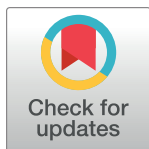RESEARCH ARTICLE

The effect of transverse ocular magnification adjustment on macular thickness profile in different refractive errors in community-based adults

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Abstract

Purpose

Changes in retinal thickness are common in various ocular diseases. Transverse magnification due to differing ocular biometrics, in particular axial length, affects measurement of retinal thickness in different regions. This study evaluated the effect of axial length and refractive error on measured macular thickness in two community-based cohorts of healthy young adults.

Methods

A total of 2160 eyes of 1247 community-based participants (18–30 years; 23.4% myopes, mean axial length = 23.6mm) were included in this analysis. Macular thickness measurements were obtained using a spectral-domain optical coherence tomography (which assumes an axial length of 24.385mm). Using a custom program, retinal thickness data were extracted at the 9 Early Treatment of Diabetic Retinopathy Study (ETDRS) regions with and without correction for transverse magnificent effects, with the corrected measurements adjusting according to the participant's axial length. Linear mixed models were used to analyse the effect of correction and its interaction with axial length or refractive group on retinal thickness.

Results

The raw measures (uncorrected for axial length) underestimated the true retinal thickness at the central macula, while overestimating at most non-central macular regions. There was an

axial length by correction interaction effect in all but the nasal regions (all $p<0.05$). For each 1mm increase in axial length, the central macular thickness is overestimated by 2.7–2.9µm while thicknesses at other regions were underestimated by 0.2–4.1µm. Based on the raw thickness measurements, myopes have thinner retinas than non-myopes at most non-central macular. However, this difference was no longer significant when the corrected data was used.

Conclusion

In a community-based sample, the raw measurements underestimate the retinal thickness at the central macula and overestimate the retinal thickness at non-central regions of the ETDRS grid. The effect of axial length and refractive error on retinal thickness is reduced after correcting for transverse magnification effects resulting from axial length differences.

Introduction

The retinal thickness profile is a useful indicator in early detection and monitoring of various diseases [1, 2]. Using optical coherence tomography (OCT) imaging, central retinal thickening has been associated with exudative macular degeneration [3] and diabetic macular oedema [4], while thinning has been associated with loss of retinal nerve fibre layer (RNFL) [5, 6] and refractive error [7].

OCT imaging has been extensively used to assess the central and peripheral retinal thickness profile. Using OCT, changes in retinal thickness associated with axial length and/or refractive errors have been reported [8–11]; however, findings have not been always consistent. Studies have generally found that the central macular (fovea) thickness is positively associated with axial length, indicating myopic eyes exhibited a thicker central macula than non-myopic eyes [10, 12–19]. However, evaluation of the peri- and/or para-macular regions show conflicting findings; some studies have found thinner retinal thickness in inner and outer rings with axial elongation [8–12, 14, 15, 17–22] while others found no significant association [23–30]. In addition to considering the potential confounding factors such as the difference in the method of measuring retinal thickness, refractive error, and participants' demographics of these studies, it is worth noting that some of these studies have not corrected for variations in the transverse magnification of the OCT images due to differences in ocular biometrics [8, 9, 12–22, 28, 30–32].

Variations in transverse magnification are largely due to differing axial lengths [33] and lead to changes in the transverse area of a pixel in the OCT image. Thus, while imaging eyes that are longer (more myopic) relative to the assumed axial length of the OCT system, a larger retinal area is captured. Since the retina is thickest at the parafoveal area and thins towards the fovea and the periphery, imaging of the retina over a larger area causes lower thickness values from more peripheral data points to be included in the analysis, while foveal thickness may be overestimated as the retina is thickest at the regions immediately surrounding the fovea (parafoveal regions). This leads to an underestimation of the peripheral macular thickness in longer eyes (e.g. in myopia), compared to those with shorter axial lengths (e.g. emmetropia and hyperopia). Using a Cirrus OCT, Odell et al. [34] found that the actual scan size of a 6 mm scan protocol may vary from 5.3 to 7.0 mm in a sample with axial length range 21.5 to 28.3 mm. This has practical implications, as altering the size of the OCT scanning area and other

transverse boundaries results in under- or over-estimation of macular thickness. Thus, when assessing retinal thickness at a particular distance from the fovea, the placement of the measurement region should be adjusted to compensate for transverse magnification effects.

Unfortunately, many studies [8, 9, 12–22, 28, 30–32] do not account for transverse magnification effects when measuring retinal thickness with OCT, likely because there is usually no built-in function in OCT software to correct for participants' ocular biometrics, including axial lengths. Some studies have corrected for transverse magnification using custom-written programs; however, such an approach is not readily available or feasible in the clinical practice [35–41]. The influence of transverse magnification correction on posterior tissue thickness measurements has been evaluated [35–38]; however, most have explored the effect of transverse magnification on the peripapillary retinal fibre layer thickness (RNFL) [35, 36, 38–41], or recruited mainly myopic participants and were thus are not representative of the general population [29]. There are limited population- or community-based studies exploring the effect of transverse magnification correction on retinal thickness or the association between axial length and retinal thickness, especially in a sample with a wide range of refractive errors.

Retinal thickness measurements may serve as an important biomarker in several ocular disease. However, accurate retinal thickness measurement is affected by transverse magnification effects, which are mainly caused by differing axial lengths. With myopia prevalence expected to increase in the next few decades [42]; it is becoming increasing critical to account for transverse magnification effects during OCT measurements. Given that axial length is a relatively easy measurement to obtain in a clinical setting, and has a major impact on transverse magnification, it may be justified to adjust for transverse magnification effects caused by differing axial lengths, where possible. To demonstrate how transverse magnification affects retinal thickness measurements, this study evaluated the effect of correction for transverse magnification based on differing axial lengths on two community-based samples with a wide range of refractive errors.

Methods

Study sample

Young healthy community-based adults were recruited from two cohort studies–Generation 2 (Gen2) of the Raine Study [43] and the Kidskin Young Adults Myopia Study (K-YAMS) [44]. Methodology for the eye examinations in both studies have been described previously [43, 44]. Briefly, for the Raine Study, 2,900 pregnant women were seen at the King Edward Memorial Hospital from May 1989 to November 1991, to whom 2,868 offspring were born, forming the original study cohort (termed "Gen2"). Since their birth, the Gen2 participants have been undergoing a series of health and medical examinations at various age. At the 20-year follow-up of the Raine Study between 2010 and 2012, the Gen2 participants had a comprehensive eye examination that included spectral-domain optical coherence tomography (SD-OCT) imaging.

The Kidskin Study was a non-randomised controlled trial in Western Australia that tested the value of an educational intervention on sun-protection behaviour in 5- to 6-year-old children in primary schools. The outcome measure was the number of melanocytic naevi on the backs of these children. Between 2015 and 2019, when they were 25–30 years of age, participants were invited to attend a comprehensive eye examination as part of the K-YAMS. The purpose of that eye examination was to explore whether these early educational interventions influence myopia development [45].

Both studies were conducted in accordance with the Declaration of Helsinki and were approved by the University of Western Australia Human Research Ethics Committee

(Approval reference numbers RA/4/20/5722 and RA/4/1/6807) and all participants provided informed consent prior to data being collected.

Eye examination

The eye examination included autorefraction and keratometry (Nidek ARK-510A Autorefractometer [Nidek Co Ltd, Tokyo, Japan]), ocular biometry (IOLMaster v 5 [Carl Zeiss Meditec AC, Jena, Germany]), and SD-OCT imaging Spectralis HRA+OCT [Heidelberg Engineering, Heidelberg, Germany]) [43, 44]. Autorefraction was taken at least 20 minutes after instillation of one drop of 1% tropicamide. The autorefractometer averages the measurements of three readings, and refraction was quantified using spherical equivalent, determined as spherical dioptre + ½ cylindrical dioptre. The IOLMaster calculates the mean of five A-scan measurements to obtain the axial length used for analyses. A-scan measurements that fall outside one standard deviation of the mean are removed from the computation.

A Spectralis spectral-domain OCT (SD-OCT) was used to image the macula, with an axial and transverse resolution of 3.9 and 5.6 μm, respectively. Macular thicknesses of both eyes were obtained using a 31-line raster scan of 30˚ horizontal and 25˚ vertical area centred on the fovea [46], obtained using high-resolution mode and with "Automated Real Time (ART)" of 9 taken per raster scan. Prior to imaging, the corneal radius was entered into the instrument to correct for ocular magnification effects due to corneal curvature, as per the manufacturer's protocol. However, since the Heidelberg system does not provide the option to alter the axial length, all scans were taken with the default axial length of 24.385 mm, similar to the process in clinical practice. Scans with signal-to-noise ratio of less than 20 were considered to be of inadequate quality and were discarded from the analysis. Eyes with amblyopia, retinal disorders, and optic disc pathologies were excluded from the study.

The raw SD-OCT scans were exported in E2E format using the built-in export function and analysed using a non-commercial custom program that was developed on MATLAB version R2017b (MathWorks, Inc. Natick, MA, USA) [46]. The transversal scaling (Scaling X) value for each eye, which differed between participants depending on the scan focus and corneal curvature adjustment, was extracted from the "image information" tab of the Heidelberg Eye Explorer. Using the Scaling X and axial length information, the program determines the lateral boundaries of the Early Treatment of Diabetic Retinopathy Study (ETDRS) grid (**Fig 1A**) by adjusting the transversal scale using the participant's axial length and accounting for the Spectralis' pre-set axial length of 24.385 mm [47], using the following equation:

Corrected transversal scale = Scan default transversal scale × (axial length/24.385).
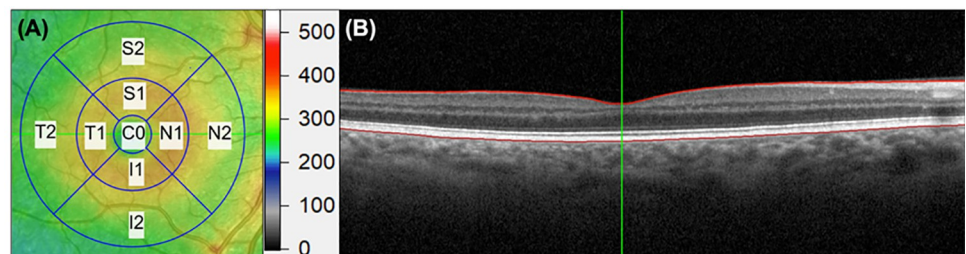
Fig 1. (A) The 9 Early Treatment of Diabetic Retinopathy Study (ETDRS) grid including central macula 0.5 mm radius around the fovea (C), the inner superior (S1), inner inferior (I1), inner temporal (T1), and inner nasal (N1) regions (between 0.5 and 1.5 mm radius around the fovea) and outer superior (S2), outer inferior (I2), outer temporal (T2), and outer nasal (N2) regions (between 1.5 and 3.0 mm radius around the fovea) macular rings. (B) A representative OCT B-scan with segmentation of the inner limiting membrane and retinal pigmented epithelium layer (red lines). Green line marks the foveal centre.

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The program detects the inner limiting membrane layer and retinal pigmented epithelium (**Fig 1B**), and the axial distance between these layers was determined as the full retinal thickness. The thickness values were extracted along each A-scan (axial thickness) [48] and averaged in each ETDRS region to provide the raw (uncorrected for axial length) and corrected retinal thickness.

Statistical analysis

All statistical analyses were conducted using R software v3.6.3 (The R Foundation for Statistical Programming, Vienna, Austria; available at https://www.r-project.org/). The Kolmogorov–Smirnov test was used to confirm that none of the variables departed significantly from a normal distribution. A P value of <0.05 was considered statistically significant.

Linear mixed models (LMMs) were used to analyse the effect of -correction and its interaction with axial length on retinal thickness. The LMMs were generated with random intercepts and slopes for participants to account for the within-participant correlation between two eyes, and correction for gender. To analyse the effect of correction in different refractive groups (myopes; spherical equivalent of $\leq$ -0.50D vs. non-myopes) [49], separate LMMs were generated with refractive groups (myopes and non-myopes) included in the models instead of axial length. Given retinal thickness is known to vary between sexes [50] and possibly ethnicities [51, 52] these were adjusted for in the LMMs. Separate analyses were conducted for the Raine Study and K-YAMS cohorts to evaluate the agreeability between cohorts, as a sensitivity analysis. In all analyses, the restricted maximum likelihood methods were used, and pairwise comparisons with Bonferroni adjustments were conducted for any significant main effects and interactions.

Results

Demographic information

A total of 1589 eyes of 953 participants from the Raine Study and 573 eyes of 294 participants from the K-YAMS were included in the analysis (see **Fig 2** for number of participants or eyes excluded along with reason for exclusion). Demographic and refractive information of the study cohorts are shown in **Table 1**. Distribution of refractive error and axial length are shown in **Fig 3**. The raw and -corrected retinal thickness values in myopes and non-myopes are shown in **S1** and **S2 Figs.**

Main effect of correction

There was a small but statistically significant difference in corrected and raw retinal thickness while adjusting for sex and ethnicity in most macular ETDRS regions (all p < 0.001). As shown in **Fig 4**, raw measures underestimated the retinal thickness at the central macula, while overestimating retinal thickness at most non-central macular regions in both the Raine and K-YAMS studies.

Axial length by correction interaction effect

There was a significant axial length-by-correction interaction effect in all but the nasal regions (all p < 0.05). **Fig 5** shows the axial length-by-correction interaction effect in each region while adjusting for sex and ethnicity in both the Raine Study and KYAMS cohorts. These findings indicate that for each 1mm increase in axial length, the central macular thickness is overestimated by 2.7 to 2.9μm when the measurements are not corrected for transverse magnification effects (**Fig 3**) but the thickness at the other regions is underestimated by 0.2 to

Raine Study   **K-YAMS**

Attended eye examination

| n= 1,344 | | n= 303 |

Remove:

- *Erroneous/poor-quality scans* — 8 eyes of 4 participants — 69 eyes of 39 participants

- *Pathology* — 4 eyes of 2 participants with previous iritis / 2 eyes of 1 participant with bilateral ODD — 2 eyes of 1 participant with bilateral macular dystrophy / 1 eye of 1 participant with previous BRVO

- *Amblyopia* — 32 eyes of 32 participants with unilateral amblyopia / 8 eyes of 4 participants with bilateral amblyopia — 12 eyes of 12 participants with unilateral amblyopia

- *No refraction data* — 984 eyes of 690 participants — 20 eyes of 16 participants

Final sample

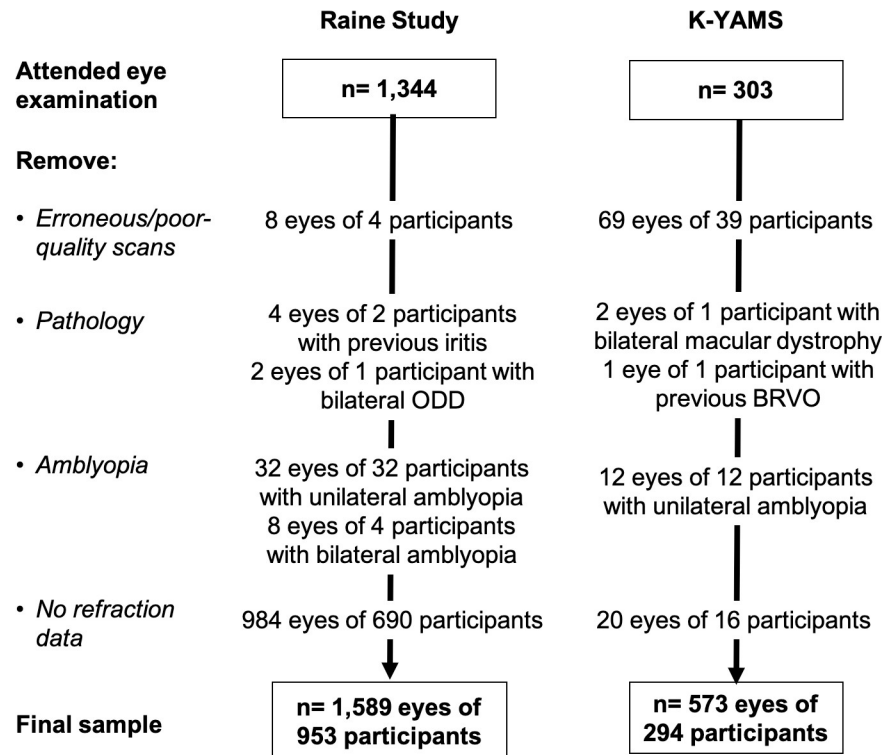| n= 1,589 eyes of 953 participants | | n= 573 eyes of 294 participants |

Fig 2. Sample size and reasons for exclusion from the data analysis in both the Raine Study and K-YAMS cohorts. BRVO = branch retinal vein occlusion, ODD = optic disc drusen.

4.1μm, with the outer temporal region being most affected. As seen in **Fig 5**, the amount of under- or overestimation per 1mm change in axial length was very similar for both cohorts.

The simple effects of axial length on the raw and corrected retinal thickness were analysed separately to explore the effect of correction for transverse magnification on the previously reported association between axial length and retinal thickness.

Table 1. Demographic information of the study participants included.

Factors	The Raine Study Gen2 (n = 953)	K-YAMS (n = 294)
Age (years)	20.1 ± 0.4 (18 to 22)	27.5 ± 1.1 (25 to 30)
Gender: female	467 (49%)	179 (61%)
Spherical equivalent (D)	-0.08 ± 1.55 (Range = -11.25 to +7.25)	-0.35 ± 1.95 (Range = -11.50 to +8.00)
Refractive group (number of eyes)		
• Myopes	345 (22%)	160 (28%)
• Non-myopes	1244 (78%)	413 (72%)
Axial length (mm)	23.6 ± 0.9 (Range = 20.3 to 28.0)	23.6 ± 1.1 (Range = 19.4 to 28.0)
Ethnicity		
• Caucasian	820 (86%)	253 (86%)
• East Asians	20 (2%)	3 (0.1%)
• Other/mixed	113 (12%)	38 (13%)

K-YAMS = Kidskin Young Adult Myopia Study; continuous variables expressed as mean ± standard deviation (and range); categorical variables expressed as number and percentage
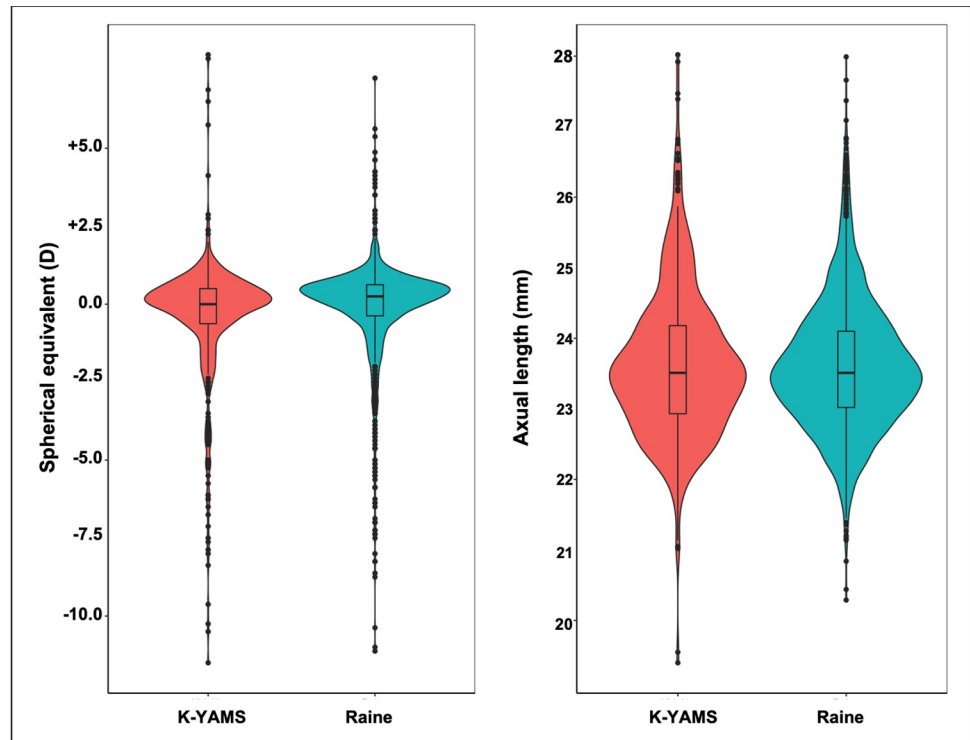
Fig 3. Distributions of refractive errors (D) and axial lengths (mm) in the Raine Study and K-YAMS cohorts.

Using the raw retinal measurements, each millimetre increase in axial length was associated with thinner retinal in the non-central region by -2.1 to -3.0 μm in the Raine Study Gen2 cohort and by -2.0 to -3.4 μm in the K-YAMS cohort (all p<0.001; **Table 2**). Using the corrected data, longer axial length remained significantly associated with thinner retinal thickness
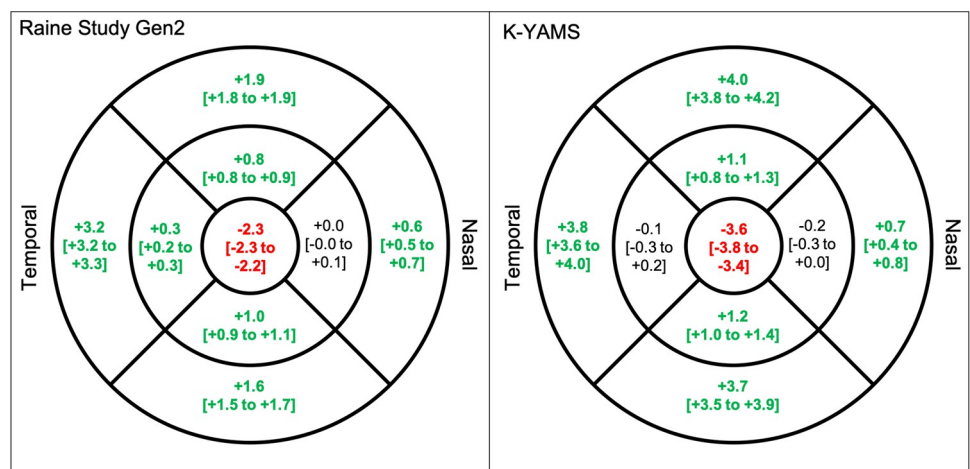
Fig 4. Estimated difference [and 95% confidence interval] in corrected and raw retinal thickness (μm) in (left) the Raine Study Gen 2 (mean axial length = 23.6 ± 0.9 mm) and (right) K-YAMS participants (mean axial length = 23.6 ± 1.1 mm). Significant difference (p< 0.05) shown in bold, with red and green values representing underestimation and overestimation by the raw measurements, relative to the transverse magnification-corrected retinal thickness, respectively. Adjusted for sex and ethnicity. Note that the mean axial lengths of both cohorts are shorter than that assumed by the Spectralis SD-OCT (24.385 mm).

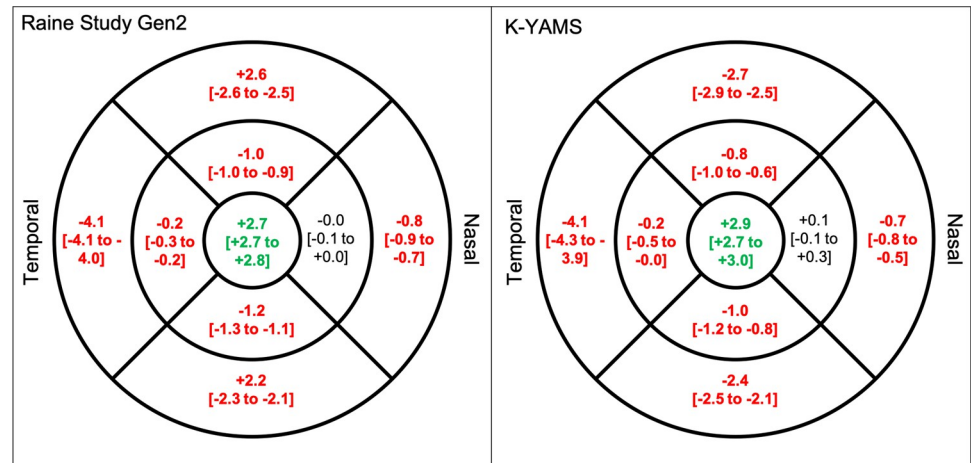**Fig 5. Under- and overestimation of retinal thickness (μm) per 1mm increase in axial length by the raw measurements, relative to the transverse magnification-corrected thickness [and 95% confidence interval] in (left) the Raine Study Gen2 (mean axial length = 23.6 ± 0.9 mm) and (right) K-YAMS participants (mean axial length = 23.6 ± 1.1 mm).** Note that the mean axial length of both cohorts is shorter than that assumed by the Spectralis SD-OCT (24.385 mm). Significant interaction effects (p< 0.05) shown in bold and red (underestimation) or green (overestimation). Adjusted for sex and ethnicity.

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outside the central macula, albeit at generally smaller magnitudes than observed with the raw measurements (**Table 2**). These findings indicate that the effect of longer or shorter axial length on macular thickness may be smaller than previously reported, but still statistically significant. At the central macula, there was no association between retinal thickness and axial length found when using the raw measurements. However, a negative association between retinal thickness and axial length was observed in both cohorts with the corrected measurements. At the outer inferior, temporal and superior regions, longer axial length was associated with thinner retinal thickness before, but not with the corrected measurements.

Table 2. Estimated difference in retinal thickness (μm) per 1mm increase in axial length.

Macular region[a]	The Raine Study Gen2				K-YAMS			
	Raw		Corrected[b]		Raw		Corrected[b]	
	Estimate (95%CI)	p-value	Estimate (95%CI)	p-value	Estimate (95%CI)	p-value	Estimate (95%CI)	p-value
Central	0.2 [-1.1 to 1.4]	0.77	-2.5 [-3.7 to -1.2]	<0.001**	0.7 [-1.2 to 2.6]	0.47	-2.2 [-4.1 to -0.2]	0.029*
Nasal inner	-2.3 [-3.2 to -1.4]	<0.001**	-2.3 [-3.2 to -1.4]	<0.001**	-3.3 [-4.5 to -2.0]	<0.001**	-3.7 [-4.9 to -2.4]	<0.001**
Nasal outer	-2.8 [-3.8 to -1.9]	<0.001**	-1.9 [-2.8 to -0.9]	<0.001**	-3.3 [-4.5 to -2.0]	<0.001**	-2.8 [-4.1 to -1.6]	<0.001**
Superior inner	-2.5 [-3.3 to -1.6]	<0.001**	-1.5 [-2.4 to -0.6]	0.001**	-3.4 [-4.7 to -2.0]	<0.001**	-3.1 [-4.4 to -1.8]	<0.001**
Superior outer	-2.6 [-3.5 to -1.8]	<0.001**	0.0 [-0.9 to 0.8]	0.95	-2.6 [-3.9 to -1.3]	<0.001**	-0.1 [-1.4 to 1.2]	0.88
Temporal inner	-2.2 [-3.0 to -1.3]	<0.001**	-1.8 [-2.6 to -0.9]	<0.001**	-2.0 [-3.3 to -0.7]	0.002**	-2.3 [-3.5 to -1.1]	<0.001**
Temporal outer	-3.0 [-3.8 to -2.1]	<0.001**	1.2 [0.4 to 2.0]	0.003**	-2.6 [-3.8 to -1.4]	<0.001**	0.9 [-0.3 to 2.1]	0.13
Inferior inner	-2.4 [-3.4 to -1.4]	<0.001**	-1.2 [-2.2 to -0.2]	0.020*	-3.0 [-4.3 to -1.7]	<0.001**	-2.5 [-3.8 to -1.2]	<0.001**
Inferior outer	-2.1 [-3.2 to -1.1]	<0.001**	0.1 [-0.9 to 1.1]	0.87	-2.6 [-4.0 to -1.3]	<0.001**	-0.7 [-2.1 to 0.6]	0.28

CI = confidence interval; TM = transverse magnification.

[a] Early Treatment of Diabetic Retinopathy regions

[b] corrected for transverse magnification effects due to differences in axial lengths. Statistically significant at

*p< 0.05 and

**p< 0.01

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Table 3. The mean magnitude of the difference (in μm) and 95% confidence intervals (CI) in retinal thickness of myopes (spherical equivalent ≤ -0.50D), in comparison to non-myopes, based on the raw and corrected data from the Raine Study Gen2 and K-YAMS cohorts.

| Macular region[a] | The Raine Study Gen2 cohort | | | | K-YAMS cohort | | | |
| | Raw | | Corrected[b] | | Raw | | Ccorrected[b] | |
	Estimate [95%CI]	P-value	Estimate [95%CI]	P-value	Estimate [95%CI]	P-value	Estimate [95%CI]	P-value
Central	1.0 [-1.1 to 3.2]	0.34	0.5 [-1.6 to 2.6]	0.64	-0.63 [-3.3 to 2.0]	0.64	-2.3 [-5.0 to 0.4]	0.09
Nasal inner	-1.4 [-2.7 to -0.1]	0.041*	-1.6 [-3.0 to -0.2]	0.024	-0.66 [-1.1 to 2.5]	0.47	-1.8 [-3.5 to -0.1]	0.035
Nasal outer	-2.5 [-4.0 to -1.1]	0.001**	-2.1 [-3.6 to -0.5]	0.010*	-0.10 [-1.8 to 1.6]	0.91	-0.3 [-1.9 to 1.3]	0.72
Superior inner	-1.9 [-3.3 to -0.5]	0.007**	-1.5 [-2.8 to -0.1]	0.040*	-1.72 [-3.6 to 0.2]	0.09	-1.6 [-3.3 to 0.1]	0.06
Superior outer	-2.7 [-4.2 to 1.3]	<0.001**	-1.0 [-2.5 to 0.4]	0.17	-2.48 [-1.5 to -0.5]	0.017*	-1.4 [-3.4 to -0.5]	0.15
Temporal inner	-0.7 [-2.0 to 0.6]	0.29	-0.95 [-2.4 to 0.5]	0.20	1.09 [-0.7 to 2.9]	0.23	-1.5 [-3.0 to 0.1]	0.07
Temporal outer	-3.1 [-4.6 to -1.5]	<0.001**	-0.2 [-1.7 to 1.4]	0.83	-2.24 [-4.0 to -0.4]	0.016*	-0.6 [-2.3 to 1.1]	0.47
Inferior inner	-3.2 [-5.3 to -1.1]	0.003**	-2.1 [-4.0 to -0.1]	0.039*	-1.75 [-0.2 to 3.6]	0.06	-1.6 [-3.4 to 0.2]	0.08
Inferior outer	-3.1 [-5.1 to -1.0]	0.004**	-1.0 [-3.0 to 1.0]	0.34	-1.69 [-3.6 to 0.3]	0.09	-0.8 [-2.7 to 1.2]	0.45

CI = confidence interval; K-YAMS = Kidskin Young Adult Myopia Study; TM

[a] Early Treatment of Diabetic Retinopathy regions

[b] corrected for transverse magnification effects due to differences in axial lengths. Statistically significant at

*p< 0.05 and

**p< 0.01

Main effect of refractive error

Table 3 shows the main effect of myopia, relative to no-myopia, using the raw and corrected macular thickness data. Using the raw data, in the Raine Study Gen2, myopes have thinner retinas compared to non-myopes at most non-central macular regions. However, this difference was no longer significant in most macular regions when the corrected data was used. In the K-YAMS cohort, based on the raw thickness, myopes have significantly thinner retinas at the outer temporal and outer superior than non-myopes (by -1.7 and -2.5 μm, respectively); however, this difference was not statistically significant based on the corrected thickness.

Discussion

This study evaluated the effect of transverse magnification due to differing axial lengths on the macular thickness in the ETDRS grid in two community-based cohorts with a wide range of refractive errors. This study found that, on average, the raw OCT measurements (which assume a more myopic sample than the community-based cohorts) underestimates the retinal thickness at the central macula and overestimate the retinal thickness at non-central regions. Moreover, the main effect of axial length and refractive error disappears or reduces after correction in most of the non-central macular regions. On the other hand, in the central macula, there was an inverse association between corrected thickness measurements and axial length, which was not observed when the raw measurements were used. It is worth noting that the Spectralis SD-OCT used in this study assumes a default axial length of 24.385 mm, which is longer than the mean axial length of 23.60 mm of the participants in this study. This means that the raw OCT measures were averaged over a smaller area (< 6mm diameter) in the current cohorts, result in an underestimation of the retinal thickness at the central macular and overestimation at the more peripheral regions. However, the effect of transverse magnification on an individual's retinal thickness measurements would depend on the relation between participant's axial lengths (and other ocular biometrics measures) and that assumed by the OCT system. For example, an opposite effect would be found in eyes longer than 24.385 mm, with

the raw measurements providing an overestimation of the retinal thickness at the central macula but an underestimation at the non-central macular.

A comparison on the estimated effect on the association between axial length and retinal thickness between the raw and corrected data indicated that the main effect of axial length on retinal thickness was weaker with corrected data, relative to the raw measurements. Nonetheless, the association between axial length and retinal thickness remained significant in most macular regions after correcting for transverse magnification. These results demonstrated that although some, but not all, of the differences retinal thickness found between eyes with and without myopia could be attributed to the miscalculation of the retinal thickness, the axial length still has a significant effect on retinal thickness.

Results from this study showed differences in retinal thickness between myopic and non-myopic eyes is reduced (depending on the region) after correction for transverse magnification due to differing axial lengths. Consistent with our findings, Liu et al. [29] initially found a significant difference in central retinal thickness between myopes and hyperopes but further analyses showed no significant difference between refractive groups after adjusting for ocular magnification.

Transverse magnification effects have also been shown to affect peripapillary RNFL thickness measurements [36, 38–41]. A disc-centred scan would result in a smaller scan area in smaller eyes, thus over-estimating RNFL thickness because of the higher density of nerve fibres closer to the optic disc. In eyes with longer axial lengths, the scan area would be larger than the intended protocol, leading to an under-estimation of RNFL thickness. Hirasawa et al. [35] evaluated the peripapillary RNFL thickness in eyes with axial lengths of 21.2 to 28.3 mm and found that for every millimetre increase in axial length, the global RNFL thickness was underestimated by 1.2μm. Other studies evaluating the effect of ocular magnification correction on RNFL thickness also found an inverse correlation between axial length and RNFL thickness which is not significant after correction of ocular magnification [36, 40, 41]. It is worth noting that the RNFL thickness, as evaluated by Hirasawa et al., is thinner that the total retinal thickness and thus a smaller magnitude of under- or overestimation in tissue thickness with each millimetre change in the axial length is expected in their study compare to our findings. Given the importance of retinal fibre layer thickness follow-up in glaucoma, further exploration of the effect of transverse magnification adjustment on peripapillary RNFL thickness may be especially relevant in younger populations. For example, when monitoring young adults or children with juvenile or secondary glaucoma, refractive error is likely to change as the eye elongates. Thus, without transverse magnification correction, the RNFL thickness is likely to appear to be thinning faster than it actually is as the eye elongates.

Commercially available OCT instruments are usually calibrated to a predetermined default axial length of around 24.5 mm (e.g. Cirrus, Spectralis, and Copernicus OCT instruments axial length default is 24.46, 24.38, and 24.00 mm, respectively), which generally provide reliable thickness measurement in emmetropic or low myopic eyes; however, elongated or shortened eyes required some adjustment for transverse magnification to cover the same scan area. Results from this study confirm that the axial length plays a key role in measurements and calculations of the retinal thickness profile using OCT, and adjustment for transverse magnification is something that OCT manufacturers could consider incorporating in their software. Most OCT devices' software already allows the input of corneal curvature to correct for some of the magnification effects. Including axial length correction in the OCT instrument's software prior to imaging will improve the accuracy of their measurements. The correction for transverse magnification due to differing axial lengths will become more crucial as almost half of the global population becomes myopic by year 2050 [42] and the accuracy of the retinal and

choroidal thickness in high myopes may provide further insight into the mechanism underlying myopia development.

This study included a wide range of refractive errors, which allows evaluation of different refractive errors/axial length values on macular thickness in relation to transverse magnification. Another strength of the current study is that the Raine Study participants have been shown to be generally representative of the Western Australia young adult population in terms of socio-economic/demography [53]. The inclusion of two cohorts analysed separately served as a sensitivity analysis and allowed us to validate the findings from each study. A main limitation of this study is that it only included young adults. More studies are perhaps needed on other age groups and in people with various ocular diseases to provide further insight into the potential effects of the transverse magnification on posterior tissue thickness calculation using OCT. Another limitation of the study is that the custom program does not account for lens thickness or anterior chamber depth in the corrected measurements. However, axial length is the major driver behind transverse magnification effects [33].

In conclusion, results from this study show raw OCT measures of retinal thickness in the ETDRS grid underestimate the retinal thickness at the central macula and overestimate the retinal thickness at non-central regions. Moreover, the main effect of axial length and refractive error disappear or reduce after correction for transverse magnification due to differences in axial length in most of the non-central macular regions. Although the effect size found in this study seems rather small, as the world population becomes increasingly myopic, the results of this study will be more meaningful in the future. Hence, commercial OCTs should consider incorporating axial length in calculation of thickness measurements.

Supporting information

S1 Fig. Uncorrected full retinal thickness (μm) in the all (top row), myopic (middle row), and non-myopic (bottom row) participants in the Raine Study (left) and K-YAMS (right) cohorts, expressed in terms of median (in bold) [and interquartile range].
(DOCX)

S2 Fig. Transverse magnification-corrected full retinal thickness (μm) in the all (top row), myopic (middle row), and non-myopic (bottom row) participants in the Raine Study (left) and K-YAMS (right) cohorts, expressed in terms of median (in bold) [and interquartile range].
(PDF)

Acknowledgments

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