Normative Study to Correlate the Effects of Morphological Variables on Macular and Choroidal Thickness Using SD-OCT

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To cite this article:
Sumeet Chopra, Preet Kanwar Singh Sodhi, Akashdeep Goel, Sehajpreet Kaur, Gurkirat Singh Bajwa. Normative Study to Correlate the Effects of Morphological Variables on Macular and Choroidal Thickness Using SD-OCT. International Journal of Ophthalmology & Visual Science. Vol. 4, No. 1, 2019, pp. 1-6. doi: 10.11648/j.ijovs.20190401.11

Received: January 2, 2019; Accepted: January 21, 2019; Published: February 13, 2019

Abstract: To determine macular and choroidal thickness in healthy north Indian eyes and determine its variation with age and height using SD-OCT. The macula of 400 randomly selected healthy subjects (800 eyes) with no retinal and choroidal pathology was imaged with Cirrus SD-OCT. Macular thickness from all 9 regions of Early Treatment Diabetic Retinopathy Study was evaluated. Choroid was visualized by enhanced depth imaging technique. Choroidal thickness was measured subfoveally and at 500 microns intervals upto 1500 microns temporal and nasal to the fovea. The mean age of the subjects was 33.60 years ± 14.033 and mean height was 163.5 cms ± 11.715. Mean central macular thickness (CMT) was 242.59 µm ± 16.802 and mean subfoveal choroidal thickness was 325.18 µm ± 47.087. CMT correlated significantly (Pearson’s correlation coefficient) with age (r=0.120, p<0.001) and height (r=0.258, p<0.001). Choroidal thickness decreased with age and the correlation was statistically significant. Choroidal thickness also decreased with height with a statistically significant correlation, but no specific pattern was found. This normative database of choroidal and macular thickness by OCT will serve as baseline for diagnosing retinal pathologies and help in future research.

Keywords: Choroidal Thickness, Macular Thickness, Normative Study, Spectral-Domain Optical Coherence Tomography (SD-OCT), North Indian

1. Introduction

Macular edema is a common cause of visual impairment, and the degree of macular thickening is significantly correlated with visual acuity. [1] The assessment of the macular region is an important parameter in the management of several ophthalmic conditions like diabetic retinopathy, age-related macular degeneration, central serous chorio-retinopathy (CSCR), retinal vein occlusion etc where an increase in retinal thickness can be seen due to fluid accumulation.

Choroidal abnormalities such as vascular hyperpermeability or loss and thinning are critical to the onset and progression of many chorioretinal diseases such as central serous chorioretinopathy, Vogt–Koyanagi–Harada disease, high myopia-related chorioretinal atrophies, age-related macular degeneration and polypoidal choroidal vasculopathy. The choroidal thickness (CT) may be affected by many local and systemic conditions.

With the recent development of enhanced depth imaging (EDI), in-vivo assessment of choroid has become an area of interest. EDI helps in better visualization of choroid and the chorio-scleral junction, which allows an accurate quantitative assessment of the choroid, which was not possible before. [2]
Studies have reported significant differences in macular thickness amongst subjects of different race, gender and age. [3, 4] Thus it is desirable that measurements derived from the normative population be as close as possible to the population for which the instrument is to be used.

Recent literature has shown the effect of age, sex, axial length (AXL), refractive error, and diurnal variation on the Choroidal Thickness. [5, 6] Various studies have reported a normal range of choroidal thickness. [7-9] Previous reports on CT are mostly from the western world and from the Asian countries including Japan and China. Hence, we undertook this prospective study for evaluating the normal retinal and choroidal thickness in normal healthy north Indian subjects and also evaluated the effect of various morphological variables on the thicknesses.

2. Materials and Methods

This prospective observational study consisted of 400 randomly selected subjects (800 eyes), who visited the OPD, at Department of Ophthalmology, Dayanand Medical College & Hospital, Ludhiana, Punjab, India in whom the chorio-scleral junction could be identified with an image quality of ≥ 6/10. Prior approval from the Institutional Review Board of the institute was taken and informed consent was obtained from each subject. This study was conducted in accordance with the tenets of the Declaration of Helsinki for research involving human subjects. All subjects had a best corrected visual acuity of 20/20. Patients with any retinal or choroidal pathology, Refractive error of > ± 6 Diopters sphere or > ± 3 diopters cylinder, media opacities, intra ocular pressure >21 mm, history of use of any drug causing retinopathy, history of any systemic disease with known ocular involvement, pregnant females, history of use of oral contraceptive pills, glaucoma were excluded from study.

Both eyes per subject were scanned. All scans had an image quality factor of 6/10 or greater and were taken as close to fovea as possible, such that the thinnest point of the macula was imaged. OCT scanning was performed using CIRRUS HD-OCT (MODEL 5000, SD-OCT, CARL ZEISS MEDITEC, INC, DUBLIN, USA) with software version 6.5.

The fast macula thickness map was used, which comprises 3 concentric circles centred at the fovea that divided the macula into 3 zones; the fovea (1 mm diameter), the inner macula (1 to 3 mm) and the outer macula (3 to 6 mm). The 3 mm inner ring and 6 mm outer ring are further divided into four equal regions. The choroid was visualized by enhanced depth imaging (EDI) technique with spectral domain optical coherence tomography using a standardized scanning protocol. A single line of 6 mm length centered horizontally on the fovea was used for the visualization of the choroid. The vertical distance between the posterior edge of the hyper reflective RPE layer and the chorio-scleral interface was measured manually using the software calipers. Choroidal thickness was measured sub foveally and 500 microns intervals up to 1500 microns temporal and nasal to the fovea.

All the data including OCT parameters were stored in a MS Excel 2007 spreadsheet. Statistical analysis was done using SPSS software version 18.0.

3. Results

We included 800 eyes of 400 healthy subjects for analysis in this study. There were 206 men (412 eyes) and 194 women (388 eyes). Mean age of the subjects was 33.60 years ± 14.033 and mean height was 163.5 cm ± 11.715. All patients were phakic.

![Figure 1. Normative Data for Retinal Thickness in Various ETDRS Sub Fields.](image)

Mean foveal thickness was 242.59 µm ± 16.802. The inner circle of ETDRS grid showed maximum retinal thickness and there was a decrease towards periphery. The retina was the thickest on nasal side with maximum thickness of inner nasal macula (Figure 1).

| Area of Measurement | Mean Choroidal Thickness (µm) ± Standard Deviation |
|---------------------|-----------------------------------------------|
| Temporal 1500µm     | 293.40 ± 46.686                               |
| Temporal 1000µm     | 306.59 ± 46.358                               |
| Temporal 500µm      | 316.32± 46.723                                |
| Sub Foveal          | 325.18± 47.087                                |
| Nasal 500µm         | 314.42± 47.889                                |
| Nasal 1000µm        | 302.81± 49.649                                |
| Nasal 1500µm        | 286.09± 52.013                                |

Table 1. Normative Data for Choroidal Thickness.

Mean sub foveal choroidal thickness was 325.18 µm ± 47.087. The choroid was thickest at subfoveal area. A gradual decrease of choroidal thickness was noted towards periphery. This decrease was more on nasal side than on the temporal side (Table 1).
Central foveal thickness was minimum in age < 20 years and maximum in the older age group with age > 60 years while it was almost similar in age groups from 21-60 years (Table 2). The central foveal thickness had a significant positive correlation with age (r = 0.120, p < 0.001) with an increase of 1.43 µm thickness per decade. The retinal thickness in the superior outer quadrant had a statistically significant negative correlation with age with a decrease of 0.067 µm per decade (Table 3).

### Table 3. Retinal thickness correlation with age.

| ETDRS Sub Field | Minimum Thickness (µm) | Maximum Thickness (µm) | Mean Thickness (µm ± S.D.) | Change per Decade (µm) | Correlation (r) | Significance (p-Value) |
|------------------|------------------------|------------------------|---------------------------|------------------------|------------------|------------------------|
| Central Foveal   | 190                    | 305                    | 242.59±16.802             | 1.43                   | 0.120            | 0.000                  |
| Temporal Inner   | 219                    | 338                    | 301.71±14.505             | -0.18                  | -0.017           | 0.314                  |
| Superior Inner   | 208                    | 360                    | 315.46±15.283             | -0.4                   | -0.022           | 0.270                  |
| Nasal Inner      | 267                    | 357                    | 316.49±15.386             | 0.11                   | -0.010           | 0.384                  |
| Inferior Inner   | 250                    | 349                    | 312.84±15.450             | 0.22                   | 0.020            | 0.283                  |
| Temporal Outer   | 222                    | 357                    | 254.96±13.751             | 0.42                   | 0.043            | 0.114                  |
| Superior Outer   | 241                    | 395                    | 273.83±14.595             | -0.69                  | -0.067           | 0.030                  |
| Nasal Outer      | 247                    | 341                    | 292.09±15.791             | -0.43                  | -0.038           | 0.139                  |
| Inferior Outer   | 205                    | 321                    | 261.42±13.910             | -0.16                  | -0.016           | 0.329                  |

Choroidal thickness was the least in the individuals with age> 60 years (Table 4). The subfoveal choroidal thickness had a significant negative correlation with age (r=-0.297, p <.001) with a decrease of 9.97 µm per decade (Table 5).

### Table 5. Choroidal thickness correlation with age.

| Area of Measurement | Group A (≤20 Years) | Group B (21-30 Years) | Group C (31-40 Years) | Group D (41-50 Years) | Group E (51-60 Years) | Group F (>60 Years) | Total N=800 | Overall p value |
|---------------------|---------------------|-----------------------|-----------------------|-----------------------|-----------------------|---------------------|-------------|----------------|
| Temporal 1500µm     | 134                 | 443                   | 293.40±46.686         | -10.29                | -0.309                | 0.000               |             |                |
| Temporal 1000µm     | 144                 | 436                   | 306.59±46.358         | -9.95                 | -0.301                | 0.000               |             |                |
| Temporal 500µm      | 154                 | 439                   | 316.32±46.723         | -10.19                | -0.306                | 0.000               |             |                |
| Sub Foveal          | 157                 | 436                   | 325.18±47.087         | -9.97                 | -0.297                | 0.000               |             |                |
| Nasal 500µm         | 160                 | 448                   | 314.42±47.889         | -9.14                 | -0.268                | 0.000               |             |                |
| Nasal 1000µm        | 141                 | 438                   | 302.81±49.649         | -7.97                 | -0.225                | 0.000               |             |                |
| Nasal 1500µm        | 112                 | 413                   | 286.09±52.013         | -7.01                 | -0.189                | 0.000               |             |                |
Retinal thickness was the maximum in group-Z i.e. with a height more than 165 cms, while it was almost similar in other height groups (Table 6). The retinal thickness had a significant positive correlation with height with a variation in the range of 2.250-5.550 µm in the each height group in various ETDRS sub fields (Table 7).

### Table 6. Mean Retinal Thickness (µm) Variations with Height ± S.D.

| ETDRS Sub Field | Group X (≤150 Cms) N=110 | Group Y (151-165 Cms) N=352 | Group Z (>165 Cms) N=338 | Total N=800 | Over all p value |
|-----------------|--------------------------|----------------------------|--------------------------|-------------|-----------------|
| Foveal          | 238.95 ± 16.193          | 238.69 ± 16.427            | 247.83 ± 15.992          | 242.59 ± 16.802 | <0.001         |
| Temporal Inner  | 298.50 ± 10.982          | 297.84 ± 14.065            | 306.78 ± 14.459          | 301.71 ± 14.505 | <0.001         |
| Superior Inner  | 311.69 ± 10.596          | 312.11 ± 14.837            | 320.17 ± 15.798          | 315.46 ± 15.283 | <0.001         |
| Nasal Inner     | 313.00 ± 10.868          | 312.87 ± 15.540            | 321.40 ± 15.156          | 316.49 ± 15.386 | <0.001         |
| Inferior Inner  | 309.68 ± 11.298          | 309.25 ± 15.172            | 317.61 ± 15.664          | 312.84 ± 15.450 | <0.001         |
| Temporal Outer  | 250.99 ± 9.613           | 252.49 ± 14.626            | 258.82 ± 13.006          | 254.96 ± 13.751 | <0.001         |
| Superior Outer  | 270.95 ± 10.866          | 273.44 ± 16.985            | 275.16 ± 12.716          | 273.83 ± 14.595 | 0.025          |
| Nasal Outer     | 289.98± 12.022           | 291.04± 16.121             | 293.86± 16.372           | 292.09± 15.791 | 0.020          |
| Inferior Outer  | 259.40± 12.302           | 259.80± 14.568             | 263.77± 13.383           | 261.42± 13.910 | <0.001         |

The maximum choroidal thickness was observed in Group-Y i.e. with height range from 151-165 cms and it showed a fall in other groups that is with higher and lower height groups (Table 8). The choroidal thickness had a significant negative correlation with height with a decrease in the range of 4.020 to 5.580 µm at various points of measurements (Table 9).

### Table 7. Retinal thickness correlation with height.

| ETDRS Sub Field | Minimum Thickness (µm) | Maximum Thickness (µm) | Mean Thickness (µm) ± S.D. | Change per Group (µm) | Correlation (r) | Significance (p-Value) |
|-----------------|------------------------|------------------------|---------------------------|-----------------------|-----------------|------------------------|
| Central foveal  | 190                    | 305                    | 242.59 ± 16.802           | -5.55                 | 0.258           | 0.000                  |
| Temporal Inner  | 219                    | 338                    | 301.71 ± 14.505           | -5.34                 | 0.288           | 0.000                  |
| Superior Inner  | 208                    | 360                    | 315.46 ± 15.283           | -5.115                | 0.261           | 0.000                  |
| Nasal Inner     | 267                    | 357                    | 316.49 ± 15.386           | -5.415                | 0.275           | 0.000                  |
| Inferior Inner  | 250                    | 349                    | 312.84 ± 15.450           | -5.295                | 0.268           | 0.000                  |
| Temporal Outer  | 222                    | 357                    | 254.96 ± 13.751           | -4.32                 | 0.245           | 0.000                  |
| Superior Outer  | 241                    | 395                    | 273.83 ± 14.595           | -2.25                 | 0.120           | 0.000                  |
| Nasal Outer     | 247                    | 341                    | 292.09 ± 15.791           | -2.58                 | 0.127           | 0.000                  |
| Inferior Outer  | 205                    | 321                    | 261.42 ± 13.910           | -2.685                | 0.151           | 0.000                  |

### Table 8. Mean Choroidal Thickness (µm) Variations with Height ± S.D.

| Area of Measurement | Group X (≤150 Cms) N=110 | Group Y (151-165 Cms) N=352 | Group Z (>165 Cms) N=338 | Total N=800 | Over all p value |
|---------------------|--------------------------|-----------------------------|--------------------------|-------------|-----------------|
| Temporal 1500µm     | 288.96 ± 46.586          | 297.00 ± 47.269             | 291.09 ± 45.969          | 293.40 ± 46.686 | 0.142           |
| Temporal 1000µm     | 304.77 ± 48.705          | 309.97 ± 45.412             | 303.66 ± 46.457          | 306.59 ± 46.358 | 0.184           |
| Temporal 500µm      | 313.17 ± 48.646          | 319.97 ± 45.231             | 313.53 ± 47.482          | 316.32 ± 46.723 | 0.145           |
| Sub foveal          | 321.93 ± 49.868          | 328.80 ± 45.171             | 322.47 ± 47.987          | 325.18 ± 47.087 | 0.155           |
| Nasal 500µm         | 310.25 ± 50.341          | 317.54 ± 46.269             | 312.53 ± 48.667          | 314.42 ± 47.889 | 0.241           |
| Nasal 1000µm        | 298.67 ± 50.955          | 305.79 ± 48.607             | 301.05 ± 50.258          | 302.81 ± 49.649 | 0.294           |
| Nasal 1500µm        | 281.59 ± 52.693          | 288.95 ± 51.212             | 284.58 ± 52.602          | 286.09 ± 52.013 | 0.337           |

### Table 9. Choroidal thickness correlation with height.

| Area of Measurement | Minimum Thickness (µm) | Maximum Thickness (µm) | Mean Thickness (µm) ± S.D. | Change per group (µm) | Correlation (r) | Significance (p-Value) |
|---------------------|------------------------|------------------------|---------------------------|-----------------------|-----------------|------------------------|
| Temporal 1500µm     | 134                    | 443                    | 293.40 ± 46.686           | 4.020                 | -0.067          | 0.029                  |
| Temporal 1000µm     | 144                    | 436                    | 306.59 ± 46.358           | 5.580                 | -0.094          | 0.004                  |
| Temporal 500µm      | 154                    | 439                    | 316.32 ± 47.623           | 5.385                 | -0.090          | 0.005                  |
| Sub foveal          | 157                    | 436                    | 325.18 ± 47.087           | 5.445                 | -0.090          | 0.005                  |
| Nasal 500µm         | 160                    | 448                    | 314.42 ± 47.889           | 4.785                 | -0.078          | 0.014                  |
| Nasal 1000µm        | 141                    | 438                    | 302.81 ± 49.649           | 4.980                 | -0.078          | 0.013                  |
| Nasal 1500µm        | 112                    | 413                    | 286.09 ± 52.013           | 4.335                 | -0.065          | 0.033                  |
4. Discussion

The assessment of the macular and choroidal region is an important parameter in the management of several ophthalmic diseases. Prior to labeling the macula or choroid as abnormal, it is important to determine the range of normal macular and choroidal thickness and the factors on which they depend.

Our study consisted of 487 subjects initially out of which those 400 were included in whom the chorio-scleral junction could be identified with an image quality of ≥ 6/10. Out of the 400 included patients 206 (51.50%) were males and 194 (48.50%) were females. All the patients were phakic and both eyes were evaluated. The mean age of the subjects was 33.60 ±14.033 years (range 9-67 years).

The mean foveal thickness was 242.59 µm ± 16.802. Previous studies have shown that Asians and African-Americans have thinner maculae when compared to Caucasians. [10, 11] The mean thickness in the central 1 mm diameter area was found to be 176.4μm in Chinese, [12] 181.2 ± 18.4 µm in Indians, [13] 183.2 ± 1.3 µm in Thai, [14] 209.5 ± 26.7 µm in Japanese, [15] and 212 ± 20 µm in Caucasians [16] using different OCT machines. Our study showed almost similar retinal thickness with the studies done by Song et al. [17], Gupta et al. [18] using Cirrus HD-OCT. The difference in the measurements is due to the fact that time domain (TD-OCT) measures retinal thickness as the distance between internal limiting membrane (ILM) and the retinal nerve fiber layer (RNFL) in this region.

We found no specific pattern of retinal variation with height, although a small negative statistically significant correlation was found below the fovea (r=-.090 p=.005), so its clinical significance cannot be commented on.

Using the criteria of mean ± 2 Standard Deviations, which includes 95% of the population, we suggest that 210-275 µm be taken as the normal range for central foveal thickness in the north Indian population using CIRRUS OCT.

On evaluating the macular thickness in the 9 ETDRS regions in our population, the nasal macula (inner and outer areas) was significantly thicker than the temporal macula, a finding consistent with previous studies. [4, 18, 20] This could be because of the thicker papillo-macular bundle of the retinal nerve fiber layer (RNFL) in this region.

We found no specific pattern of retinal variation with height. Normal central retinal thickness for a north Indian population is 242.59 µm ± 16.802 and subfoveal choroidal thickness is 325.18 µm ± 47.087 using Cirrus HD-OCT. Central macular thickness is positively correlated (r=0.120, p <.001) while subfoveal choroidal thickness is negatively correlated (r=-0.297, p <.001) with age. Central macular thickness is positively correlated (r=0.090, p=.005) with height, although a small negative statistically significant correlation was found below the fovea (r=-.090 p=.005), so its clinical significance cannot be commented on.

According to our knowledge, this is the first study which describes normative values in healthy North Indian subjects. Intra-observer and Intra-observer variations could alter the results, these could not be evaluated in the study done. Intra-eye variations were evaluated though, which didn’t show any statistically significant co-relation.

5. Conclusions

A normative database was established for the north Indian population of the retinal and choroidal thickness which is important to diagnose the abnormalities. Normal central retinal thickness for a north Indian population is 242.59 µm ± 16.802 and subfoveal choroidal thickness is 325.18 µm ± 47.087 using Cirrus HD-OCT. Central macular thickness is positively correlated (r=0.120, p <.001) while subfoveal choroidal thickness is negatively correlated (r=-0.297, p <.001) with age. Central macular thickness is positively correlated (r=0.090, p=.005) with height.

Acknowledgements

The authors acknowledge the role of the entire staff of Department of Ophthalmology, Dayanand Medical College and Hospital, Ludhiana, Punjab where the study was conducted. The management’s role for the conduct of study is also acknowledged. The role of Dr Sanjeev Maheshwari for biostatics and preparation of the manuscript is also deeply acknowledged.
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