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Jonuscheit, Sven; Doughty, Michael; Martin, Raul; Rio-Cristobal, Ana

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Relationship between Corneal Thickness and Radius to Body Height

Sven Jonuscheit, PhD, FAAO, Michael J. Doughty, PhD, Raúl Martín, PhD, and Ana Rio-Cristobal, PhD

Vision Sciences, Department of Life Sciences (SJ, MJD), Anterior Eye Research Group (SJ, MJD), Institute for Applied Health Research, Glasgow Caledonian University, Glasgow, United Kingdom, Departamento de Física Teórica, Atómica y Óptica (RM, AR-C), and Instituto Universitario de Oftalmobiología Aplicada (IOBA Eye Institute) (RM, AR-C), Universidad de Valladolid, Valladolid, Spain

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ABSTRACT

Purpose. To investigate the possible association between body stature (height) and corneal thickness and radius in younger-adult Caucasians, especially within the context of previously published literature. **Methods.** Body height and weight were measured in 109 healthy subjects, with an average age of 24 ± 6 years (mean ± SD). Subjects underwent an ophthalmic assessment including anterior segment imaging by Scheimpflug topography and specular microscopy. Central and peripheral corneal thickness as well as corneal radius were analyzed. The relationship between body stature and corneal parameters was assessed using simple and multiple regression analysis. Effect size was determined by generating regression and correlation coefficients. **Results.** Body height ranged from 1.54 to 1.86 m (mean ± SD 1.67 ± 0.08 m), central corneal thickness from 465 to 629 μm (554 ± 33 μm), while corneal radius measured between 7.16 to 8.49 mm (7.75 ± 0.24 mm). Body height was weakly associated with central corneal thickness and peripheral corneal thickness ($r \geq -0.180$), and moderately with corneal radius ($r = 0.351$). Based on the regression equations, central corneal thickness decreases by 8 μm, while corneal radius increases by 0.11 mm for each 0.1 m difference in body height. No significant correlations were found for similar assessments using body weight or body mass index. **Conclusions.** Differences in corneal radius and corneal thickness can be linked to body stature. However, effect sizes were consistently small and no more 13% of the variability in corneal curvature could be explained by variations in body stature.

Key words: corneal thickness, corneal radius, body height, body weight, body stature, effect size

Corneal thickness is an important anatomical characteristic of the anterior eye and a useful indicator of corneal health,[1] a specific indicator for corneal abnormalities[2] and an essential determinant for suitability of refractive surgery.[3]

An analysis, however, of the literature reporting human corneal thickness over a 30-year period indicated that a wide range of values could be encountered for nominally healthy adults and, at best, values between 473 and 595 µm would be within normal limits.[1] While some of the differences between studies can be attributed to the use of different measuring devices or different underlying optical principles,[1,4] no substantial or consistent differences in central corneal thickness in adults appeared to exist for those of Caucasian origin when age, gender or refractive error were considered. The latter aspect has been confirmed in more recent studies.[5]

A factor not considered in the meta-analysis undertaken in 2000 on the expected normal values for corneal thickness in adults[1] was that of the stature of an adult individual, as assessed by height or body mass. Early, growth-related changes in the cornea, including in its thickness, can be expected to occur in infancy and perhaps into early childhood.[6,7] Similarly, age-related changes in eye growth, notably the axial length of the eye, can be expected over the same time period and extending to early adult years with such changes likely being dependent on the refractive error that develops in the growing eye.[8,9]

The issue of adult body stature and the cornea has been considered in a number of recent population-based assessments, with body height as a factor contributing to inter-individual corneal thickness variability[10-13] and to differences in radius of curvature of the cornea.[14-16] Consideration has also been given to body weight and corneal thickness[10,13,14,17-19] or body mass index (BMI) and corneal thickness.[18,20-23]

The rationale behind these previous population-based studies, and analyses including corneal thickness, appears to have been principally directed towards understanding disease-related changes especially as associated with the onset of severe myopia and other ocular diseases, especially in non-Caucasian individuals. For the most part, individuals over the age of 40 years were those that were studied, and while the outcomes of the analyses have indicated that there could be statistically significant correlations between body height and corneal thickness, for example, the effect size (or magnitude) of any such relationship was not addressed or elaborated upon in most of these studies.[10-23] Stated another way, it is unclear how substantial any inter-dependency between body stature and corneal thickness or other corneal parameters such as anterior corneal radius of curvature (corneal radius) might be in fully grown younger adults, as opposed to growing children or teenagers. Without this specific information on effect size, it is not possible to assess whether such associations are of clinical relevance (e.g. does body height need to be considered in interpretation of pachymetry or keratometry-based findings)?

The purpose of this study was to further investigate the anatomical and statistical relationship between body stature and both corneal thickness and corneal radius in normal healthy young adult Caucasian subjects with a particular focus on the effect size of such relations. The secondary aim was to re-examine the existing literature on the topic. The outcome of this study provides valuable information because the relationship between body stature in adults and ocular dimensions may be useful in understanding the process of emmetropization.[15]

SUBJECTS AND METHODS

The study adhered to the tenets of the Declaration of Helsinki and the protocol was approved at the respective institutional ethical review boards at Glasgow Caledonian University and the University of Valladolid. Following written informed consent subjects were asked to complete a version of an Ocular Comfort Questionnaire,[7] which includes questions on the eye and general health, on current spectacle and contact lens wear, and medication use. Subjects with active ocular inflammation, previous ocular surgery, and rigid contact lens wear were excluded. Soft contact lens wearers were instructed to remove their contact lenses at least 24 hours prior to participating in the study. All measurements were taken during waking hours and between 10 am and 5 pm to minimize the effect of diurnal variations.[24,25]

Body Measurements

Subjects were asked to remove shoes and any jackets or overcoats prior to obtaining height and weight measurements. Body height was measured using a standard height scale and recorded in meters (m) to 0.01 m accuracy. Body weight was assessed using a calibrated scale and recorded in kilograms (kg), to 0.1 kg accuracy. In order to obtain a quantifiable index of body height to weight, the body mass index (BMI) was calculated as weight in kilograms divided by the height in meters squared (kg/m^2).[26]

Instrumentation and Ocular Assessments

Subjects underwent an ophthalmic assessment. Habitual visual acuity was obtained using a standard Snellen chart. Slit-lamp biomicroscopy and optical coherence tomography of the anterior segment (Topcon 3D OCT2000, Topcon Corporation, Tokyo, Japan) were carried out to confirm ocular health of the anterior segment. Non-contact specular microscopy of the central cornea (Topcon SP2000, Topcon Corporation, Tokyo, Japan) was performed to rule out corneal endotheliopathy or any other notable corneal endothelial abnormalities. The anterior segment was then assessed using the Pentacam Scheimpflug system (Pentacam, Oculus GmbH, Wetzlar, Germany). Two Pentacam measurements of the same eye were performed, with the subjects being asked to blink and reposition between scans and with the automatic release mode used to minimise observer-related variability. Corneal thickness was extracted from topographic maps at 1 mm increments including the apex (central corneal thickness) and peripheral nasal and temporal locations up to 5 mm away from the apex at 11 locations along the horizontal corneal meridian. The mean corneal radius was recorded. The mean of two scans was used for analyses.

Statistical Analysis

One eye per subject was used for analyses, which were carried out using the Stata SE version 13.1 software (Stata Corporation, College Station, TX). Descriptive statistics including the mean and standard deviation were generated, and the normality of data set distribution tested using the Shapiro-Wilk test. Appropriate parametric and non-parametric tests were used to assess differences. Spearman's rank correlation and linear regression analysis were used to assess associations between body stature and ocular measurements. Simple and multiple regression models were applied. Effect size was determined by generating regression and correlation coefficients and the coefficient of determination where appropriate. A sub-group analysis was carried out for two refractive groups, namely myopic and emmetropic subjects. Myopia was defined as spherical equivalent refractive error of < -0.50 D and emmetropia as >= -0.50 <= +0.50 D. A p-value of $\leq$ 0.05 was considered statistically significant.

RESULTS

Subject Demographics, Body and Corneal Measurements

One hundred and nine eyes of 109 healthy Caucasian subjects (72% female) with a mean (± SD) age of 24 ± 6 years were assessed. The body height measures ranged from 1.54 to 1.86 m and were rather heterogeneous and not normally distributed (p = 0.003, Shapiro-Wilk test). The mean height was 1.67 ± 0.08 m. The mean body weight was 65.0 ± 12.3 kg, and the resultant mean BMI was 23.21 ± 3.86 kg/m^2.

Central corneal thickness ranged from 465 to 629 μm and was normally distributed ($p = 0.886$). The mean central corneal thickness for all subjects was 554 ± 33 μm. Corneal thickness increased progressively and asymmetrically from the corneal apex to the periphery with a significantly greater thickness at all nasal locations as compared to the corresponding temporal sites ($p < 0.001$, related samples t-test). Corneal thickness increased by 32 % to 733 ± 42 μm at 4 mm and by 51 % to 833 ± 50 μm at 5 mm nasally from the apex. For the temporal aspect, corneal thickness increased by 21 % to 674 ± 41 μm at 4 mm, and by 40 % to 773 ± 49 μm at 5 mm temporally from the apex. Therefore, the corresponding nasal peripheral corneal thickness at both, the 4 and 5 mm locations, was on average about 10 % greater than the corresponding temporal values. The mean corneal radius was 7.75 ± 0.24 mm (range 7.16 to 8.49 mm) and the data were normally distributed ($p = 0.167$). Corneal power averaged 43.63 ± 1.32 D (range 39.75 to 47.15). Subgroup analysis of myopic and emmetropic individuals revealed that myopic ($n = 49$) and emmetropic ($n = 55$) subjects had a similar mean corneal radius with 7.73 ± 0.26 mm, and 7.76 ± 0.22 mm respectively ($p = 0.536$, One-way ANOVA), while corneal power was 43.73 ± 1.47 D for myopic and 43.53 ± 1.21 D for emmetropic individuals ($p = 0.457$).

Correlations between Body Height, Corneal Thickness and Corneal Curvature

Assessments were made of whether or not corneal thickness showed any predictable association with body height (Figure 1). For central corneal thickness (Figure 1A), a weak and just statistically significant association was observed with taller subjects having lower corneal thickness values (Spearman's correlation, $p = 0.043$, rho = -0.195). However, this association failed to reach statistical significance when simple linear regression was applied ($p = 0.061$, Pearson's $r = -0.180$). The regression coefficient, also termed the slope of the regression, was -77.6 μm/m, indicating that for each 0.1 m (10 cm) increase in body height the central corneal thickness would decrease by approximately 7.8 μm.

A statistically significant, but weak inverse association was observed for nasal peripheral corneal thickness 4 mm from the apex (Figure 1B, p = 0.004, r = - 0.271), but this relationship failed to reach statistical significance temporally (Figure 1C, p = 0.078, r = - 0.169). Using Pearson's regression or applying Spearman's correlation analyses, central, mid-peripheral, and peripheral corneal thickness were inversely associated with body height at most locations along the horizontal meridian and consistently slightly stronger for nasal corneal thickness as compared to temporal measurements (Table 1). Using Spearman's correlation, the strongest correlation was observed at 4 mm nasally (p = 0.003, rho = -0.280).

Statistically significant and positive associations were noted between height and corneal radius, with a taller stature being associated with a flatter corneal curvature (simple linear regression, p = < 0.002, Pearson's r = 0.351). The effect size (regression coefficient) was + 1.09 mm/m, indicating that for each 0.1 m (10 cm) difference in body height, corneal radius would differ by 1.1 mm (Figure 2). Similar results were observed when applying Spearman's correlation analysis (p = 0.002, rho = 0.351).

Applying regression analysis to the myopic and emmetropic subgroups, a slightly stronger effect size was observed between height and corneal radius for the myopic (Figure 2B; p = 0.002, r = 0.423), but not for the emmetropic subjects (Figure 2C; p = 0.099, r = 0.225). Applying Spearman's analyses, the association was again confirmed in myopic subjects (p = 0.003, rho = 0.415), but the relationship failed to reach statistical significance in emmetropes (p = 0.105, rho = 0.220).

Multiple regression models (all subjects) with age, gender, height, and weight as independent variables, returned body height as the only significant factor associated with corneal radius while controlling for the other independent variables (p = 0.015, R^2 = 0.13). Multiple regression also indicated statistically significant inter-dependencies of body height with central corneal thickness (when adjusted for corneal radius) ($p \leq 0.018$). Corneal thickness and radius were not associated ($p = 0.350$, $r = 0.091$).

DISCUSSION

The present cross-sectional analyses, on younger Caucasian adults, indicate that body stature could have a small contributory effect in determining corneal thickness of an individual. Perhaps more importantly, this body height-related effect is more pronounced for the progressive increases in thickness from the central cornea to the periphery. Such an association also appears to be linked to corneal curvature so that, overall, thinner and flatter corneas could be predicted for taller individuals and *vice versa*. The instrument used in the present studies was the Pentacam, which provides repeatable central, mid-peripheral, and peripheral corneal thickness readings, allowing for high resolution and repeatable assessments of regional (geographic) differences in corneal thickness.[27] Corneal thickness and other biometric measurements of the cornea are valuable in clinical assessments of corneal health[2] and increasingly important in corneal and anterior segment surgical procedures.[14] Assuming that the algorithms for generating corneal thickness profiles and the corneal curvature do provide independent measurement outcomes, the present analyses indicate that body stature could have a slightly greater effect on corneal radius than corneal thickness values.

Recent work has indicated that genetic factors have a greater contribution to the development of refractive error than environmental factors.[28] As body height is strongly influenced by genetics,[29] it seems appropriate to investigate the link between height and corneal radius in detail. Our study provides further evidence for the complex and multifactorial nature of the process steering emmetropization. The present study provides an important extension of previous research on the possible influence of body stature on corneal metrics, with a particular focus on a less frequently assessed cohort of younger Caucasian adults. However, the present analyses indicate that the effect size of any such relationship in younger adults was small.

Refractive error, and especially the development of myopia, is a considerable public health concern.[30] Wu and colleagues discuss the complexity of refractive error development, including the influence of genetic and environmental factors. The results of their biometric study on more than 2000 adult Burmese subjects aged 40 years and older, indicate that body stature may be associated with the development of refractive error, in that a moderate association (correlation coefficient 0.302) between body height and axial length was observed.[11] The present study supports the notion of a possible association between body stature and refractive development in that body height and corneal radius were correlated.

Even though correlation does not imply causality,[31] the present study adds a new and interesting perspective to the issue of refractive error development, specifically in younger Caucasian adults. Previous research has linked corneal radius with refractive error and corneal radius has been shown to be independently associated with refractive error, even though the balance between structural components is the key determinant for the development of myopia. A recent study by Richdale and co-workers also indicated that a steeper corneal radius can be linked with increasing myopic refractive error in adults aged 30 to 50 years. The magnitude of the effect size (i.e. the regression coefficient) was -0.16, which was slightly lower compared to the effect size for the association between height and corneal radius noted in the present study (0.35).[32]

These findings and those of the present study support the sentiment that many factors including ocular variables, body stature, and environmental factors contribute jointly to the ultimate refractive error of an individual. Extending the concept of multi-causality, it could be anticipated that each of the contributing elements accounts for a limited proportion of the variability in refractive error only, leading to comparatively small effect sizes, even when the number of study participants is substantial.

Body stature (as assessed by measurements such as body height and weight) has been included in various analyses undertaken in a number of population-based studies to identify correlates of body development and risk factors for various ocular and systemic diseases.[10-14,17,18,21] These studies provide little or no indication of the effect size and / or the clinical significance of body stature on corneal parameters (e.g. how much of a difference in body height would be needed to have a clinically important impact on corneal thickness or curvature). This type of outcome is different to simply assessing whether or not statistically significant effects or interactions were present.

In such studies, assessments of the relationship between body stature and corneal thickness or corneal radius have been undertaken, albeit not with such analyses being the primary study aim. Multiple regression models have been devised with corneal thickness or corneal radius as inter-dependent parameters alongside body stature. For example, body height has been considered as a factor contributing to differences in corneal thickness,[10-13,17,19,22] as well as radius of curvature of the cornea,[14-16] but usually with inconsistent detail being provided to indicate the effect size or even the overall predictability of these effects. For most of these previously published cross-sectional studies, positive correlation coefficients were generally only around 0.1,[10,11,17,18] although one study which included younger adults reported a correlation coefficient of 0.44 for the association between body height and corneal thickness.[12] No body height effect was noted in other reports,[18,33] despite a significant effect for body weight being noted.[18] These publications have not usually included examples of regression plots that could be derived from univariate analysis and which could indicate important characteristics such as the distribution of the data. Similarly, in most of the publications on this topic, little indication has been provided on the proportionality of the predicted interactions, especially as based on the effect size generated from regression analyses. Scatterplots and effect size analysis are provided in the present studies and help to highlight the tenuous nature of any possible correlations between body stature and corneal metrics.

In the cohort evaluated in the present studies, the relationship between body height and corneal thickness was inverse, whereas a positive relationship was noted between height and corneal radius. This is consistent with the outcome of a recent study reporting on older Caucasian subjects, where application of multiple regression analyses, including age as a factor, also indicated a negative correlation could exist between corneal thickness and body height.[13] Multivariate analyses indicated that each 10 cm increase in body height would be associated with a 3.18 μm decrease in central corneal thickness. The outcome of the present study is in agreement with these results i.e. taller people might have slightly thinner corneas and with the overall effect being of 8 μm/0.1m (10 cm) height difference. In other multivariate analyses, an effect was noted,[19] but no details were provided (especially as to whether the effect was positive or negative), while in other reports no predictable relationship was evident.[10-12,17] The effect size for the relationship between body stature and corneal radius was similarly small.

Most of the previously published studies were conducted on older adults with the minimum age usually being 40 years and extending to at least 80 years. In such studies, any contribution of stature (body height) to corneal parameters should be considered to be a residual effect of body and eye growth in infancy and childhood. The same limitation applies to the present cross-sectional studies on young adults, and it would useful for longitudinal studies to be undertaken on body stature and corneal thickness during early childhood years alongside measures of axial length and refractive error.

Overall, while numerous studies have indicated that central corneal thickness in adults has a wide range, there does not appear to be a substantial influence of body stature on central corneal thickness. While customizing refractive surgery based on an ever-increasing number of metrics could improve surgical outcomes, body stature is unlikely to be a significant parameter, since effect size in this and in previous studies was consistently small. The same conclusion can be applied to IOP assessments, where the magnitude of any corneal difference is likely well below that which might affect tonometry outcomes.[1] This seems to apply to different age and ethnic groups. Our structured review of the literature indicated that a detailed analyses on the topic does not appear to have been undertaken recently. However, earlier studies also show that larger sample sizes, such as those of population-based studies, while allowing for useful complex multivariate regression models and the controlling of a wide range of possible confounding variables, do not lead to any better predictability or to a larger effect size.

This study adds to the literature by providing a detailed review of the literature of the topic, a detailed consideration of effect sizes, and the addition of new data relating to the refractive error development specifically in younger Caucasian adults. The outcome of this study has relevance to the correction of myopia, including the surgical correction of refractive error, in particular laser refractive surgery. Studies investigating the effect of corneal radius on laser ablation depth have shown that the effective ablation depth decreases with an increasing corneal radius.[34] Based on the outcome if our study, taller patients are likely to have flatter corneas and therefore require lesser ablation depths for a given surgical correction of their refractive error.

The study is potentially limited by the relatively small sample and by the restriction to one ethnic group. Further research is needed to assess whether or not body stature and corneal parameters are related in populations and ethnic groups with a high prevalence of myopia.

In summary, the evidence for meaningful inter-dependence of body height and corneal parameters appears to be weak and ambiguous. The same applies to considerations of inter-related metrics such as body weight and BMI. The effect sizes of any such relationships are relatively small with no more than 13% of variability in corneal parameters being accounted for by body height, while controlling for variations in age, gender, and weight. The outcome of the present studies and the objective analysis of the literature do not support the notion of including body stature in routine clinical practice such as pre-operative assessments.

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Corresponding author:

Sven Jonuscheit
Vision Sciences, Department of Life Sciences
Glasgow Caledonian University
Cowcaddens Road
Glasgow, G4 0BA
UNITED KINGDOM
e-mail: sven.jonuscheit@gcu.ac.uk

Table 1. Outcome of simple linear regression and Spearman's correlation analysis between body height (independent variable) and corneal thickness at central, mid-peripheral, and peripheral locations.

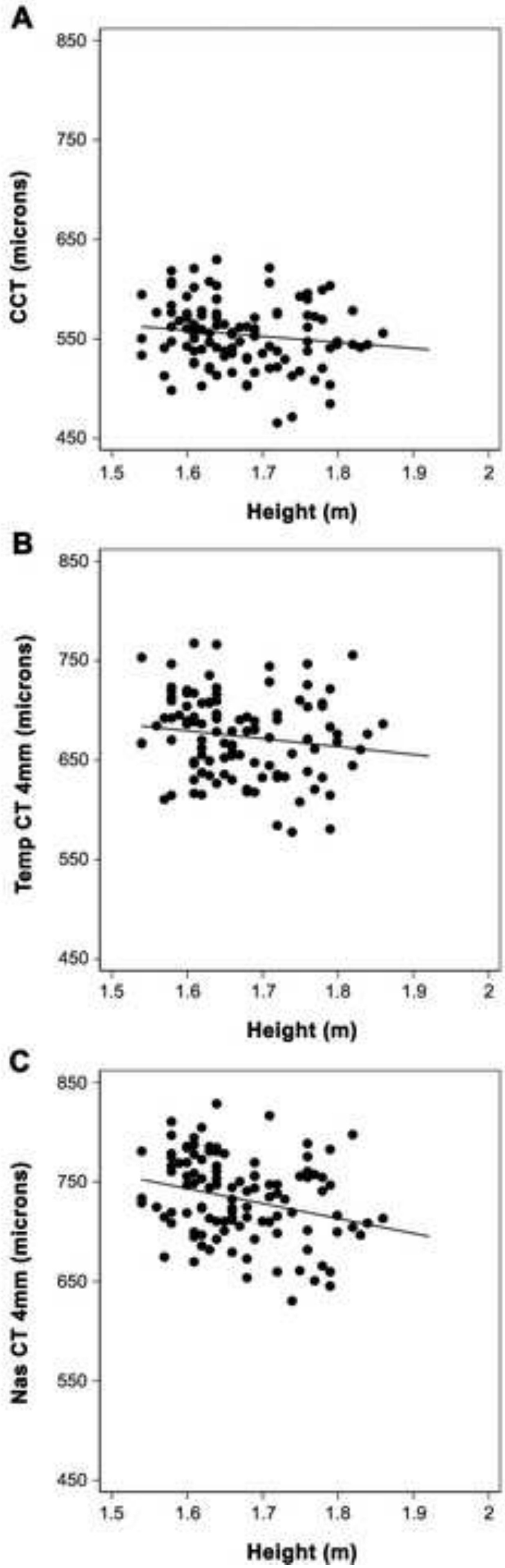
Corneal thickness location (dependent variable)	Linear regression (Pearson's r)	p-value	Spearman's rho	p-value
Temporal 5 mm	-0.194	0.043*	-0.227	0.018*
Temporal 4 mm	-0.169	0.0780	-0.201	0.036*
Temporal 3 mm	-0.170	0.078	-0.195	0.043*
Temporal 2 mm	-0.119	0.218	-0.192	0.044*
Temporal 1 mm	-0.157	0.103	-0.178	0.064
CCT (apex)	-0.180	0.061	-0.195	0.043*
Nasal 1 mm	-0.207	0.031*	-0.213	0.026*
Nasal 2 mm	-0.233	0.015*	-0.231	0.016*
Nasal 3 mm	-0.241	0.012*	-0.250	0.008*
Nasal 4 mm	-0.271	0.004*	-0.280	0.003*
Nasal 5 mm	-0.188	0.051	-0.211	0.028*

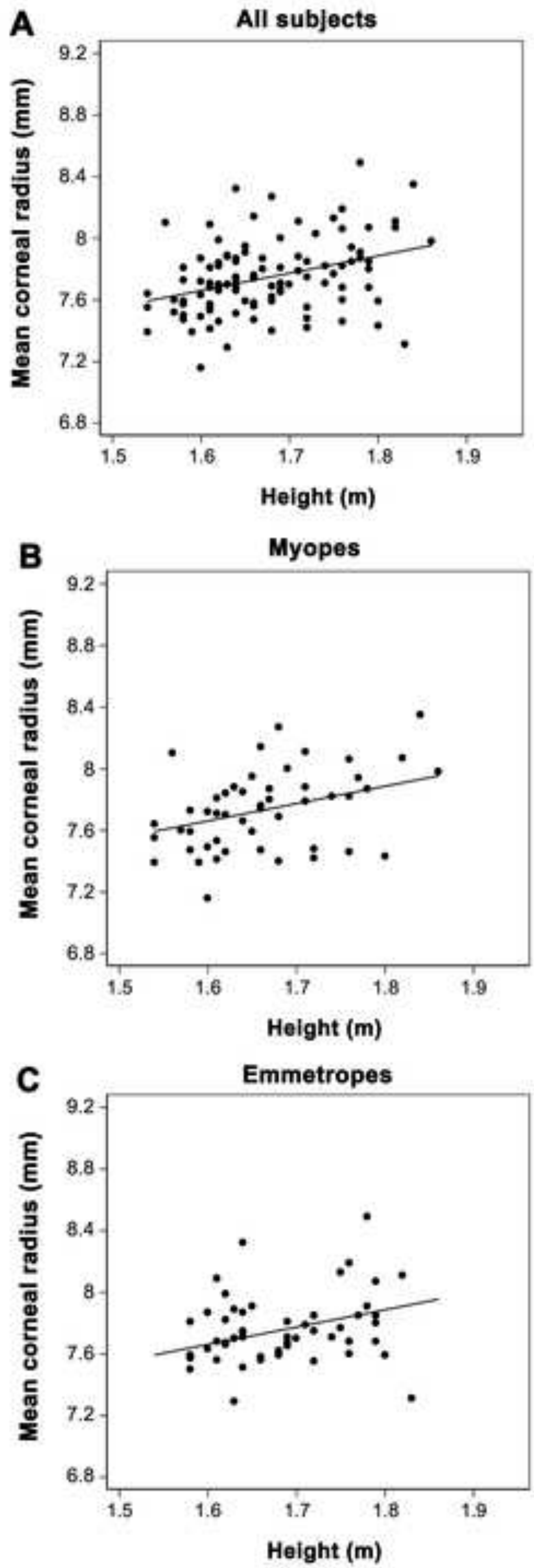
The asterisk * indicates a statistically significant relationship.

FIGURE LEGENDS

Figure 1. Scatterplots to illustrate the observed relationship between body height (in meters) and **(A)** central corneal thickness, **(B)** nasal corneal thickness at 4 mm, and **(C)** temporal corneal thickness at 4 mm. All thickness measures are given in μm. The lines are those from application of a simple linear regression analysis.

Figure 2. Scatterplots to illustrate the observed relationship between body height (in meters) and anterior corneal curvature in **(A)** all subjects, **(B)** myopic, and **(C)** emmetropic subgroups. Curvature measures are given in mm. The lines are those from application of a simple linear regression analysis.


A
850
750
650
550
450
CCT (microns)
1.5
1.6
1.7
1.8
1.9
2
Height (m)
B
Temp CT 4mm (microns)
Height (m)
C
Nas CT 4mm (microns)
Height (m)


A
All subjects
Mean corneal radius (mm)
9.2
8.8
8.4
8
7.6
7.2
6.8
1.5
1.6
1.7
1.8
1.9
Height (m)
B
Myopes
Mean corneal radius (mm)
Height (m)
C
Emmetropes
Mean corneal radius (mm)
Height (m)