Available online at www.sciencedirect.com
ScienceDirect
Vision Research xxx (2007) xxx–xxx
Vision Research
www.elsevier.com/locate/visres

Emmetropization and optical aberrations in a myopic corneal refractive surgery chick model

E. García de la Cera [a], G. Rodríguez [b], A. de Castro [a], J. Merayo [b], S. Marcos [a],*

[a] *Instituto de Óptica, Consejo Superior de Investigaciones Científicas, Serrano 121, 28006 Madrid, Spain*
[b] *Instituto Universitario de Oftalmobiología Aplicada (IOBA), Universidad de Valladolid, Valladolid, Spain*

Received 29 March 2007; received in revised form 13 June 2007

Abstract

We studied the potential of myopic corneal refractive laser surgery to induce myopia (axial elongation) and potential interactions between aberrations (generally resulting from the procedure) and myopia development in chicks (Gallus domesticus). Ten white Leghorn chicks were monolaterally treated one day post-hatching with photorefractive keratectomy (PRK), with a nominal dioptric change of −9.9 D (imposed hyperopia). Axial length was measured using an adapted ultrasonic biometer; corneal radius of curvature was measured using a custom-built videokeratometer and spherical error and high order aberrations were measured using custom-built Hartmann–Shack aberrometer post-operatively on days 9, 12, 14 and 16 after hatching. Two-weeks after surgery, there were no significant differences in corneal radius of curvature between treated and control eyes. Astigmatism increased on average by a factor of 2.6 and 3rd and higher order aberrations by a factor of 5.3 after PRK. Both treated and control eyes were close to emmetropia, and no axial elongation was found in the treated eyes. The inability of the refractive procedure to achieve significant reductions in the corneal power could be attributed to the biomechanical properties of the chick eye. High order aberrations induced significant contrast decrease (by a factor of 1.7 at 4.5 c/deg). However, reduced image quality neither produced myopic refractive error nor axial elongation in the treated eyes. Both normal and treated eyes emmetropized, indicating that increased amounts of aberrations do not appear to be a risk factor for myopia.

Keywords: Emmetropization; Experimental myopia; Refractive surgery; Optical aberrations; Refractive error

1. Introduction

The quality of visual experience in early stages of post-natal development is critical for proper eye growth and normal emmetropization. Abnormal visual experience has been associated to the development of myopia (Smith, 1998; Wallman, 1993; Wildsoet, 1997). Animal models in which retinal image has been degraded exhibit abnormal eye growth. It is well established that form deprivation imposed by diffusers (Hayes, Fitzke, Hodos, & Holden, 1986; Troilo & Wallman, 1991; Wallman & Adams, 1987) and defocus imposed by negative lenses (Diether & Schaeffel, 1997; Schaeffel, Glasser, & Howland, 1988; Schaeffel & Howland, 1991) cause excessive elongation in chick eyes and therefore myopia. Treatments with lenses in young chicks produce a change of the refractive state of the treated eye, which adjusts its growth to compensate for the imposed defocus (Kee, Marzani, & Wallman, 2001; Schaeffel et al., 1988). For example, Schaeffel et al. (1988) achieved −2.2 D after 15 days of treatment with −4 D lenses placed at day 9 post hatching, while control eyes with a normal visual environment remained slightly hyperopic in the same period of time. In humans, several pathologies that produce an absence of normal visual experience, such as congenital cataracts, eyelid closure or corneal opacities have been associated to myopia (Gee & Tabbara, 1988; Hoyt, Stone, Fromer, & Billson, 1981; Robb, 1977).

An increasingly popular technique to correct refractive errors in humans is corneal refractive surgery. Corneal power is changed using excimer laser, reshaping the ante-

---

* Corresponding author. Fax: +34 915645557.
E-mail address: susana@io.cfmac.csic.es (S. Marcos).

0042-6989/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.visres.2007.06.005

rior surface of the cornea by laser ablation of corneal tissue. Corneal photorefractive keratectomy (PRK) has been shown to produce reliable refractive results in humans, with efficacies of 90%, and stability (changes in spherical equivalent less than 1 D, 6 and 12 months after surgery) of 85.8% (Tuunanen & Tervo, 1998). The potential use of corneal refractive surgery to produce a permanent change in corneal power seems attractive as an alternative to current methods used to impose experimental refractive errors in laboratory animals and to study mechanisms of refractive error development. PRK has been used to alter emmetropization in the rabbit (Bryant et al., 1999) and infant Rhesus Monkeys (Zhong et al., 2004). In both cases, the axial length changed to compensate for the induced defocus. In this study, we will evaluate the feasibility of a refractive surgery myopia model in chicks. In addition, we will evaluate the optical outcomes of the refractive surgery model in chick, by measuring the effective change in corneal curvature and refraction (a refractive surgery model in adult chickens had been previously used to test the effect of refractive surgery on corneal transparency (Merayo-Lloves, Yañez, Mayo, Martín, & Pastor, 2001).

Several studies, primarily in human patients, have shown that while laser refractive surgery is in general successful at correcting defocus and astigmatism, high order aberrations are generally induced (Moreno-Barriuso, Merayo-Lloves, Marcos, Navarro, Llorente & Barbero, 2001) and these affect the quality of the retinal image (Marcos, 2001). Several studies (Atchison, Collins, Wildsoet, Christensen, & Waterworth, 1995; Paquin, Hamam, & Simonet, 2002) in humans report that myopic eyes show higher amounts of higher order aberrations than emmetropic eyes, although not all studies have found significant differences between myopes and emmetropes (Cheng, Bradley, Hong, & Thibos, 2003). Cross-sectional studies cannot reveal whether increased aberrations are a cause or a consequence of myopia. A group of hyperopes and myopes (matched in age and absolute ametropia) showed differences in axial length, corneal asphericity and optical aberrations, suggesting that the differences in aberrations across refractive groups may be the result of different structural properties (Llorente, Barbero, Cano, Dorronsoro, & Marcos, 2004). However, others have suggested that increased aberrations (and consequently degraded retinal image) can be a cause of axial elongation and as a consequence myopia development, and methods for myopia control based on correction of optical aberrations have even been proposed Thorn et al., 2003). The cause/effect relationship between aberrations and myopia can better be studied through longitudinal measurements, particularly in animal models where visual experience can be more easily manipulated. In a previous study we measured optical aberrations, axial length and refraction in chicks (0–13 days of age) monolaterally treated with diffusers (García de la Cera, Rodriguez, & Marcos, 2006b). We found that, for a fixed pupil diameter, optical aberrations decreased with age both in the normal eye (following normal emmetropization) and the treated eye (that progressively developed myopia), although myopic eyes showed increased amounts of aberrations. These results suggested that in this model, where myopia had been achieved by severe retinal image quality degradation with diffusers (with no feedback loop), increased aberrations were a cause rather than a consequence of myopia development. Also, a recent study showed that chick eyes that had undergone ciliary nerve section showed larger amounts of higher-order aberrations but did not become myopic, implying that retinal image degradation imposed by certain amounts of aberrations do not necessarily affect the emmetropization process (Tian & Wildsoet, 2006). On the other hand, Campbell et al. (Kisilak, Campbell, Hunter, Irving, & Huang, 2006) found that increased aberrations immediately preceded myopia development in chicks treated with negative lenses, suggesting some role of ocular aberrations in emmetropization.

If, as found in human patients, corneal refractive surgery induces significant amounts of high order aberrations, a refractive surgery model could be used as a model of permanently imposed abnormally high aberrations. Retinal image degradation caused by high order aberrations may be particularly relevant in the chick eye, which (unlike other species (García de la Cera, Rodriguez, Llorente, Schaeffel, & Marcos, 2006a)) shows naturally very low amounts of high order aberrations (García de la Cera et al., 2006b) allowing the study of potential interactions between aberrations and myopia development. If corneal power is altered (by flattening the anterior cornea) and high order aberrations are induced in the laser treatment, but axial elongation still occurs to compensate for the imposed defocus, we will conclude that the presence of aberrations does not interfere with normal emmetropization.

2. Methods

2.1. Subjects and experimental protocols

Ten White-Leghorn chicks were monocularly treated (OD) with myopic corneal refractive surgery with excimer laser (PRK) one-day post hatching (day 0), while the left eye was not treated and was used as control. All experimental protocols followed the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and had been approved by the Institutional Review Boards. Chicks were labeled for identification with color wires attached around their feet. Chicks were reared under fluorescent lighting (12 h/12 h light/dark cycle conditions) in a cage inside a controlled heated room (24–28 °C). They were allowed to eat and drink *ad libitum*. Adequate measures were taken to minimize pain or discomfort. Axial length was measured in all chicks on their first day after hatching and prior to surgery (Day 0). Post-operative measurements were done on both eyes on days 9, 12, 14 and 16. Measurements were not done immediately following surgery since corneal re-epithelization and wound healing processes, as well as increased tear secretion, would have prevented from obtaining reliable results. Measurements consisted of Hartmann–Shack aberrometry and keratometry in five chicks and ultrasound biometry in all chicks. Measurements were done with the animals awake and under natural viewing conditions.

2.2. Refractive surgery

Refractive surgery was performed using an excimer laser SVS Apex PlusTM (Summit Technology). Chicks underwent refractive surgery under total and topical anesthesia (0.02 ml Ketamine, 0.1 g/ml). Prior to laser treatment, the corneal epithelium was removed mechanically, and then laser treatment was applied on Bowman's layer (178 pulses). Finally the cornea was irrigated with buffered saline solution (BSS). The nominal myopia correction programmed into the laser system was −9.9 D, with an optical zone of 3.5 mm and a nominal corneal tissue depth ablation of 45 µm. Pachymetry measurements on 8 newborn chick eyes (used in trial surgeries) showed a pre-operative corneal thickness of 190 ± 6 µm. Computer simulations using theoretical ablation profiles (based on Munnerlyn or the parabolic approximation of the Munnerlyn equation (Cano, Barbero, & Marcos, 2004) predicted similar refractive outcomes using chick corneal dimensions than human corneal dimensions. All surgeries were uneventful and all chicks recovered (i.e. they opened the eyes normally and exhibited no signs of photosensitivity) 8 days after surgery.

2.3. Hartmann–Shack aberrometry and refraction

Aberrations were measured using a custom-built Hartmann–Shack (HS) aberrometer designed for measurements in awake animals. Measurements of the refractive state with streak retinoscopy were attempted in treated eyes, but the bad quality of the reflections (showing scissor-type images) prevented us from obtaining reliable results. The HS aberrometry data were repetitive and consistent, and the spherical error was obtained from 2nd order aberrations.

The HS system, described elsewhere(García de la Cera et al., 2006a,b) has been developed and used for measurements on chicks and mice in previous studies in our laboratory. The animal were sited on an elevated platform in front of the system, which was mounted on an *x*–*y* translational stage, allowing correct centering and focusing of the pupil. The eye pupil was continuously monitored and aligned to the optical axis of the instrument. The animal fixated the illumination spot (from a 680 nm-superluminescent diode) during a few seconds, allowing obtaining 5–10 Hartmann–Shack images per eye. Typically, HS image frames contained 17–21 spots in the pupillary zone. Pupil diameters were 2.7 ± 0.3 mm on average. The best HS images were selected for processing (Matlab, Mathworks, Nattick MA), following a procedure described in detail in previous studies (García de la Cera et al., 2006b). A program written in Matlab computed the centroids of the retinal spots and estimated the wave aberrations using modal fitting (up to 5th order Zernike expansion) of the ray deviations. We obtained defocus, astigmatism, and RMS high order aberrations from Zernike coefficients for the maximum pupil size, and also scaled down to 2-mm pupils for comparative purposes. Point spread functions and modulations transfer functions were computed from the wave aberrations assuming a pupil with homogeneous transmittance.

2.4. Keratometry

Measurements of the corneal radius of curvature were obtained using a custom-built infrared (IR) photokeratometer, implemented specifically for this study. This method has been applied in birds previously, and it is described by Schaeffel and Howland (Schaeffel & Howland, 1987; Schaeffel, Howland, & Farkas, 1986). Our keratometer consists of a ring of eight Infrared (IR) LEDs placed around a circumference of 80 mm diameter and an 8-bit CCD camera (Teli, 1360 × 1023 pixels) provided with a 105 mm focal length camera lens and extension tubes. The chick was held in front of the camera, at a distance of 27 mm from the LED ring and 71 mm from the CCD. Sequences of images were captured when the pupil appeared in focus and the image of LED-ring was well aligned with the pupil center. The image capture was controlled by computer using a program written in Visual Basic (Microsoft Corporation, Redmond, Washington). The pupillary images were processed using routines written in Matlab (Mathworks, Nattick MA). The Purkinje images of the LEDs were detected, and their positions were automatically estimated using a centroiding algorithm (Rosales & Marcos, 2006). The diameter of the LED ring on the image was computed, using a scale of 0.019 mm/pixels. A calibration curve, obtained experimentally using a set of calibrated spheres was used to convert from ring diameters to corneal radius of curvature: 1 mm (ring diameter)/3.9 mm (corneal radius). Differences in corneal curvature across 4 meridians (45, 90, 135, and 180 deg) allowed estimation of corneal astigmatism.

2.5. Ultrasound biometry

Axial length was obtained by an adapted ultrasound biometer (Allergan Humphrey Mod. 826). Measurements were conducted under topical anesthesia with a drop of (lidocaine 1%). The probe was enlarged to adapt it to the chick eye's dimensions as described in the literature (Schaeffel & Howland, 1991). The axial length for each eye was specified as the average of at least five measurements.

2.6. Statistical analysis

Agreement of repeated measurements was tested using confidence intervals (CI), with confidence levels of 95%. Statistical differences between control and control eyes where tested using paired-*t* test, with significance levels of $p < .05$. Significance of linear correlations was tested using Pearson's coefficient of correlation, with significance levels of $p < .05$.

3. Results

3.1. Refractive error

Refractive error and astigmatism were obtained from the defocus Zernike term for 2 mm pupil size. Fig. 1 shows the average spherical refractive errors and astigmatism in treated and control eyes on 4 different days, starting 8 days after surgery. Both eyes were close to emmetropia, and although spherical refractive error tended to decrease slightly with age (−0.03 D/day and in control eye and −0.07 D/day) these changes were not statistically significant. There were no statistically significant differences in refractive error (paired *t*-test) between the treated and control eyes in any of the days.

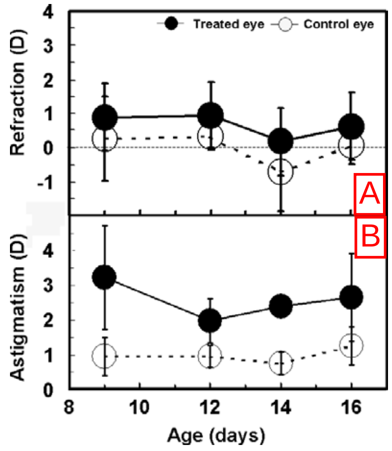

Fig. 1. Spherical error and astigmatism obtained from defocus and astigmatism Zernike terms during the experiment period (from 8 to 15) days post-operatively (9–16 days post-hatching). Solid symbols correspond to eyes treated with refractive surgery, and open symbols to untreated contralateral eyes. Error bars represent ±standard deviations.

Individually, we only found significant differences in chick #1, day 14 ($p = .0014$), chick #3, day 16 ($p = .0176$) and chick #4, day 12 ($p = .0243$). The changes and amounts in refractive state were consistent with previous data in the literature, and surprisingly, these were not modified by refractive surgery. Measurements tended to be slightly noisier in treated eyes than in the control eyes, with average standard deviations for repeated measurements of 0.99 D and 0.57 D, respectively. The 95% confidence interval (CI) for repeated measurements was ±0.97 D and ±0.57 D, respectively. Inter-subject variability was also larger in treated eyes than in the control eyes (0.98 D in treated eye and 0.66 D in control eyes), and 95% CI were ±1.26 and ±0.62, respectively. Astigmatism was almost constant throughout the measurement period. Treated eyes showed higher values of astigmatism (2.6 ± 0.5 D) on average than the control eyes (1.0 ± 0.2 D), and these differences were statistically significant in all days ($p = .0013$).

3.2. Optical aberrations

Fig. 2 shows examples of wave aberrations for 3rd and higher order in the treated and control eye of the same chick, on day 16 and their corresponding PSFs for 2-mm pupils. The higher number of contour lines in the wave aberration map and larger PSF in the treated eye were indicative of larger optical degradation. Fig. 3 shows average 3rd and higher order (A), 3rd order aberrations (B) and spherical aberrations (Z_{40} term) (C) in treated and control eyes on 4 different days, starting 9 days after hatching (8 after surgery). Third and higher order root-mean-square wave front error (RMS) was higher in the surgical eyes

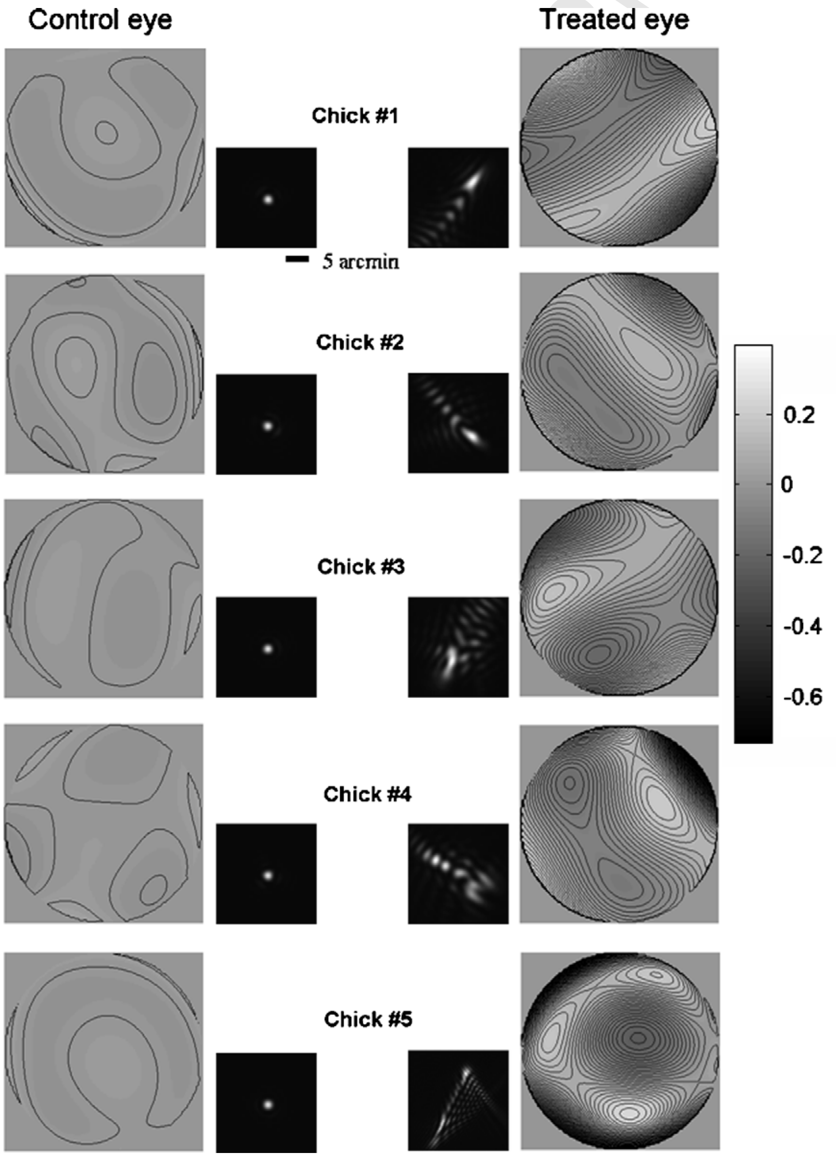

Fig. 2. Examples of wave aberration maps from all chicks (treated and control eyes) for 3rd and higher order Zernike coefficients at day 16 and their corresponding PSF for 3rd and higher order aberrations. Data are for 2-mm pupil diameters. Map contour lines are plotted in 0.01 μm steps.

Please cite this article in press as: Garci'a de la Cera, E. et al., Emmetropization and optical aberrations in a myopic corneal ..., *Vision Research* (2007), doi:10.1016/j.visres.2007.06.005

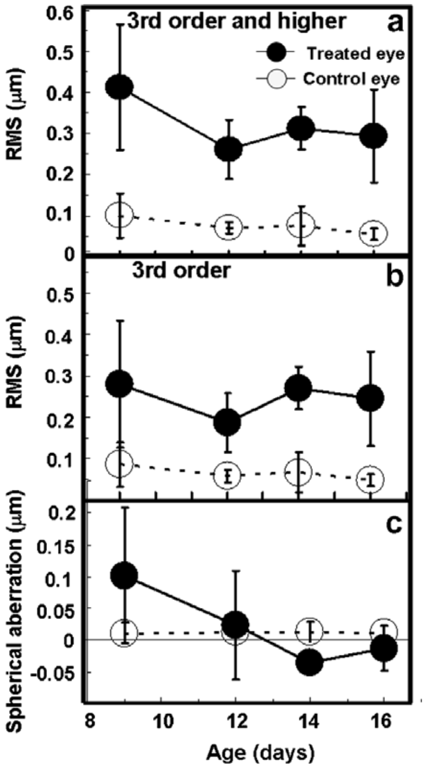

Fig. 3. Mean 3rd and higher order RMS (a), 3rd order RMS (b), spherical aberration Zernike coefficient (Z_{40}) (c) for days #9, #12, #14 and #16 (post hatching) for treated (solid symbols) and control (open symbols) eyes. Error bars represent ±standard deviations. Data are for 2-mm pupil diameters.

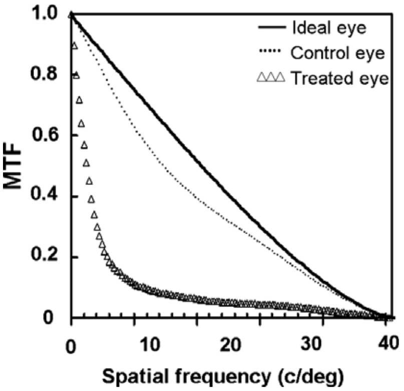

Fig. 4. Mean MTFs (radial profile) for treated (circles) and control (cross) chick eyes, for 3rd and higher order aberrations and 2 mm pupil diameter. For comparison the theoretical MTF of a diffraction-limited eye is also represented. MTFs were computed for a wavelength of 680 nm.

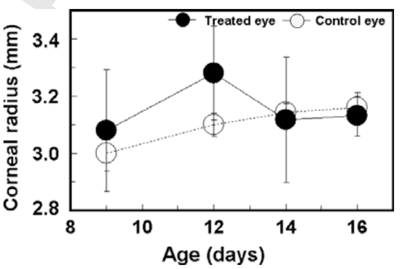

Fig. 5. Average corneal radius of curvature during the experiment period (8–15 days post-operatively). Solid symbols correspond to eyes treated with refractive surgery, and open symbols to control contralateral eyes. Error bars represent ±standard deviations.

(4.3 times larger, on average) than the control eyes, and the differences were highly statistically significant in all days ($p < .001$, paired t-test). The increase in RMS was primarily driven by 3rd order aberrations. There were no significant changes in aberrations with time during the studied period. In the control eyes, spherical aberration was not significantly different from zero ($p = .56$), it presented very little inter subject variability and it remains unchanged across days. In the treated eyes, spherical aberration showed larger inter-subject variability, and tended to decrease with time from positive values to negative values in the studied period, although the differences between treated and control eyes were only significant on day 14. The increase of high order aberrations in the treated eyes resulted in significantly lower modulation transfer functions (MTFs). Fig. 4 shows MTFs (averaged across eyes) on day 16, for 3rd and higher order in both the treated and control eyes, for 2 mm pupil diameters. Contrast was reduced with surgery at all spatial frequencies. For example, for 4.5 and 10 c/deg modulation transfer (from 3rd and higher order aberrations) was 1.7 and 2.6 times higher in control than treated eyes.

3.3. *Corneal radius of curvature*

Fig. 5 shows average corneal radius of curvature in treated and control eyes on 4 different days. In the control eyes corneal radius of curvature increases slightly and the correlation with time was significant (at a rate of 0.023 mm/day, −0.84 D/day, $p = .02$), while longitudinal changes in the treated eye were less systematic and the increase was not statistically significant. There were no statistically significant differences in corneal radius of curvature (paired t-test) between the treated and control eyes in any of the days. The mean values of corneal radius (3.15 ± 0.09 mm, or 120 ± 4 D, in treated eye and 3.10 ± 0.07 mm, or 122 ± 3 D, in the control eyes) were consistent with previous data on normal eyes in the literature, and surprisingly, these did not appear to have been modified by refractive surgery 8 days after the procedure. Average standard deviations for repeated measurements were similar in treated eyes than in control eyes (0.10 mm, averaging across days and chicks). The 95% CI for repeated measurements was ±0.08 mm in treated eyes and ±0.04 mm in control eyes, averaging across days and chicks. Inter subject variability was larger in treated eyes (Standard deviation: ±0.18 mm, 95% CI = ± 0.09 mm, averaging across days) than in control eyes (Standard deviation: ±0.04 mm, 95% CI = ± 0.07 mm).

Consistent with the HS measurements of total astigmatism, differences in radii of curvature between the steepest and flattest meridian were higher for the treated eyes

Please cite this article in press as: Garci'a de la Cera, E. et al., Emmetropization and optical aberrations in a myopic corneal ..., *Vision Research* (2007), doi:10.1016/j.visres.2007.06.005

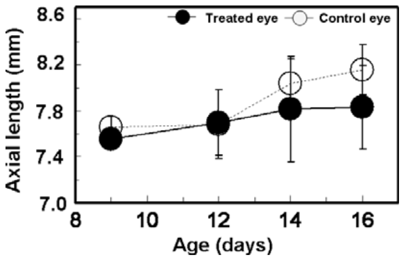

Fig. 6. Axial length during the experiment period (8–15 days post-operatively). Solid symbols correspond to eyes treated with refractive surgery, and open symbols to control contralateral eyes. Error bars represent ±standard deviations.

(0.28 ± 0.13 mm, averaging across eyes and days) than for control eyes (0.08 ± 0.06 mm), although the differences were not statistically significant.

3.4. Axial length

Fig. 6 shows axial length in treated and control eyes on 4 different days. Axial length increased significantly with age from Day 0 (prior to treatment, not shown in the graph, 7.39 ± 0.09 mm in the treated eyes and 7.35 ± 0.03 mm in the control eyes) and Day 16 (7.8 ± 0.6 mm in the treated eyes and 8.16 ± 0.16 mm in the control eyes). Differences in axial length between treated and control eyes were not statistically significant (paired *t*-test) in any of the days. The mean values of axial length were consistent with previous data on normal eyes in the literature, and again were not altered by the treatment. Inter subject variability was slightly higher in treated eyes (0.11 mm, average across eyes and days) than in control eyes (0.08 mm) and 95% CI were ±0.14 and ±0.17 mm, respectively.

4. Discussion

We have applied corneal refractive surgery to new born chicks. We did not find that refractive surgery was an efficient way to induce axial elongation: (1) corneal curvature eyes treated with myopic PRK was not significantly different to control eyes 8 days after treatment; (2) treated eyes exhibited significantly higher amounts of high order aberrations, but the reduction in retinal contrast did not interfere with the emmetropization process.

Chicks have been extensively shown to respond to form deprivation and lens treatments by altering axial ocular growth (Hayes et al., 1986; Troilo & Wallman, 1991; Wallman & Adams, 1987). In a previous study using the same chick strain, from the same hatchery as that used in the present study, and similar time course for treatment and measurements, we found interocular differences between eyes treated with frosted occluders and control contralateral eyes of −16 ± 3 D for refraction and of treatment and axial length of 0.81 ± 0.3 mm by day 13. Numerous studies have shown that functional hyperopia induced by negative lenses induces axial growth that tends to compensate for the induced defocus, at least partially (Choh, Lew, Nadel, & Wildsoet, 2006; Diether & Schaeffel, 1997; Priolo, Sivak, Kuszak, & Irving, 2000; Schaeffel et al., 1988; Schippert & Schaeffel, 2006; Wildsoet & Wallman, 1995). Some studies found consistently lower amounts of myopia than the power imposed by the negative lens, while others found even larger amounts of myopia that produced by form deprivation when high power lenses were used. For example, Diether and Schaeffel (1997) achieved −3.82 ± 2.48 D using −7.5 D lenses; Schaeffel, Glasser et al. (1988) found similar myopia (−1.5 D) for treatments with either −4 or −8 D while Wildsoet and Wallman (1995) achieved −8.6 D after treatment with −15 D lenses and Priolo and Sivak (2000) achieved −12.8 ± 0.7 D with −10 D lenses in eyes treated one day after hatching.

Differences in the effectiveness of the treatment can be affected by the large amplitude of accommodation in chicks (in the experiments performed under natural conditions) and the start day of the treatment (the younger, the more effective).

We attempted to impose hyperopic defocus in chicks (as in negative lens experiments) directly on the cornea, using PRK. Previous studies showed induction of refractive errors in experimental models in infant rhesus monkeys and young rabbits. The hyperopic defocus imposed by treating infant monkey eyes with 3 D myopic PRK, produced consistent hyperopic shifts, corneal flattening and compensatory axial elongation (Zhong et al., 2004). Results from a study in which rabbits (5 and 10 weeks of age) monocularly treated with 5–6 D myopic PRK showed also initially refractive changes which tended to be compensated by increased rate in axial length in the treated eyes (Bryant et al., 1999). In addition to the regression from induced refractive errors in the young group, at the end of the observation period no significant differences were observed in the corneal curvatures between the treated and the control eyes. Surprisingly, hyperopic errors were found in the treated eyes, along with increased axial lengths and similar corneal curvature than in control eyes.

In the present study in chicks, one week after surgery, the refractive treatment with PRK with a nominal negative correction of −9.9 D, no significant change in corneal curvature remained and it did not produce the increased axial elongations previously obtained with a negative lens with the same amount of correction, nor did it produce statistically significant anisometropia. Measurements immediately after surgery would have allowed us to assess whether surgery produced the expected corneal curvature and refractive changes. Unfortunately, tear secretion and epithelial changes prevent those measurements to be reliable (even if they were conducted under anesthesia). In this study we did not attempt to measure corneal transparency or scattering following surgery (although transparency measurements in vitro had been performed in this model by one of the authors, del Val et al., 2001). If haze increased during wound healing, this certainly was not sufficient to induce form deprivation myopia. Refraction, axial length

Please cite this article in press as: Garci'a de la Cera, E. et al., Emmetropization and optical aberrations in a myopic corneal ..., *Vision Research* (2007), doi:10.1016/j.visres.2007.06.005

and corneal radius of curvature in the control eyes in this study were similar to previous studies. For example, refraction and axial length of untreated 13-day old chick eyes from a previous study on the same chick strain (0.9 ± 0.7 D and 7.9 ± 0.2 mm) (García de la Cera et al., 2006b) were similar to those find here despite the differences in the refraction measurement techniques (retinoscopy in the previous study, and Hartmann–Shack here). Published corneal radius of curvature of untreated 2-week old chicks (3.18 ± 0.03 mm) (Li, Howland, & Troilo, 2000) were similar to these of our study. While some corneal flattening was observed in the treated eyes during the first days of the observation period, the change in corneal power was consistently below the accommodation ability of chicks and in most cases not statistically significantly different from the corneal curvature of the control eyes. If the treatment was effective in reshaping the cornea at all, regression in less than two weeks following surgery may have cancelled the nominally imposed corneal curvature. This effect, also described in a PRK rabbit model, may have occurred more rapidly in chicks for several reasons: (1) the treatment was applied earlier –one day after hatching-, and regression had been associated with earlier treatment (5 versus 10 weeks in the rabbit experiment); (2) chick corneas exhibit higher elasticity than mammalian corneas (Glasser, Troilo, & Howland, 1994; Troilo & Wallman, 1987). It has been proved that under normal physiological conditions, a pressure-mediated mechanism would be able to alter corneal curvature in chicks by about only 3 D (Glasser et al., 1994). However it is likely that the decreased intraocular pressure and decreased corneal thickness following PRK (Schipper, Senn, Thomann, & Suppiger, 1995) play a major role in increasing corneal curvature and cause regression.

While we have found that, unlike other species, PRK was not effective in changing corneal power of chicks, and therefore as an alternative to spectacle-rearing procedures, high order aberrations were systematically induced by the procedure. As a result, modulation transfer functions in treated eyes were significantly lower than in control eyes. Unlike in human eyes (Marcos, Barbero, Llorente, & Merayo-Lloves, 2001; Moreno-Barriuso et al., 2001), spherical aberration did not increase significantly with the procedure (although longitudinal variations were found), perhaps as a result of regression mechanisms similar to defocus. Astigmatism was significantly higher in treated than control eyes (see Fig. 1B). Q1 Other asymmetric aberrations such as coma increased significantly, producing increased blur in the retinal images (see Fig. 2) and consistently decreased contrast (see Fig. 4—MTF) in the treated eyes with respect to control eyes. Bartman and Schaeffel (Bartmann & Schaeffel, 1994) found 9 D of induced myopia in chicks wearing diffusers that caused a 4-time decrease in the modulation transfer at 4.5 c/deg. For the same frequency, in this experiment, high order aberrations decreased modulation transfer functions by 2. When astigmatism was considered, the MTF decreased from 0.69 (normal eyes) to 0.21 (treated eyes) for this spatial frequently. Previous studies in chicks had shown that induced astigmatism actually resulted in low but significant hyperopic (and not myopic) refractive error (McLean & Wallman, 2003). In infant monkeys it has been shown that induced astigmatism produces both hyperopic and myopic refractive errors (Kee, Hung, Qiao-Grider, Roorda, & Smith, 2004). Thus, presence of laser induced astigmatism could prevent myopia development in the treated eye. We did not find that the contrast degradation produced by high order aberrations induced neither refractive changes nor significant changes in axial length. This was consistent with recent findings in chicks that had undergone ciliary nerve section (Tian & Wildsoet, 2006). The treated chicks showed higher amounts of higher-order aberrations but they did not become myopic. For the same pupil size (2-mm) we found slightly lower HOA aberration values than (Tian & Wildsoet, 2006) for the control eyes and of the same order of magnitude for the treated eyes (0.53 D versus 2–3 D using the equivalent defocus power metric (Cheng, Bradley, & Thibos, 2004). On the other hand, this was in contrast with studies suggesting that increased aberrations may precede myopia development (Kisilak et al., 2006). Along with differences in magnitude which may set a threshold for image blur below which the emmetropization process was not affected, the nature of the image degradation induced by diffusers (scattering) may be different from that induced by aberrations. We found that predominant induced aberrations were non-rotationally symmetric. It could be that this type of aberrations (as previously found for astigmatism, (McLean & Wallman, 2003) may not necessarily trigger myopia development. Future research on the potential involvement of specific high order aberrations (i.e. spherical aberration) in myopia development could be addressed by using phase-plates or customized contact lenses with a better a priori control on the magnitude and type of aberration induced.

Acknowledgments

The authors acknowledge funding from FIS2005-04382 (Ministerio de Educación y Ciencia, Spain), and an European Young Investigator Award (EURHORCs) to Susana Marcos. The authors also acknowledge support from the Unidad Asociada IO-CSIC/IOBA-Universidad de Valladolid.

References

Atchison, D., Collins, M., Wildsoet, C., Christensen, J., & Waterworth, M. (1995). Measurement of monochromatic ocular aberrations of human eyes as a function of accommodation by the Howland aberroscope technique. *Vision Research, 35*, 313–323.

Bartmann, M., & Schaeffel, F. (1994). A simple mechanism for emmetropization without cues from accommodation or colour. *Vision Research, 34*(7), 873–876.

Bryant, M. R., Kampmeier, J., Er, H., Sanchez-DiMartino, D., Shah, S. S., & McDonnell, P. J. (1999). PRK-induced anisometropia in the rabbit as a model of myopia. *Graefes Archive for Clinical and Experimental Ophthalmology, 237*(2), 161–165.

Cano, D., Barbero, B., & Marcos, S. (2004). Comparison of real and computer-simulated outcomes of LASIK refractive surgery. *Journal of the Optical Society of America A, 21*, 926–936.

Cheng, X., Bradley, A., Hong, X., & Thibos, L. (2003). Relationship between refractive error and monochromatic aberrations of the eye. *Optometry and Vision Science, 80*, 43–49.

Cheng, X., Bradley, A., & Thibos, L. N. (2004). Related articles. Predicting subjective judgment of best focus with objective image quality metrics. *Journal of Vision, 23*(4), 310–321.

Choh, V., Lew, M. J. Y., Nadel, M. W., & Wildsoet, C. F. (2006). Effects of interchanging hyperopic defocus and form deprivation stimuli in normal and optic nerve-sectioned chicks. *Vision Research, 46*(6–7), 1070–1079.

del Val, J. A., Barrero, S., Yanez, B., Merayo, J., Aparicio, J. A., Gonzalez, V. R., Pastor, J. C., & Mar, S. (2001). Experimental measurement of corneal haze after excimer laser keratectomy. *Applied Optics, 40*(10), 1727–1734.

Diether, S., & Schaeffel, F. (1997). Local changes in eye growth induced by imposed local refractive error despite active accommodation. *Vision Research, 37*(6), 659–668.

García de la Cera, E., Rodriguez, G., Llorente, L., Schaeffel, F., & Marcos, S. (2006a). Optical aberrations in the mouse eye. *Vision Research, 46*(16), 2546–2553.

García de la Cera, E., Rodriguez, G., & Marcos, S. (2006b). Longitudinal changes of optical aberrations in normal and form-deprived myopic chick eyes. *Vision Research, 46*(4), 579–589.

Gee, S., & Tabbara, K. (1988). Increase of ocular axial length in patients with corneal pacification. *Ophthalmology, 1988*(95), 1276–1278.

Glasser, A., Troilo, D., & Howland, H. C. (1994). The mechanism of corneal accommodation in chicks. *Vision Research, 34*(12), 1549–1566.

Hayes, B. P., Fitzke, F. W., Hodos, W., & Holden, A. L. (1986). A morphological analysis of experimental myopia in young chickens. *Investigative of Ophthalmology and Visual Science, 27*, 981–991.

Hoyt, C. S., Stone, R. D., Fromer, C., & Billson, F. A. (1981). Monocular axial myopia associated with neonatal eyelid closure in human infants. *American Journal of Ophthalmology, 91*(2), 197–200.

Kee, C., Hung, L., Qiao-Grider, Y., Roorda, A., & Smith, E. L. (2004). Effects of optically imposed astigmatism on emmetropization in infant monkeys. *Investigative Ophthalmology & Visual Science, 45*(6), 1647–1659.

Kee, C. S., Marzani, D., & Wallman, J. (2001). Differences in time course and visual requirements of ocular responses to lenses and diffusers. *Investigative Ophthalmology & Visual Science, 42*(3), 575–583.

Kisilak, M. L., Campbell, M. C. W., Hunter, J. J., Irving, E. L., & Huang, L. (2006). Aberrations of chick eyes during normal growth and lens induction of myopia. *Journal of Comparative Physiology A, Neuroethology Sensory Neural and Behavioral Physiology, 192*(8), 845–855.

Li, T., Howland, H. C., & Troilo, D. (2000). Diurnal illumination patterns affect the development of the chick eye. *Vision Research, 40*(18), 2387–2393.

Llorente, L., Barbero, S., Cano, D., Dorronsoro, C., & Marcos, S. (2004). Myopic versus hyperopic eyes: axial length, corneal shape and optical aberrations. http://journalofvision.org/4/4/5/. Journal of Vision, 4, 288.

Marcos, S. (2001). Aberrations and visual performance following standard laser vision correction. *Journal of Refractive Surgery, 17*, 596–601.

Marcos, S., Barbero, B., Llorente, L., & Merayo-Lloves, J. (2001). Optical response to LASIK for myopia from total and corneal aberrations. *Investigative Ophthalmology and Visual Science, 42*, 3349–3356.

McLean, R., & Wallman, J. (2003). Severe astigmatic blur does not interfere with spectacle lens compensation. *Investigative Ophthalmology Visual Science, 44*(2), 449–457.

Merayo-Lloves, J., Yañez, B., Mayo, A., Martín, R., & Pastor, J. C. (2001). Experimental model of corneal haze. *Journal of Refractive Surgery, 17*, 696–699.

Moreno-Barriuso, E., Merayo-Lloves, J., Marcos, S., Navarro, R., Llorente, L., & Barbero, S. (2001). Ocular aberrations before and after myopic corneal refractive surgery: LASIK-induced changes measured with laser ray tracing. *Investigative Ophthalmology and Visual Science, 42*, 1396–1403.

Paquin, M. P., Hamam, H., & Simonet, P. (2002). Objective measurement of optical aberrations in myopic eyes. *Optometry and Vision Science, 79*(5), 285–291.

Priolo, S., Sivak, J. G., Kuszak, J. R., & Irving, E. L. (2000). Effects of experimentally induced ametropia on the morphology and optical quality of the avian crystalline lens. *Investigative Ophthalmology & Visual Science, 41*(11), 3516–3522.

Robb, R. M. (1977). Refractive errors associated with Hemangiomas of eyelids and orbit in infancy. *American Journal of Ophthalmology, 83*(1), 52–58.

Rosales, P., & Marcos, S. (2006). Phakometry and lens tilt and decentration using a custom-developed Purkinje imaging apparatus: validation and measurements. *Journal of the Optical Society of America A, Optics Image Science and Vision, 23*(3), 509–520.

Schaeffel, F., Glasser, A., & Howland, H. (1988). Accommodation, refractive error and eye growth in chickens. *Vision Research, 28*, 639–657.

Schaeffel, F., & Howland, H. C. (1987). Corneal accommodation in chick and pigeon. *Journal of Comparative Physiology A, Sensory Neural and Behavioral Physiology, 160*(3), 375–384.

Schaeffel, F., & Howland, H. C. (1991). Properties of the feedback loops controlling eye growth and refractive state in the chicken. *Vision Research, 31*, 717–734.

Schaeffel, F., Howland, H. C., & Farkas, L. (1986). Natural accommodation in the growing chicken. *Vision Research, 26*(12), 1977–1993.

Schipper, I., Senn, P., Thomann, U., & Suppiger, M. (1995). Intraocular-pressure after excimer-laser photorefractive keratectomy for myopia. *Journal of Refractive Surgery, 11*(5), 366–370.

Schippert, R., & Schaeffel, F. (2006). Peripheral defocus does not necessarily affect central refractive development. *Vision Research, 46*(22), 3935–3940.

Smith, E. III, (1998). Environmentally induced refractive errors in animals. *Myopia and Nearwork*, 57–90.

Thorn, R., Held, J., Gwiazda, & He, J. C. U. (2003). Patent Application US 2003/0058404 A1. US.

Tian, Y. B., & Wildsoet, C. F. (2006). Diurnal fluctuations and developmental changes in ocular dimensions and optical aberrations in young chicks. *Investigative Ophthalmology & Visual Science, 47*(9), 4168–4178.

Troilo, D., & Wallman, J. (1987). Changes in corneal curvature during accommodation in chicks. *Vision Research, 27*(2), 241–247.

Troilo, D., & Wallman, J. (1991). The regulation of eye growth and refractive state: an experimental study of emmetropization. *Vision Research, 31*, 1237–1250.

Tuunanen, T. H., & Tervo, T. T. (1998). Results of photorefractive keratectomy for low, moderate, and high myopia. *Journal of Refractive Surgery, 14*(4), 437–446.

Wallman, J. (1993). Retinal control of eye growth and refraction. *Progress in Retinal Research, 12*, 133–153.

Wallman, J., & Adams, J. I. (1987). Developmental aspects of experimental myopia in chicks: susceptibility, recovery and relation to emmetropization. *Vision Research, 27*, 1139–1163.

Wildsoet, C., & Wallman, J. (1995). Choroidal and scleral mechanisms of compensation for spectacle lenses in chicks. *Vision Research*(35), 1175–1194.

Wildsoet, C. F. (1997). Active emmetropization—Evidence for its existence and ramifications for clinical practice. *Ophthalmic and Physiological Optics, 17*(4), 279–290.

Zhong, X. W., Ge, J., Nie, H. H., Chen, X. L., Huang, J., & Liu, N. (2004). Effects of photorefractive keratectomy-induced defocus on emmetropization of infant rhesus monkeys. *Investigative Ophthalmology & Visual Science, 45*(10), 3806–3811.

Please cite this article in press as: Garci'a de la Cera, E. et al., Emmetropization and optical aberrations in a myopic corneal ..., *Vision Research* (2007), doi:10.1016/j.visres.2007.06.005