

1 **Full title:** Short- and long-term changes in corneal power are not correlated  
2 with axial elongation of the eye induced by orthokeratology in children.

3

4 **Running head:** Corneal power and axial length with orthokeratology

5

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35 **ABSTRACT**

36

37 **Purpose:** To assess the relationship between short- and long-term changes in power at  
38 different corneal locations relative to the change in central corneal power and the 2-year  
39 change in axial elongation relative to baseline in children fitted with orthokeratology contact  
40 lenses (OK).

41

42 **Methods:** Thirty-one white European subjects 6-12 years of age and with myopia -0.75 to -  
43 4.00DS and astigmatism  $\leq 1.00$ DC were fitted with OK. Differences in refractive power 3 and  
44 24 months post-OK in comparison to baseline and relative to the change in central corneal  
45 power were determined from corneal topography data in 8 different corneal regions (i.e. N  
46 (nasal)1, N2, T(temporal)1, T2, I(inferior)1, I2, S(superior)1, S2), and correlated with OK-  
47 induced axial length changes at 2-years relative to baseline.

48

49 **Results:** After two years of OK lens wear, axial length increased by  $0.48 \pm 0.18$ mm ( $p < 0.001$ );  
50 which corresponded to an increase of  $1.94 \pm 0.74\%$  ( $[2\text{-years change in axial length}/\text{baseline}$   
51  $\text{axial length}] * 100$ ). However, the change in axial elongation in comparison to baseline was not  
52 significantly correlated with changes in corneal power induced by OK relative to baseline for  
53 any of the corneal regions assessed (all  $p > 0.05$ ).

54

55 **Conclusion:** The reduction in central corneal power and relative increase in paracentral and  
56 pericentral power induced by OK over 2 years were not significantly correlated with  
57 concurrent changes in axial length of white European children.

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60 **Key words:** cornea, power, topography, myopia progression, orthokeratology, contact lenses

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64 **INTRODUCTION**

65 Myopia is globally recognized as a significant public health concern  
66 associated with increased ocular-related morbidity and considerable  
67 healthcare costs.<sup>1-3</sup> It is the most common refractive error; affects around 30%  
68 of the world's population; and its prevalence has been estimated a significant  
69 increase to affect around 50% of the world's population by 2050.<sup>4</sup> The  
70 prevalence of myopia in young adolescents has been increasing in recent  
71 decades to reach 10–25% in industrialized societies of the West and epidemic  
72 levels of 60–80% in East Asia.<sup>4-6</sup> Of particular concern is that there appears to  
73 have been a commensurate increase in high myopia (i.e.  $\leq -6.00D$ )<sup>7-10</sup> leading  
74 to a higher risk of potentially blinding ocular pathologies such as glaucoma,  
75 macular degeneration and vitreous and retinal detachments.<sup>11-14</sup> That the  
76 myopic eye is, in terms of propensity to ocular pathology, a vulnerable eye<sup>3</sup>  
77 has prompted interest in therapies to ameliorate its progression. Several  
78 treatment options have been used in the past with limited success to eliminate  
79 or, at least, reduce myopia progression.<sup>15-18</sup> However, recent studies have  
80 reported orthokeratology contact lens wear (OK) to significantly reduce axial  
81 length growth by 30 to 50% in comparison to spectacle and soft contact lens  
82 wear.<sup>19-24</sup> In this regard, of the optical treatment options currently available OK  
83 is the method with the largest demonstrated efficacy in reducing myopia  
84 progression across different ethnicities.<sup>25</sup> Furthermore, OK lens wear has a  
85 relatively low rate of adverse events and discontinuations<sup>26</sup> and is well  
86 accepted by parents and children.<sup>27</sup>

87

88 Orthokeratology induces a flattening of central corneal curvature to  
89 temporarily correct myopia. In addition, there is a concurrent relocation of  
90 epithelial tissue or fluid within or between epithelial cells from the center to the  
91 mid-periphery that produces a decrease and increase in central and mid-  
92 peripheral corneal thickness, respectively.<sup>28</sup> Such induced changes in corneal  
93 curvature following OK lens wear can be precisely monitored with currently  
94 available corneal topographers and have important refractive implications.<sup>29-31</sup>  
95 In fact, a strong correlation has been previously reported between the amount  
96 of apical corneal power change and refractive power change following OK,  
97 although the change in power has been found to underestimate the change in  
98 manifest refractive error.<sup>32</sup> Furthermore, in myopic subjects, the change in  
99 central corneal thickness induced by OK has been shown to account for  
100 concomitant changes in refraction.<sup>31</sup> A number of animal studies have shown  
101 that peripheral refraction is important in the emmetropization process such  
102 that relative peripheral hyperopic and myopic defocus can induce and inhibit  
103 myopia progression, respectively.<sup>33-41</sup> Of relevance to myopia control in  
104 humans therefore is that relative peripheral hyperopic defocus is reduced in  
105 OK<sup>42, 43</sup> compared with the increase that occurs in single vision spectacle lens  
106 wear<sup>44</sup> and the neutral effect of bifocal soft or gas-permeable contact lens  
107 wear.<sup>45, 46</sup> Peripheral myopic defocus induced by OK has consequently been  
108 hypothesized in several studies as the basis for its efficacy in myopia  
109 control.<sup>47</sup>  
110  
111 Recently, Zhong et al. evaluated whether corneal power changes induced by  
112 a proprietary OK lens design (i.e. Hiline Optics, China) are predictive of

113 myopia progression in 32 Chinese children aged from 9 to 14 fitted with OK  
114 for 2 years.<sup>48</sup> Using a TMS-4 corneal topographer instrument (Tomey  
115 Corporation, Japan), corneal apical refractive power was provided  
116 automatically and corneal sagittal powers were recorded manually at four  
117 locations along the nasal, temporal, and inferior corneal axes (i.e. 1, 2, 3 and  
118 4 mm intervals from the apex).<sup>48</sup> The study compared the pre- and post-OK  
119 changes in peripheral corneal sagittal refractive powers (relative to the central  
120 apical power) and the 2-year change in axial length.<sup>48</sup> It was reported that the  
121 larger the relative post-OK change in relative positive peripheral corneal  
122 power along the nasal, temporal and inferior cornea the smaller the axial  
123 elongation after 24 months of lens wear.<sup>48</sup> In the Zhong et al. study, however,  
124 sagittal corneal power changes pre- and post-OK were measured manually  
125 and hence susceptible to human error.<sup>48</sup> Corneal topography sagittal maps  
126 measure corneal curvature at any given point on the cornea as the  
127 perpendicular distance from the corneal surface to the optical axis, which is  
128 then converted to sagittal power using the paraxial power formula for a single  
129 refracting surface.<sup>49-51</sup> Although sagittal maps provide useful measurements  
130 of the shape of the cornea in the form of curvature, their ability to represent  
131 corneal refractive power is limited.<sup>49-51</sup> Contemporary corneal topographers  
132 feature built-in software with refractive power difference maps that are able to  
133 measure directly changes in corneal power pre- and post-OK. Furthermore,  
134 difference refractive maps can provide mean changes in corneal power  
135 across certain regions of the cornea and are thus likely to better reflect  
136 corneal power changes following OK lens wear rather than assessing the  
137 change in corneal power at isolated corneal points (Figure 1). In addition,

138 unlike sagittal maps, refractive maps account for spherical aberration and with  
139 reference to Snell's law describe how light is refracted through an aspheric  
140 surface such as the human cornea.<sup>49-51</sup> Therefore, difference refractive  
141 corneal topography maps offer particular advantages when assessing  
142 refractive changes following OK lens wear in comparison to no lens wear.

143

144 The present study examines the correlation between changes in axial length  
145 and short- (3 months post-OK) and long-term (24 months post-OK) changes  
146 in corneal power induced by OK with reference to data from our previous  
147 study, Myopia Control with Orthokeratology contact lenses in Spain (MCOS).  
148 MCOS evaluated, as the primary outcome measure, differences in growth of  
149 axial length over a 2-year period in white European children with myopia  
150 wearing OK contact lenses and distance single-vision spectacles.<sup>23</sup> Thirty-one  
151 children were prospectively allocated to OK and 30 to distance single-vision  
152 spectacles. No statistically significant differences were found in any of the  
153 baseline demographics and refractive and biometric data between groups,  
154 including central corneal power and corneal shape (p-value). However, we  
155 reported a statistically significant difference in axial length elongation relative  
156 to baseline between the OK (mean  $\pm$  standard deviation,  $0.47\pm 0.18\text{mm}$ ) and  
157 distance single-vision spectacles ( $0.69\pm 0.32\text{mm}$ ) groups ( $p = 0.005$ ).<sup>23</sup>

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162 **METHODS**

163 This study was part of a larger study designed to assess different aspects of  
164 OK lens wear specifically prescribed for the control of myopia progression in  
165 children.<sup>23, 26, 27, 52-56</sup> Normal, healthy, white European subjects 6 to 12 years  
166 of age with moderate levels of myopia [mean spherical equivalent (MSE) -  
167 0.75 to -4.00D] and astigmatism  $\leq 1.00$ D) and free of systemic or ocular  
168 disease were fitted with Menicon Z Night contact lenses for overnight use  
169 (Menicon Co., Ltd, Nagoya, Japan). An OK fit was considered to be  
170 successful if the subject showed a CCLRU score regarding anterior eye  
171 segment signs of  $\leq 1$  unit,<sup>57</sup> a “bull’s eye” corneal topography pattern and  
172 unaided monocular and binocular visual acuities within  $\pm 1$  line of the best-  
173 corrected spectacle decimal visual acuity. All patients underwent ocular  
174 examinations including slit-lamp examination, manifest refraction, and corneal  
175 topography at baseline and then following 1 day, 2 weeks, 3 months and 6-  
176 month intervals over a 2-year period. Axial length was measured at the time of  
177 enrolment and 6, 12, 18, and 24 months after the initiation of the treatment.  
178 Follow-up visits were scheduled to fall within 2 hours of awakening. A  
179 decrease in one line of visual acuity accompanied by a change in subjective  
180 refraction at any of the follow-up visits<sup>58</sup> was considered clinically significant  
181 and was remedied by supplying new contact lenses. Full informed consent  
182 and child assent was obtained from the parents/guardians prior to the start of  
183 all experimental work and data collection. Patient participation in the study  
184 could be discontinued at the examiner’s discretion should significant  
185 symptoms or slit-lamp findings occur. Subjects were instructed that they could  
186 withdraw from the study at anytime. The study was conducted in accordance

187 with the Tenets of the Declaration of Helsinki and approved by the Institutional  
188 Ethical Committee Review Board of Novovision Ophthalmology Clinic.

189

190 Cycloplegic auto-refraction was performed following the instillation of three  
191 drops of cyclopentolate HCl 1% separated 10 min apart in each of the  
192 subjects' eyes using a multidose bottle (Alcon Cusí, Masnou, Barcelona,  
193 Spain). Ten minutes after the instillation of the third drop, three auto-refraction  
194 measurements were taken and a mean obtained (Topcon RM 8000B, CA,  
195 USA).

196

197 Measurements of axial length were taken with the Zeiss *IOLMaster* (Carl  
198 Zeiss Jena GmbH). Three separate measurements of axial length were  
199 recorded and a mean obtained.<sup>59</sup> The 2-year change in axial length relative to  
200 baseline was calculated as a percentage to normalize between-subjects  
201 differences in changes in axial length relative to the baseline axial length [(2-  
202 years change in axial length/baseline axial length)\*100].

203

204 Corneal topography measurements were performed with the Wavelight  
205 Allegro Topolyzer (WaveLight Laser Technologies AG, Erlangen, Germany).  
206 The instrument incorporates a high resolution placido ring corneal  
207 topographer which detects 22,000 elevated data points of measurement  
208 evenly distributed from 22 ring edges with a accuracy and reproducibility of  
209  $\pm 0.10D$  as claimed by the manufacturer. The instrument has been reported to  
210 display excellent reliability in measuring corneal power (i.e. an intraclass  
211 correlation coefficient  $\geq 0.971$ ).<sup>60</sup> The first measurement taken for each eye,



212 which provided an optimum index value according to the manufacturer's  
213 recommendations, was used for the study. Baseline, 3- and 24-months  
214 topographic outputs were taken as representative of the pre-, short- and long-  
215 term post-OK treatment status, respectively.<sup>28</sup> Corneal topography was  
216 analyzed using Oculus Keratograph software (Version 1.76, Oculus  
217 Optikgeräte GmbH, Germany). Differences in refractive power between  
218 baseline and 3- and 24-months were quantified using the 'refractive compare'  
219 display map provided by the instrument software. The map displays average  
220 values of change in corneal power for 4 different quadrants (nasal, temporal,  
221 inferior and superior) and between the paracentral (i.e. 3 to 5mm ring  
222 diameters) and pericentral cornea (i.e. 5 to 8mm ring diameters). The map  
223 thus generates for analysis 8 discrete corneal regions N1, N2, T1, T2, I1, I2,  
224 S1, S2 and a single central corneal area, C (Figures 1 and 2). However, data  
225 from the superior pericentral cornea (i.e. S2) were not analyzed owing to  
226 intrusion by the upper lid and lashes. The change in corneal power induced by  
227 OK for each corneal region was measured relative to the change in central  
228 corneal power (e.g.  $[N1_{\text{post-OK}} - N1_{\text{pre-OK}}] - [C_{\text{post-OK}} - C_{\text{pre-OK}}]$ ). Additionally,  
229 central and total multifocality were also calculated. Central multifocality was  
230 defined as the greatest difference in corneal power following subtraction of the  
231 change in central corneal power from the change in corneal power at any of  
232 the 7 different corneal regions measured (relative to the change in central  
233 corneal power). Total multifocality was defined as the greatest difference in  
234 corneal power between any two of the 7 different corneal regions assessed  
235 relative to the change in central corneal power.

236

237 **Statistical analysis**

238 A 1-way within-subjects analysis of variance (ANOVA) was used to assess  
239 whether OK lens wear induced differences in corneal power changes between  
240 different regions in the paracentral (i.e. N1, T1, I1 and S1) and pericentral (i.e.  
241 N2, T2 and I2) cornea separately. Equality of variances and sphericity were  
242 tested using the Levene and Mauchly tests, respectively. *Post-hoc* t-tests with  
243 Bonferroni correction were used to assess differences between pairs of  
244 comparisons. Differences in power at each individual corneal location relative  
245 to baseline between 3 and 24 months of OK lens wear as well as between  
246 central and total multifocality were assessed using a paired t-test. Simple  
247 linear regressions were used to demonstrate the relationship between the 2-  
248 years' change in axial elongation relative to baseline (i.e. the dependent  
249 variable) and the change in corneal power at each of the different corneal  
250 locations assessed as well as with central and total multifocality. Data from  
251 right eyes only were used for analysis and expressed as mean  $\pm$  standard  
252 deviation. Statistical analyses were performed with *SigmaPlot* (Systat  
253 software Inc, California, USA). The level of statistical significance was set at  
254 5%.

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262 **RESULTS**

263 The subjects' demographic and baseline data have been reported  
264 elsewhere.<sup>23, 52</sup> In brief, thirty-one children were prospectively fitted with OK  
265 contact lenses, but two children discontinued the study; one due to discomfort  
266 with contact lens wear and another to unknown reasons.<sup>26</sup> One subject  
267 completed the study, but was excluded from the analysis as corneal  
268 topography data were unreliable. At the start of the study, the mean age of the  
269 remaining 28 subjects was  $9.6 \pm 1.6$  years; 15 were male and 13 were female.

270

271 Three and 24 months of OK lens wear produced a significant reduction in  
272 myopia (MSE) from  $-2.20 \pm 1.13D$  to  $-0.19 \pm 0.23D$  and  $-0.33 \pm 0.29D$ ,  
273 respectively (both  $p < 0.001$ ); the change in MSE between 3 and 24 months  
274 was also statistically significant ( $p = 0.005$ ). The cylindrical component of the  
275 refraction did not change significantly between any of the 3 pairwise  
276 comparisons (i.e. baseline vs. 3-months, baseline vs. 24-months and 3- vs.  
277 24-months) (all  $p > 0.05$ ). Central corneal power decreased by  $-1.89 \pm 0.91D$  at  
278 3 months and by  $-1.84 \pm 0.97$  at 24 months in comparison to baseline; the  
279 difference in corneal power change relative to baseline between short- and  
280 long-term OK lens wear was not statistically significant ( $p = 0.710$ ). Axial length  
281 increased from  $24.53 \pm 0.78mm$  at baseline to  $25.01 \pm 0.82mm$  following 2-years  
282 of OK lens wear ( $p < 0.001$ ). The 2-years change in axial length (i.e.  
283  $0.48 \pm 0.18mm$ ) corresponded to an increase of  $1.94 \pm 0.74\%$  (i.e. [2-years  
284 change in axial length/baseline axial length]\*100).

285

286 Short- and long-term OK lens wear induced an asymmetric change in power  
287 in the paracentral cornea ( $p=0.003$  and  $p<0.001$ , respectively) that was  
288 attributable to the difference in power between N1 and T1 at 3 months  
289 ( $p=0.001$ ) and between T1 and N1, I1 and S1 at 24 months (all  $p<0.05$ )  
290 (Figure 3). Similarly, significant differences in power were found between  
291 different regions of the pericentral cornea at both 3 ( $p=0.021$ ) and 24 months  
292 ( $p=0.02$ ) relative to baseline that were attributable to the difference in power  
293 between N2 and T2 at both 3 and 24 months (both  $p<0.05$ ) (Figure 3). Short-  
294 and long-term OK lens wear induced similar changes in corneal power relative  
295 to changes in central corneal power at each of the 7 corneal regions assessed  
296 (all  $p>0.05$ ) with the exception of S1 where the change in corneal power was  
297 significantly more positive following long- in comparison to short-term OK lens  
298 wear ( $p=0.037$ ).

299

300 After 3 and 24 months of OK treatment, the greatest differences in power  
301 between the central cornea and any other corneal region (i.e. central  
302 multifocality) were  $-2.69\pm 1.16$  D and  $-2.53\pm 1.39$  D, respectively; central  
303 multifocality was not statistically different between short- and long-term OK  
304 lens wear ( $p=0.474$ ). After 3 and 24 months of OK treatment, the greatest  
305 differences in power between any two corneal regions (i.e. total multifocality)  
306 were  $-2.94\pm 1.22$  D and  $-2.70\pm 1.41$  D; total multifocality was not statistically  
307 different at 3 in comparison to 24 months ( $p=0.333$ ). The difference between  
308 central and total multifocality was, however, statistically significant following  
309 both short- and long-term OK lens wear (both  $p<0.001$ ).

310

311 The change in axial elongation over 2 years relative to baseline was not  
312 significantly correlated with changes in corneal power induced by OK over 3  
313 or 24 months relative to baseline at any of the corneal regions assessed (all  
314  $p>0.05$ ) (Table 1). Similarly, the mean changes in corneal power at the nasal  
315 (i.e. mean of N1 and N2), temporal (i.e. mean of T1 and T2), inferior (i.e.  
316 mean of I1 and I2), horizontal (i.e. mean of N1, N2, T1 and T2), vertical (i.e.  
317 mean of I1, I2 and S1), paracentral (i.e. mean of N1, T1, I1 and S1) or  
318 pericentral corneal regions (i.e. mean of N2, T2 and I2) following either 3 or  
319 24 months of OK lens wear were not significantly correlated with the 2-year  
320 change in axial length relative to baseline (all  $p<0.05$ ) (Table 1 and Figures 4  
321 and 5).

322

323 Neither central nor total multifocality following short- or long-term OK lens  
324 wear were significantly correlated with the 2-year change in axial length  
325 relative to baseline (all  $p<0.05$ ) (Table 1).

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333 **DISCUSSION**

334 The decrease in central corneal power and concomitant increase in  
335 paracentral and pericentral corneal power found in this study is consistent  
336 with previous reports of central corneal flattening and peripheral steepening  
337 following OK lens wear.<sup>28-31</sup> Following 3 months of OK lens wear, Zhong et al.  
338 reported significant increases (compared with baseline) in sagittal power at  
339 the nasal 2 and 3mm, temporal 3mm and inferior 2, 3 and 4mm corneal  
340 locations; peaking was evident at the 3mm location (i.e. 6mm corneal ring)  
341 compared with the apical center.<sup>48</sup> The present study found increases in  
342 corneal power at both the paracentral and pericentral locations but these were  
343 greater in the pericentral region (i.e. 5 to 8mm ring diameter) than in the  
344 paracentral region (i.e. 3 to 5mm ring diameter) following both 3 and 24  
345 months of OK lens wear. That OK induced asymmetrical power changes  
346 along different areas of the cornea agrees with the results of Maseedupally et  
347 al.<sup>61</sup> The latter finding might be attributed to the fact that the normal corneal  
348 shape is not rotationally symmetric and exhibits some hemi-meridional  
349 variation.<sup>62-64</sup> Therefore, the wearing of a rotationally symmetric OK contact  
350 lens on the eye will result in asymmetrical power changes along different  
351 regions of the cornea. Additionally, the greater changes in corneal power  
352 found for the nasal cornea in comparison with the temporal cornea are in  
353 agreement with previous studies<sup>48, 61, 65</sup> and might be attributable to temporal  
354 decentration of the OK treatment leading to greater flattening and thus  
355 reduction of corneal power of the temporal cornea in comparison with the  
356 nasal cornea.<sup>65</sup> It should be noted that changes in central, paracentral and  
357 pericentral corneal powers following OK lens wear have important refractive

358 implications which in turn are affected by pupil size. Incident light rays parallel  
359 to the visual axis will be susceptible to an increase in spherical aberration as  
360 pupil diameter increases.<sup>66</sup> The increase in spherical aberration is generally  
361 relatively moderate when the central area of corneal flattening following OK  
362 treatment encompasses the pupil. However, when light rays simultaneously  
363 pass through corneal regions of marked difference in refractive power (i.e.  
364 central and paracentral/pericentral corneal regions), which might occur with  
365 off-axis (i.e. oblique) incidence and/or in subjects with larger pupils, that would  
366 produce a peripheral astigmatic refraction (i.e. relative hyperopia and myopia  
367 for light rays passing through the central and paracentral/pericentral corneal  
368 regions, respectively). Although the resulting pattern of astigmatic refraction  
369 and the position of the sagittal and tangential image shells relative to the  
370 retina might have important implications in terms of regulating myopia  
371 progression, the physiological and optical mechanisms for modulating ocular  
372 growth are unclear.<sup>67</sup>

373

374 Hiraoka et al. reported an increase in corneal multifocality from  $1.69\pm 0.42$  to  
375  $4.92\pm 2.50$  D ( $\Delta=3.23$ D) following 12 months of OK lens wear,<sup>68</sup> whereas the  
376 present study found central and total multifocality to be  $2.69\pm 1.16$  and  
377  $2.94\pm 1.22$ D, respectively following 3 months of OK lens wear and  $2.53\pm 1.39$   
378 and  $2.70\pm 1.41$ D, respectively following 24 months of OK lens wear. Hiraoka et  
379 al. found a statistically significant negative correlation between changes in  
380 corneal multifocality and the 1-year change in axial elongation,<sup>68</sup> whereas in  
381 the present study neither central nor total multifocality were significantly  
382 associated with the 2-year change in axial length relative to baseline. The

383 discrepancy might be attributable to differences between studies in the  
384 determination of multifocality as Hiraoka et al. measured corneal multifocality  
385 as the difference between the maximum and minimum corneal optical powers  
386 (in diopters) calculated within the central 4-mm pupillary.<sup>68</sup> The greater levels  
387 of multifocality found by Hiraoka over the central cornea could potentially be  
388 associated with changes in axial length. Furthermore, the finding that the  
389 changes in relative positive corneal power for the paracentral and pericentral  
390 cornea were not significantly correlated with the change in the axial length is  
391 in disagreement with the results of Zhong et al.<sup>48</sup> It is feasible that differences  
392 in OK lens designs and corneal topography between Caucasian and Chinese  
393 individuals<sup>69</sup> could produce different profiles of refraction in the peripheral  
394 cornea which, in turn, might differentially affect the axial elongation of the eye.  
395 The clear lack of correlation between changes in paracentral and pericentral  
396 corneal power and change in axial length found in this study was not  
397 anticipated given the well documented evidence from animal models that  
398 peripheral myopic and hyperopic defocus can modulate change in axial  
399 length.<sup>33-41</sup> However, the paracentral and relative pericentral myopic defocus  
400 induced by OK lens wear in children differs inherently from that produced by  
401 optically imposed defocus in animals where exposure to defocus is generally  
402 substantial in terms of both magnitude and duration.<sup>33-41</sup> Furthermore, large  
403 studies in humans have failed to find peripheral refraction to affect myopia  
404 progression.<sup>70, 71</sup> Other factors that could affect myopia progression and  
405 ultimately the correlation between changes in corneal power and axial length  
406 following OK treatment are ethnicity, family history and outdoor exposure. It is  
407 well established that certain ethnicities, such as those from Far East Asia (i.e.



408 Chinese, Hong Kongers, Taiwanese, South Korean, Japanese and  
409 Singaporean), are at higher risk of myopia development and progression.<sup>4, 72,</sup>  
410 <sup>73</sup> However, all subjects recruited for this study were limited to White  
411 European ethnicity. Similarly, children with myopic parents are at higher risk  
412 of developing myopia, with the risk increasing with the number of myopic  
413 parents.<sup>74-76</sup> In fact, a previous analysis of the MCOS study showed smaller  
414 increases in axial length with lower levels of parental myopia in children  
415 wearing OK lenses in comparison to children wearing spectacles.<sup>53</sup> Higher  
416 levels of time spent outdoors have been shown to be protective for myopia  
417 development.<sup>77, 78</sup> Although time spent outdoors was not controlled in the  
418 MCOS study, it may be presumed that children participating in the study were  
419 exposed to similar levels of outdoor exposure.

420

421 In summary, we conclude that, based on the results of this study, the  
422 inhibition of axial length growth found in the MCOS study is a not  
423 consequence of a relative myopic shift in the peripheral retinal image induced  
424 by changes in corneal power following OK lens wear. It should be noted,  
425 however, that changes in corneal power give only an indirect estimate of  
426 changes in relative peripheral refractive error. We envisage that the findings  
427 of this study will contribute to the debate of the role of peripheral imagery in  
428 the etiology of human myopia.<sup>47</sup>

429

430

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435

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665 **TABLE LEGENDS**

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667 **Table 1.** Univariate regression analyses. The strength of association between  
668 the different factors is indicated by linear regression equations, R-squared  
669 values and p-values.

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689 **FIGURE LEGENDS**

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691 **Figure 1.** Refractive compare map of the Oculus Keratograph software  
692 displaying the post- to pre-OK change in corneal refractive up to a 8mm ring  
693 diameter for the right eye of an individual subject. The map on the top right  
694 shows data post-OK lens wear, the one on the bottom right data pre-OK lens  
695 wear, and the larger map on the left shows the difference in corneal power  
696 (i.e. post-OK – pre-OK). The right and left sides of each of the 3 maps  
697 correspond to nasal and temporal corneal regions, respectively. The color  
698 scale on the far right represents the absolute refractive power of the cornea,  
699 whereas the color scale on the far left represents the relative change in  
700 corneal power. Warmer (i.e. red) and darker colors (i.e. blue) indicate  
701 increases and decreases in corneal power, respectively. Average values of  
702 corneal power change for certain regions of the cornea are provided on the  
703 larger map on the left.

704

705 **Figure 2.** Areas of corneal power change (i.e. post-OK – pre-OK) for the right  
706 eye. The regions located between the 3- and 5-mm diameter rings are  
707 referred to as “paracentral” corneal regions (i.e. N1, T1, I1, S1), whereas the  
708 regions located between the 5- and 8-mm diameter rings are referred as  
709 pericentral corneal regions (i.e. N2, T2, I2, S2). C, central; N, nasal; T,  
710 temporal; I, inferior; S, superior. It has been estimated that the central region  
711 and each of the 4 regions of the paracentral (i.e. N1, T1, I1, S1) and  
712 pericentral (i.e. N2, T2, I2, S2) cornea assessed by the corneal topographer

713 encompass 3,094, 1,374 and 3,352 elevated data points of measurement,  
714 respectively.

715

716 **Figure 3.** Mean changes in corneal power relative to the central corneal  
717 power at 3-months (left) and 24-months (right) relative to baseline for each of  
718 the 7 different corneal regions assessed. Data from the superior peripheral  
719 cornea (i.e. S2) were not analyzed as intrusion of the upper lid and lashes  
720 prevented reliable measurement.

721

722 **Figure 4.** Simple linear regressions between the 2-years change in axial  
723 length relative to baseline and the change in paracentral corneal power  
724 relative to central corneal power following 3- (solid triangles and line) and 24-  
725 months (open circles and dashed line) of OK lens wear.

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727 **Figure 5.** Simple linear regressions between the 2-years change in axial  
728 length relative to baseline and the change in pericentral corneal power relative  
729 to central corneal power following 3- (solid triangles and line) and 24-months  
730 (open circles and dashed line) of OK lens wear.

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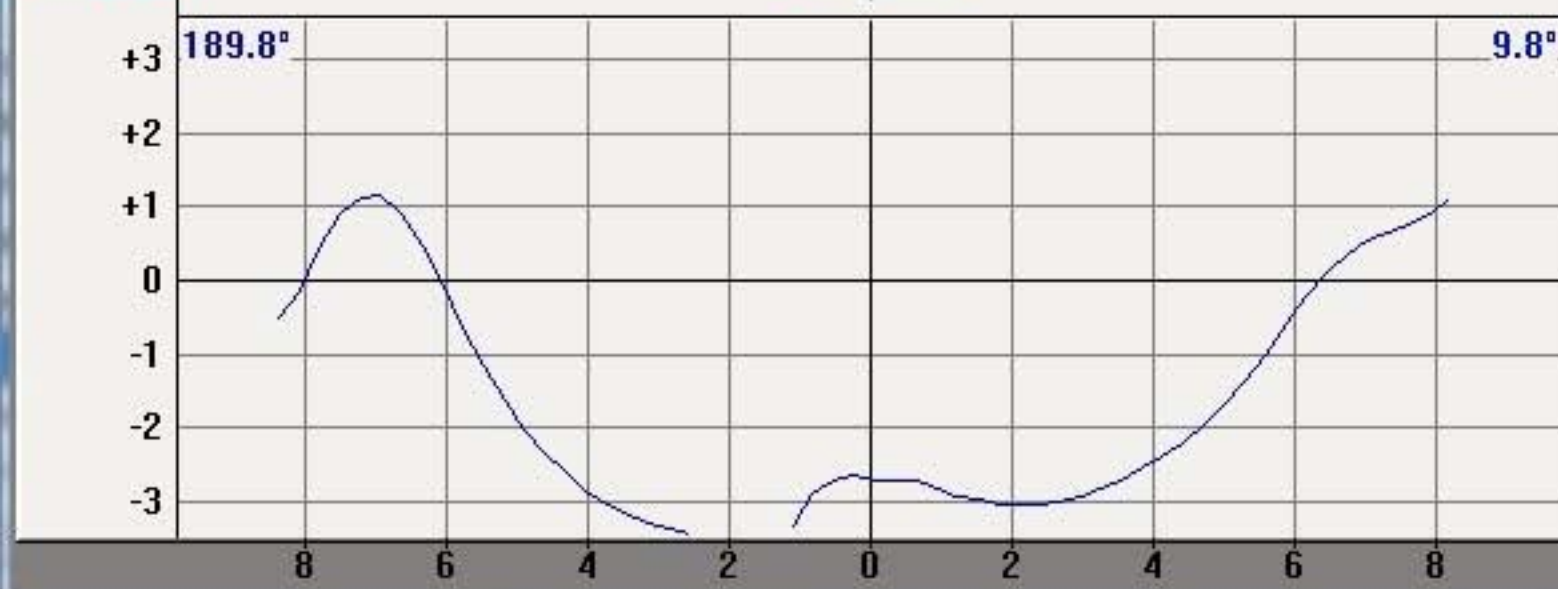
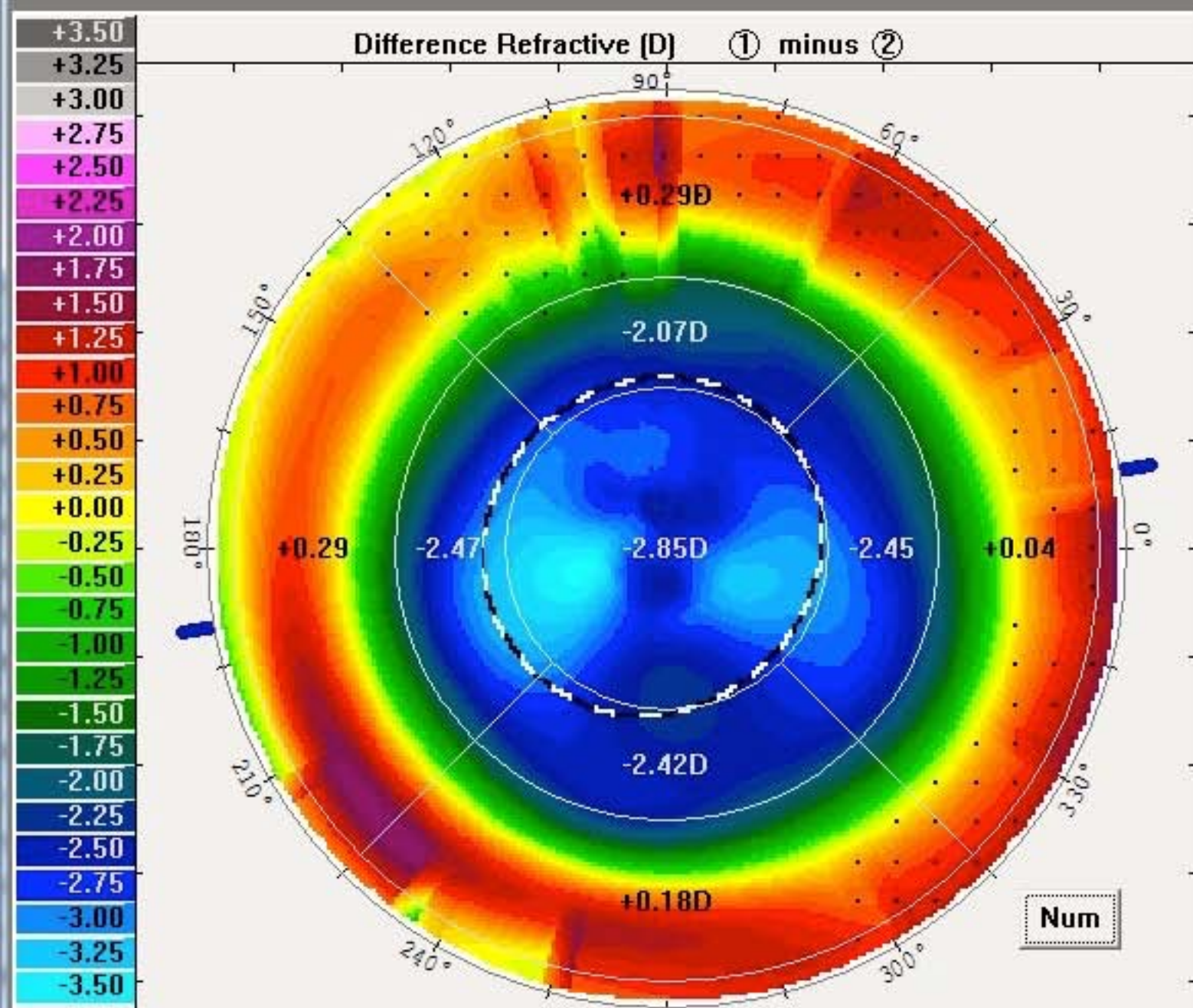
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Corneal areas	Short-term corneal power changes vs. changes in axial length		Long-term corneal power changes vs. changes in axial length	
	Regression line equations	Statistical results	Regression line equations	Statistical results
<b>N1</b>	$y = -0.020x + 1.957$	$R^2=0.000, p=0.906$	$y = -0.026x + 1.958$	$R^2=0.000, p=0.919$
<b>N2</b>	$y = -0.102x + 2.184$	$R^2=0.000, p=0.392$	$y = -0.053x + 2.092$	$R^2=0.000, p=0.628$
<b>T1</b>	$y = -0.093x + 1.924$	$R^2=0.000, p=0.777$	$y = 0.226x + 1.936$	$R^2=0.000, p=0.639$
<b>T2</b>	$y = -0.003x + 1.947$	$R^2=0.000, p=0.980$	$y = 0.012x + 1.924$	$R^2=0.000, p=0.923$
<b>I1</b>	$y = -0.159x + 1.992$	$R^2=0.000, p=0.500$	$y = 0.050x + 1.924$	$R^2=0.000, p=0.895$
<b>I2</b>	$y = -0.006x + 1.957$	$R^2=0.000, p=0.951$	$y = -0.009x + 1.977$	$R^2=0.000, p=0.943$
<b>S1</b>	$y = -0.004x + 1.943$	$R^2=0.000, p=0.979$	$y = 0.022x + 1.931$	$R^2=0.000, p=0.902$
<b>Mean N: (N1+N2)/2</b>	$y = -0.108x + 2.111$	$R^2=0.000, p=0.514$	$y = -0.045x + 2.011$	$R^2=0.000, p=0.784$
<b>Mean T: (T1+T2)/2</b>	$y = -0.023x + 1.959$	$R^2=0.000, p=0.915$	$y = 0.043x + 1.909$	$R^2=0.000, p=0.848$
<b>Mean I: (I1+I2)/2</b>	$y = -0.044x + 1.998$	$R^2=0.000, p=0.784$	$y = 0.009x + 1.932$	$R^2=0.000, p=0.964$
<b>Mean H: (N1+N2+T1+T2)/4</b>	$y = -0.094x + 2.050$	$R^2=0.000, p=0.649$	$y = -0.017x + 1.962$	$R^2=0.000, p=0.934$
<b>Mean V: (I1+I2+S1)/3</b>	$y = -0.048x + 1.987$	$R^2=0.000, p=0.810$	$y = 0.031x + 1.913$	$R^2=0.000, p=0.892$
<b>Mean Para (N1+T1+I1+S1)/4</b>	$y = -0.044x + 2.032$	$R^2=0.000, p=0.734$	$y = 0.059x + 1.920$	$R^2=0.000, p=0.880$
<b>Mean Peri: (N2+T2+I2)/3</b>	$y = -0.077x + 1.967$	$R^2=0.000, p=0.766$	$y = -0.013x + 1.968$	$R^2=0.000, p=0.916$
<b>Central multifocality</b>	$y = 0.102x + 2.215$	$R^2=0.000, p=0.415$	$y = 0.047x + 2.060$	$R^2=0.000, p=0.656$
<b>Total multifocality</b>	$y = 0.146x + 2.372$	$R^2=0.023, p=0.212$	$y = 0.044x + 2.060$	$R^2=0.023, p=0.674$

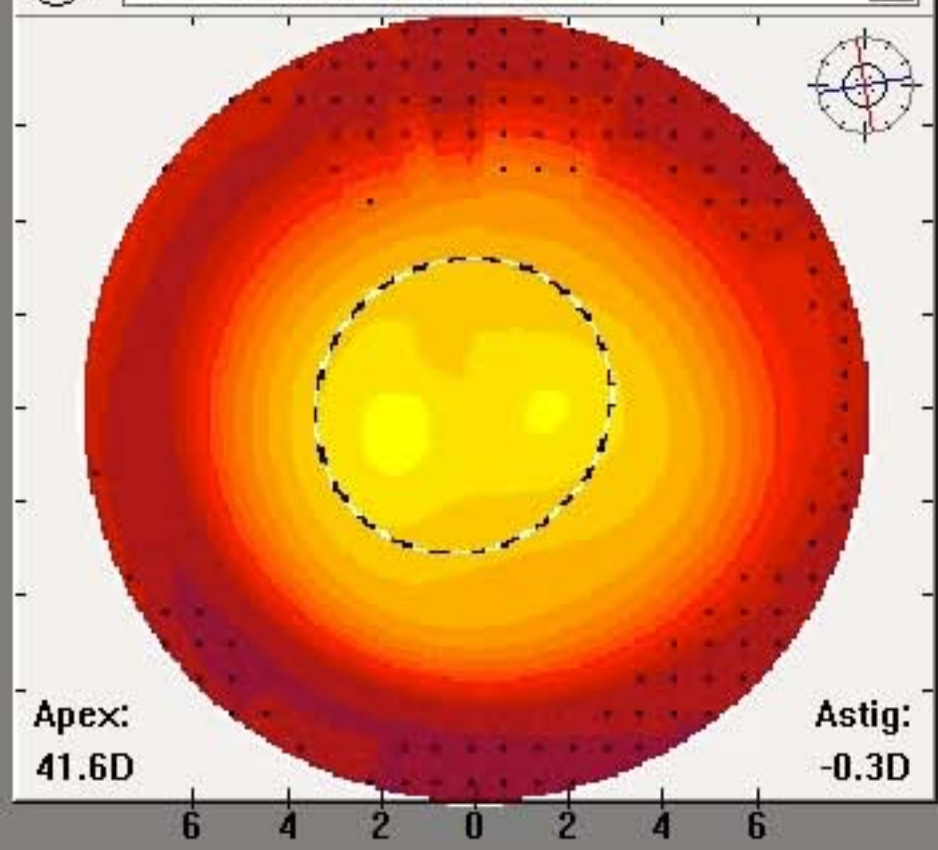
Table 1. Simple linear regressions between the change in axial length at 2-years relative to baseline and the change in corneal power at each of the corneal areas relative to baseline and the change in central corneal power following short- (3 months) and long-term (24 months) OK lens wear. N, nasal; T, temporal; I, inferior; S, superior; H, horizontal; V, vertical; Para, paracentral; Peri, pericentral.



Name: \_\_\_\_\_



① POST-ORTHOKERATOLOGY



② PRE-ORTHOKERATOLOGY

