Research Article

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Shaping OCT Norms in Children: The Impact of Age, Refraction, Gender, and Ethnicity

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ABSTRACT

Purpose: To establish a normative database of optical coherence tomography (OCT) parameters in children and examine the effects of spherical refraction, age, gender, and ethnicity on these measurements.

Methods: OCT measurements were performed using spectral-domain OCT (HD-OCT Cirrus 6000) on children aged 3 to 17.9 years. A total of 274 eyes from 137 children were included. Mean age was 10.41 ± 3.79 years and mean spherical equivalent refraction was +0.23 ± 2.79 diopters. Optic nerve and macular parameters were assessed, and a normative database was established distinguishing between children younger and older than 10 years. Only participants without any ophthalmological pathology with an OCT scan quality signal of 7 or above were included.

Results: The study provides a normative database for optic nerve head parameters, retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), and macular thicknesses in a normal pediatric population. Age showed a significant negative correlation with rim area and the temporal quadrant of RNFL thickness and a positive correlation with central macular thickness. Refraction demonstrated a significant positive correlation with rim area, RNFL, GCL, and macular thicknesses. Ethnicity was correlated with disk area, cup-to-disk ratios, cup volume, and RNFL thickness, and central macular thickness was significantly thicker in boys.

Conclusions: This study provides reference normative data for Cirrus OCT measurements in normal children. These were significantly influenced by age, refraction, gender, and ethnicity. The tendency of diminution in spherical equivalent with age likely led to a thinning of RNFL, GCL, and macular thicknesses, whereas reorganization of the foveal zone during childhood possibly explained the increase in central macular thickness with age.

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INTRODUCTION

Pediatric patients present unique challenges in ocular disease diagnosis and monitoring due to the difficulty in obtaining consistent and reliable visual assessments. Traditional diagnostic tools used for adults, such as visual field tests, often require a level of cooperation that is impractical for young children. In contrast, table-mounted optical coherence

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tomography (OCT) provides objective measurements of ocular structures and is suitable for children as young as 3 years. Despite the advancements in OCT technology, there is a significant need for a normative database specific for pediatrics. Previous studies have established databases for children, but they often rely on older machines or a small pediatric sample with a limited age range, or do not cover the full range of optic nerve and macular parameters.

Beyond age and refraction, several spectral-domain OCT (SD-OCT) studies have shown that gender and ethnicity may influence OCT parameters. Banc and Ungureanu[1] reviewed OCT normative data in children before June 2020, finding that most studies showed no association between age and retinal nerve fiber layer (RNFL) thickness, with inconsistent correlations reported by others. Studies published after June 2020 reported mixed findings: most found no correlation between age and RNFL thickness,[2-4] whereas one study found a negative correlation.[5] Two recent studies observed a positive correlation between age and macular thickness.[2,4] Regarding refraction, Banc and Ungureanu[1] noted a positive correlation between spherical equivalent refraction (SER) and RNFL thickness, contrasting with recent findings that found no correlation between SER and RNFL thickness, SER and ganglion cell layer (GCL) thickness, or SER and macular thickness.[2,4] Two studies observed a positive correlation between SER and macular thickness.[5,6] Concerning gender, the review[1] found no effect on RNFL thickness but also noted thicker central macular thicknesses in males, which recent studies largely support.[3-6] In contrast, one study found no correlation between gender and macular or GCL thicknesses.[7] Concerning ethnicity, Banc and Ungureanu[1] identified only four studies with mixed results: two studies[8,9] noted smaller cup and vertical disk diameters, and thinner RNFL thickness of supratemporal sector in White individuals compared to Black and Hispanic individuals, whereas two other studies[10,11] found no correlation. To the best of our knowledge, research after June 2020 remains lacking on the effect of ethnicity.

An article by Rozema et al[12] described the concept of emmetropization, which was defined as the process by which the eye achieves near-zero refractive error, primarily through axial elongation and adjustments in corneal and lens power. In our study, by including ages from 3 to 17.9 years, we aimed to establish a normative database of OCT parameters and to investigate whether gender, ethnicity, and eye elongation affect these measurements by studying the effects of age and SER.

PATIENTS AND METHODS

Study Population

The study involved 137 children and was conducted as a prospective multicenter cross-sectional study at two hospital sites (Cliniques Universitaires Saint-Luc and CHU HELORA, Hôpital de Nivelles) from February 2022 to May 2023. Participants included 85 girls and 52 boys aged 3 to 17.9 years. Eligibility criteria included a SER between -6.00 and +6.00 diopters (D) and normal visual function, by means of absent anisometropia and presence of normal stereopsis. Participants had no personal or family history of strabismus and no neurological or metabolic conditions, and were born at term. All procedures were performed in strict adherence to the tenets of the Declaration of Helsinki. In addition, the experimental protocol received approval from the local ethics committee. Children and their parents or representatives signed the informed consent before any examination was performed.

Ocular Examination

All patients participated on a voluntary basis and were screened using automated refraction without cycloplegia, performed with the ARK-1 autorefractor (Nidek Co Ltd). They were then classified in one of three categories of non-cycloplegic SER[19]: emmetropia: from -0.50 to +0.50 D; hyperopia: from +0.51 to +6.00 D; and myopia: from -0.51 to -6.00 D. Stereopsis was then assessed based on the Lang I stereotest, in which participants had to correctly identify all three images to be included.

OCT Imaging

The Cirrus HD-OCT 6000 (Carl Zeiss Meditec AG) device was used to obtain images, using the macular cube 512 × 128 and optic disk cube 200 × 200 protocols to assess macular, GCL, and peripapillary RNFL thickness. Macular analysis included measurements of central subfield thickness (central 1-mm disk) and macular thickness in two concentric circles of 3- and 6-mm diameter centered at the fovea, which were further divided into four quadrants, according to the nine areas of the Early Treatment Diabetic Retinopathy Study (ETDRS) guidelines. A signal strength of 7/10 or higher was considered acceptable. Only scans with a clear fundus image and without movement artefacts were accepted. All imaging was performed by an experienced author (IH). Multiple measurements were taken, and the best-centered image was selected for analysis.

Statistical Analysis

Data were entered into Microsoft Excel (Microsoft Corporation) and analyzed using JMP Pro 17.1.0 software. The *t*-test or Wilcoxon tests were used to compare continuous data between groups (ie, the gender groups, refraction groups, and ethnicities). Pearson's correlation coefficient analyzed linear relationships between age and SER. Multivariate regression analyzed the effects of age, SER, ethnicity, and gender on OCT parameters. In all analyses, P values lower than .05 were considered statistically significant.

Use of Generative Artificial Intelligence (AI) and AI-assisted Technologies in the Writing Process

An AI language model (ChatGPT, GPT-4 architecture, developed by OpenAI, no specific version or extension numbers) was employed during the manuscript preparation process on the following dates: September 17, 2024; September 19, 2024; September 20, 2024; and September 24, 2024. The AI was used to assist with synthesizing and reducing the word count to enhance readability and conciseness. All editing and final content decisions were made under the direct oversight and control of the authors.

RESULTS

A total of 201 participants were enrolled. Sixty-four patients were excluded because of history of strabismus, anisometropia, premature birth, or neurometabolic diseases. A total of 274 eyes from 137 patients were included, comprising 85 girls and 52 boys, with ages ranging from 3 to 17.9 years. Both right and left eyes were included for separate analysis. Demographic and ocular characteristics are detailed in **Table 1** and **Figures 1-2**.

The normative database was established, distinguishing between individuals younger and older than 10 years (**Table 2**). The 10-year cut-off was chosen based on the mean age of our cohort (10.41 years) and a balanced sample size across age groups. Statistical analysis using *t*-tests for different cut-offs (8, 9, 10, 11, and 12 years) showed that the most significant differences occurred with the 10-year cut-off.

Optic Nerve Measurements

Normative data for optic nerve head parameters and RNFL thickness in children are detailed in **Table 2**. In the older subgroup (ie, older than 10 years), average RNFL thickness, rim area, disk area, and RNFL thickness of the inferior quadrant were significantly decreased ($P < .05$). Comparison between RNFL quadrants revealed that the ISNT rule was not followed, because the inferior quadrant did not appear to be significantly thicker than the superior quadrant (paired *t*-test; $P = .1315$ for the right eye and $P = .9391$ for the left eye).

Myopic children had a significantly smaller rim area compared to those with hyperopia (Steel-Dwass method, $P = .0426$; right eye). The average RNFL and superior and inferior RNFL quadrants were significantly thinner for myopia compared to hyperopia (P = .0044, .0243, .0173; right eye) and emmetropia (P = .0003, .0004, .0012; right eye). Gender comparative analysis showed no significant differences between genders. Ethnic group comparison showed that Blacks had a significantly higher cup volume and average cup-to-disk ratio (P = .0424 and .0133; right eye) compared to Whites. North Africans had a greater average RNFL thickness, superior RNFL quadrant, and cup volume (P = .0494, .0189, and .0215; right eye) compared to Whites.

On multivariate regression analysis, age showed a significant negative correlation with rim area ($P = .0273$; right eye) and with the temporal RNFL quadrant ($P = .0439$; left eye). SER demonstrated a significant positive correlation with rim area and average (**Figure 3A**), inferior, superior, and nasal RNFL thicknesses. Ethnicity significantly influenced disk area, cup-to-disk ratios, cup volume, and RNFL thicknesses (**Table 3**).

In the variance analysis using regression models, age and SER together accounted for 10.25% ($R^2 = 0.1025$, $P = .0007$; right eye) of the variance in average RNFL thickness. In the multivariate analysis, SER, age, ethnicity, and gender together explained 20.71% ($P < .0001$; right eye) of the variance in average RNFL thickness.

GCL Measurements

Normative data for GCL thickness in children aged 3 to 17.9 years are detailed in **Table 2**. In the older subgroup, average GCL thickness, supranasal, inferonasal, inferior, and superior GCL thicknesses were significantly decreased ($P < .05$). The average and

TABLE 1

Demographic and Ocular Characteristics of the Population

Characteristics	N	% (of 137 Participants)	Mean SER (Diopters) Right Eye	Mean SER (Diopters) Left Eye	Age (Years) Mean ± SD	Age (Years) Range
Total participants	137 (274 eyes, RE: 137, LE: 137)	100%	+0.18 ± 2.73	+0.27 ± 2.85	10.41 ± 3.79	3.15 to 17.84
Age group (y)						
3 to 4.9	10	7.30%	+0.83 ± 0.75	+0.69 ± 0.80	4.15 ± 0.60	3.15 to 4.92
5 to 6.9	24	17.52%	+1.12 ± 1.26	+1.22 ± 1.09	5.99 ± 0.68	5.04 to 6.98
7 to 8.9	21	15.33%	+1.38 ± 1.71	+1.55 ± 1.98	7.91 ± 0.47	7.10 to 8.73
9 to 10.9	20	14.60%	+0.13 ± 1.05	+0.38 ± 0.92	9.76 ± 0.63	8.88 to 10.85
11 to 12.9	22	16.06%	-0.82 ± 2.09	-0.69 ± 2.14	11.91 ± 0.65	11.01 to 12.99
13 to 15.9	24	17.52%	+0.10 ± 1.73	-0.01 ±1.85	14.54 ± 0.99	13.14 to 15.90
16 to 17.9	16	11.67%	-1.64 ± 1.80	-1.45 ± 1.88	16.76 ± 0.62	16.04 to 17.84
Age group (y)[a]						
≤ 10	69	50.4%	+0.97 ± 2.32	+1.06 ± 2.55	7.01 ± 1.92	3.15 to 9.90
> 10	68	49.6%	-0.61 ± 2.65	-0.52 ± 2.62	13.86 ± 2.49	10.03 to 17.84
Gender						
Female	85	62%	+0.17 ± 2.72	+0.23 ± 2.85	10.75 ± 3.75	3.15 to 17.04
Male	52	38%	+0.21 ± 2.73	+0.35 ± 2.85	9.84 ± 3.79	3.22 to 17.84
Ethnicity						
White	71	51.8%	+0.42 ± 2.74	+0.43 ± 2.87	10.37 ± 3.69	3.15 to 17.80
North African	42	30.7%	-0.22 ± 2.73	-0.09 ± 2.85	10.97 ± 3.79	3.22 to 17.84
Asian	11	8.0%	-0.75 ± 2.55	-0.60 ± 2.74	10.49 ± 3.25	4.28 to 15.69
Mixed race	7	5.1%	+1.57 ± 2.51	+1.75 ± 2.73	8.11 ± 2.20	4.01 to 11.54
Black	6	4.4%	+0.64 ± 2.59	+1.06 ± 2.77	9.39 ± 2.97	6.84 to 13.63
Refractive error						
Hyperopia	RE: 59, LE: 58	RE: 43.1%, LE: 42.3%	+1.70 ± 2.67	+1.82 ± 2.79	8.73 ± 3.58	3.15 to 17.04
Emmetropia	RE: 40, LE: 42	RE: 29.2%, LE: 30.7%	+0.02 ± 2.65	+0.11 ± 2.82	10.18 ± 3.67	3.88 to 17.80
Myopia	RE: 38, LE: 37	RE: 27.7%, LE: 27.0%	-2.00 ± 2.81	-1.97 ± 2.85	13.25 ± 3.45	5.04 to 17.84

LE = left eye; RE = right eye; SD = standard deviation; SER = spherical equivalent
[a]Cut-off = 10 years.

minimum GCL thicknesses, as well as the thickness of the six GCL quadrants, were significantly thinner for myopia compared to emmetropia (P = .0003, .0144, .0030, .0018, .0001, .0003, .0004, .0019; right eye) and hyperopia (P = .0002, .0065, .0007, .0004, .0001, < .0001, .0007, .0041; right eye). No significant difference was found in GCL parameters between genders and ethnicities. The supranasal quadrant was the thickest of all quadrants (P = .0019, right eye).

In the multivariate analysis, SER showed a significant positive relationship with average, minimum, and the six quadrants of GCL thickness (**Table 3**). Average GCL thickness increased by +1.21 µm per diopter of SER (P < .0001; right eye), as illustrated in **Figure 3B**.

In the variance analysis of the average GCL thickness, age and SER together accounted for 14.58% (R^2 = 0.1458, P = .0047; right eye). Multi-

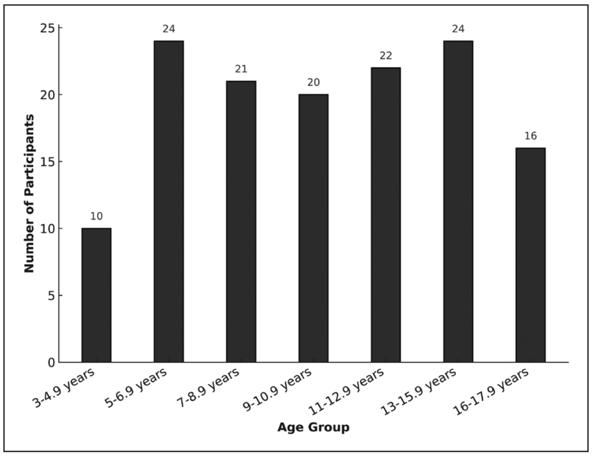

Figure 1. Age distribution of the 137 participants.

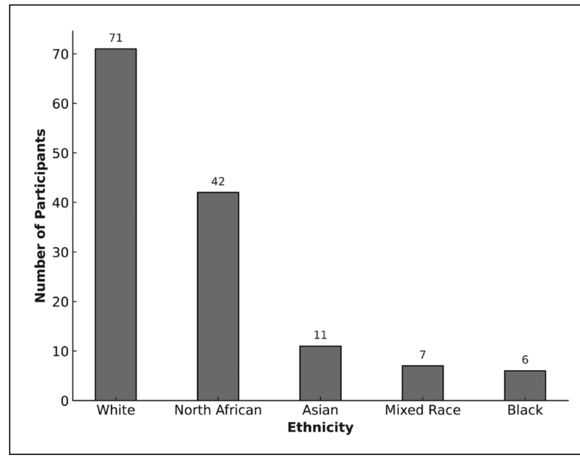

Figure 2. Ethnicity distribution of the 137 participants.

variate analysis showed that gender, ethnicity, SER, and age explained 18.47% of the variance (P = .0004; right eye).

Macular Measurements

Normative data for macular parameters in children aged between 3 and 17.9 years are detailed in **Table 2**. In the older subgroup, inferior and temporal outer-circle macular thicknesses were significantly decreased, whereas central macular subfield thickness was significantly increased (P < .05). The superior outer circle thickness was significantly thinner for myopia compared to emmetropia (P = .0186; right eye) and the superior, temporal, and inferior sectors were also thinner compared to hyperopia (P = .0127, .0369, .0173; right eye). Compared to girls, boys exhibited a significantly thicker central macular subfield and nasal and temporal inner circle thicknesses (P = .0061; right eye). No significant difference was found in macular parameters when comparing between ethnicities. In the comparative analysis, the inner circle was the thinnest in the temporal quadrant (P < .0001; both eyes). In the outer circle, the nasal quadrant was the thickest (P < .0001; both eyes) and the temporal quadrant was the thinnest (P < .0001; both eyes).

In the multivariate regression analysis, age had a significant positive association with central macular subfield thickness, increasing by 1.41 µm per year (P = .0042; right eye), as depicted in **Figure 3C**. SER had a significant positive correlation with average macular thickness and the outer circle thicknesses. Gender significantly influenced central macular subfield thickness and inner circle thicknesses, with boys having the thickest measurements (**Table 3**).

In the variance analysis, variance in central macular subfield thickness was 17.10% (P = .0009; right eye), mainly influenced by gender, with boys having significantly thicker central macular subfields.

DISCUSSION

A normative database was established based on a cut-off of 10 years. In addition, this study shows that age, SER, gender, and ethnicity influence OCT measurements.

To date, and to the best of our knowledge, this is the only study on the Cirrus SD-OCT that presents a complete database of optic nerve head parameters, RNFL thickness, GCL thickness, and macular thickness in children aged 3 to 17.9 years. Unlike most studies, which are single-center, only two other studies[13,14] are prospective multicenter studies. In addition, our study is the only one that compares OCT values between different ethnicities. The inclusion of different ethnicities ensures that the database is applicable to a wide range of children.

The comparison of our OCT values with those from other studies using different SD-OCT models and involving various ethnicities is presented in **Table A** (available in the online version of this article). This table shows that the RNFL, GCL, and central macular thickness values are thicker with the Spectralis and the RTVue 100 Avanti OCT devices than with the Cirrus SD-OCT. SD-OCT devices such as the Cirrus, Spectralis, and RTVue 100 have different software algorithms, image acquisition and calibration protocols, contributing to varying outcomes.[15] Studies using the Cirrus OCT in the Middle East and Asia reported thinner RNFL, GCL, macular thicknesses, and volume than our study.

TABLE 2

Distribution of ONH Parameters, RNFL Thicknesses, GCL Thicknesses, and Macular Parameters in Children < and ≥ 10 Years, Mean ± SD (5th to 95th Percentile)

Parameter	< 10 Years Right Eye	< 10 Years Left Eye	≥ 10 Years Right Eye	≥ 10 Years Left Eye
ONH				
Rim area (mm^2)	1.568 ± 0.261 (1.505 to 1.630)	1.579 ± 0.260 (1.516 to 1.641)	1.440 ± 0.233 (1.384 to 1.497)	1.445 ± 0.251 (1.384 to 1.506)
Disk area (mm^2)	1.946 ± 0.343 (1.864 to 2.028)	1.957 ± 0.377 (1.867 to 2.048)	1.830 ± 0.321 (1.752 to 1.907)	1.808 ± 0.387 (1.714 to 1.902)
Average C/D ratio	0.390 ± 0.171 (0.349 to 0.431)	0.382 ± 0.178 (0.340 to 0.425)	0.397 ± 0.198 (0.349 to 0.445)	0.404 ±0.187 (0.359 to 0.450)
Vertical C/D ratio	0.368 ± 0.164 (0.328 to 0.407)	0.351 ± 0.166 (0.311 to 0.390)	0.366 ± 0.187 (0.320 to 0.411)	0.383 ± 0.176 (0.340 to 0.425)
Cup volume (mm^3)	0.107 ± 0.119 (0.0786 to 0.136)	0.111 ±0.132 (0.0792 to 0.143)	0.126 ± 0.143 (0.0917 to 0.161)	0.128 ± 0.147 (0.0927 to 0.164)
RNFL thickness (µm)				
Average	100.6 ± 9.4 (98.4 to 102.9)	100.7 ± 11.5 (98.0 to 103.5)	97.5 ± 10.0 (95.1 to 100.0)	96.8 ± 10.2 (94.3 to 99.3)
Quadrants				
Inferior	129.5 ± 17.2 (125.4 to 133.6)	126.9 ± 24.0 (121.1 to 132.7)	123.5 ± 17.1 (119.4 to 127.7)	121.1 ± 18.8 (116.5 to 125.6)
Superior	126.5 ± 14.2 (123.1 to 129.9)	130.8 ± 18.6 (126.3 to 135.3)	123.4 ± 16.0 (119.5 to 127.3)	127.0 ± 16.5 (123.0 to 131.0)
Nasal	75.3 ± 12.6 (72.3 to 78.3)	72.0 ± 12.8 (68.9 to 75.1)	73.7 ± 12.1 (707.8 to 76.6)	70.3 ± 11.9 (67.4 to 73.1)
Temporal	71.3 ± 9.9 (68.9 to 73.7)	71.5 ± 13.2 (68.3 to 74.7)	69.8 ± 10.6 (67.2 to 72.3)	67.8 ± 9.8 (65.4 to 70.2)
Clock hours				
1	112.2 ± 21.0 (107.2 to 117.3)	134.1 ± 25.3 (128.1 to 140.2)	110.1 ± 20.1 (105.2 to 115.0)	131.6 ± 22.1 (126.3 to 137.0)
2	96.1 ± 17.7 (91.8 to 100.3)	80.1 ± 12.4 (77.1 to 83.0)	93.0 ± 18.0 (88.7 to 97.4)	83.4 ± 23.6 (77.6 to 89.1)
3	58.8 ± 11.6 (56.0 to 61.6)	53.2 ± 9.1 (51.0 to 55.3)	60.4 ± 15.4 (56.7 to 64.2)	53.7 ± 11.7 (50.8 to 56.5)
4	71.1 ± 14.1 (67.7 to 74.4)	75.0 ± 15.9 (71.2 to 78.9)	70.6 ± 14.7 (67.0 to 74.1)	72.4 ± 16.2 (68.5 to 76.3)
5	108.8 ± 23.8 (103.1 to 114.5)	145.5 ± 21.8 (140.2 to 150.7)	97.7 ± 23.6 (92.0 to 103.4)	134.7 ± 26.1 (128.4 to 141.0)
6	137.5 ± 25.0 (131.5 to 143.5)	138.9 ± 28.6 (132.1 to 145.8)	126.1 ± 30.9 (118.6 to 133.6)	127.8 ± 29.9 (120.6 to 135.0)
7	142.2 ± 24.9 (136.2 to 148.2)	107.2 ± 22.6 (101.7 to 112.6)	140.2 ± 22.3 (134.8 to 145.6)	100.5 ± 25.1 (94.4 to 106.6)
8	76.4 ± 15.3 (72.8 to 80.1)	67.3 ± 17.4 (63.1 to 71.5)	80.1 ± 27.5 (73.5 to 86.8)	69.7 ± 15.8 (65.9 to 73.5)
9	53.9 ± 7.6 (52.1 to 55.8)	54.9 ± 11.7 (52.1 to 57.7)	54.0 ± 10.9 (51.4 to 56.7)	55.2 ± 11.5 (52.4 to 58.0)
10	83.7 ± 15.0 (80.1 to 87.3)	92.9 ± 18.1 (88.5 to 97.2)	80.3 ± 17.0 (76.2 to 84.5)	87.3 ± 20.3 (82.4 to 92.2)
11	137.9 ± 20.3 (133.1 to 142.8)	123.3 ± 21.0 (118.3 to 128.4)	136.4 ± 25.0 (130.4 to 142.5)	118.9 ± 24.7 (112.9 to 124.9)
12	129.2 ± 26.2 (122.9 to 135.6)	136.8 ± 26.8 (130.4 to 143.2)	123.7 ± 30.1 (116.4 to 131.0)	126.4 ± 29.2 (119.3 to 133.5)

TABLE 2 (cont'd)

Distribution of ONH Parameters, RNFL Thicknesses, GCL Thicknesses, and Macular Parameters in Children < and ≥ 10 Years, Mean ± SD (5th to 95th Percentile)

	< 10 Years		≥ 10 Years	
Parameter	Right Eye	Left Eye	Right Eye	Left Eye
GCL thickness (µm)				
Average	85.8 ± 5.5 (84.5 to 87.1)	86.0 ± 5.9 (84.6 to 87.5)	84.0 ± 5.3 (82.7 to 85.2)	84.3 ± 5.4 (83.0 to 85.6)
Minimum	83.4 ± 5.8 (82.0 to 84.8)	83.4 ± 5.7 (82.0 to 84.8)	82.4 ± 5.6 (81.0 to 83.8)	83.0 ± 5.2 (81.7 to 84.2)
Sectors				
Superior	85.9 ± 6.0 (84.5 to 87.4)	86.8 ± 6.1 (85.3 to 88.3)	84.1 ± 5.8 (82.7 to 85.5)	84.7 ± 5.5 (83.3 to 86.0)
Supranasal	87.4 ± 5.8 (86.1 to 88.8)	87.4 ± 6.0 (86.0 to 88.9)	85.4 ± 6.0 (83.9 to 86.8)	85.8 ± 6.0 (84.2 to 87.2)
Inferonasal	86.3 ± 5.8 (84.9 to 87.6)	86.4 ± 6.3 (84.9 to 87.9)	84.3 ± 5.9 (82.8 to 85.7)	84.8 ± 5.9 (83.3 to 86.2)
Inferior	85.0 ± 5.9 (83.5 to 86.3)	84.8 ± 6.1 (83.3 to 86.2)	82.8 ± 5.6 (81.4 to 84.1)	82.9 ± 5.9 (81.4 to 84.3)
Inferotemporal	86.0 ± 6.3 (84.4 to 87.5)	85.7 ± 6.4 (84.1 to 87.2)	84.2 ± 5.1 (83.0 to 85.4)	84.1 ± 5.4 (82.8 to 85.4)
Supratemporal	84.5 ± 6.0 (83.0 to 85.9)	84.9 ± 6.1 (83.5 to 86.4)	83.0 ± 5.1 (81.8 to 84.2)	83.6 ± 5.4 (82.3 to 84.9)
Macular parameters				
Central macular subfield thickness (µm)	246.4 ± 19.1 (241.8 to 251.0)	246.2 ± 18.4 (241.7 to 250.6)	255.7 ± 22.2 (250.3 to 261.1)	257.0 ± 21.1 (251.9 to 262.1)
Average macular volume (mm^3)	10.1 ± 1.3 (9.8 to 10.4)	10.2 ± 0.5 (10.1 to 10.3)	10.1 ± 1.0 (9.8 to 10.3)	10.2 ± 0.5 (10.0 to 10.3)
Average macular thickness (µm)	283.7 ± 12.0 (280.8 to 286.6)	283.6 ± 12.7 (280.6 to 286.7)	283.4 ± 19.6 (278.6 to 288.1)	282.2 ± 13.4 (278.9 to 285.4)
Inner circle (µm)				
Superior	322.7 ± 13.6 (319.5 to 326.0)	321.7 ± 15.7 (318.0 to 325.5)	322.0 ± 16.4 (318.0 to 326.0)	323.6 ± 16.1 (319.7 to 327.5)
Nasal	319.5 ± 13.9 (316.1 to 322.8)	320.0 ± 14.6 (316.5 to 323.5)	322.3 ± 16.9 (318.2 to 326.3)	323.3 ± 16.4 (319.4 to 327.3)
Inferior	318.7 ± 14.2 (315.3 to 322.1)	317.8 ± 14.4 (314.3 to 321.2)	317.7 ± 15.4 (314.0 to 321.4)	318.0 ± 15.0 (314.3 to 321.6)
Temporal	309.0 ± 14.4 (305.6 to 312.5)	307.5 ± 14.7 (304.0 to 311.0)	308.1 ± 15.3 (304.4 to 311.8)	309.1 ± 15.5 (305.3 to 312.9)
Outer circle (µm)				
Superior	285.1 ± 13.7 (281.8 to 288.4)	285.8 ± 14.4 (282.4 to 289.3)	282.4 ± 15.9 (278.6 to 286.3)	282.4 ± 18.3 (278.0 to 286.8)
Nasal	301.7 ± 14.6 (298.2 to 305.2)	302.6 ± 16.3 (298.7 to 306.5)	299.1 ± 16.8 (295.0 to 303.1)	299.7 ± 16.3 (295.7 to 303.6)
Inferior	274.1 ± 13.4 (270.9 to 277.4)	274.6 ± 14.5 (271.1 to 278.0)	269.0 ± 14.9 (265.4 to 272.6)	270.9 ± 14.1 (267.5 to 274.4)
Temporal	267.6 ± 12.9 (264.5 to 270.7)	267.4 ± 13.7 (264.2 to 270.7)	261.6 ± 13.6 (258.3 to 264.9)	263.0 ± 13.5 (259.7 to 266.3)

C/D = cup-to-disk; GCL = ganglion cell layer; ONH = optic nerve head; RNFL = retinal nerve fiber layer; SD = standard deviation

Regional variations in SER, such as the higher prevalence of myopia in Asia, as well as environmental,[16] nutrional,[17] and hormonal factors,[18] may contribute to the thinner OCT values observed in these

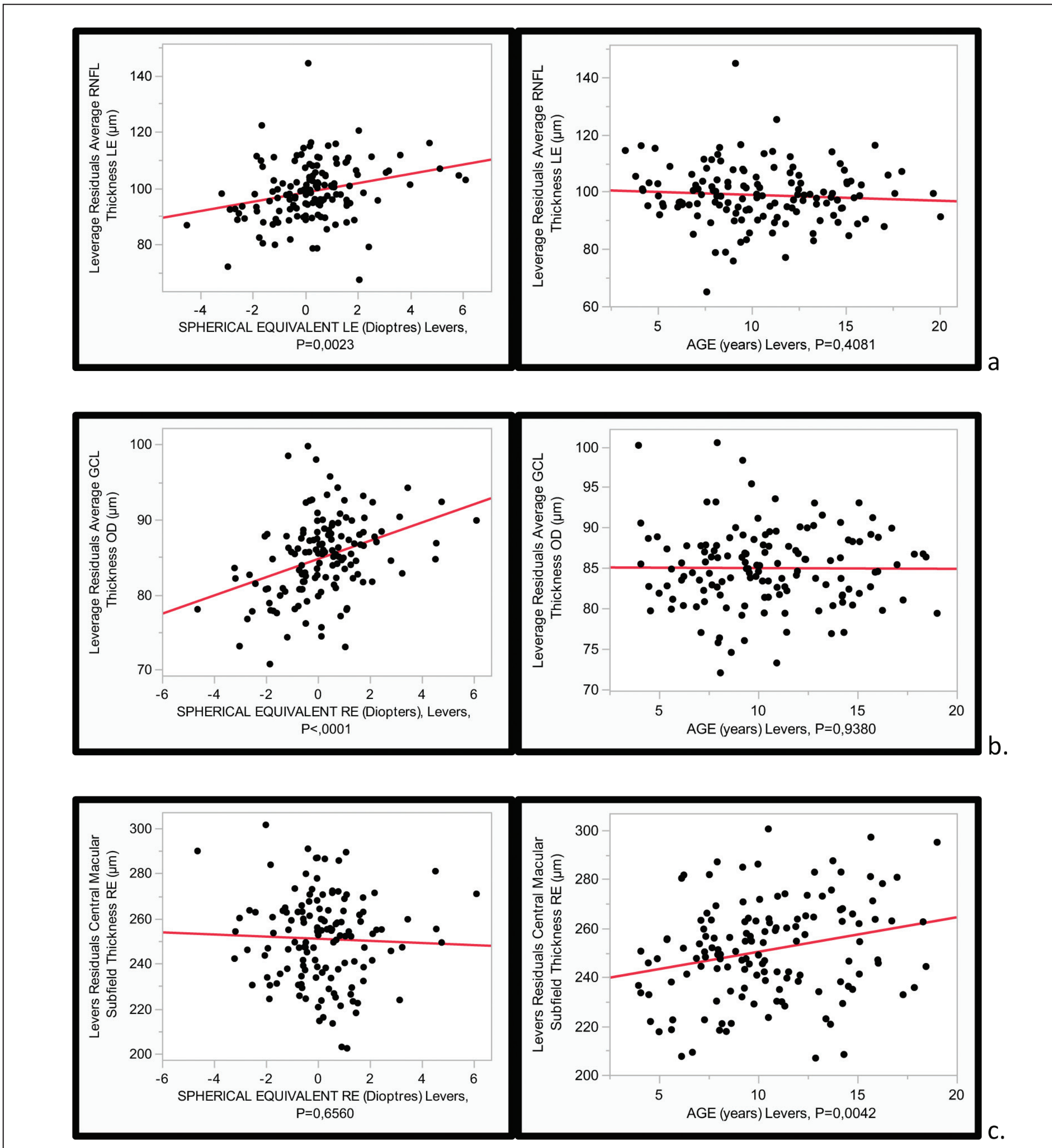

Figure 3. Multivariate regression analysis for (A) average retinal nerve fiber layer (RNFL) thickness of the left eye ($P = .0023$ for refraction, $P = .4081$ for age), and (B) average ganglion cell layer (GCL), thickness of the right eye ($P < .0001$ for refraction, $P = .9380$ for age), and (C) central macular subfield thickness of the right eye ($P = .6550$ for refraction, $P = .0042$ for age).

populations. On the other hand, European studies showed similar RNFL, GCL, and macular values compared to our study. However, our study reported smaller rim area, disk area, and cup volume values compared to the other studies, and particularly another European study by Altemir et al.[19] This difference could be attributed to the fact that their study, published in 2013, used an earlier version of the Cirrus OCT, whereas our study used the Cirrus 6000. The latter offers improved image resolution and speed, more advanced image processing algorithms and software enhancements, and enhanced optics and light source to reduce noise and artifacts. These improvements contribute to more accurate measurements and may result in different values compared to older versions of the Cirrus OCT. A notable finding

TABLE 3

Multivariate Regression Analysis for OCT Parameters by Age, SER, Ethnicity, and Gender[a]

Parameter	Age, Regression Coefficient (*P*)		SER, Regression Coefficient (*P*)		Ethnicity, F Ratio Coefficient (*P*)		Gender, F Ratio Coefficient (*P*)	
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye
ONH parameters								
Rim area (mm^2)	-0.013 (.0273)	-0.012 (.0592)	0.026 (.0483)	0.030 (.0210)	1.29 (.2755)	1.10 (.3617)	0.0021 (.9638)	0.013 (.9101)
Disk area (mm^2)	-0.013 (.1030)	-0.0078 (.3843)	0.020 (.2498)	0.027 (.1677)	4.06 **(.0039)**	2.66 **(.0357)**	0.0075 (.9310)	0.20 (.6591)
Average C/D ratio	0.0020 (.6411)	0.0037 (.3748)	-0.0017 (.8612)	-0.0026 (.7690)	4.06 **(.0039)**	4.29 **(.0027)**	0.062 (.8038)	0.15 (.6968)
Vertical C/D ratio	0.0025 (.5568)	0.0037 (.3491)	0.00061 (.9467)	-0.0052 (.5465)	3.76 **(.0063)**	3.07 **(.0188)**	0.24 (.6224)	0.25 (.6202)
Cup volume (mm^3)	0.0016 (.5879)	0.0022 (.4935)	-0.0035 (.5942)	-0.0037 (.5938)	5.42 (.0005)	4.15 (.0034)	0.38 (.5413)	0.75 (.3876)
RNFL thickness (μm)								
Average	-0.073 (.7407)	-0.20 (.4081)	1.91 **(.0001)**	1.65 **(.0023)**	3.90 (.0050)	3.07 (.0187)	0.76 (.3835)	0.22 (.6406)
Inferior	-0.062 (.8734)	-0.21 (.6707)	3.49 **(< .0001)**	2.95 (.0070)	3.41 (.0110)	1.81 (.1307)	0.55 (.4613)	0.007 (.9349)
Superior	-0.23 (.5084)	-0.11 (.7874)	1.64 **(.0341)**	1.68 (.0566)	4.69 **(.0015)**	3.26 **(.0139)**	0.044 (.8348)	0.009 (.9245)
Nasal	0.32 (.2580)	0.11 (.7022)	2.61 **(< .0001)**	2.27 **(.0002)**	1.91 (.1120)	2.65 **(.0365)**	1.59 (.2100)	1.61 (.2065)
Temporal	-0.30 (.2358)	-0.57 (.0439)	-0.18 (.7477)	-0.23 (.7030)	0.49 (.7463)	0.55 (.7002)	0.76 (.3849)	0.096 (.7570)
GCL thickness (μm)								
Average	-0.0096 (.9380)	-0.015 (.9092)	1.21 **(< .0001)**	1.02 **(.0004)**	1.42 (.2314)	1.28 (.2798)	0.045 (.8320)	0.0001 (.9935)
Minimum	0.049 (.7163)	0.15 (.2399)	0.96 **(.0014)**	0.87 (.0016)	0.79 (.5368)	1.28 (.2806)	0.0001 (.9937)	0.3613 (.5488)
Superior	-0.078 (.5719)	-0.10 (.4513)	0.97 **(.0018)**	0.87 **(.0032)**	1.36 (.2525)	1.79 (.1343)	0.63 (.4281)	0.44 (.5096)
Supranasal	-0.065 (.6313)	0.0096 (.9438)	1.19 **(< .0001)**	1.11 **(.0002)**	1.90 (.1141)	1.78 (.1372)	0.051 (.8221)	0.036 (.8494)
Inferonasal	-0.030 (.8153)	-0.013 (.9280)	1.39 **(< .0001)**	1.16 **(.0002)**	2.12 (.0822)	1.04 (.3889)	0.50 (.4827)	0.028 (.8669)
Inferior	-0.065 (.6115)	-0.059 (.6691)	1.34 **(< .0001)**	1.11 **(.0003)**	2.01 (.0970)	1.70 (.1533)	1.90 (.1709)	1.67 (.1990)
Inferotemporal	0.043 (.7399)	0.036 (.7927)	1.27 **(< .0001)**	1.02 **(.0007)**	1.31 (.2708)	0.86 (.4892)	0.25 (.6173)	0.35 (.5557)
Supratemporal	0.080 (.5444)	0.088 (.5105)	1.01 **(.0006)**	0.89 **(.0022)**	0.46 (.7681)	0.84 (.5046)	1.07 (.3026)	1.23 (.2686)
Macular parameters								
Central macular subfield thickness (μm)	1.41 **(.0042)**	1.42 **(.0023)**	-0.47 (.6560)	-0.82 (.4003)	1.30 (.2720)	1.40 (.2378)	11.80 **(.0008)**	10.30 **(.0017)**
Average macular volume (mm^3)	-0.0052 (.8618)	0.000037 (.9974)	-0.011 (.8669)	0.038 (.1196)	0.047 (.9957)	0.30 (.8545)	0.98 (.3242)	0.0005 (.9830)
Average macular thicknesses (μm)	0.49 (.2132)	0.042 (.8926)	2.15 **(.0134)**	1.08 (.1112)	0.70 (.5961)	0.34 (.8529)	0.0048 (.9450)	0.0036 (.9525)

TABLE 3 (cont'd)

Multivariate Regression Analysis for OCT Parameters by Age, SER, Ethnicity, and Gender[a]

Parameter	Age, Regression Coefficient (*P*)		SER, Regression Coefficient (*P*)		Ethnicity, F Ratio Coefficient (*P*)		Gender, F Ratio Coefficient (*P*)	
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye
Inner circle								
Superior	0.32 (.3884)	0.47 (.2258)	1.01 (.2119)	0.34 (.6844)	0.58 (.6811)	0.40 (.8069)	2.73 (.1009)	0.75 (.3869)
Nasal	0.67 (.0731)	0.54 (.1448)	0.85 (.3015)	0.14 (.8558)	0.43 (.7841)	0.54 (.7057)	6.77 (.0104)	4.08 **(.0454)**
Inferior	0.23 (.5295)	0.26 (.4687)	1.20 (.1305)	0.51 (.5003)	0.43 (.7851)	0.28 (.8875)	2.99 (.0860)	2.14 (.1461)
Temporal	0.35 (.3291)	-5.15 (.3783)	0.81 **(.3025)**	-2.44 (.8461)	1.09 (.3644)	0.23 (.9205)	5.47 **(.0209)**	1.49 (.2247)
Outer circle								
Superior	0.086 (.8085)	-0.47 (.2329)	2.31 **(.0035)**	0.90 (.2839)	0.70 (.5926)	1.17 (.3278)	0.068 (.7945)	0.93 (.3363)
Nasal	-0.0018 (.9963)	-0.24 (.5375)	2.14 **(.0106)**	1.04 **(.2217)**	0.8536 (.4939)	0.34 (.8481)	0.1604 (.6894)	0.078 (.7801)
Inferior	-0.25 (.4515)	-0.20 (.5540)	2.35 **(.0018)**	1.55 **(.0371)**	1.42 (.2316)	0.15 (.9617)	0.10 (.7512)	0.27 (.6075)
Temporal	-0.14 (.6612)	-0.11 (.7304)	2.24 **(.0014)**	1.45 **(.0403)**	0.59 (.6708)	0.53 (.7152)	1.08 (.3002)	0.097 (.7555)

C/D = cup-to-disk; GCL = ganglion cell layer; OCT = optical coherence tomography; ONH = optic nerve head; RNFL = retinal nerve fiber layer; SER = spherical equivalent refraction

[a]Only the measurements that exhibit statistically significant differences are in bold.

in our study is the non-adherence to the ISNT rule. Banc and Ungureanu[1] state that non-adherence to the ISNT rule is not unusual in the pediatric population. In this review, among all seven Cirrus SD-OCT studies that addressed the ISNT rule, six reported adherence,[20,21] with only one not observing it.

In line with Rozema et al,[12] who studied eye elongation, the bivariate analysis revealed a Pearson correlation of -0.43 for the right eye and -0.41 for the left eye between SER and age ($P < .0001$). Multivariate analysis revealed that age showed a statistically significant negative correlation with rim area and temporal quadrant of RNFL thickness, which may be explained by axial elongation. As opposed to our results, most of the OCT studies in children[1-4,7] found no correlation between age and RNFL thickness. SER showed a significant positive correlation with rim area, RNFL, GCL, and macular thicknesses. The effect of the SER is controversial in the literature, with mixed findings. Some studies found no correlation between SER and RNFL thickness[2,4] or macular parameters,[4] whereas others showed a correlation.[1,5-7] Our results demonstrated that emmetropization affects OCT parameters. Two studies[8,9] reported an effect of age on optic nerve head parameters (cup diameter and vertical disk diameter) and superior-temporal quadrant of RNFL thickness, whereas two others[10,11] showed no effect of age. Gender was significantly correlated with central macular subfield and inner-circle macular thicknesses, with boys having thicker values, which was supported by several studies.[1,3-7] However, the variance analysis of different OCT parameters indicated that the variables studied (age, refraction, ethnicity, and gender) did not fully explain the observed variance of OCT parameters. This suggests the involvement of additional factors not accounted for in this study (eg, genetics,[22] environment,[16] nutrition,[17] and hormones[18]).

Foveal development is thought to be complete by 5 years of age and involves a centrifugal migration of the inner retinal layers and centripetal migration of the photoreceptor layer. Rotruck et al[11] demonstrated a decrease in the GCL, ganglion cell complex, and inner nuclear layer at the macula, accompanied by a logarithmic increase in the photoreceptor layer during the first 5 years of life, similar to the findings of Lee et al.[23] In line with these findings, Alabduljalil et al[24] observed a significant increase in total retinal thickness at the foveal center and at what the authors called “Sector 1” (1 mm around the fovea, corresponding to the central macular subfield) during early childhood, with a notable increase in photoreceptor thickness during the first 24 months of life. On the other hand, as opposed to Rotruck et al,[11] Alabduljalil et al[24] noted no change in the inner retinal layer thickness over the first 5 years. In our study, and in line with these observations, we observed a significant increase in central macular subfield thickness with age, and a statistically non-significant decrease in GCL thickness, which could be explained by the foveal reorganization during early childhood. In addition, Vajzovic et al[25] reported that foveal cone packing continues throughout childhood, reaching a thickness of more than 10 cell bodies between the ages of 13 and 16 years. In our study, this increase in central macular subfield thickness from ages 3 to 17.9 years probably reflects the thickening of the photoreceptor layer and the thinning of the inner retinal layers.

This prospective multicenter study reduces single-center bias by including populations from multiple hospital centers. It provides a comprehensive OCT database covering all parameters and includes children aged 3 to 17.9 years, with different ethnicities and a balanced distribution across age groups. However, all of the patients in our study were hospital-based and did not reflect the general population. Cycloplegia was not used for SER classification. Sankaridurg et al[26] observed that only 61% of children were correctly classified into refractive error groups without cycloplegia. Their study used the same definition to classify patients into refractive error groups, both with and without cycloplegia, without considering accommodative tonus. Rozema et al[12] suggested the definition of non-cycloplegic emmetropia as 0.00 ± 0.50 D, which we have adopted.

CONCLUSION

We have established reference normative data for the Cirrus OCT measurements of optic nerve head parameters, RNFL, GCL, and macular thicknesses in a healthy pediatric population. Our findings indicate that these measurements were influenced by age, refraction, gender, and ethnicity. We also observed that emmetropization likely led to a thinning of RNFL, GCL, and macular thicknesses, whereas reorganization of the foveal zone during childhood may explain the increase in central macular thickness with age.

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Table A

Reported Optic Nerve Head Parameters, Average RNFL Thickness, Average GCL Thickness, and Macular Parameters in Normal Pediatric Population in the Literature

Study	OCT	N (Participants / Eyes)	Refraction, diopters (mean, range)	Age, years (mean, range)	Ethnicity	Rim area ± SD, mm²	Disc area ± SD, mm²	Cup volume ± SD, mm³	Average RNFL Thickness ± SD, µm	Average GCL-IPL Thickness ± SD, µm	Macular Parameters: Average Thickness ± SD, µm	Macular Parameters: Central Thickness ± SD, µm	Macular Parameters: Volume ± SD, mm³
Non-Cirrus													
Bhoiwala[27] 2015	RTVue 100 Avanti	77 / 77	RE : +0.89 LE : +0.81, -1.25 to +3.00	5.08, range NA	NA (USA)	NA	**2.01** ± 0.40	NA	**103.93** ± 10.59	**98.37** ± 5.94	NA	NA	NA
Perez-Garcia[28] 2016	Spectralis	162 / NA	+0.03, NA	8.1, 3-14	Caucasian (Spain)	NA	NA	NA	**100.45** ± 1.98	NA	NA	**263.69** ± 4.54	NA
Asia													
Goh[29] 2017	Cirrus	139 / 243	-3.20, -12.88 to +7.75	9.47, 3 to 18	Asian (Singapore)	NA	NA	NA	**99** ± 11.45	**82.59** ± 6.29	NA	**245.12** ± 19.79	NA
Güragaç[7] 2016	Cirrus	318 / 318	-0.21, -4.00 to +3.00	10.2, 3 to 17	Asian (Turkey)	NA	NA	NA	**96.49** ± 10.10	NA	**279.27** ± 12.59	**245.28** ± 19.47	**9.97** ± 0.44

Middle East													
Al-Haddad[21] 2013	Cirrus	108 / 108	-0.02, -4.25 to +5.00	10.7, 6-17	Middle-East (Lebanon)	NA	NA	NA	**95.6** ± 8.7	NA	**279.6** ± 12.5	**249.1** ± 20.2	**10.1** ± 0.5
Raffa[30] 2023	Cirrus	135 / NA	NA	10.19, 4-18	Middle-East (Saudi Arabia)	**1.6** ± 0.3	**2.0** ± 0.4	**0.3** ± 1.1	**93.88** ± 10.0	NA	**275.9** ± 17.7	**240.6** ± 28.2	**9.9** ± 0.6
Europe													
Altemir[19] 2013	Cirrus	357 / 714	NA, -3.00 to +4.50	9.00, 6-14	Caucasian 96% Other 4% (Spain)	RE : **1.59** ± 0.34 LE : **1.57** ± 0.34	RE : **2.06** ± 0.39 LE : **2.03** ± 0.39	NA	RE : **98.50** ± 7.93 LE : **97.76** ± 7.93	NA	RE : **282.61** ± NA LE : **282.31** ± NA	NA	RE : **10.18** ± 0.37 LE : **10.17** ± 0.37
Queiros[20] 2015	Cirrus	153 / 306	-0.39, -5.00 to +5.00	9.54, 4-17	Caucasian (Portugal)	NA	NA	NA	**97.90** ± 9.32	NA	**282.26** ± 11.59	**250.35** ± 19.28	**10.17** ± 0.41
Haffane 2024 Current study	Cirrus	137 / 274	RE : +0.18 LE : +0.27, -5.125 to +6.00	10.41, 3-18	Caucasian 51.8% North African 30.7% Other 17.5% (Belgium)	RE :**1.50** ± 0.25 LE : **1.51** ± 0.26	RE : **1.89** ± 0.34 LE : **1.88** ± 0.39	RE : **0.12** ± 0.13 LE : **0.12** ± 0.14	RE : **99.10** ± 9.82 LE : **98.80** ± 11.02	RE : **84.88** ± 5.47 LE : **85.18** ± 5.69	RE : **283.53** ± 16.15 LE : **282.91** ± 13.02	RE : **251.03** ± 21.19 LE : **251.52** ± 20.47	RE : **10.06** ± 1.18 LE : **10.18** ± 0.47

NA: Not Available; LE: Left Eye ; RE: Right Eye; SD: Standard Deviation