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Refractive, biometric and corneal topographic parameter changes during 12 months of orthokeratology

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Background: The aim of this study was to monitor refractive, topographic and biometric changes in Singaporean myopic children fitted with orthokeratology over a period of 12 months.
Methods: Data from 62 myopic eyes from an Asian population corrected with orthokeratology were retrospectively collected from an optometric clinic in Singapore. Anterior segment parameters were analysed with a Pentacam. Axial length was measured using the IOLMaster and refraction was assessed by subjective examination before the treatment and after one night, one week, and one, three, six and 12 months. A logistic regression model was built to evaluate the probability of slower (< 0.10 mm/year) or faster eye growth (≥ 0.10 mm/year).
Results: Subjects had a mean age of 12.2 ± 3.9 years (range 5–19 years), and 71 per cent were female. Baseline myopia was −3.95 ± 1.59 D (range −1.50 and −8.75 D). Statistically significant differences were found after 12 months of treatment for refractive error, parameters of the central anterior corneal surface (curvature and elevation) and central corneal thickness. Topographic and thickness changes stabilised after one week of treatment. During 12 months of orthokeratology treatment there was a significant increase of axial length (difference = 0.11 ± 0.18 mm, $p < 0.001$) while refraction remained stable. Changes in axial length of subjects above 11 years were not statistically significantly independent of the baseline myopia, and in subjects with baseline myopia greater than 4.00 D. Logistic regression showed that each additional year of age and each additional dioptre of baseline myopia decreased the probability of faster axial elongation (odds ratio [OR] = 1.23, 2.19 95% CI; OR = 1.08, 3.47 95% CI, respectively).
Conclusion: Corneal parameters in orthokeratology treatment were stable after one week, particularly for myopes under 4.00 D. Axial length did not change significantly in children older than 11 years of age or in subjects with myopia above 4.00 D undergoing orthokeratology treatment.

Key words: corneal parameters, corneal refractive therapy, myopia progression, orthokeratology

Myopia affects approximately 28 per cent of the global population.[1] This prevalence varies considerably in different regions of the world reaching over 90 per cent in some East Asian populations. In these regions, there is a great interest in solutions to prevent myopia onset and to reduce its progression. Depending on the mechanism involved, different clinical approaches have been developed, including the use of drugs (such as atropine[2,3] or pirenzepine[4,5]), monofocal, bifocal or multifocal spectacle lenses,[6,7] reverse geometry rigid gas-permeable contact lenses (orthokeratology),[8–10] or multifocal soft contact lenses.[11]

The induction of myopic defocus on the peripheral retina is a hypothetical mechanism for slowing myopia progression.[12,13] Promising treatments ensuring this effect include orthokeratology and multifocal contact lenses.[14] The use of orthokeratology to change the cornea into an oblate shape[15] with a central flat treated area surrounded by a paracentral area of increased power, induces a peripheral myopic astigmatic defocus.[16]

The first longitudinal study (LORIC)[8] confirming the effectiveness of orthokeratology to slow myopia progression and axial length was performed in Asian children over a two-year period. The results showed 46 per cent less axial elongation in the orthokeratology group comparing with controls who used single-vision spectacles. Similar retention rates could be found in a study with Caucasian children, with retention effect of about 56 per cent[9] over two years. Hiraoka et al.[17] observed a retention effect of 30 per cent in a period of five years of orthokeratology treatment. The same study suggests that the greater retention rate was obtained during the first three years.

Considering that the cornea is the most powerful optical element of the eye, with direct impact on the refractive status, the present study aims to evaluate the stability of axial length and corneal and anterior segment parameters over a period of 12 months in low to high myopic children, adolescents and young adults. This information is relevant to understanding the interpretation of refractive and biometric changes in the context of the longitudinal follow-up of refractive error changes, particularly in myopia control studies.

Methods

Subjects and inclusion criteria

The clinical records of 62 subjects who underwent orthokeratology treatment at the Vision Research Centre Pte Ltd (Singapore) were retrospectively analysed. Only patients with myopia between −1.00 D and −8.00 D of sphere and astigmatism below −1.50 D were included. Only the right eye from each patient was considered for statistical analysis. When the right eye did not meet the previous inclusion criterion, the left eye was used.

The inclusion criteria required that the subjects did not suffer from any current eye disease or injury, were not taking any ocular or systemic medication and had not undergone ocular surgery. Comprehensive optometric and ophthalmological examinations were performed prior to orthokeratology lens fitting.

After explaining the nature of the study, each subject signed a consent form before being enrolled. The study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the Institutional Ethical Committee Review Board of Vision Research Centre.

Only subjects who were successfully treated, in respect of residual refractive error (≤ ±0.50 D), visual acuity (≥ 6/6 or higher uncorrected visual acuity), surface regularity and centring of the treatment zone (less than 0.5 mm of decentralisation), were selected for inclusion in the sample.

In order to analyse separately the potential differences in changes of the measured parameters induced by orthokeratology as a function of age, two age groups were formed, as shown in Table 1 – younger (less than 11 years of age) and older (more than 11 years of age). To analyse the changes as a function of the basal refractive status, three refractive groups were established according to the spherical refraction at baseline. Age groups were divided according to the middle point (10–12 years) of the progression slope for early-onset myopia models.[18]

Outcomes

Corneal parameters were measured with the Pentacam (Oculus, Inc. GmbH, Wetzlar, Germany) before treatment, after one night, one week, one month, three months, six months and 12 months, following commencement of the treatment. This instrument has been previously validated[19] and used to measure corneal parameters in eyes undergoing orthokeratology.[20,21]

The internal anterior chamber depth (IACD), central corneal thickness (CCT), apical tangential curvature (ATC), anterior flat K (A-FK), anterior steep K (A-SK), anterior central elevation (A-CE), anterior nasal elevation at 2.5 mm from centre of the cornea (A-NE), anterior temporal elevation at 2.5 mm from centre of the cornea (A-TE), posterior central curvature (P-CC), posterior flat K (P-FK), posterior steep K (P-SK), posterior central elevation (P-CE), posterior nasal elevation (P-NE), and posterior temporal (P-TE) were determined. Only scans classified as 'OK' by the instrument were considered.

Axial length (AL) was measured by Zeiss IOLMaster biometer (Carl Zeiss GmbH, Jena, Germany).[22] Three separate measurements of AL were recorded to posteriorly calculate the average. Non-cycloplegic subjective refraction was monocularly performed, always by the same optometrist, using the clinically accepted endpoint of maximum plus (that is, the best visual acuity with the maximum plus), followed by cross-cylinder to locate the axis within five degrees and its power within 0.25 D.[23]

Orthokeratology lens characteristics

Sigmoid reverse geometry rigid gas-permeable lenses (Wave Contact Lenses) were used. These lenses are software-designed based on topography data. The lens material used for these patients was Boston XO (Bausch + Lomb). Other considerations when designing an accurate orthokeratology correction include refractive error, horizontal visible iris diameter and pupil size. Wave corneal mould design data were electronically submitted to the laboratory in order to manufacture each unique contact lens.

After the first night of treatment, the patients attended the clinic wearing their lenses. They were instructed to insert the lenses 10 minutes before sleep with a drop of artificial tear. The subjects were instructed to remove the lenses 10 minutes after waking up and to again apply a drop of artificial tear solution. The measurements across the study were performed between 9:00 and 11:00 hours and at least two hours after lens removal. This protocol minimised the influence of treatment regression and diurnal variations in corneal thickness that might potentially influence anterior corneal topography,[24] ensuring that all measurements were taken 30 minutes after this period.

Statistical analysis

The SPSS software package v.22 (IBM, Armonk, NY, USA) was used for statistical analysis. The Kolmogorov–Smirnov test was applied to evaluate the normality of the data distribution. A one-way repeated measures analysis of variance or Friedman test was conducted to determine whether there was a statistically significant difference in the performance visits for parametric and non-parametric variables, respectively. A post hoc analysis with a Bonferroni adjustment was conducted for post hoc comparisons.

Stepwise logistic regression analysis was performed on the dataset to determine the best predictors of a faster AL growth (≥ 0.10 mm/year). It has been shown that non-myopes can increase their AL up to 0.10 mm/year on average without developing myopia.[25]

A sensitivity and specificity analysis was performed on the development dataset by using the equation generated by the parameter that was the single best predictor of AL increment.

	n	Age (years)	M (D)	AL (mm)
Younger (≤ 11 years)	30 (48%)	9 ± 1	−3.70 ± 1.74	24.36 ± 1.08
Older (> 11 years)	32 (52%)	15 ± 3	−4.18 ± 1.42	25.07 ± 0.89

Table 1. Characterisation of age/gender after distribution of subjects respecting baseline age, myopia (M) and axial length (AL)

Parameters	Visit baseline	Visit 1 1 night	Visit 2 1 week	Visit 3 1 month	Visit 4 3 months	Visit 5 6 months	Visit 6 12 months	p	Post hoc test[§]
Refractive									
M (D)	−3.95 ± 1.59	−1.01 ± 1.05	−0.31 ± 0.51	−0.23 ± 0.39	−0.23 ± 0.41	−0.22 ± 0.30	−0.10 ± 0.28	**< 0.001**[‡]	B1,B2,B3,B4,B5,B6,12,13,14,15,16
J_0 (D)	0.26 ± 0.33	0.04 ± 0.17	0.04 ± 0.17	0.02 ± 0.13	0.03 ± 0.13	0.02 ± 0.13	0.01 ± 0.08	**< 0.001**[‡]	B1,B2,B3,B4,B5,B6
J_{45} (D)	−0.06 ± 0.18	0.01 ± 0.08	0.00 ± 0.04	0.00 ± 0.00	−0.01 ± 0.05	0.00 ± 0.03	0.00 ± 0.00	**0 .018**[‡]	x
Biometric									
AL (mm)	24.73 ± 1.04	24.72 ± 1.04	24.71 ± 1.04	24.73 ± 1.03	24.78 ± 1.01	24.81 ± 1.00	24.84 ± 1.00	**< 0.001**[‡]	B2,15,16,24,25,26,35,36
IACD (mm)	3.21 ± 0.25	3.16 ± 0.23	3.16 ± 0.24	3.16 ± 0.24	3.13 ± 0.25	3.14 ± 0.25	3.13 ± 0.24	**< 0.001**[‡]	B1,B2,B3,B4,B5,B6
ACV (mm^3)	153.39 ± 33.60	167.27 ± 40.62	164.44 ± 44.05	171.05 ± 38.59	176.82 ± 41.62	184.81 ± 40.93	178.98 ± 30.44	**< 0.001**[†]	B4,B5,B6
CCT (μm)	565.90 ± 34.12	558.60 ± 31.80	552.02 ± 27.96	550.98 ± 29.92	547.50 ± 29.60	547.29 ± 29.58	552.40 ± 33.55	**< 0.001**[†]	B2,B3,B4,B5,12,13,14,15
Topographic									
ATC (mm)	43.66 ± 1.73	41.27 ± 1.76	40.28 ± 1.94	40.43 ± 2.14	40.61 ± 1.75	40.62 ± 1.71	40.50 ± 2.18	**< 0.001**[†]	B1,B2,B3,B4,B5,B6,1B,12,13
A-FK (mm)	43.62 ± 1.66	42.13 ± 1.63	41.37 ± 1.68	41.24 ± 1.57	41.16 ± 1.63	41.02 ± 1.63	40.78 ± 1.83	**< 0.001**[†]	B1,B2,B3,B4,B5,B6,12,13,14,15,16,25,26,35,36,46
A-SK (mm)	44.68 ± 1.87	43.28 ± 1.79	42.46 ± 1.66	42.48 ± 1.68	42.22 ± 1.82	42.14 ± 1.76	41.98 ± 1.96	**< 0.001**[‡]	B1,B2,B3,B4,B5,B6,12,13,14,15,16
A-CE (μm)	2.77 ± 1.57	−2.55 ± 2.91	−5.39 ± 3.42	−5.35 ± 4.29	−5.69 ± 3.99	−6.19 ± 3.85	−6.84 ± 4.52	**< 0.001**[‡]	B1,B2,B3,B4,B5,B6,12,13,14,15,16
A-NE (μm)	2.21 ± 5.34	4.66 ± 4.69	8.06 ± 4.49	9.11 ± 5.12	9.65 ± 5.84	10.97 ± 5.06	11.82 ± 4.95	**< 0.001**[‡]	B1,B2,B3,B4,B5,B6,12,13,14,15,16,25,26
A-TE (μm)	1.03 ± 8.52	4.58 ± 4.53	7.32 ± 4.87	8.13 ± 5.28	8.76 ± 5.56	10.16 ± 3.90	11.13 ± 5.17	**< 0.001**[‡]	B1,B2,B3,B4,B5,B6,12,13,14,15,16,25,26
P-CC (mm)	−6.10 ± 0.37	−6.15 ± 0.34	−6.05 ± 0.30	−6.06 ± 0.35	−6.04 ± 0.30	−6.02 ± 0.31	−6.04 ± 0.30	**< 0.001**[‡]	B5,12,14,15,16
P-FK (mm)	−6.18 ± 0.37	−6.22 ± 0.33	−6.17 ± 0.31	−6.19 ± 0.33	−6.19 ± 0.30	−6.18 ± 0.31	−6.22 ± 0.29	**0.014**[‡]	x
P-SK (mm)	−6.54 ± 0.35	−6.60 ± 0.30	−6.53 ± 0.33	−6.52 ± 0.32	−6.54 ± 0.32	−6.55 ± 0.31	−6.57 ± 0.31	**< 0.001**[‡]	12,13
P-CE (μm)	1.53 ± 4.49	2.65 ± 3.30	0.65 ± 2.73	0.24 ± 3.37	0.50 ± 3.14	0.92 ± 3.07	0.84 ± 3.53	**< 0.001**[‡]	B2,B3,B4,B6,12,13,14,15,16
P-NE (μm)	10.10 ± 7.39	9.15 ± 7.87	9.68 ± 7.04	9.92 ± 7.20	9.06 ± 7.11	9.69 ± 8.22	8.05 ± 6.95	**0.125**[‡]	x
P-TE (μm)	8.39 ± 7.39	7.87 ± 7.09	8.74 ± 6.72	8.37 ± 6.63	8.02 ± 6.31	9.42 ± 7.52	8.32 ± 7.64	**0.698**[‡]	x

ACV: anterior chamber volume, AL: axial length, ATC: apical tangential curvature, A-CE: anterior central elevation, A-FK: anterior flat K, A-NE: anterior nasal elevation, A-SK: anterior steep K, A-TE: anterior temporal elevation, CCT: central corneal thickness, IACD: internal anterior chamber depth, P-CC: posterior central curvature, P-CE: posterior central elevation, P-FK: posterior flat K, P-NE: posterior nasal elevation, P-SK: posterior steep K, P-TE: posterior temporal elevation.

Bold values of statistical significance (p) highlights values < 0.05.

[†]Repeated measures analysis of variance.

[‡]Friedman test.

[§]The post hoc test presents the pairwise comparison, only for those that revealed to be statistically significant differences between visits, for example B1, between visit baseline and visit 1.

Table 2. Refractive, biometric and topographic (mean ± SD) evaluation of the population at baseline and at several times after starting orthokeratology treatment. Refractive error components (M, J_0 and J_{45}) obtained by non-cycloplegic subjective refraction (n = 62 eyes).

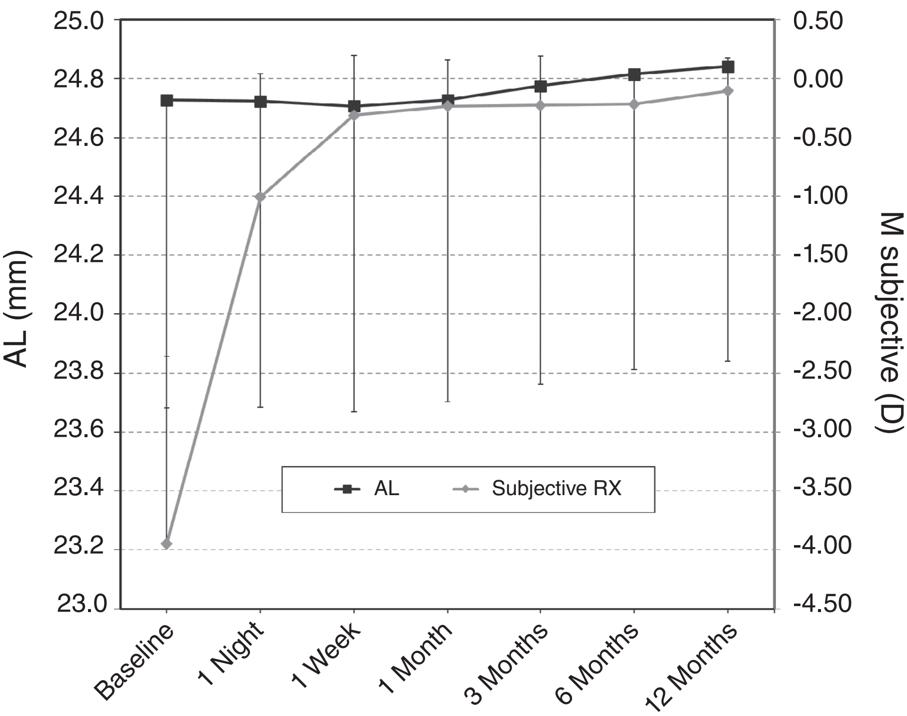

Figure 1. Refractive myopia (M) (left axis of ordinates, grey line) and axial length (AL) (right axis of ordinates, black line) during 12 months of orthokeratology treatment (n = 62 eyes). Vertical bars indicate standard deviation values. The x-axis scale has equal continuous intervals for easier viewing of changes, although the intervals are not similar.

For statistical purposes, a p-value lower than 0.05 was considered statistically significant.

Results

Measurements were performed on 62 eyes from 62 subjects with a mean age of 12.2 ± 3.9 years (range 5–19 years), of which 44 were female (71.0 per cent) and 18 were male (29.0 per cent). Mean baseline spherical equivalent obtained by subjective refraction was −3.95 ± 1.59 D (from −1.50 to −8.75 D).

Table 1 shows the demographic distribution of subjects stratified by two age groups – under and above 11 years of age. Table 2 presents several refractive, topographic and pachymetric parameters measured from the general sample at different follow-up visits. The post hoc test presents the pairwise comparison, only for those revealed to be statistically significant. Figure 1 shows the values of subjective refraction and AL over the 12 months of follow-up. Table 3 shows the differences of refractive, biometric and topographic parameters (mean ± SD) of the population according different periods of time over 12 months of evaluations, as a function of gender and age group.

Subjective refraction and AL

The baseline myopia of the general sample was −3.95 ± 1.59 D by subjective evaluation. On average, the desired orthokeratology treatment was achieved after one week and remained constant thereafter, as seen in Table 2. Astigmatic components J_0 and J_{45} followed the same trend. The average change in AL after 12 months was 0.11 ± 0.18 mm ($p < 0.001$).

CCT and anterior chamber depth

The CCT values decreased during the first week of treatment (552.02 ± 27.96 µm). The average thinning observed was 13.50 ± 34.96 µm after 12 months (p = 0.003). The CCT decreased in age and gender groups during the 12-month study period. However, the decrease was only statistically significant when comparing visits with the baseline and the first night.

Internal measurement of anterior chamber depth showed an average reduction of 50 µm after one night of lens wear ($p < 0.001$) from 3.21 to 3.16 mm and 80 µm from 3.21 to 3.13 mm after 12 months ($p < 0.001$).

Anterior and posterior topographic corneal parameters

An average change of 2.83 ± 1.24 D and 2.70 ± 1.42 D was observed in the flat and steep corneal meridians, respectively. The change in ATC was 3.16 ± 1.78 D after 12 months.

No significant difference between one week and one month (−0.03 ± 2.61 µm, p = 0.700) was observed in anterior elevation. Conversely, the peripheral anterior elevation showed an increase after one week remaining stable thereafter. The average change was 9.61 ± 6.98 for A-NE and 10.10 ± 9.68 µm for A-TE ($p < 0.001$ for both), which was compatible with central elevation loss of 9.61 ± 4.80 µm ($p < 0.001$).

The posterior tangential curvature data did not vary over 12 months of ß treatment. Despite a slight variation in the first week, there was a transient, non-significant change over 12 months of treatment (average change: 0.04 ± 0.23 and 0.03 ± 0.13 mm for flat and steep Ks, respectively; $p > 0.05$). There is also no evidence of change in central or peripheral posterior elevation values during orthokeratology treatment (Table 2).

Analysis by refractive and age groups

Figure 2 shows the change in AL after 12 months of orthokeratology treatment for younger and older subjects. A positive correlation is observed, demonstrating that higher baseline refractive errors display a smaller axial elongation. Younger subjects generally show larger changes of AL compared to older subjects. Interestingly, several older subjects showed a reduction in AL (n = 20, between 10 and 150 µm) after 12 months of orthokeratology treatment, with 13 out of 20 showing a reduction equal or superior to 50 µm.

Analysis by logistic regression

The strongest parameter selected as a significant predictor in the stepwise logistic regression (r^2 = 0.564, $p < 0.001$) was age and baseline myopia. From this analysis, the following equation to calculate the

	Visit baseline	Visit 1 1 night	Visit 2 1 week	Visit 3 1 month	Visit 4 3 months	Visit 5 6 months	Visit 6 12 months	p-value	Post hoc test†
M (D)									
Female	−3.85 ± 1.32	−0.91 ± 0.94	−0.31 ± 0.47	−0.24 ± 0.38	−0.16 ± 0.36	−0.18 ± 0.21	−0.10 ± 0.28	< 0.001¶	B1,B2,B3,B4,B5,B6,12,13,14,15,16
Male	−4.20 ± 2.13	−1.24 ± 1.28	−0.31 ± 0.61	−0.21 ± 0.44	−0.39 ± 0.50	−0.32 ± 0.44	−0.13 ± 0.29	< 0.001¶	B2,B3,B4,B5,B6,12,13,16
p	0.525‡‡	0.374¶	0.693††	0.435††	0.116††	0.456††	0.529††	–	
Younger	−3.70 ± 1.74	−0.90 ± 1.06	−0.40 ± 0.58	−0.28 ± 0.36	−0.28 ± 0.46	−0.25 ± 0.37	−0.15 ± 0.28	< 0.001¶	B1,B2,B3,B4,B5,B6,13,15,16
Older	−4.18 ± 1.42	−1.11 ± 1.04	−0.23 ± 0.42	−0.20 ± 0.42	−0.18 ± 0.37	−0.19 ± 0.21	−0.06 ± 0.28	< 0.001¶	B1,B2,B3,B4,B5,B6,12,13,14,15,16
p	0.238§	0.411§§	0.282§§	0.151§§	0.220§§	0.951§§	0.098§§	–	
AL (mm)									
Female	24.56 ± 1.10	24.55 ± 1.09	24.54 ± 1.09	24.57 ± 1.09	24.63 ± 1.08	24.67 ± 1.07	24.69 ± 1.08	< 0.001‡	B2,B4,B5,B6,12,13,14,15,16,23,24,25,26,34,35,36,45,46
Male	25.14 ± 0.77	25.13 ± 0.77	25.12 ± 0.76	25.11 ± 0.76	25.13 ± 0.74	25.16 ± 0.73	25.20 ± 0.68	0.034‡	35
p	0.044§	0.045§	0.045§	0.062§	0.078§	0.079§	0.070§	–	
Younger	24.36 ± 1.08	24.37 ± 1.08	24.35 ± 1.09	24.38 ± 1.08	24.46 ± 1.07	24.54 ± 1.07	24.59 ± 1.08	< 0.001‡	B4,B5,B6,12,14,15,16,23,24,25,26,34,35,36,45,46,56
Older	25.07 ± 0.89	25.05 ± 0.89	25.04 ± 0.88	25.05 ± 0.87	25.07 ± 0.87	25.07 ± 0.88	25.08 ± 0.87	0.132‡	B1,B2
p	0.007§	0.009§	0.008§	0.009§	0.018§	0.084§	0.113§	–	
ACDint (mm)									
Female	3.18 ± 0.22	3.13 ± 0.22	3.15 ± 0.23	3.15 ± 0.23	3.10 ± 0.23	3.13 ± 0.25	3.11 ± 0.24	< 0.001¶	B1,B4,B5,B6,24,26,34
Male	3.30 ± 0.28	3.23 ± 0.25	3.20 ± 0.26	3.19 ± 0.27	3.21 ± 0.28	3.17 ± 0.25	3.18 ± 0.23	< 0.001¶	B1,B2,B3,B4,B5,B6
p	0.063§§	0.091§§	0.310§§	0.281§§	0.095§§	0.442§§	0.281§§	–	
Younger	3.21 ± 0.23	3.16 ± 0.21	3.17 ± 0.23	3.18 ± 0.23	3.15 ± 0.22	3.17 ± 0.24	3.16 ± 0.22	< 0.001¶	B1,B2,B3,B4,B5,B6
Older	3.22 ± 0.27	3.16 ± 0.26	3.15 ± 0.26	3.14 ± 0.26	3.12 ± 0.28	3.11 ± 0.25	3.10 ± 0.25	< 0.001¶	B1,B3,B4,B5,B6,16,26
p	0.044‡‡	0.844††	0.811††	0.767††	0.622††	0.597††	0.331††	–	
CCT (µm)									
Female	561.7 ± 36.2	553.4 ± 30.3	548.7 ± 29.3	545.3 ± 27.8	542.7 ± 30.4	543.1 ± 29.2	548.2 ± 34.8	0.001‡	B4,B5,13,14,15
Male	576.2 ± 26.5	571.2 ± 32.6	560.1 ± 23.1	564.8 ± 31.2	559.3 ± 24.5	557.7 ± 28.7	562.6 ± 28.5	< 0.001‡	B2,B4,12,13,15,
p	0.131§	0.045§	0.149§	0.018§	0.044§	0.077§	0.126§	–	
Younger	568.1 ± 30.8	567.6 ± 33.0	556.0 ± 26.0	558.4 ± 30.2	547.8 ± 33.0	552.6 ± 27.3	555.1 ± 31.1	< 0.001‡	B2,B4,B5,12,13,14,15,16,
Older	563.8 ± 37.3	550.2 ± 28.6	548.2 ± 29.5	544.0 ± 28.4	547.2 ± 26.5	542.3 ± 31.1	549.8 ± 36.0	0.005‡	13,15
p	0.622§	0.030§	0.277§	0.507§	0.939§	0.173§	0.539§	–	
IACD (mm)									
Female	43.74 ± 1.89	41.56 ± 1.81	40.43 ± 2.14	40.85 ± 2.13	40.69 ± 1.72	40.84 ± 1.81	40.58 ± 2.46	< 0.001‡	B1,B2,B3,B4,B5,B6,12,14
Male	43.46 ± 1.27	40.58 ± 1.43	39.92 ± 1.30	39.42 ± 1.83	40.44 ± 1.84	40.09 ± 1.36	40.31 ± 1.30	< 0.001‡	B1,B2,B3,B4,B5,B6,12,14
p	0.498§	0.046§	0.358§	0.015§	0.617§	0.120§	0.582§	–	
Younger	44.10 ± 1.71	41.74 ± 1.80	40.91 ± 1.95	40.74 ± 2.57	41.01 ± 1.66	41.00 ± 1.73	40.96 ± 2.05	< 0.001‡	B1,B2,B3,B4,B5,B6,12
Older	43.25 ± 1.67	40.84 ± 1.63	39.68 ± 1.76	40.14 ± 1.62	40.24 ± 1.77	40.27 ± 1.64	40.07 ± 2.24	< 0.001¶	B1,B3,B4,B5,B6,16,26
P	0.052§	0.043§	0.011§	0.278§	0.084§	0.093§	0.119§§	–	

Table 3. Differences of refractive (M), biometric and topographic parameters (mean ± SD) of the population according different periods of time of total 12 months of evaluations in function of gender and age groups

Table 3. Continued

	Visit baseline	Visit 1 1 night	Visit 2 1 week	Visit 3 1 month	Visit 4 3 months	Visit 5 6 months	Visit 6 12 months	p-value	Post hoc test†
P-CC (mm)									
Female	−6.07 ± 0.42	−6.15 ± 0.37	−6.05 ± 0.33	−6.05 ± 0.37	−6.03 ± 0.33	−6.03 ± 0.33	−6.04 ± 0.33	0.001¶	14,15,16
Male	−6.20 ± 0.22	−6.15 ± 0.26	−6.04 ± 0.20	−6.09 ± 0.27	−6.06 ± 0.22	−6.02 ± 0.25	−6.06 ± 0.19	0.007¶	B5
P	0.334§§	0.999§§	0.909§	0.708§	0.780§	0.903§	0.777§	–	
Younger	−6.15 ± 0.32	−6.20 ± 0.30	−6.08 ± 0.29	−6.14 ± 0.32	−6.06 ± 0.26	−6.06 ± 0.29	−6.09 ± 0.26	0.001¶	14,15,16
Older	−6.06 ± 0.42	−6.10 ± 0.37	−6.02 ± 0.30	−5.99 ± 0.36	−6.02 ± 0.33	−5.99 ± 0.33	−6.00 ± 0.33	0.003¶	B5,15
p	0.318§§	0.244§	0.444§	0.075§	0.537§	0.145§§	0.220§	–	

AL: axial length, ATC: apical tangential curvature, CCT: central corneal thickness, IACD: internal anterior chamber depth, M: spherical equivalent, P-CC: posterior central curvature.
Younger (≤ 11 years) and Older (> 11 years).

†The post hoc test presents the pairwise comparison, only for those that revealed to be statistically significant differences between visits, for example B1, between visit baseline and visit 1.

‡Repeated measures analysis of variance.

§Student's t-test.

¶Friedman test.

††Kruskal Wallis test.

‡‡Analysis of variance.

§§Mann–Whitney U-test.

probability level for the presence of an increment ≥ 0.10 mm/year could be derived:

$$P(AL) = \frac{e^{8.111-0.496*Age+0.659*M_{Baseline}}}{1+e^{8.111-0.496*Age+0.659*M_{Baseline}}}$$

The threshold for determining the presence of a myopic increment ≥ 0.10 mm/year pattern was chosen to be 0.44 (receiver operating characteristic curve area = 0.882, $p < 0.001$) to maximise specificity (0.824) with high sensitivity (0.821).

Discussion

The present study shows a change in ATC which flattens a total of 3.16 ± 1.78 D after 12 months. A 9.61 ± 4.80 μm decrease in anterior central elevation (A-CE) was also observed, which is consistent with an increase in elevation at temporal and nasal locations 2.5 mm from the centre of 10.10 ± 9.68 versus 9.61 ± 6.98 μm, respectively. There is a minor asymmetry with higher elevation changes at the temporal side, as found in a previous study with a different orthokeratology lens design.[21]

Similar to a recent meta-analysis[26] the present results show that the greatest change in CCT during orthokeratology are expected to occur during the first week of treatment. Alharbi et al.[27] observed a reduction of 70 per cent of CCT after the first night while in the present study, a reduction of 54 per cent was achieved. Alharbi et al.[27] also reported that the changes in CCT up to 15 μm could be observed after three months of treatment. In the present study, for subjects with a similar level age and myopia, less than half of this change (about 6 μm) was observed, and after one year the decrease was 9.63 ± 12.33 μm.

These differences can be compared with differences in orthokeratology lens geometry used in the study of Alharbi et al.;[27] CCT was greater (579.1 ± 19.3 μm) compared to the present sample (544.0 ± 29.0 μm) and there were probably differences in ethnicity and different measuring methodologies (optical pachometry versus Pentacam).[28] These anatomical changes induce optical changes resulting on an inversion of the pattern of the peripheral refraction after

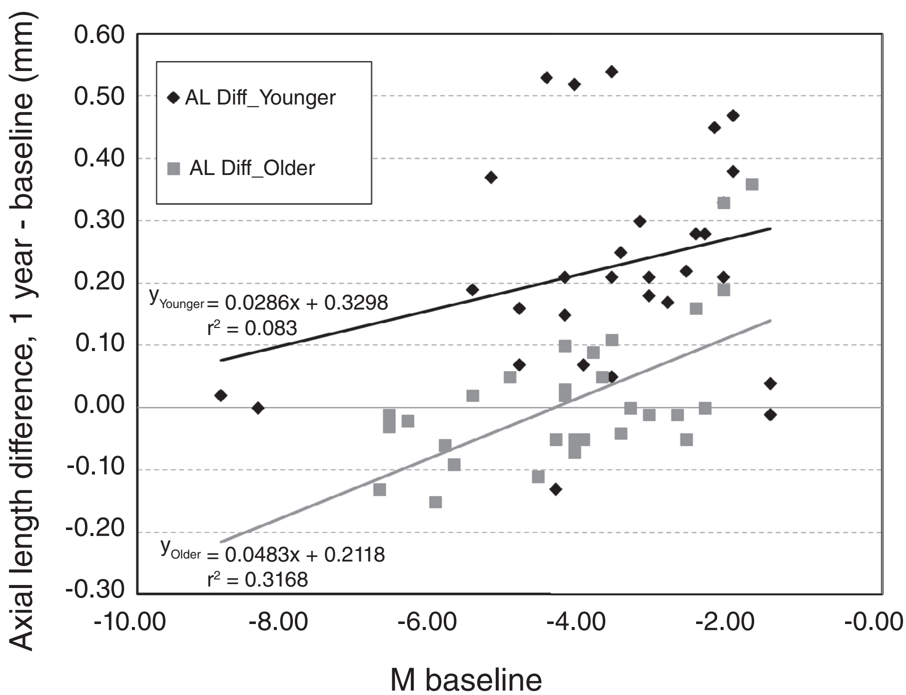

Figure 2. Axial length difference during 12 months of orthokeratology treatment in function of baseline myopia (M) of all subjects to younger and older subjects

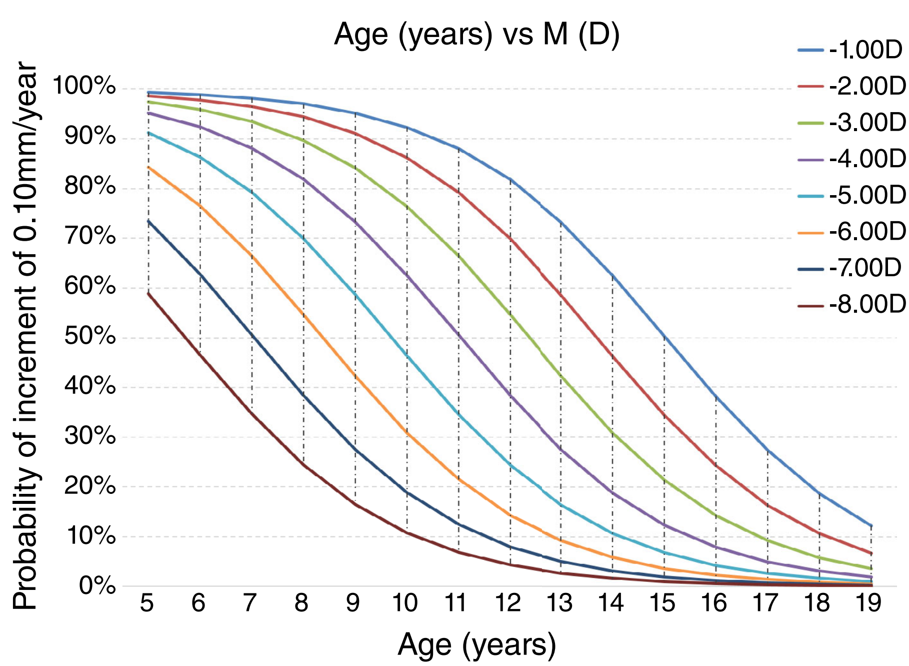

Figure 3. Logistic regression analysis performed on the dataset with best predictors of a faster axial length growth (≥ 0.10 mm/year): age and spherical equivalent baseline

orthokeratology, following the myopia induced in the periphery with a 1:1 relation with axial baseline spherical equivalent myopia.[29,30]

The present study indicates that posterior corneal shape parameters do not change during orthokeratology treatment over 12 months. A previous study[31] demonstrated that the shape changes that guarantee refractive correction in orthokeratology essentially occur in the anterior surface of the cornea. The present results support this previous finding.[31] The previous study followed patients during a short period of 14 days, but in the light of the present results, the absence of posterior elevation changes remain after 12 months.

AL in this sample showed a trend toward increasing over the period of follow-up. In a recent meta-analysis[26] combining results from seven studies (218 subjects), with the majority using IOLMaster (5/7), a mean axial elongation in orthokeratology groups of 0.27 mm after two years was demonstrated. In the present sample, the AL increased on average 0.11 mm after one year. Interestingly, a significant number of subjects showed a reduction in AL values. In previous studies,[8,32] the reduction of AL was not reported, and patients were followed over longer periods of time, and subjects between six and 12 years of age were enrolled. Older subjects in clinical trials may show faster axial elongation that masks the eventual shortening,[33] thus reducing the possibility of finding the decrease observed in the present sample.

In the present work, the findings were also different between younger and older cohorts. Only two out of 32 subjects in the present sample of children (up to 11 years of age) showed such an AL reduction, while 20 out of 30 in the older group (over 11 years of age) showed AL reduction, with 13 out of 20 presenting a reduction equal or higher than 50 μm. This phenomenon in the older group is in agreement with data from Lipson et al.[34] It does not mean that children do not experience such behaviour, but their faster axial elongation potentially compensates for that. This AL reduction can be at least in part explained by the fact that the choroidal thickness increases during orthokeratology, thus shortening the vitreous chamber rather than changing in the outer scleral layer; however, this needs to be further investigated.

Chen et al.[35] found significant correlation between the increase of choroidal thickness after orthokeratology treatment and reduction of AL, but with low predictive values (12 per cent). This suggests that other factors are potentially related with this effect, namely the reduction of thickness in corneal central epithelium.[36] IOLMaster measures distance between the central anterior corneal surface and the retinal pigment epithelium in the foveal area. The axial shortening found in the present study can be attributed to the thinning of the corneal epithelium or to the forward movement of the retina, presumably related to choroidal thickening that has been reported previously during orthokeratology[35,37] or both. The present results showed no relation between the changes in CCT and the AL changes during orthokeratology treatment, which suggests that choroidal thickening might be responsible for AL shortening. However, this cannot be confirmed because choroidal thickness has not been measured alone.

Myopia control treatments such as the use of atropine[38] and imposing myopic defocus for short periods of time[39] also can induce thickening of the measured choroidal layer. Different defocus stimuli in myopic healthy eyes were tested by Chiang et al.[39] over short periods of time. The choroidal layer was revealed to be sensitive to the sign of defocus. Inducing myopic defocus led to an increase, and inducing hyperopic defocus led to a decrease in choroidal thickness. The present study found that after 12 months, subjects with higher myopia showed a slight decrease in AL compared to the baseline condition, whereas this is less frequent in lower myopia and especially at younger ages. However, as previously reported, some of the subjects (one-third) could experience AL shortening even in a control group (without imposing a treatment or change in prescription).[35] Certainly this shortening effect during orthokeratology treatment deserves further attention in the future.

Another interesting outcome is the behaviour of AL growth over 12 months under orthokeratology treatment according to myopia/age group. After 12 months of orthokeratology, in subjects less than 11 years, the axial elongation was significantly greater than in subjects older than 11 years. As well, AL in children increased at least 0.10 mm in 73 per cent of cases and 57 per cent increased at least 0.20 mm. Conversely, in older subjects, only 19 per cent and six per cent of subjects increased at least 0.10 mm and 0.20 mm, respectively, after 12 months of orthokeratology treatment.

Previously, another study[17] suggested that myopia retention with orthokeratology will be more successful for myopia control purposes in the first three years. Five years extended evaluation showed a loss of effect after the third year, potentially related with the slower natural increase of myopia rather than loss of efficacy of the treatment. Hiraoka et al. considered that orthokeratology treatment must be maintained after three years to preserve the favourable effect previously obtained. They hypothesised that cessation could provoke a rebound effect similar to what happens with atropine-based treatments,[17] and is still to be confirmed to affect optical treatments.

It was previously suggested that older subjects can benefit more from orthokeratology treatment if axial elongation is faster in early ages.[40] Additionally, independently of age, subjects with high myopia (< −4.00 D) do not register significant changes in AL, as previously suggested.[10] Also, in a high myopia group, only 20 per cent of subjects demonstrated an increased AL of at least 0.10 mm, and of those only seven per cent increased more than 0.20 mm.

Logistic regression showed that each additional year of age and each additional dioptre of baseline myopia decreased the probability of faster progression (odds ratio [OR] = 1.23, 2.19 95% CI; OR = 1.08, 3.47 95% CI, respectively). These results are in agreement with the exponential models of myopia progression proposed by Thorn et al.[18] Jones et al. found that by the age of 10 to 12 years there is an inflexion of the trend for axial elongation and this is in agreement with the present results.[41]

The probability of faster axial elongation is at the maximum for each level of baseline myopia up to 10 to 12 years of age and decreases thereafter (Figure 3). A population-based survey has been recently used to evaluate the potential for myopia progression in a sample between the ages of five and 20 years.[42] Complementary to their observations, the present results suggest that older myopes, even with lower values of myopia, require close observation, and potentially a more vigorous intervention because their probability of faster axial elongation (≥ 0.10 mm/year) is very high. Moreover, such intervention must be implemented as soon as possible, as this risk for faster progression and therefore the therapeutic potential effect will tend to decline around 11 years of age. A limitation of this model is that it can only be applied to the Asian population within the ages of the current sample. Further studies in different ethnic groups, age ranges and during longer periods of time should provide further information for the management of myopia progression based on the potential for axial elongation.

In summary, this study systematically evaluated a clinical population over 12 months for changes at anterior and posterior cornea curvature and elevation, corneal thickness and AL during orthokeratology. No significant changes were found in parameters of posterior shape of the cornea. The parameters of corneal anterior surface changed differently according to basal axial myopia and age of subjects. The axial elongation did not vary significantly during 12 months of orthokeratology in participants aged over 11 years, or for subjects with myopia greater than −4.00 D. Results showed that AL shortening was present more frequently in older subjects and in high myopia cases. Future studies must be developed to clarify the ocular parameter(s) involved in AL decrease during orthokeratology in older and high myopes.

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