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Study of Macular Thickness Using Spectral Domain Optical Coherence Tomography in Healthy Indian Subjects

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ABSTRACT

Purpose: *To generate normative data for SD-OCT (Topcon 3D OCT 2000) estimated macular thickness in Indian eyes and establish its relation with age sex and refractive error.*

Materials and methods: *In this cross sectional , observational, hospital based study 800 eyes of 400 healthy Indian individuals underwent a macula OCT scan using Topcon SD OCT. Macular thickness was measured in 9 ETDRS regions .The effect of age , sex , refractive error on foveal thickness was determined.*

Results: *The mean central foveeal thickness was 226.4025 ±22.5063 µm. Males were found to have a significantly thicker macula (P< 0.05) than females with the central foveal thickness of 229.8153 ± 21.4222 vs 220.7748 ±23.14742 . Central foveal thickness was found to have very weak correlation with age which was not statistically significant. All other regions (the parafoveal and perifoveal thickness) showed statistically significant negative correlation with age.*

Conclusion: *We provide the largest normative data for SD OCT Topcon 3D OCT 2000. We also suggest that demographic factor like gender should be considered while interpreting any OCT measurements. The normal range of central macular thickness for Indian population should be 181 µm to 270 µm for Topcon SD OCT. Age and refractive error do not show a significant correlation with central macular thickness.*

Keywords- *Topcon 3D OCT 2000, macular thickness, SD-OCT.*

INTRODUCTION

Optical coherence tomography (OCT) is a new diagnostic technology for high-resolution, cross-sectional, quantitative imaging of the retina. [1] OCT is a non-invasive non-contact technique which uses near infrared low coherent light passing through a Michelson interferometer to obtain two dimensional images of the retina and optic nerve head. [1], [2]

The RT measurements obtained by SD-OCT are consistently greater than those obtained by TD-OCT. RT measurement differences may also vary by SD-OCT model. Consideration of these measurement differences is essential when OCT-determined RT measurement data are used in clinical settings. [3]

All instruments use vitreoretinal interface or internal limiting membrane as Inner retinal border whereas Outer retinal boundary varies with different machines. There are four hyper reflective outer retinal layers. (Christine.A. Crusio)

1. External limiting membrane
2. Inner Segment-Outer Segment junction of photoreceptors

3. OS tips and apical processes of RPE (basal complex)
4. RP–Bruchs complex

Thus various models of SD-OCT also differ in their measurement due to different retinal segmentation algorithms used. **Macular thickness measurements using different OCT systems are not interchangeable** [4,5,6-10]. We used the Topcon SD-OCT, which uses the inner border of RPE, where the outer segment tips meet the apical processes of RPE (basal complex) as the outer retinal boundary for macular thickness measurements.

Ethnic differences in macular thickness and volume have been described in a number of studies. [11-16] Central and inner macular thickness and volume were shown to be significantly thinner in blacks and Asians than in whites, not only in adults [13-16] but also in children. [11,12].

According to Tiwari et al, age was positively correlated with the mean thickness of the central macula but negatively correlated with the inner and outer macular thicknesses [17]. Similar findings have been reported in previous studies by, Xin Rong Duan et al, Guedes Vet al and Sung KR et al [18,15,19]. but inconsistent with others, [20 ,13, 14, 21, 22, 23]

Hence there are non cnclusive reports on correlation of macular thickness with age.

In the study by Tewari *et al.* [17] and Grover *et al* [24] no significant difference was seen in the average foveal thickness and minimum foveal thickness in men and women. However, other similar studies by Song *et al.* [25] Wong *et al* [26] and Massin *et al.* [27] found males to have significantly higher average retinal thickness as compared to females.

A number of recent studies show that refractive errors do not correlate significantly with central retinal thickness measurements [26, 28, 3, 29]

Refraction was not found to have any significant effect on macular thickness, in studies by Tewari *et al* [17]., and Massin *et al.* [21] Lim *et al.* [30] in their study on myopes found that myopes had thinner parafovea and thicker foveas.

Therefore, data documenting normal macular measurements and variations associated with demographic and ocular variables in healthy Indian subjects on SD OCT are imperative to clinicians around the world to help them make informed decisions on pathologic changes in this ethnic group.

MATERIALS AND METHODS

This was a cross sectional, observational, hospital based study. 800 eyes of 400 healthy volunteers were recruited from the outpatient department of SMS Medical College, jaipur from November 2011 to November 2013. Macular thickness was measured using SD OCT (Topcon3D OCT2000). Informed consent was taken from all participants using consent form. All subjects underwent a complete ophthalmic examination including best corrected visual acuity estimation, slit lamp examination, non contact tonometry, dilated stereoscopic fundus examination.

Exclusion Criteria

1. age <5 yrs
2. BCVA < 6/6 on Snellen's visual acuity chart
3. eyes with media opacities preventing fundus assessment
4. IOP > 21 mm Hg
5. Patients with systemic diseases known to affect macula : diabetes , hypertension
6. Patients on medications known to cause maculopathy e.g.chloroquine
7. Patients with known neuro-ophthalmologic disease

All participants were subjected to macular imaging using Spectral Domain OCT following papillary dilatation. Both eyes of each participant was included in the study. The OCT images were taken using good centration. The Radial 3D OCT scan was used.

Statistical analysis was performed using t test and Pearsons correlation. Where indicated, linear regression was used to describe parametric associations and to generate graphic representations of the same.

RESULTS

Prospective data on the macular thickness of 418 subjects were recorded. However, 18 patients had to be excluded from the final analysis due to poor scan quality <60 (n = 6), presence of minor retinal pigment epithelial irregularities (n = 3), early epiretinal membrane (n = 3), non-clinically detectable small serous pigment epithelial detachment (n = 2), and poor centration of the ETDRS grid (n = 4). Eight hundred eyes of 400 subjects aged between 5 to 73 years were evaluated. The baseline parameters are shown in [Table 1]. The visual acuity of all 400 subjects for each eye was 6/6.

The macular thickness was determined in 9 ETDRS regions. The means, standard deviations, and ranges are shown in [Table 2]. Looking at the macular topography, the fovea was the thinnest area (226.4025 ±22.5063 µm). The inner macula was thicker than outer macula in all four regions superior, inferior, nasal and outer ($p<0.001$) ,thus the retina thinned towards the periphery. The nasal macula (inner and outer) was found to be significantly thicker ($p<0.001$) than the temporal macula. The superior quadrant was the thickest amongst all nine ETDRS regions. In the inner region of the macula superior quadrant was thickest, followed by the nasal, inferior and temporal quadrants. In contrast, in the outer region, the nasal quadrant was the thickest, followed by the superior, inferior and temporal quadrants.

Preliminary statistical analysis showed no difference in macular thickness between right and left eyes in any of the ETDRS regions.

Table 1:. Demographic data

Baseline Parameters	Subjects n = 400, Eyes N= 800
Male: female	498:302
Mean age (SD) in years	32.18 (13.14)
Range in years	5 – 73
Mean spherical refractive error(SD) D	0.11 (1.08)
Range of refractive error	-4 to +3 D

Table -2 Macular Thickness In Nine ETDRS Region

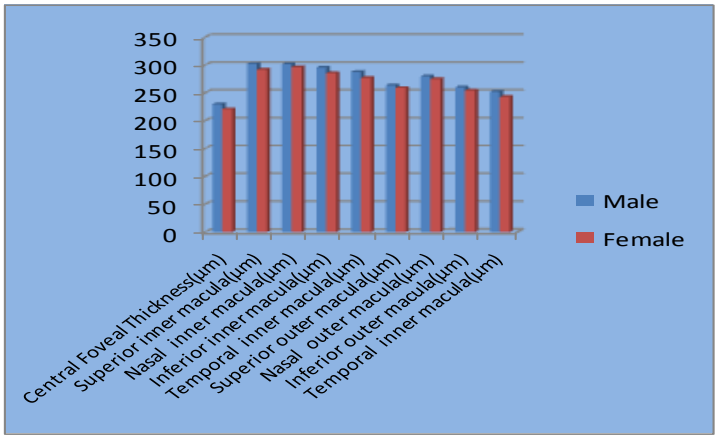
Statistics	µm								
	Central	NIM	TIM	SIM	IIM	NOM	TOM	SOM	IOM
Mean	226.4025	297.1413	283.6063	298.3188	291.6713	277.8088	248.5525	261.7325	257.7475
Std. Deviation	22.5063	21.3919	22.32564	20.90882	21.9822	19.54872	19.58083	16.65827	17.73801
Range	171	160	236	166	218	227	235	184	205
Minimum	141	187	158	182	177	157	113	163	159
Maximum	312	347	394	348	395	384	348	347	364

Table 3: Comparison On Basis Of Gender

ETDRS region	Sex	N	Mean	Std. Deviation	Std. Error Mean	t value	
Central	Male	498	229.8153	21.42222	0.959953	5.611646	**S**
	Female	302	220.7748	23.14742	1.331984		
NIM	Male	498	301.6205	19.49458	0.873573	7.891428	**S**
	Female	302	289.755	22.34477	1.285797		
TIM	Male	498	287.5281	20.43038	0.915507	6.545278	**S**
	Female	302	277.1391	23.80082	1.369583		
SIM	Male	498	302.1687	19.47634	0.872755	6.878849	**S**
	Female	302	291.9702	21.66084	1.246441		
IIM	Male	498	295.3936	21.90564	0.981615	6.297365	**S**
	Female	302	285.5331	20.72788	1.192756		
NOM	Male	498	279.6285	17.52723	0.785414	3.403379	**S**
	Female	302	274.8079	22.19596	1.277234		
TOM	Male	498	251.992	17.75895	0.795797	6.544828	**S**
	Female	302	242.8808	21.09886	1.214103		
SOM	Male	498	263.4137	15.76582	0.706483	3.694407	**S**
	Female	302	258.9603	17.71475	1.019369		
IOM	Male	498	259.8775	17.51766	0.784985	4.411571	**S**
	Female	302	254.2351	17.56774	1.01091		

COMPARISON ON BASIS OF GENDER

Females were found to have a significantly thinner macula ($P< 0.05$) than males in all 9 ETDRS regions as depicted in table 3. The central foveal thickness was found to be 229.8153 ± 21.4222 vs 220.7748 ±23.14742 for males vs females. (table 3)



Correlation with age

Central foveal thickness was found to have very weak correlation with age which was not statistically significant. All other regions (the parafoveal and perifoveal thickness) showed statistically significant negative correlation with age, when analyzed using pearsons coefficient of partial correlation as shown in table 4. Macular OCT Parameter in the Study group and their comparison with age using Pearson 'r'.

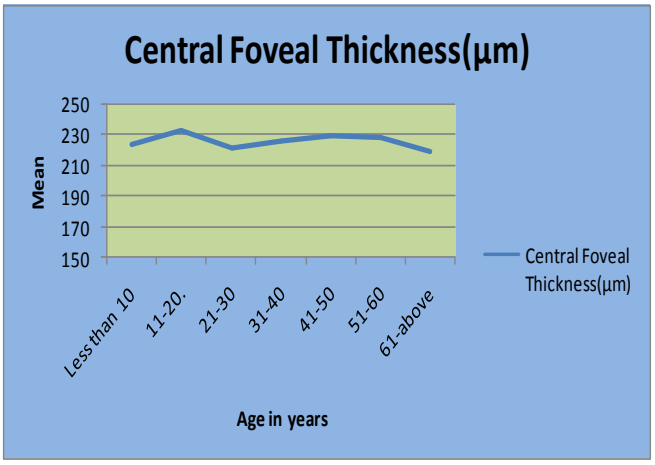


Table 4: Correlation with age

ETDRS region	Minimum	Maximum	Mean retinal Thickness Mean ±S.D(µm)	Pearson 'r'	
Central Foveal Thickness	141	312	226.4025±22.5063	-0.04552	P=0.198353
Superior inner macula	187	347	297.1413±21.3919	-0.05014	P=0.156523
Nasal inner macula	158	394	283.6063±22.32564	-0.16299	P=0.001
Inferior inner macula	182	348	298.3188±20.90882	-0.24477	P=0.001
Temporal inner macula	177	395	291.6713±21.9822	-0.21755	P=0.001
Superior outer macula	157	384	277.8088±19.54872	-0.15579	P=0.001
Nasal outer macula	113	348	248.5525±19.58083	-0.12989	P=0.05
Inferior outer macula	163	347	261.7325±16.65827	-0.20005	P=0.001
Temporal inner macula	159	364	257.7475±17.73801	-0.15569.	P=0.001

All areas except the fovea had a decline with advancing age. The central foveal thickness did not correlate with age with a more or less linear graph. The only exception being average CFT in 11 to 20 years of age which shows an increase, though not statistically significant.

CORRELATION WITH REFRACTIVE ERROR

There was no significant correlation between macular thickness and refractive error in hypermetropic eyes(upto + 4D) In myopic eyes thickness in central macula and in outer temporal region was positively correlated with refractive error while no other region showed statistically significant correlation(upto – 4D).

DISCUSSION

Normal Macular Tomography

In our study, the central macular thickness was **226.4025** ± 22.5063 µm. Previous study on Indian eyes using Stratus OCT by Tewari *et al.* [17] showed a thinner central foveal thickness of 149.16 ± 21.15 µm. the discripency , can be partly explained by difference in retinal algorithms of Stratus OCT and Topcon 3D OCT. Further difference can be attributed to demographics (proportion of male subjects and age distribution) and small sample size in previous study.

In our study, the fovea was the thinnest area (226.4025 ±22.5063 µm). The inner macula was thicker in all four quadrants ie superior, inferior nasal and temporal compared to outer macula ($p<0.001$), thus the retina thinned towards the periphery. The nasal macula (inner and outer) was found to be significantly thicker ($p<0.001$) than the temporal macula . The superior quadrant was the thickest in the inner region of the macula, followed by the nasal, inferior and temporal quadrants. In contrast, in the outer region, the nasal quadrant was the thickest, followed by the superior,inferior and temporal quadrants. The observed macular thickness parameters of being thinnest at the fovea with an increase in the parafoveal area with decrease in perifoveal thickness are consistent with the normal anatomic contour and mirrors previous reports on OCT of the normal macula in the Caucasians [31,20] and chinese population.[18] Previous studies using different types of OCT or retinal thickness analyzer also reported a similar pattern of macular thickness by regions, which is speculated to be related to *the crowding of nerve fibers within the inner region* [32,17,11, 33,29,12,34,35,15,36,21,37] *and along the papillomacular bundle* within the outer region of the macula.[32,11]

Using the criteria of mean ± 2 SDs, which includes 95% of the population, we suggest that ***181 µm to 270 µm*** be taken as the ***normal range***

for central foveal thickness in the Indian population for Topcon SD OCT. This implies that average CFT being **226.4025** , any patient with macular thickness of **below 180 µm or above 270 µm should be considered outside normal limits and should be further evaluated.**

In other studies done using Topcon OCT Mehreen Adhi et al on subjects from pakistan, foveal thickness of 229.01±20.464 µm was found. [38] Giani et al [07] recently reported foveal thickness of 229±24 µm, while Sull AC et al [04] reported a foveal thickness of 231±16 µm in healthy subjects from New England using Topcon OCT system. However, Hyang et al [08] reported foveal thickness of 221.76±15.95, and Bruce et al [39] reported foveal thickness of 244.83±17.84 µm in healthy subjects using Topcon OCT. However, in a study from Wisconsin, New York the CFT was found to be 274.3 ±72.4 µm using Topcon OCT[40] . The same study showed CFT using stratus OCT as 249.8±72.4 µm. This difference in measurements can be explained on ethnic grounds.

Correlation of Macular Thickness with age

In our study***, the central foveal thickness did not correlate significantly with age.*** (r =-0.045, p=0.198) However, in all other regions (parafoveal and perifoveal) thickness showed a significant negative correlation with age (r = -0.05 to -0.244,p=0.001 to 0.156). These results suggest that young adults tend to have a deeper foveal depression and relatively thick inner and outer macular regions, whereas older adults tend to have less variation in macular thickness with a smaller magnitude in thickness changes from the foveola toward the central macula and inner and outer macular regions. *The decreased thickness variation outside the central macula may result from* ***the loss of ganglion cell and the thinning of the retinal nerve fiber layer*** *associated with aging, which cannot be reflected in the central foveal area because there is no retinal nerve fiber layer.*[19] *This decline in the retinal thickness with age is also supported by* ***histologic decrease in the density of phodtoreceptors, ganglion cells, and retinal pigment epithelial cells with age.*** [41,42].

All areas except the central fovea had a decline with advancing age. The central foveal thickness did not correlate with age with a more or less linear graph. The only exception being average CFT in 11 to 20 years of age which shows an increase, though not statistically significant. Besides central region, thickness was found to increase in all other regions also from 1st to 2nd decade of life. Eriksson U et al [43] found similar pattern of increase in foveal thickness. The age related thinning

of the macula was not found in children, 5-16 yearsof age . In fact, there was a trend towards a retinal thickening with age in this group. Huynh et al. examined 1,543 six-year-old children. [44] The central macular thickness reported in their study was thinner (194µm) than in the present study, and a statistically significant positive correlation with age was found. One could speculate that this ***apparent 'thickening' in early age*** could be an effect of the developing macula in childhood [45, 46] resulting in a slight thickening of the central retina before it is fully developed, but the finding could also be due to algorithm problems in a growing eye.

The negative correlation between age and parafoveal and perifoveal macular thickness in our study was consistent with other studies. [31,47and 48] that showed significant association between age and macular thickness in all ETDRS areas, except the center

Tiwari et al [17] had similar findings for inner and outer macula but showed positive correlation of foveal thickness with age. According to J Huang et al, age was positively correlated to retinal thickness on some 49but not all subfields. The increased variation in central macular thickness in older persons compared with younger persons may be *related to* ***the thickening of the internal limiting membrane and the centripetal force of the posterior vitreous*** *resulting in elevation of the fovea with aging* [33]. In another study, a

significant increase in center point foveal thickness and mean foveal thickness with age. They have suggested the **presence of interstitial edema from foveal capillary dropout with age** as a probable reason. It is likely that individual retinal layers (like the RNFL) are preferentially affected by age and that this is not detected in measurements of the whole retina. [50] However we did not find any significant change in central macular thickness with age.

In contrast, few studies [51,08,04,38,03] failed to show a statistically significant association between retinal thickness and age, which may be due to the small sample size and the age distribution.

Thus, we suggest that parafoveal and perifoveal thickness tends to decrease with age but the central foveal thickness which is most widely used for clinical purposes is not affected by age.

Comparison on basis of Sex

Our study showed that men had greater central foveal thickness as compared to women (*P<0.05)*. Females were found to have a significantly thinner macula (*P*< 0.05) than males in all 9 ETDRS regions as depicted in table 3. The central foveal thickness was found to be 229.8153 ± 21.4222 vs 220.7748 ±23.14742 for males vs females.

In the study by Tewari *et al.* [17] and Grover *et al.*,[24] no significant difference was seen in the average foveal thickness and minimum foveal thickness in men and women. However, other similar studies [25, *26*, 27, 48, 49, 38,26, 03] found males to have significantly higher average retinal thickness as compared to females.. The presence of thinner foveas in females could probably explain the higher incidence of macular holes seen in them.

Correlation with refractive error

In our study, overall refractive error was not found to have any significant effect on macular thickness. There was no significant correlation between macular thickness and refractive error in hypermetropic eyes (p ranging from 0.039 to -0.039). In myopic eyes thickness in central macula and in outer temporal region was weakly positively correlated with refractive error while no other region showed statistically significant correlation (p ranging from 0.07 to 0.15). This was similar to other studies [76,85.73] A number of recent studies show that refractive errors and keratometry readings do not correlate significantly with central retinal thickness. [99, 74, 25, 78]. Lim *et al.* [100] in their study on myopes found that myopes had thinner parafovea and thicker foveas.

CONCLUSION

Keeping in view the various determinants of macular thickness. This is *first study* to use SD OCT (TOPCON 3D OCT 2000) with largest normative database for establishing macular thickness in Indians and to determine effect of age, sex and refractive error on it.

The macular thickness was determined in 9 ETDRS regions. The fovea was the thinnest area (**226.4025 ±22.5063 µm**).Using the criteria of mean ± 2 SDs, which includes 95% of the population, we suggest that ***181 µm to 270 µm*** be taken as the ***normal range*** for central foveal thickness in the Indian population for Topcon SD OCT.

Females were found to have a significantly thinner macula (*P*< 0.05) than males in all 9 ETDRS regions. The central foveal thickness was found to be 229.8153 ± 21.4222 vs 220.7748 ±23.14742 for males vs females.

Central foveal thickness was found to have very weak correlation with age which was not statistically significant. All other regions showed statistically significant negative correlation with age.

There was no significant correlation between macular thickness and refractive error.

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