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Retinal nerve fiber layer and optic disc measurements by spectral domain OCT: normative values and associations in young adults

Abstract

Purpose To determine normative values and associations of retinal nerve fiber layer (RNFL) and optic disc parameters in normal eyes measured by spectral domain optical coherence tomography (OCT). Methods In a population-based setting, 1521 young adults were examined as part of the Sydney Adolescent Vascular and Eye Study (SAVES). Their mean age was 17.3 ± 0.6 years. RNFL and optic disc parameter measurements were made using Cirrus HD-OCT 4000.

Results The average RNFL was found to be 99.4 \pm 9.6 µm. RNFL thickness was least for the temporal quadrant $(69.9 \pm 11.2 \,\mu m)$, followed by the nasal $(74.3 \pm 12.8 \,\mu m)$, superior (124.7 \pm 15.7 μ m) and inferior $(128.8 \pm 17.1 \,\mu m)$ quadrants. The mean disc area in this population was 1.98 ± 0.38 mm² with a mean rim area of 1.50 ± 0.30 mm² and a mean cup/disc ratio of 0.44 ± 0.18 . Multivariate-adjusted RNFL thickness was marginally greater in East Asian than in white participants $(100.1 \mu m \text{ vs }$ 99.5 μ m; P = 0.0005). The RNFL was thinner with greater axial length $(P<0.0001)$, less positive spherical equivalent refractions $(P<0.0001)$, smaller disc area and rim area $(P<0.0001)$.

Conclusion This study documents normative values for the RNFL and optic disc measured using Cirrus HD-OCT in young adults. The values and associations reported in this study can inform clinicians on the normal variation in RNFL and optic disc parameters.

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Keywords: retinal nerve fiber layer; optic disc; optical coherence tomography; Sydney Childhood Eye Study

Introduction

In glaucoma, thinning of the retinal nerve fiber layer (RNFL) can occur before the onset of detectable visual field loss.^{[1,2](#page-6-0)} Optical coherence tomography (OCT) is an imaging modality which can be used to non-invasively measure retinal parameters. It is of great use in diagnosis and monitoring of diseases affecting retinal and optic nerve structure and can also be used to detect RNFL thinning in glaucomatous eyes.^{[3](#page-6-0)}

Spectral domain OCT is currently the most advanced commercially available application of OCT technology. It allows faster scanning and higher resolution images than time domain OCT technology.^{[4,5](#page-6-0)} The Cirrus HD-OCT 4000 (Carl Zeiss Meditec, Dublin, CA, USA) is a spectral domain OCT instrument that scans the optic disc and peripapillary RNFL in a 6-mm² area consisting of 200×200 scanning grid. The instrument software has an in-built normative database to compare with RNFL parameters. RNFL and optic disc parameters, however, are known to vary owing to particular demographic[6–8](#page-6-0) and ocular factors.[7,9–12](#page-6-0) Most studies to have assessed variation in these parameters have been performed using the older time domain Stratus OCT. As results using

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the Cirrus HD-OCT and Stratus OCT are not interchangeable, 13 studies assessing these relationships with Cirrus HD-OCT are needed.

The purpose of this study is to determine normal values for Cirrus HD-OCT-measured RNFL and optic disc parameters in a large population-based sample of young adults aged 16–19 years, and to determine whether demographic and ocular factors impact on these measurements. We believe that this young population is ideal for such investigations as they are relatively free of confounding ocular disease.

Materials and methods

Population

The Sydney Adolescent Vascular and Eye Study (SAVES) is a 5-year follow-up of the Sydney Myopia Study (SMS), and is part of the Sydney Childhood Eye Study. The SMS was a population-based survey of refraction and other eye conditions in a sample of school students, across 34 primary and 21 high schools conducted between 2003 and 2005. As part of this survey, all schools in Sydney were stratified into 10 deciles based on socio-economic status (SES) of the areas in which they were located, with three high schools chosen from the top SES decile and the remainder randomly selected from the bottom 9 deciles. SES data were obtained from the Australian Bureau of Statistics 2001 national census. The high school students were examined in grade 7 between 2004 and 2005. As part of SAVES, 20 of the 21 high schools were re-visited during 2009 and 2010 and students in grades 11 and 12 were offered the opportunity to participate.

Procedures

Each participant under age 18 years was required to provide written consent from one parent, and those participants over 18 years of age were permitted to consent independently. The study followed the tenets of the Declaration of Helsinki. The study was approved by the Human Research Ethics Committee, University of Sydney and the New South Wales Department of Education and Training.

Examinations were conducted during 2009 and 2010 by a team of doctors, optometrists, and orthoptists. Monocular visual acuity was assessed using a logarithm of the minimum angle of resolution (logMAR) chart, read at 244 cm (8 feet).^{[14](#page-6-0)} Both cyclopentolate (1%) and tropicamide (1%) were administered twice (5 min apart) to achieve cylcoplegia; in addition, phenylephrine (2.5%) was used if adequate mydriasis (≥ 6 mm) was not achieved and for individuals with very dark iris pigmentation. Axial length (AL) was measured using

non-contact partial coherence interferometry (IOLMaster; Carl Zeiss, Jena, Germany). Autorefraction (RK-F1; Canon, Tokyo, Japan) was performed at least 25 min after the eye drops. Fundus photography (CF 60DSI) was also performed. All tests were conducted on both eyes.

Scans of RNFL thickness and the optic disc were performed using a Cirrus HD-OCT 4000, which performs low-coherence interferometry with an 840-nm superluminescent light-emitting diode to produce high-resolution tomograms. Data for RNFL and optic disc parameters were acquired using the 'Optic Disc Cube $200 \times 200'$ protocol, after pupil dilation. This protocol scans a 6-mm square grid ('cube') by acquiring a series of 200 horizontal scan lines each composed of 200 A-scans.

A single operator (HL) performed the optic disc scans on each participant. The operator was required to ensure adequate pupil alignment, optimal fundus focus and illumination as well as centration of the optic disc before each scan. Scans were repeated in an attempt to obtain signal strengths $\geq 8/10$ and to avoid blink or eye movement artifacts.

Cirrus HD-OCT software (version 5.0) was used for image analysis. RNFL thickness was calculated by layerseeking algorithms for the entire cube. A total of 256 specific A-scans aligned in a circle of 3.46 mm diameter centered on the optic disc are extracted to provide average RNFL thickness and data in clock hours and quadrants. This circle is automatically placed by the software. In some cases where the operator deemed the circle to be eccentrically located, it was manually moved to be centered on the optic disc before data were exported for analysis.

The OCT software provides calculation of optic nerve head parameters. The software delineates the disc edge by the termination of Bruch's membrane. The neuroretinal rim width and area is determined by measuring the amount of neuroretinal tissue within the boundaries of the optic nerve. The software thus calculates optic disc rim and optic cup area. The total area of the optic disc is the sum of the rim and cup areas. The average cup/disc ratio (CDR) is the square root of the ratio of the area of the cup to the area of the disc. The vertical CDR is the ratio of vertical cup diameter to vertical disc diameter. Cup volume is the volume between the plane created by the cup outline at the vitreous interface and the posterior surface of the optic nerve head.

Statistics

Statistical analysis was performed using SAS, Version 9.2 (SAS Institute, Cary, NC, USA). For the purposes of this report, only scans of the right eye with signal strengths greater than 7 were used in analysis. The Kolmogorov–Smirnov test

was used to assess for normality of the distributions. Paired t-tests were used to compare RNFL quadrant data. For comparison of parameters between sex and ethnicity, mixed linear models 15 were employed adjusting for age, height, AL, and sex/ethnicity with the school attended included as a random effect. Mixed linear models were also employed in assessing the relationships of RNFL thickness with AL, refraction, and optic disc parameters, adjusting for age, height, AL, sex, and ethnicity with the school attended included as a random effect.

Results

Of the 2294 students offered examinations, 1550 (67.6%) students between the ages of 16 and 19 years had OCT scanning performed. Of these, 9 participants were excluded because of signal strengths < 8 for optic disc scans; 5 were excluded because of ocular pathology, including retinitis pigmentosa, posterior staphyloma and prior optic nerve injury, and another 15 were excluded because their best corrected visual acuity was 20/40 or worse, leaving 1521 with OCT scans included in analysis. Table 1 presents baseline characteristics from the sample. The mean age of the sample was 17.3 ± 0.6 years and 49.6% were male.

Table 2 presents the distributions of RNFL and optic disc parameters. The average RNFL for this population was 99.4 \pm 9.7 μ m with a range of 61–138 μ m. The inferior RNFL quadrant was the thickest at $128.5 \pm 17.2 \,\mu m$ followed by the superior quadrant at $124.8 \pm 15.9 \,\mu$ m. The two thinnest quadrants were the nasal RNFL at $74.2 \pm 12.6 \,\mu m$ and the temporal RNFL at $69.9 \pm 11.6 \,\mu m$.

Table 1 Characteristics of participants

Characteristic	All $(n=1521)$	White $(n=841)$	East Asian $(n=301)$
Age, years	$17.3 \pm 0.6^{\circ}$	17.4 ± 0.48	17.4 ± 0.7
Male, n $(\%)$,	755 (49.6)	448 (53.3)	129 (42.9)
Ethnicity n , $(\%)$			
White	841 (55.3)		
East Asian	301 (19.8)		
South Asian	101(6.6)		
Middle Eastern	133(8.7)		
Other	145 (9.5)		
SER, D	$0.08 \pm 1.56^{\rm b}$	0.55 ± 1.02	-1.12 ± 2.12
AL, mm	$23.7 \pm 0.9^{\circ}$	23.5 ± 0.8	24.1 ± 1.2
Height, cm	169.4 ± 9.6	171.9 ± 9.5	164.9 ± 8.7
Weight, kg	66.2 ± 22.0	$67.6 + 14.8$	$61.5 + 38.8$

Abbreviations: AL, axial length; D, Diopter, SER, spherical equivalent refraction.

 a Range = 16–19 years.

 $^b Range = -8.0$ to 6.3 D.</sup>

 c Range = 20.8–28.2 mm.

These differences in thickness between RNFL quadrants were highly statistically significant $(P<0.0001)$. The thickest RNFL clock hour segments were at the 7 (inferotemporal) and 11 (superotemporal) o'clock positions, with the thinnest at the 3 (nasal) and 9 (temporal) o'clock positions. The mean disc area in this population was 1.98 ± 0.38 mm² with a mean rim area of 1.50 ± 0.30 mm² and a mean CDR of 0.44 ± 0.18 . CDRs ranged from 0.05 to 0.80.

Females ($n = 766$) had a thicker temporal RNFL compared with males ($n = 755$) in data adjusted for age, height, AL, and ethnicity (mean difference $2.7 \mu m$, $P = 0.0007$). [Figure 1a](#page-3-0) presents clock hour RNFL thickness for males and females and shows that the sex differences occur mainly in the temporal inferior and superior clock hours (unadjusted data). Females also had smaller disc areas, smaller cup volumes and smaller CDRs (mean differences 0.08 mm^2 , 0.06 mm^3 , and 0.05 , respectively, all $P \leq 0.004$).

In white children compared with East Asian children, RNFL average, superior, temporal, and inferior were thicker in East Asian children, the largest difference was seen in the superior quadrant (mean difference 6.2 μ m, $P < 0.0001$; the nasal quadrant was thicker in white children (mean difference $4.9 \mu m$ $P < 0.0001$) (data

Table 2 Distribution of RNFL and optic disc parameters $(n = 1521)$

	Mean (SD)	Median	Range
RNFL, µm			
Average RNFL	99.4 $(9.7)^a$	99.0	$61 - 138$
Temporal	69.8 (11.5)	68.5	$40 - 135$
Superior	124.8 $(15.9)^a$	124.3	$61 - 186$
Nasal	74.3 (12.6)	73.2	$31 - 117$
Inferior	128.5 (17.2)	127.7	$53 - 214$
Clock hour 9 temporal	54.1 (9.1)	53.2	$31 - 136$
Clock hour 10	83.6 (15.7)	82.1	$41 - 157$
Clock hour 11	$139.7 (22.2)^a$	139.8	$64 - 213$
Clock hour 12 superior	$123.2 (26.5)^a$	122.8	$48 - 208$
Clock hour 1	111.6 (20.7)	109.8	$50 - 184$
Clock hour 2	94.7 (18.6)	94.1	$42 - 156$
Clock hour 3 nasal	58.2 (11.2)	56.8	$8 - 114$
Clock hour 4	70.0 (15.6)	68.8	$19 - 141$
Clock hour 5	104.8 (22.6)	103.0	$33 - 191$
Clock hour 6 inferior	139.5 (28.1)	138.2	$52 - 259$
Clock hour 7	141.3 (22.4)	142.7	$61 - 250$
Clock hour 8	71.9 (15.6)	69.9	38-169
Optic disc			
Rim area (mm ²)	1.50(0.30)	1.47	$0.50 - 2.82$
Disc area (mm ²)	1.98 (0.38)	1.94	$1.01 - 4.29$
Cup/disc area ratio	0.44(0.18)	0.47	$0.05 - 0.80$
Vertical cup/disc ratio	0.42(0.17)	0.45	$0.05 - 0.84$
Cup volume (mm^3)	0.13(0.14)	0.09	$0 - 1.12$

Abbreviation: RNFL, retinal nerve fiber layer.

^a Normal distribution (Kolmogorov–Smirnov > 0.05).

adjusted for age, sex, height, and AL). In Figure 1b, RNFL thickness for the two ethnic groups is presented, demonstrating a thicker RNFL temporally and superiorly in the East Asian group (unadjusted data). The East

Figure 1 Graphs showing (a) sex and (b) ethnic differences in peripapillary retinal nerve fiber layer mean thickness by clock hours in right eyes. Error bars in both figures are 95% confidence intervals. Inf, inferior; nas, nasal; sup, superior; temp, temporal.

Asian group was found to have smaller rim areas with larger disc areas, resulting in larger CDR (mean difference 0.08 mm², 0.14 mm², and 0.11, respectively, all $P \leq 0.0007$).

Both greater AL and more myopic refraction were associated with decreased RNFL thickness in data adjusted for age, sex, height, and ethnicity $(P < 0.0001)$. Increasing optic disc area and rim areas were found to be associated with greater average RNFL thickness (both $P < 0.0001$). Larger CDR was associated with lower average RNFL thickness ($P = 0.02$). After adjusting for age, sex, height, and ethnicity, the positive association of disc area and rim area with average RNFL thickness was maintained, however there was no significant relationship of a CDR with average RNFL ($P = 0.06$) after adjustment. Figure 2 demonstrates the relationships of average RNFL thickness with AL, spherical equivalent refraction, and disc parameters.

Discussion

In this study, we report normative values for RNFL thickness and optic disc parameters measured by Cirrus HD-OCT in a large population-based sample of young adults. We found that the average RNFL and superior RNFL were normally distributed. However, optic disc parameters did not have normal distributions. We also found significant associations between Cirrus

Figure 2 Relationship of average RNFL thickness to (a) quintiles of axial length (b) quintiles of spherical equivalent refraction (c) quintiles of disc area (d) quintiles of rim area (e) quintiles of cup/disc ratio. Error bars represent 95% confidence intervals. Axial length quintiles (mm): $1 = 20.8-22.89$, $2 = 22.9-23.4$, $3 = 23.4-23.8$, $4 = 23.8-24.3$, $5 = 24.3-28.2$. Spherical equivalent quintiles (D): $1 = -8.0$ to -0.6 , $2 = -0.6$ to 0.3, $3 = 0.3 - 0.6$, $4 = 0.6 - 0.9$, $5 = 1.0 - 6.3$. Disc area quintiles (mm²): $1 = 1.0 - 1.7$, $2 = 1.7 - 1.8$, $3 = 1.8 - 2.0$, $4 = 2.0 - 2.3$, $5 = 2.3 - 4.3$. Rim area quintiles (mm²): $1 = 0.5 - 1.2$, $2 = 1.2 - 1.4$, $3 = 1.4 - 1.5$, $4 = 1.5 - 1.7$, $5 = 1.7 - 1.9$. Cup/disc ratio quintiles: $1 = 0.1 - 0.3$, $2 = 0.3 - 0.4$, $3 = 0.4 - 0.5$, $4 = 0.5 - 0.6$, $5 = 0.6 - 0.8$.

1566

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HD-OCT-measured RNFL thickness and ethnicity, AL, and optic disc parameters.

Based on our literature search, few large populationbased studies of RNFL and optic disc parameters measured by Cirrus HD-OCT have been reported.[16–20](#page-6-0) The largest OCT study to date is by Knight et al,^{[16](#page-6-0)} who presented data on 271 normal subjects aged 18–84 years. They had an average RNFL thickness of 94.0 μ m (SE 0.6) (adjusted for age and disc area) in their multi-ethnic population. This value is similar but slightly less than our value of $99.4 \pm 9.7 \,\mu m$. The older population (although data was adjusted for age) and the adjustment for disc area may have accounted for the difference. The disc area and rim area for their total population were 1.81 mm² and 1.32 mm², respectively, which are smaller than our values for these parameters. This may be explained by age differences and possible differences in AL between samples. Their values for CDRs were 0.47 (average) and 0.47 (vertical), which were similar to the current study. Hong et al,^{[17](#page-6-0)} who examined 269 (96% male) normal Korean military personnel aged 19 to 26 years, found an average RNFL thickness of $98.2 \pm 8.6 \,\mu m$, which is very similar to our value in males of $98.8 \pm 9.8 \mu m$ and slightly less than our value for East Asians of $100.1 \pm 9.4 \,\mu m$. This study did not present optic disc data.

Mwanza et aI^{18} aI^{18} aI^{18} presented optic disc data measured by Cirrus HD-OCT in 146 normal eyes. They found smaller disc areas $(1.83 \pm 0.35 \text{ mm}^2)$ and smaller rim areas (1.27 mm^2) and slightly larger CDR (0.51 ± 0.16) compared with our study. Large studies $(n>100)$ that measured normal disc size using Stratus OCT^{10,21-25} have reported disc areas between 2.34±0.41 and 2.63 ± 0.55 mm², which are larger than our value of 1.98 ± 0.38 mm². These studies also report cup-disc area ratios between 0.17 ± 0.11 and 0.37 ± 0.20 , which are substantially smaller than our value of 0.44 ± 0.18 . These discrepancies are most likely due to differences in the

scanning pattern and optic disc and cup delineation algorithms between Stratus and Cirrus OCT.

In Table 3, values for OCT measured RNFL thickness in large studies is presented. The studies by Bendschneider et al^{[26](#page-7-0)} using Spectralis HRA + OCT (Heidelberg Engineering, Heidelberg, Germany) and Hirasawa et al^{27} al^{27} al^{27} using the spectral domain Topcon 3D OCT1000 (Tokyo, Japan), report values remarkably similar to those found in our study. We would expect these two studies to measure thinner values, as they included older populations by comparison with our study, and it is known that RNFL thickness decreases with age.^{7,26,28} It should be noted, however, that measurements obtained using either the Spectralis $HRA + OCT$ or Topcon OCT are not interchangeable with those using the Cirrus HD-OCT.[29,30](#page-7-0) The Stratus OCT normative studies presented in Table 3 also have values within 10 μ m of those presented in our study, which is within the limit of resolution of time domain OCT.^{[7,31](#page-6-0)} Meaningful comparison with Stratus measurements, however, is difficult due to differences in the scanning pattern and segmentation algorithms.

Our study found only small to non-significant sex differences in RNFL thickness with the Cirrus HD-OCT, similar to findings from studies using time domain OCT.^{[7,22,32](#page-6-0)} However, we did find small, but statistically significant, sex differences in optic disc parameters. Most previous studies have reported a lack of association of sex with optic disc parameters[.33–35](#page-7-0) However, larger optic disc size has previously been reported in males, $36,37$ consistent with our finding of a slightly larger disc area in males. The average CDR sex difference of 0.05 is not likely to be of any clinical relevance, particularly as the more sensitive parameter of RNFL thickness did not differ between sexes.

Ethnic differences in RNFL thickness were previously reported with older time domain OCT.[6–8](#page-6-0) The thinner nasal RNFL in East Asians could be explained by the

Table 3 Reports of RNFL thickness values measured by OCT in large studies ($n>100$)

Paper	OCT	OCT type	Country	N	Age mean (range), years	Average RNFL, µm	Temporal RNFL, um	Superior RNFL, um	Nasal RNFL, μ <i>m</i>	<i>Inferior</i> RNFL, um
Current study	Cirrus	SD	Australia	1521	$17.3(16-19)$	99.4 ± 9.7	69.8 ± 11.5	$124.8 + 15.9$	74.3 ± 12.6	$128.5 + 17.2$
Knight et al ¹⁶	Cirrus	SD	USA	271	$46.2(18 - 84)$	94.0 SE:0.6	64.0 SE:0.6	119.0 SE:0.9	69.8 SE:0.7	123.2 SE:1.0
Hong <i>et al</i> ¹⁷	Cirrus	SD	Korea	269	$21.3(19-26)$	98.6 ± 8.7				
Girkin et al ¹⁹	RTVue	SD	USA ^a	219	53.4	101.9 ± 9.8				
Hirasawa et al ²⁷	Topcon	SD	Japan	251	>20	101.9 ± 8.4	78.6 ± 13.3	123.9 ± 13.6	79.6 ± 13.6	125.5 ± 13.1
Bendschneider et al^{26}	Spectralis SD		Germany	170	\sim 20–79	97.2 ± 9.7	68.8 ± 11.1	118.0 ± 14.5	76.4 ± 15.0	123.7 ± 16.4
Turk et al ²⁰	Spectralis SD		Turkey	107	$10.5(6-16)$	106.5 ± 9.4				
Huynh et al^{22}	Stratus	TD	Australia 2132		$(11.1 - 14.4)$	103.6 ± 10.6	74.6 ± 12.8	129.7 ± 17.5	82.0 ± 16.7	128.3 ± 18.6
Huynh et al^9	Stratus	TD	Australia	1369	6.7	103.7 ± 11.4	75.7 ± 14.7	129.5 ± 20.6	81.7 ± 19.6	127.8 ± 20.5
El Dairi et al 10	Stratus	TD	USA	286	$8.6(3-17)$	$108(92 - 125)$	78 (56-105)	143 (112–177)	83 (56-120)	129 (102-160)
Budenz et al ⁷	Stratus	TD	USA	328	47.4 (18-85)	100.1 ± 11.6	69.0 ± 12.7	$124.2 + 17.9$	$80.9 + 18.1$	126.1 ± 17.8

Abbreviations: RNFL, retinal nerve fiber layer; SD, spectral domain; SE, standard error; TD, time domain.

^a European descent.

greater prevalence of myopia in this population, which may be associated with a temporal shift in the arcuate nerve fiber bundles.^{[17](#page-6-0)} In a study by Knight *et al*,^{[16](#page-6-0)} the European/white sample had an average RNFL of 90.1 μ m (SE 0.8) and their Chinese/East Asian sample had average RNFL of $96.4 \mu m$ (SE 1.1), compared with our values of $99.5 \pm 9.8 \mu m$ and $100.1 \pm 9.4 \mu m$ for these two groups, respectively. Therefore, there is a greater disparity between these ethnic groups compared with our sample, even though their use of disc area adjustment should have reduced the value for the Chinese sample. Because the Knight et al^{16} al^{16} al^{16} study had older patients, these differences may suggest that RNFL thinning with age may occur to a greater extent in white compared with East Asian populations.

We found that the East Asian group had larger disc areas, smaller rim areas, and hence larger CDRs than the white sample. In support of our findings, Wang et al^{38} al^{38} al^{38} using optic disc photographs reported larger disc size in a Chinese population than in white populations. Also in the SMS, using time domain OCT, we reported that at both 6 and 12 years of age, East Asian children had larger CDRs compared with white children.[8](#page-6-0)

We found that increasing AL and more myopic refraction was associated with thinner average RNFL. This is in agreement with previous Cirrus HD-OCT studies, $6,39$ as well as in a study using the Spectralis $HRA + OCT²⁶$ $HRA + OCT²⁶$ $HRA + OCT²⁶$ Studies using the time domain Stratus OCT instrument also reported thinner RNFL with increasing AL or myopic refraction.^{[7,9–12](#page-6-0)} Using the Topcon spectral domain OCT, Hirasawa et al^{[27](#page-7-0)} did not find a relationship with average RNFL thickness or AL in multiple regression analysis. One reason for this discrepancy could be the adjustment for optic disc size in their analysis. RNFL thinning in eyes with longer AL may be due to a magnification effect[.7,40](#page-6-0) The larger projected scan circle in these eyes would alter RNFL measurement further from the disc margin, where the RNFL is thinner.^{[41](#page-7-0)} Regardless of the true relationship between RNFL and AL, it should be noted in clinical practice when using Cirrus HD-OCT that thinner RNFL values will be found in myopic eyes or eyes with longer AL. To account for this effect, a mathematical adjustment for scan enlargement may be utilized by clinicians for patients with very long eyes.[42](#page-7-0)

Both larger disc and rim area were found to be associated with increased RNFL thickness. Increasing CDR was associated with decreased RNFL thickness only in unadjusted analysis. Utilizing a spectral domain OCT instrument (OPKO/OTI Spectral OCT/SLO), Mansoori et $al⁴³$ $al⁴³$ $al⁴³$ found no significant association between disc area and RNFL thickness, in conflict with our findings. The reasons for their reported lack of association may be due to the differences in disc margin delineation between the

two OCT instruments, or the small sample size of their study ($n = 65$). Our studies also differed with respect to age, with their study including a wider age range of 13–79 years. However, Mansoori et al^{43} al^{43} al^{43} reported significantly greater RNFL thickness with increasing rim area and lesser RNFL thickness with increasing CDR, in agreement with our unadjusted findings. The association of a thinner RNFL with increasing CDR is in keeping with the traditional assumption made during clinical assessment of the optic disc for glaucoma screening.

In agreement with our results, a study using Topcon spectral domain OCT^{27} and studies with the Stratus time domain $OCT^{7,44}$ $OCT^{7,44}$ $OCT^{7,44}$ have reported increasing RNFL thickness (measured using a 3.4-mm scanning circle) is associated with larger optic disc area. However, these findings may not relate to an actual anatomic relationship as they are not unanimously supported by human histological studies.[45,46](#page-7-0) The fixed diameter of OCT RNFL scanning may introduce an artefact of thicker RNFL measurement in eyes with larger discs, as the RNFL is sampled closer to the disc margin. Hirasawa et al^{27} al^{27} al^{27} used the spectral domain Topcon OCT instrument to study the association of RNFL thickness with different sized scanning circles, and reported that optic disc area was negatively correlated with mean RNFL thickness in the smaller scanning circles (2.2 and 2.5 mm diameter) and positively correlated with mean RNFL thickness in the larger scanning circles (3.4, 3.7, and 4.0 mm). This suggests that there may be an even more complex relationship between disc area and RNFL thickness.

Strengths of this study include its large populationbased sample of young adults without confounding ocular disease and the use of uniform examination techniques. A potential weakness of this study is that the scan data are presented without adjustment for scan magnification effects, which could produce abnormal results in individuals at the extremes of AL or refraction. However, as most clinicians rely principally on the raw output of the Cirrus HD-OCT without further calculation, our results may be applied directly to clinical scenarios.

In conclusion, we have presented normative values for Cirrus HD-OCT 4000 measured RNFL and optic disc parameters in a very large population-based sample aged 16–19 years. We further report that RNFL thickness is significantly associated with ethnicity, AL, and optic disc parameters. The values and associations reported in this study can inform clinicians about normal variations in RNFL thickness and optic disc parameters, as measured using the Cirrus HD-OCT and may help to better delineate normal variation from pathological changes.

1568

What was known before

- Normal ranges for RNFL thickness are provided in the Cirrus HD-OCT in-built database, based only on a sample 284 individuals, only for those above 18 years of age, without stratification for sex and ethnicity.
- There are few large population-based studies using Cirrus HD-OCT providing associations of RNFL parameters with sex, ethnicity, or axial length.

What this study adds

- Normative data for both RNFL and optic disc parameters measured in a large population-based sample $(n = 1521)$ of young adults.
- Data on variation on these parameters with sex, ethnicity, axial length, and spherical equivalent refraction.

Conflict of interest

The authors declare no conflict of interest.

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1569

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1570