

Measurement of Normal Macular Thickness Using Cirrus Optical Coherence Tomography Instrument in Iranian Subjects with Normal Ocular Condition

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Abstract

Purpose: To describe the macular thickness map of Iranian adult with normal retinal status as measured by Cirrus' optical coherence tomography (OCT) instrument

Methods: In this cross-sectional study, one eye of subjects with normal ocular examination and retinal status of at least one eye were recruited. The 512×128-scan pattern and scan area of 6×6 mm² with software version 4 protocol in Cirrus OCT apparatus were used for data acquisition and analysis.

Results: A total of 98 individuals participated in this study. 45.9% of the participants (i.e., 45 subjects) were male. The mean age of the subjects was 49.55±16.31 years; ranging from 23 to 80 years. The mean central subfield thickness (CST) was 251.39±20.57 µm which is the thinnest part. The mean CST in men and women were 259.33±21.26 µm and 244.64±17.48 µm, respectively (p<0.001). The thickest part of macula was located in the foveonasal area with a measurement of 320.2±14.54 µm. There was not any significant correlation among age (p=0.207), gender (p=0.290), and the CST. The nasal, superior, inferior, and temporal parts of macula, consecutively, exhibited a decrease in macular thickness. The mean macular volume was 9.95±0.49 mm³ (i.e., 10.05±0.54 mm³ in men and 9.86±0.41 mm³ in women, respectively). There is, however, a statistically-significant correlation between age and the macular volume (p<0.001). With every one year increase in age, there was a 0.012 mm³ decrease in macular volume. The average retinal thickness was 277.58±11.55 µm. Additionally, there is a significant correlation between age and average thickness (p<0.001) from statistical point of view. With every one year increase in the age, there was a 0.266 µm decrease in the average thickness.

Conclusion: The thickest part of the macula was located in the foveonasal area with a measurement of 320 µm while the thinnest part was in the central subfield area with a measurement of 251 µm. The nasal, superior, inferior, and temporal parts of macula, consecutively, exhibited a decrease in macular thickness. In younger adults and among males, the mean thickness was greater.

Keywords: Macular Thickness Map, Optical Coherence Tomography, Central Subfield Thickness, Macular Volume

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Introduction

Optical coherence tomography (OCT) has been introduced as a useful imaging method by providing high-resolution and cross-sectional information about various pathological conditions of macula¹⁻³ and has gained increased importance in the diagnosis, management, and monitoring of patients with various retinal disorders. OCT enables clinicians to quantitatively measure retinal thickness in a reliable and highly-reproducible manner.⁴⁻⁸

However, differentiation between normal and abnormal conditions may be challenging; specially when the changes are minor. The definition of normal level, specially in certain races or ethnicities, allows more accurate characterization of the abnormal conditions. In Iran, there have been no studies that define the normal levels of the topographic macular map. The macular topographic map can also be created using different OCT apparatus. We used the Cirrus instrument, as the retinal thickness measurement errors tend to occur less frequently with this device; however, segmentation errors still remain a concern.⁹

Methods

Subjects with normal retinal status and examination of at least one eye were recruited for our study. The study protocol was reviewed in advance by the review board of our research center. Each participant was informed of the purpose of the study, and provided a written consent to participate. The inclusion criteria were as follows: age range between 20 and 80 years, best corrected visual acuity (BCVA) $\geq 20/20$, refractive error between -1 and +1 diopter, and no history or evidence of systemic (diabetes mellitus, severe or uncontrolled systemic hypertension, pregnancy, cancer, kidney transplant, autoimmune disease) or ophthalmic diseases such as amblyopia, high intraocular pressure (IOP; more than 21 mmHg), glaucoma and previous ocular surgery, hazy media, or poor cooperation, which prevents high-quality image acquisition. In eligible subjects, the right eye was studied. If the right eye did not meet the criteria for inclusion, the left eye underwent measurements. All patients underwent thorough ophthalmic examinations; including refraction, visual acuity (VA), slit-lamp biomicroscopic examination, IOP

measurement by Goldmann applanation tonometer, and examination of the fundus with plus 90-D lens. The 512×128-scan pattern (128 lines, 512 A-scan per line) and a scan area of 6×6 mm² with software 4 protocol of Cirrus OCT apparatus were used for data acquisition and analysis.

We calculated the retinal thickness, in every part separately and totally and summarized the measurement results according to the Age-Related Eye Disease Study (AREDS) subfields.¹⁰

The layer-seeking algorithms discover the retinal inner (i.e., anterior) boundary and outer (i.e., posterior) boundary for the entire cube. The scans with Signal-to-Noise Ratio (SNR) of less than 6 dB were either repeated or excluded.

For each image, the artifacts and segmentation were checked and corrected manually. Each subject's highest SNR scan was used in the study. The highly reflective inner and outer borders of the retina were traced, interpolating regions hidden by blood vessel shadowing. If the segmentation lines defined by OCT deviated from the traced lines, excluding blood vessel regions, segmentation errors were noted. Scans were independently assessed for segmentation errors twice to determine the evaluation reproducibility. We performed the Shapiro-Wilk test (for demonstration of the type of distribution), the independent sample test, ANOVA, and the linear regression analysis for statistical purposes. The p-value less than 0.05 was considered to be significant.

We measured these variables: Central subfield thickness (CST) as the average thickness in the central 1 mm diameter circle of the Early Treatment Diabetic Retinal Study group (ETDRS) grid, macular volume as the topographic map also displays retinal thicknesses within the 6 mm scanned area, and average thickness is considered as the mean of thicknesses in nine ETDRS quadrant.

Results

A total of 98 individuals were included in this study. 45.9% (i.e., 45 patients) of the subjects were male. The mean age was 49.55±16.31 years; ranging from 23 to 80 years. 34.7%, 33.7%, and 31.6% of the participants were

between 21-40, 41-60, and 61-80 years of age, respectively.

Central subfield thickness

The mean CST was 251.39 ± 20.57 μm . The percentiles are provided in table 1.

Based on the Shapiro-Wilk test results, the CST had normal distribution. The mean CST in men and women were 259.33 ± 21.26 μm and 244.64 ± 17.48 μm , respectively. An independent sample *t* test revealed that this level was significantly greater in the men's group ($p < 0.001$) statistically.

However, using the linear regression analysis, we found that there was no significant correlation between age ($p = 0.207$), gender ($p = 0.290$), and the CST (Figure 1).

Macular volume

The mean macular volume was 9.95 ± 0.49 mm^3 . The percentiles are provided in table 1.

Based on the Shapiro-Wilk test results, the macular volume did not have a normal distribution. The mean macular volume in men and women were 10.05 ± 0.54 mm^3 and 9.86 ± 0.41 mm^3 , respectively. An independent sample *t* test revealed that this level was significantly larger in the men's group ($p = 0.045$) from statistical point of view.

With linear regression analysis, we concluded that, statistically, there was a significant

correlation between age and the macular volume ($p = 0.001$). With each year of increase in age, there was 0.012 mm^3 of decrease in macular volume.

We found that there was a significant correlation between gender (Figure 2) and age (Figure 3) with the macular volume.

Average thickness

The average retinal thickness was 277.58 ± 11.55 μm . The percentiles are provided in table 1.

Based on the Shapiro-Wilk test results, the average thickness has a normal distribution. The mean of retinal thickness in men and women were 280.89 ± 11.35 μm and 274.77 ± 11.06 μm , respectively (Figure 4). An independent sample *t* test revealed that, statistically, men had higher average thickness ($p = 0.008$).

Using the linear regression analysis, we concluded that there was a significant correlation between age and the average thickness ($p < 0.001$). With each year of increase in age, there was a 0.266 μm decrease in the average thickness (Figure 5).

It was concluded that significant correlation existed between age and sex and the average thickness.

Table 1. Macular thickness measurements

	Mean	SD	Minimum	Maximum	Percentile 05	Median	Percentile 95
Central point thickness (μm)	251.39	20.57	190	300	223	251	286
Macular volume (mm^3)	9.95	0.49	7.8	11	9.1	10	10.6
Average thickness (μm)	277.58	11.55	254	305	257	277.5	295
Inner superior (μm)	319.01	13.75	285	353	295	319	339
Outer superior (μm)	273.81	13.18	240	309	252	274	293
Inner nasal (μm)	320.2	14.54	279	352	300	320.5	342
Outer nasal (μm)	290.86	16.84	241	331	260	293.5	316
Inner inferior (μm)	315.78	13.47	266	346	296	317	335
Outer inferior (μm)	265.94	12.37	237	295	243	264	285
Inner temporal (μm)	305.36	13.67	275	343	283	305.5	325
Outer temporal (μm)	264.79	12.87	234	295	246	264	289

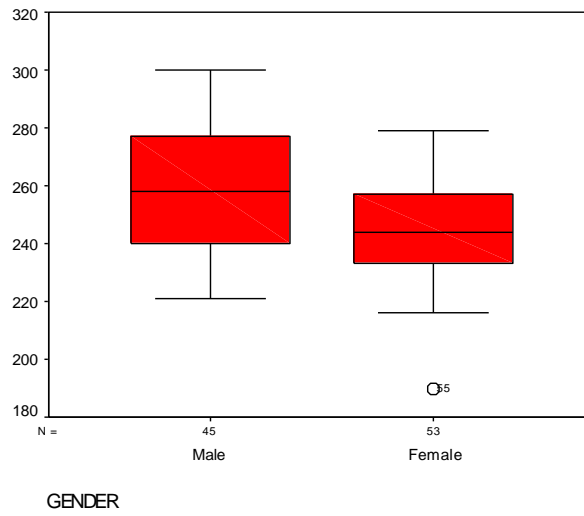


Figure 1. The distribution of central subfield thickness by gender

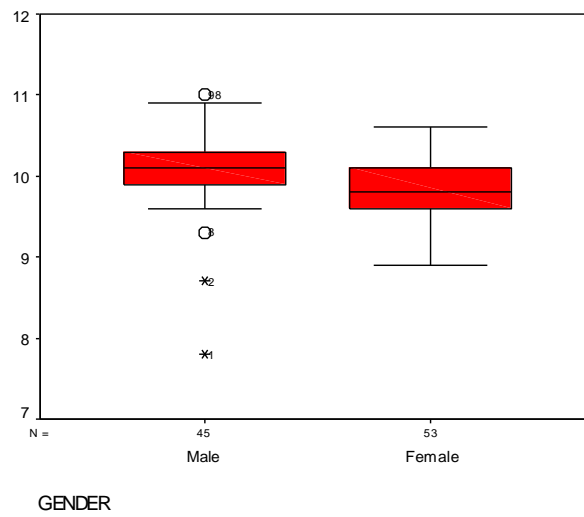


Figure 2. The distribution of macular volume by gender

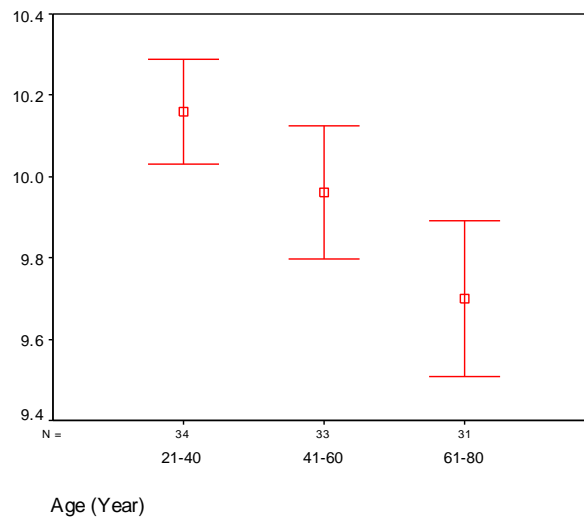


Figure 3. The mean and 95% of confidence interval of macular volume based on age group

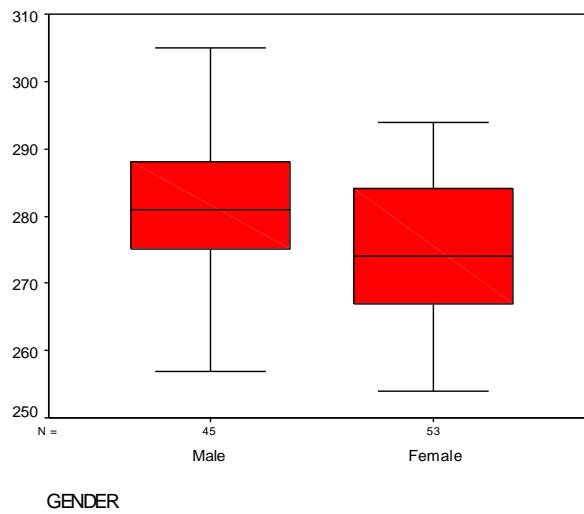


Figure 4. The distribution of average thickness by gender

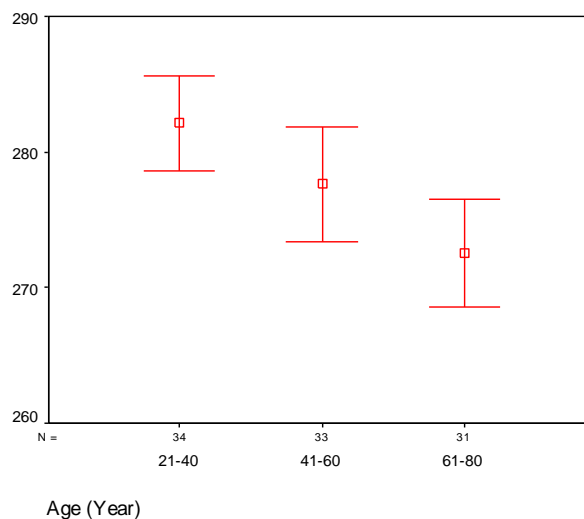


Figure 5. The mean and 95% of confidence interval of average thickness based on age group

Discussion

In this study, there was no significant correlation between age and gender, and the CST. There was a significant correlation between age and gender and the macular volume. A significant correlation between age and sex and the average thickness was seen in this survey.

Based on this study, the thickest part of macula was located in the foveonasal area (320 μm), and the thinnest part was in central subfield area (251 μm). This is due to a thicker nerve fiber layer in the peripapillary area. The nasal, superior, inferior, and temporal parts of macula, consecutively, exhibited a decrease in macular thickness. There are other studies that followed this sequence, as well.¹¹

Therefore, the nasal side of the perifoveal area was considerably thicker than the other parts. In younger patients and among males, greater amount of mean thickness is reported in recent studies.^{12,13}

Our results are in agreement with previous studies that have shown reduced retinal thickness in women compared with men.¹³⁻¹⁷ However, two recent studies using SD-OCT reported no significant difference in retinal thickness between men and women.^{11,18}

By regression analysis, after putting other possible intriguing factors, there were no significant differences between CST between men and women in this study, although foveal pit morphology was not evaluated. Intersex

differences persisted in all analysis in macular volume and average macular thickness in this study. As Wagner-Schuman et al¹⁹ concluded that their data taken together with Delori and Nolan's data,^{20,21} showed no sex-related difference in foveal pit diameter.¹⁹

Ethnic differences in macular thickness and volume have been described and central and inner macular thickness and volume were shown to be significantly thinner in blacks and Asians than in whites, not only in adults but also in children.^{15-18,22-25}

Wagner-Schuman observed similar differences between the races in macular thicknesses, with the African/African American group having a significantly reduced CST compared with the Caucasian group.

However, no significant racial differences in retinal thickness were observed in any of the other ETDRS segments.¹⁹

At the end of their article they stated that race-associated differences are more likely due to differences in foveal pit morphology. As in agreement with some previous literature they emphasized that sex-based differences tended to include multiple ETDRS segments, while race-related differences were largely confined to the central subfield.^{11,16}

In our study the central foveal thickness in central 1 mm is 251.39 μm in accordance with Grover et al's results. Our CST measurement of 251 μm versus 262-276 μm in other studies,^{11,12,26} the macular volume of 9.95 mm^3 versus 10 mm^3 ,^{3,12} and the mean macular thickness measurement of 278 μm versus 258-300 μm .^{12,28,29}

Similar to the results of Tiffany's study,¹² we also found no relationship between CST and age. These findings are in consistent with some other studies^{16,25,29-32} as opposed with the results of several previous studies that age had a positive correlation with the mean thickness of the central macula but negatively correlated with the inner and outer macular thicknesses.

The macular thickness map evaluation allows differentiation between a healthy and a diseased retina. In certain diseases such as diabetes mellitus,³³ the age-related macular degeneration, macular hole,³ and glaucoma³⁴ macular thickness map evaluation could help diagnosis and monitor the treatment. Furthermore, high reproducibility of macular thickness measurement is achieved using Cirrus' OCT instrument (i.e., 84.8-94.9%).¹¹

The weaknesses of our study are perhaps related to the OCT reproducibility (the margin of error on a 95% confidence interval (CI) for the true change in thickness in an eye measured by OCT at two different time points), the differences in image quality, and the segmentation error (misidentification of retinal boundaries which results in errors in the automated retinal thickness map measurement).

However, Cirrus HD-OCT has been demonstrated to have high intrasession repeatability in healthy subjects^{26,35} and it eliminates this weak point of our study.

There are several commercially-available OCT instruments with different acquisition protocols and segmentation. Therefore, we expected minor differences in results when measuring a normal thickness level using these apparatus.²⁶ In Cirrus measurements of mean macular thickness is 60 micron greater than that of Stratus.²⁸ This is related to the fact that Stratus OCT measures retinal thickness down to the IS/OS junction of photoreceptors, while Cirrus HD-OCT and RTVue-100 include the outer segments, and measure closer to the retinal pigment epithelium (RPE).¹¹

Conclusion

We were able to estimate the thickness and volume based on the age. With every one year increase in age, there is a 0.266 μm decrease in the average retinal thickness and 0.012 mm^3 decreases in the mean macular volume.

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