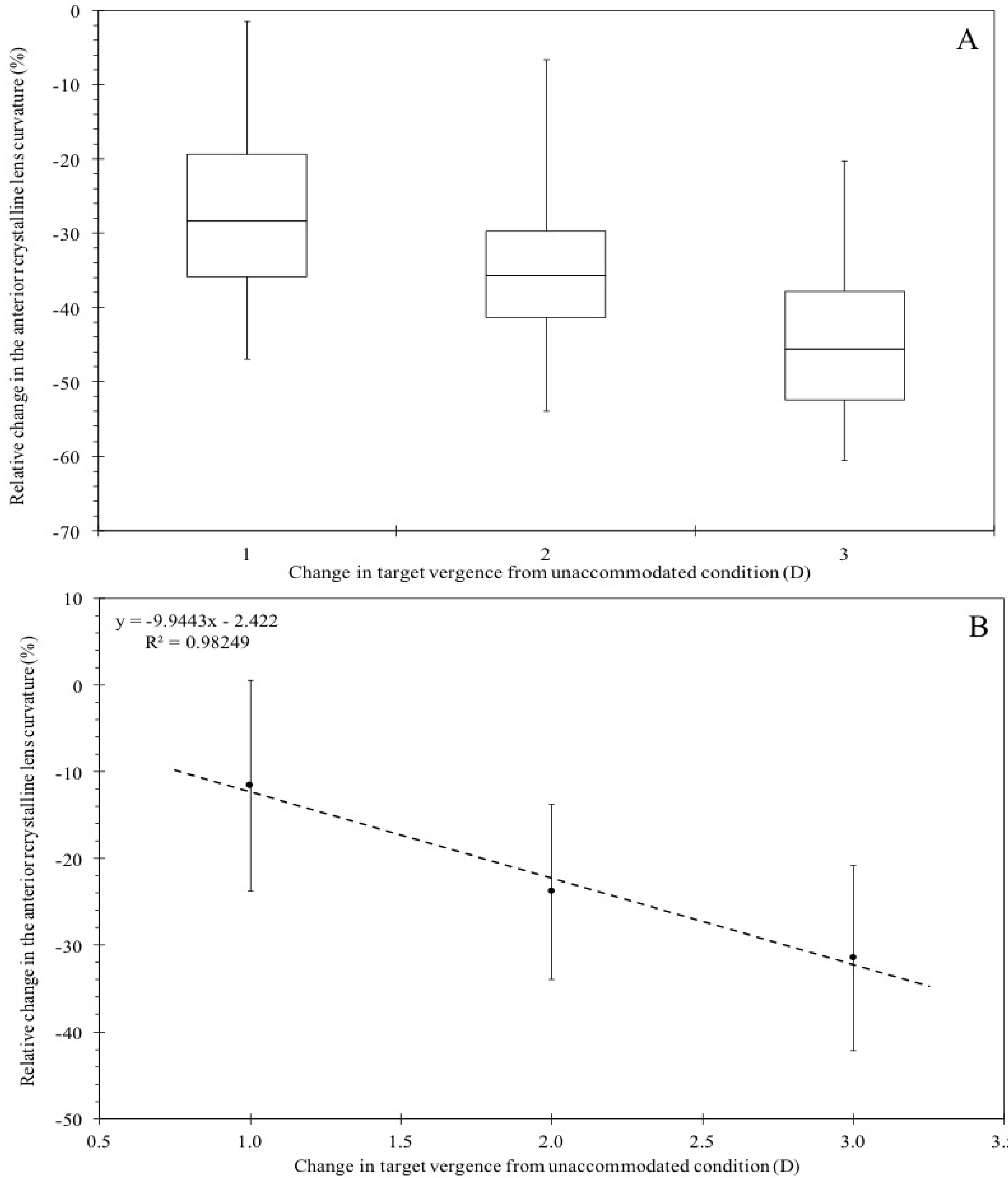
Figure 6. Box plot (panel A) and linear model (panel B) of the relative changes in the ciliary muscle area as a function of the vergence.

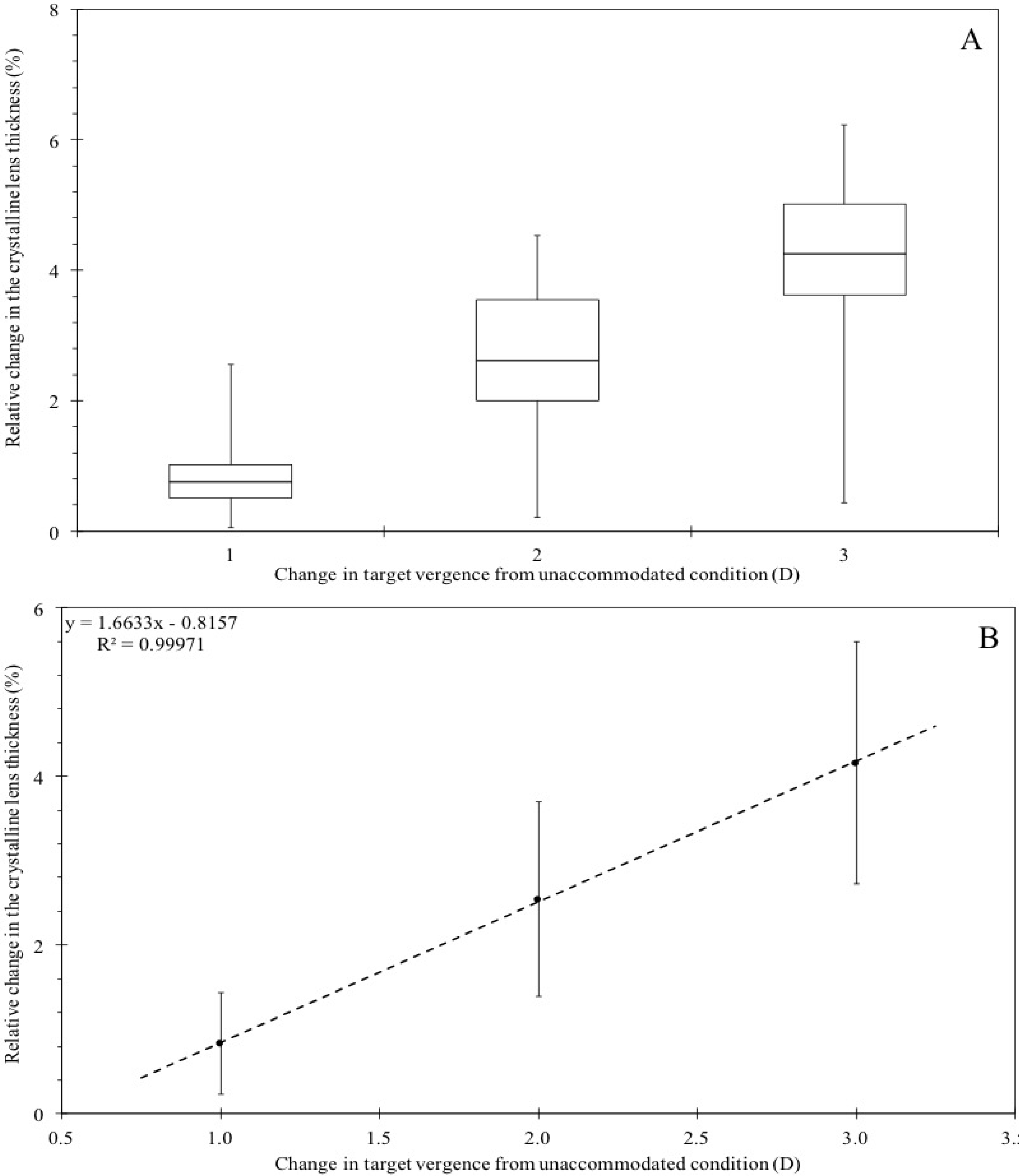

A
CCT
ACD
Anterior Lens Radius
Ciliary Muscle Area
B
Lens Thickness


A
Relative change in the central corneal thickness (%)
Change in target vergence from unaccommodated condition (D)
B
y = 0.0343x - 0.0704
R² = 0.65623
Relative change in the central corneal thickness (%)
Change in target vergence from unaccommodated condition (D)

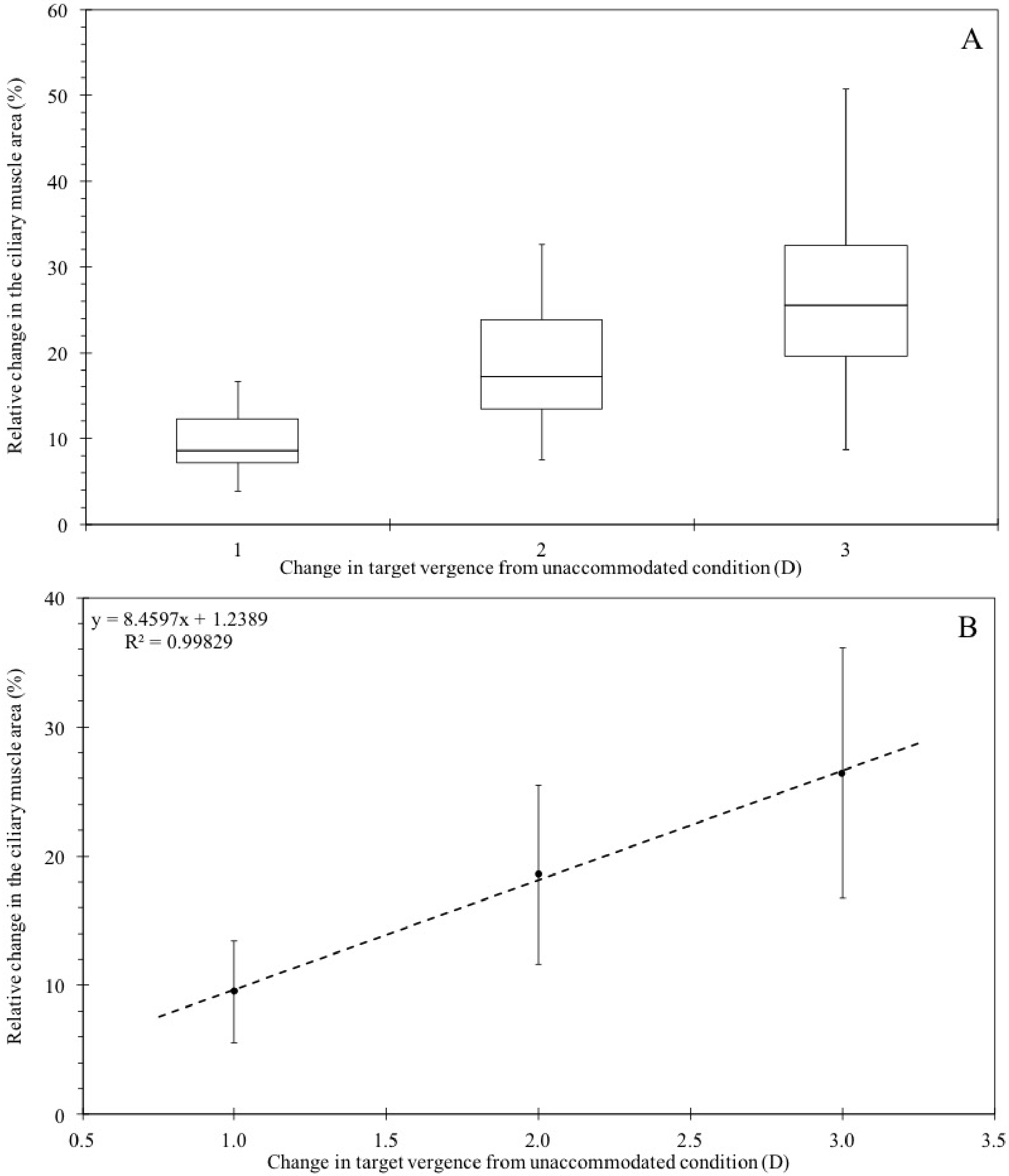


A
B
0
-2
-4
-6
-8
1
2
3
0.5
1.5
2.5
3.5
Relative change in the anterior chamber depth (%)
Change in target vergence from unaccommodated condition (D)
y = -1.8038x + 0.827
R² = 0.99743


A
B
Relative change in the anterior crystalline lens curvature (%)
Relative change in the anterior rcrystalline lens curvature (%)
Change in target vergence from unaccommodated condition (D)
y = -9.9443x - 2.422
R² = 0.98249



A
Relative change in the crystalline lens thickness (%)
0
2
4
6
8
1
2
3
Change in target vergence from unaccommodated condition (D)
B
y = 1.6633x - 0.8157
R² = 0.99971
Relative change in the crystalline lens thickness (%)
0
2
4
6
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Change in target vergence from unaccommodated condition (D)


A
Relative change in the ciliary muscle area (%)
0
10
20
30
40
50
60
1
2
3
Change in target vergence from unaccommodated condition (D)
B
y = 8.4597x + 1.2389
R^2 = 0.99829
Relative change in the ciliary muscle area (%)
0
10
20
30
40
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Change in target vergence from unaccommodated condition (D)