

Macular thickness in healthy Saudi adults

A spectral-domain optical coherence tomography study

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ABSTRACT

الأهداف: وصف سماكة المركز البقعي للشبكية بواسطة تصوير التماسك البصري المقطعي (SD-OCT) في عيون الأصحاء البالغين السعوديين.

الطريقة: هذه دراسة استطلاعية مستعرضة شملت 158 مشاركاً سليماً. كان متوسط العمر 29.9 ± 7.85 سنة. خضع جميع المشاركين في الدراسة لفحص العيون الشامل بما في ذلك تصوير التماسك البصري المقطعي وقياس طول العين المحوري. تم تضمين بيانات العين اليمنى فقط. تم تحديد معدل سماكة شبكية العين. وتم فحص العلاقة بين سماكة شبكية العين والجنس والعمر والطول المحوري للعين والتكافؤ الكروي.

النتائج: وأظهرت النتائج أن متوسط سماكة الشبكية المركزي بلغ 244.76 ± 23.62 ميكرون، وبلغ متوسط طول محوري الكروي 23.8 ± 1.062 مم (المدى: 20.5-29 مم)، وبلغ متوسط المعادل الكروي -0.31 ± 1.75 D (المدى: -5.50 إلى +4.25 D). وكانت سماكة المنطقة المركزية وحجم النقيرة أقل بكثير في النساء من الرجال (كلاهما $p < 0.001$). ولم يوجد فرق في سماكة المنطقة المركزية ($p = 0.389$) ولا حجم النقيرة ($p = 0.341$) بين الفئات العمرية الثلاث. ولوحظ وجود علاقة إيجابية بين سماكة السائل النخاعي وطول محوري ($p < 0.001$).

الخلاصة: أظهرت الدراسة ان سماكة البقعة الصفراء الطبيعي في البالغين السعوديين والتي تم قياسها بواسطة تصوير التماسك البصري المقطعي (SD-OCT) تختلف عن تلك التي سجلت في الشعوب الأخرى. وكانت المنطقة المركزية وحجم النقيرة أكثر سمكاً لدى الرجال السعوديين من النساء السعوديات وان الطول المحوري يرتبط بشكل إيجابي مع سماكة المنطقة المركزية.

Objectives: To determine the macular thickness in the eyes of healthy Saudi adults using spectral-domain optical coherence tomography (SD-OCT).

Methods: This is a prospective, cross-sectional study, including 158 healthy participants between August and December 2015. Mean subject age was 29.9 ± 7.85 years old. All participants underwent full ophthalmic

evaluation, including SD-OCT imaging, and axial length measurement. Data from the right eye were included. Mean retinal thickness was determined. Correlations between retinal thickness and gender, age, axial length, and spherical equivalence were analyzed.

Results: Mean central retinal thickness was 244.76 ± 23.62 μ m, mean axial length was 23.8 ± 1.062 mm (range: 20.5-29 mm) and mean spherical equivalent was -0.31 ± 1.75 diopters (D) (range: -5.50 to +4.25 D). Central subfield (CSF) thickness and foveal volume were significantly lower in women than in men (both $p < 0.001$). Data from the various age groups did not show statistically significant differences in the CSF thickness ($p = 0.389$) or foveal volume ($p = 0.341$). A positive correlation between CSF thickness and axial length ($p < 0.001$) was observed.

Conclusion: The normal macular thickness values in healthy Saudi individuals is different from that reported in other ethnic groups, as obtained by SD-OCT. Saudi men had thicker CSF than Saudi women and axial length was positively correlated to the central foveal thickness.

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The values of normal macular thickness in different patient populations is essential for evaluating, treating and following-up of patients with various ocular pathologies.¹ Optical coherence tomography (OCT) is a non-invasive technology that provides *in vivo* high-resolution measurements of the macular thickness that enables clinicians to detect and monitor subtle changes in macular thickness.²⁻⁷ Normative macular thickness was obtained by several studies using OCT.^{8,9} Spectral domain OCT (SD-OCT) systems are faster and more sensitive than time-domain OCT (TD-OCT) systems that provide an improved resolution, more accurate segmentation, and data points.¹⁰⁻¹² One important feature of SD-OCT raster scans is its ability to reconstruct a fundus-like image as soon as the scan is acquired.¹³ The OCT fundus images can be useful in screening OCT images for eye movement. The SD-OCT capabilities overcome many limitations of TD-OCT, such as the lack of precise correspondence between B-scans and retinal topography, the difficulty in accounting for eye motion, and the substantial need for data interpolation.¹⁴ Unstable fixation and imprecise targeting can lead to inaccuracies in retinal thickness measurement calculations.¹⁴ Several authors have published normative data for macular thickness, using the Spectralis SD-OCT technology.¹⁵⁻¹⁷ However, there is a significant variation in macular thickness values between different ethnic groups in both TD- and SD-OCT measurements.¹⁸⁻²⁰ These variations mean that different cut-off points for abnormal retinal thickness are needed to properly evaluate macular conditions in each ethnic population. The primary purpose of the current study was to determine normative macular thickness values in healthy Saudi adult subjects using the Cirrus SD-OCT. The secondary purpose was to evaluate correlations between macular thickness and age, gender, axial length, and spherical equivalence.

Methods. This cross-sectional study was performed at King Fahad Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia between August and December 2015. The study was approved by the local institutional review board. Written informed consent was obtained from each subject prior to performing any study examination. Subjects were selected from outpatient clinic medical personnel and patient relatives. Subject gender was predetermined. Inclusion criteria were as follows: 1) age ≥ 18 years and the ability to provide written informed consent, 2) Snellen best-corrected visual acuity (BCVA) better than 20/40, 3) spherical refractive error less than ± 6 diopters (D)

and astigmatism ≤ 3 D, 4) intraocular pressure (IOP) ≤ 21 mm Hg, and 5) cup-to disc ratio ≤ 0.4 .

Subjects were excluded if they met one or more of the following exclusion criteria: 1) history or clinical evidence of macular, retinal, glaucomatous, or neurological conditions affecting retinal nerve fiber thickness, 2) diagnosis of diabetes, 3) history of ocular trauma, or 4) history of intraocular surgery or retinal laser treatment. In subjects who had both eyes eligible, only data from the right eye were included in macular thickness analyses. In subjects who had only one eligible eye, data from that only eye were included in analyses.

All subjects underwent comprehensive ophthalmic examinations, including measurement of Snellen BCVA, IOP (Goldmann applanation tonometer), axial length (IOLMaster, Carl Zeiss Meditec, Inc.), and macular thickness by spectral-domain OCT (Cirrus HD-OCT; software version 6.0; Carl Zeiss Meditec, Inc.). Slit-lamp biomicroscopy and a stereo biomicroscopy fundus examination were also performed.

All OCT scans were performed by a single experienced operator through a nondilated pupil. An internal fixation light was used to center scans on the fovea. Images were generated using a high-speed volumetric raster scan pattern over a $20^0 \times 20^0$ area. Each raster scan consisted of 25 horizontal line scans that were spaced 240 μm apart. Each horizontal line scan was created from 512 A-scans. The final horizontal line used in the analyses was the average of 12 B-scans that were averaged using the automatic real-time mode to reduce speckle noise. Two scanning sessions were performed by the same operator, with patients repositioned between sessions. Only scans with a good signal strength, defined as a numerical quality score > 16 and within the blue range of the quality bar, were used in analyses. All images were checked by a single retina specialist. Scans with retinal abnormalities or segmentation errors were excluded.

Macular thickness values were automatically calculated by the built-in software (version 6.0). Macular thickness is defined as the distance between the vitreoretinal interface and the outer border of the retinal pigment epithelium. Mean retinal thickness and volume were displayed in sectors created by 3 concentric rings with diameters of 1 (central), 3 (inner), and 6 (outer) mm, corresponding to the 9 areas of the early treatment diabetic retinopathy study (ETDRS) map (**Figure 1**). The inner and outer rings were divided into 4 areas. Retinal thickness within the inner circle (1 mm diameter) was defined as the central subfield (CSF) thickness. Average macular thickness was calculated for each scanning session and the average value of the 2 sessions was used in analyses.

Pearson's correlation was used to examine correlations between the right and left eyes in mean macular thickness, CSF thickness, average inner ring thickness, average outer ring thickness, mean foveal volume, and mean total macular volume. Differences between male and female patients in mean macular thickness were compared with unpaired t-tests. Patients were divided by age into the following 3 groups: 18-30, 31-43, and ≥ 44 years old. Patients were also divided by spherical equivalent into the following 3 groups: myopia (less than -0.50 D), emmetropia (between -0.50 and +0.50 D), and hyperopia (more than +0.50 D). Moreover, patients were divided into the following groups according to axial

length: ≤ 21.99 , 22.00-22.99, 23.00-23.99, 24.00-24.99, and ≥ 25.00 mm. Comparisons between mean macular thickness of the various age, refractive error, and axial length groups were performed using analysis of variance (ANOVA). Relationships between macular thickness and each factor were assessed using multiple linear regression analysis. Statistical significance was defined as $p < 0.05$. All data were analyzed using the Statistical Package for Social Sciences software version 20 (IBM Corp., Armonk, NY, USA).

Results. The study comprised 158 Saudi; adult subjects (79 males, 50%). Mean subject age was 29.9 ± 7.85 years old (range: 18-56 years old). Mean axial length was 23.8 ± 1.062 mm (range: 20.5-29 mm) and mean spherical equivalent was -0.31 ± 1.75 D (range: -5.50 to +4.25 D). The mean retinal thickness and macular volume for the subjects with 2 eligible eyes were analyzed for correlations between the right and left eyes. The CSF thickness had an interocular correlation coefficient of 0.92 ($p < 0.001$). The 4 inner regions and 4 outer regions had correlation coefficients of 0.92 for the inner regions and 0.94 for the outer regions, (both $p < 0.001$). The interocular correlations of mean foveal volume and total macular volume were 0.93 for mean foveal volume and 0.94 for the total macular volume (both $p < 0.001$).

Mean CSF thickness was 244.76 ± 23.62 μm for all included eyes. Mean retinal thickness in the inner regions was significantly larger than that of the outer regions ($p < 0.001$). Additionally, the temporal segment was the thinnest and the nasal segment was the thickest

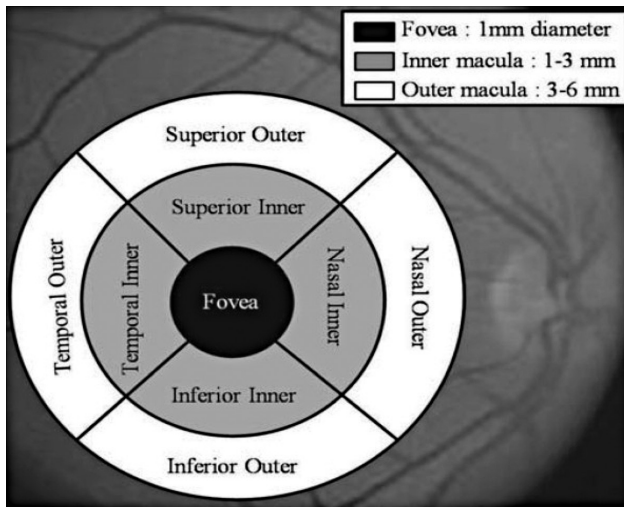


Figure 1 - Early treatment diabetic retinopathy study regions of the macula as measured by macula program of optical coherence tomography.

Table 1 - Mean retinal thickness and macular volume for the whole group and for each gender.

Parameters	Whole group	Men	Women	P-value
Subjects	158	79	79	
<i>Mean retinal thickness ($\mu\pm SD$)</i>				
Central subfield	244.76 \pm 23.62	246.97 \pm 23.56	239.53 \pm 23.19	<0.001
<i>Inner region</i>				
Superior	318.38 \pm 21.69	320.42 \pm 21.41	313.55 \pm 21.81	<0.001
Inferior	315.94 \pm 21.05	318.73 \pm 20.81	309.34 \pm 20.34	<0.001
Nasal	320.23 \pm 20.71	322.75 \pm 20.42	315.28 \pm 20.38	<0.001
Temporal	303.81 \pm 20.70	306.20 \pm 20.73	298.17 \pm 19.72	<0.001
<i>Outer region</i>				
Superior	276.37 \pm 16.58	277.37 \pm 16.35	274.00 \pm 17.06	0.244
Inferior	265.75 \pm 17.31	267.06 \pm 17.05	262.64 \pm 17.71	0.150
Nasal	293.18 \pm 21.21	295.23 \pm 19.83	288.34 \pm 23.70	<0.001
Temporal	259.56 \pm 25.24	261.20 \pm 15.45	255.68 \pm 39.76	<0.001
<i>Mean macular volume (mm^3)</i>				
Fovea	0.20 \pm 0.02	0.21 \pm 0.02	0.20 \pm 0.01	<0.001
Total	8.48 \pm 0.35	8.56 \pm 0.34	8.41 \pm 0.38	<0.001

SD - standard deviation

in both the inner and outer rings ($p < 0.001$). Mean foveal volume was $0.20 \pm 0.02 \text{ mm}^3$ and mean macular volume was $8.48 \pm 0.35 \text{ mm}^3$. When the genders were examined separately, eyes of male subjects had significantly greater mean retinal thickness and mean retinal volume values than eyes of female subjects in all inner areas. Mean CSF thickness was $246.97 \pm 23.56 \mu\text{m}$ in men and $239.53 \pm 23.19 \mu\text{m}$ in women ($p < 0.001$). Total macular volume was $8.56 \pm 0.34 \text{ mm}^3$ in men and $8.41 \pm 0.38 \text{ mm}^3$ in women ($p < 0.001$). Mean macular thickness as per ETDRS standard for the whole group and for each gender is presented in Table 1.

The comparison of data from the various age groups did not show statistically significant differences in the CSF thickness ($p = 0.386$) or foveal volume ($p = 0.341$) (Table 2). When axial length groups were compared, statistically significant differences in mean CSF thickness and mean foveal volume were found (all $p < 0.001$) (Table 3). A significantly positive correlation was obtained with axial length after adjusting for age, mean CSF thicknesses and mean foveal volumes (all $p < 0.001$). Interestingly, the mean retinal thickness of each of the 4 outer regions and total macular volume were significantly and negatively correlated with the axial length ($p < 0.001-0.023$).

Table 2 - Mean retinal thickness by age groups.

Parameters	Years			P-value
	18-30	31-43	44-56	
Subjects	83	55	20	
<i>Mean retinal thickness ($\mu\text{m} \pm \text{SD}$)</i>				
Central subfield	247.05 \pm 24.42	243.07 \pm 23.09	244.54 \pm 24.02	0.386
Inner region				
Superior	321.99 \pm 21.03	313.27 \pm 20.93	322.72 \pm 25.13	<0.001
Inferior	320.05 \pm 21.02	311.30 \pm 19.74	316.70 \pm 24.41	<0.001
Nasal	323.13 \pm 20.55	319.77 \pm 19.97	323.94 \pm 23.03	<0.001
Temporal	306.87 \pm 21.51	299.45 \pm 18.05	306.23 \pm 24.19	<0.001
Outer region				
Superior	279.64 \pm 15.45	272.57 \pm 16.95	277.82 \pm 19.13	<0.001
Inferior	269.07 \pm 16.66	263.05 \pm 16.99	263.75 \pm 22.00	<0.001
Nasal	298.54 \pm 19.35	289.43 \pm 19.89	287.01 \pm 30.99	<0.001
Temporal	262.83 \pm 19.95	255.77 \pm 32.07	261.73 \pm 19.10	<0.001
<i>Mean macular volume (mm^3)</i>				
Fovea	0.21 \pm 0.02	0.20 \pm 0.01	0.20 \pm 0.01	0.341
Total	8.78 \pm 0.36	8.79 \pm 0.33	8.56 \pm 0.32	<0.001

SD - standard deviation

Table 3 - Mean retinal thicknesses and macular volumes of various axial length groups.

Parameters	Axial length (mm)					P-value
	≤ 21.99	22.00-22.99	23.00-23.99	24.00-24.99	≥ 25.00	
Subjects	7	23	62	56	10	
<i>Mean retinal thickness ($\mu\text{m} \pm \text{SD}$)</i>						
Central subfield	231.14 \pm 20.16	239.56 \pm 21.67	243.69 \pm 22.06	249.45 \pm 24.44	253.34 \pm 16.78	<0.001
Inner region						
Superior	316.78 \pm 15.37	326.44 \pm 15.95	321.80 \pm 14.02	330.23 \pm 11.36	337.64 \pm 13.60	0.004
Inferior	330.82 \pm 18.24	339.65 \pm 17.93	331.55 \pm 13.76	342.55 \pm 12.53	346.08 \pm 11.50	0.051
Nasal	333.80 \pm 16.84	339.66 \pm 17.94	332.64 \pm 14.06	344.49 \pm 14.98	346.12 \pm 13.16	0.032
Temporal	324.72 \pm 18.39	335.75 \pm 18.85	330.77 \pm 13.92	339.57 \pm 12.17	344.08 \pm 14.09	0.009
Outer region						
Superior	279.41 \pm 16.24	286.04 \pm 16.05	273.96 \pm 12.32	282.52 \pm 12.59	286.68 \pm 12.10	0.331
Inferior	294.89 \pm 19.44	298.86 \pm 16.45	291.98 \pm 12.36	296.22 \pm 12.51	296.08 \pm 14.82	0.642
Nasal	312.65 \pm 19.63	315.45 \pm 17.55	304.20 \pm 14.55	314.24 \pm 15.16	311.28 \pm 16.60	0.762
Temporal	286.60 \pm 18.84	289.76 \pm 13.84	281.99 \pm 13.86	286.43 \pm 16.79	284.04 \pm 14.14	0.370
<i>Mean macular volume (mm^3)</i>						
Fovea	0.20 \pm 0.01	0.20 \pm 0.02	0.20 \pm 0.02	0.21 \pm 0.01	0.21 \pm 0.02	<0.001
Total	8.30 \pm 0.35	8.47 \pm 0.44	8.45 \pm 0.39	8.47 \pm 0.44	8.45 \pm 0.40	0.767

SD - standard deviation

(Table 4). As presented in Table 5, the spherical equivalence was not significantly associated with the CSF thickness and foveal volume for the 3 refractive groups ($p=0.428$ for thickness and $p=0.563$ for foveal volume). Multiple linear regression analysis revealed that gender was the only significant factor that influenced retinal thickness and macular volume.

Discussion. The SD-OCT allows the retina to be imaged with higher resolution than with TD-OCT. SD-OCT uses many sampling points in the raster scan, which makes the measurement of retinal thickness

more accurate.¹¹ Images obtained with SD-OCT have improved the understanding of several posterior retinal pathologies. However, the placement of the posterior boundary for measuring retinal thickness differs between SD-OCT instruments. Normative values of retinal thickness vary among instruments.²¹ Differences in retinal thickness have also been reported among various ethnic groups.^{18,22} Our study has obtained normative retinal thickness values in Saudi population using the Cirrus SD-OCT.

Asefzadeh et al¹⁸ concluded that CSF thickness was significantly thinner in normal eyes of non-Hispanic blacks compared with normal eyes of non-Hispanic whites ($p=0.02$) using Stratus TD-OCT measurements. Kelyt et al²² found that the fovea is thinner in healthy African Americans than in healthy Caucasians ($p<0.001$). In the Asian population, Duan et al¹⁹ reported that the CSF was thinner in Chinese ($176.4 \pm 17.3 \mu\text{m}$) adults than in Thai ($183.2 \pm 1.3 \mu\text{m}$)²⁰ and Japanese ($210.7 \pm 28.6 \mu\text{m}$)²³ adults. Variations in retinal thickness due to different ethnic groups have also been reported in several SD-OCT studies. Grover et al¹⁶ obtained a mean CSF thickness of $270.2 \pm 22.5 \mu\text{m}$. This study found thickest CSF in Asian subjects ($279.5 \pm 27.4 \mu\text{m}$), followed by whites ($272.7 \pm 20.8 \mu\text{m}$) and blacks ($256.5 \pm 16.9 \mu\text{m}$). However, the proportion of Asians among those surveyed was only 22%. Other researchers^{17,24,25} have found a mean CSF thickness between 272 and 289 μm in the Caucasian population, using a small number of participants.

Table 4 - Correlation between axial length and retinal thickness after adjusting for age.

Parameters	Partial correlation	P-value
<i>Central subfield</i>	0.233	<0.001
Inner region		
Temporal	0.125	0.105
Superior	0.036	0.318
Nasal	0.068	0.136
Inferior	0.072	0.139
<i>Outer region</i>		
Temporal	-0.156	0.002
Superior	-0.146	0.002
Nasal	-0.138	0.004
Inferior	-0.195	0.001
<i>Macular volume</i>		
Fovea	0.122	<0.001
Total	-0.019	0.023

Table 5 - Mean retinal thicknesses of various spherical equivalence groups.

Parameters	Emmetropia (-0.5 to +0.5)D	Myopic <-0.5 D	Hyperopic >+0.5 D	P-value
Subjects	89	57	12	
<i>Mean retinal thickness ($\mu\pm\text{SD}$)</i>				
Central subfield	243.93 \pm 23.51	247.40 \pm 23.22	238.33 \pm 26.70	0.428
Inner region				
Superior	317.62 \pm 20.63	319.67 \pm 22.81	317.92 \pm 25.41	0.003
Inferior	317.31 \pm 19.82	314.75 \pm 21.42	311.33 \pm 28.31	<0.001
Nasal	319.72 \pm 20.21	320.19 \pm 19.86	318.75 \pm 28.85	0.019
Temporal	304.15 \pm 19.62	304.26 \pm 21.42	299.17 \pm 26.02	<0.001
<i>Outer region</i>				
Superior	276.60 \pm 15.85	275.35 \pm 17.65	279.50 \pm 17.67	0.002
Inferior	266.94 \pm 15.51	263.54 \pm 18.96	267.33 \pm 21.96	0.005
Nasal	294.07 \pm 19.31	291.33 \pm 24.12	295.33 \pm 21.17	<0.001
Temporal	260.87 \pm 18.00	256.70 \pm 33.94	263.42 \pm 23.68	0.007
<i>Mean macular volume (mm^3)</i>				
Fovea	0.20 \pm 0.01	0.20 \pm 0.02	0.20 \pm 0.02	0.563
Total	8.63 \pm 0.35	8.60 \pm 0.35	8.43 \pm 0.38	0.070

D - diopters, SD - standard deviation

In the current study, mean CSF thickness in the Saudi population was $244.76 \pm 23.62 \mu\text{m}$, which was less than that seen in previous SD-OCT studies. In addition, we found a total macular volume of $8.48 \pm 0.35 \text{ mm}^3$ and a foveal volume of $0.20 \pm 0.02 \text{ mm}^3$. These results were comparable with those obtained in earlier studies.²⁶ Nevertheless, even when the same OCT system is used, small but significant differences in measured retinal thickness and volume may exist between scanning protocols. For example, variations in the numbers of B-scans, number of A-scans per B-scan, and image acquisition speed have been noted in some macular thickness map subfields.²⁷ These differences are taken into consideration when interpreting retinal volume and thickness data. However, the retinal layers that cause these differences are still not known. Segmentation and retinal layer thickness mapping techniques of SD-OCT may provide a better understanding of them.²⁸

Mean retinal thickness in the CSF and inner regions was found to be thinner in women than in men. Consistent with previous studies in healthy populations^{19,20,29-31}, this difference was less in the outer regions. Using the Stratus OCT in adults, Duan et al¹⁹ reported a difference of $7.9 \mu\text{m}$ ($p < 0.001$). Grover et al¹⁶ found a difference of $7.5 \mu\text{m}$ with the Spectralis SD-OCT, but this difference was not statistically significant ($p = 0.10$). Ooto et al³⁰ reported a difference of $7.45 \mu\text{m}$ ($p = 0.002$) using 3D OCT-1000 and Song et al³¹ reported a difference of $11.47 \mu\text{m}$ ($p = 0.009$) using the Cirrus SD-OCT. Moreover, Turk et al³² reported a difference of $6.96 \mu\text{m}$ ($p = 0.036$) in a paediatric study using the Spectralis SD-OCT. In the current study, we found that the CSF thickness was $7.44 \mu\text{m}$ greater in men than in woman using the Cirrus SD-OCT.

Similar to previous studies in Thai population,^{20,26} CSF thickness was not statistically affected by aging in either gender. However, we did find that CSF thickness was positively correlated with axial length. This is in agreement with previous TD-OCT^{19,29} and SD-OCT^{26,33} studies. In contrast, other SD-OCT studies^{30,31} found no correlation between CSF thickness and axial length in normal, healthy eyes, even when correlations were adjusted for age. While little is known about the relationship between spherical equivalence and CSF thickness, we did not find a statistically significant difference in CSF thickness between each spherical equivalence group.

The limitation of our study includes: the non-random selection of eyes; the enrollment of the only eye (right or left) of 5 subjects who had only single eye could have induced bias;³⁴ and the unequal distribution of spherical equivalence and axial length in the studied groups that may have affected data analysis.

In conclusion, this study demonstrated the normative values for retinal thickness in the adult Saudi population, as obtained by the Cirrus SD-OCT. The results showed that Saudi men have a thicker CSF than women, and that the axial length correlates positively with central foveal thickness. Age, gender, and axial length should be taken into consideration for macular retinal thickness and total macular volume measurements. The diagnosis and monitoring of retinal pathologies in clinical practice should be adjusted to account for differences in baseline retinal thickness among ethnic groups.

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