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Effect of Age on Macular Thickness in Healthy Individuals Using SD-OCT

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I. Introduction

OCT was first demonstrated by Huang D et al, in 1991.[1] The first *in vivo* tomograms of the human optic disc and macula were demonstrated in 1993.[2,3] It enables noncontact, noninvasive imaging of the anterior eye as well as imaging of morphologic features of the human retina including the fovea and optic disc[4,5]using near infrared low coherent light passing through a Michelson interferometer to obtain two dimensional images of the retina and optic nerve head.

Optical coherence tomographyis of two types- Time domain OCT and Spectral- domain or Fourier Domain OCT. The time domain OCT 3000become available in 2002, with an axial resolution of 10µm and scan velocity of 400 axial scans per second. In 2004, higher resolution Spectral Domain OCT (SD-OCT) was introduced in clinical practice with reported resolution of 1 to 5 µm as well as improved visualization of retinal morphologic and pathologic features.[6]

The changes in macular thickness (MT) are commonly seen in eyes with pathologies, like age related macular degeneration, diabetic retinopathy etc., but can also be attributed to normal aging process. The knowledge of normal macular thicknesss with respect to the age must be known in order to distinguish pathological changes from normal aging process.

II. Aims And Objectives

- To find out the normal Macular Thickness using spectral domain optical coherence tomography (OCT)
- To find out the effect of age on Macular Thickness

III. Materials And Methods

This was descriptive type of observational, cross-sectional, hospital based study done at Upgraded Department of Ophthalmology, SMS Hospital and Medical College, Jaipur. 400 eyes of randomly selected healthy volunteers were recruited from OPD from January 2013 to September 2017.

Macular thickness was measured using SD OCT (TOPCON 3D OCT 2000). Radial 3D OCT Scan was done for macula. All subjects underwent a complete history – Age, Sex, Intra ocular surgery, current ocular and systemic medications to rule out Diabetes, Hypertension and complete Ophthalmic examination including BCVA, Non-contact Tonometery for baseline IOP and Visual field (HVF: 24-2) – to rule out Glaucoma suspects), Slit-lamp examination, Fundoscopy – direct and indirect.

INCLUSION CRITERIA: Healthy subjects from age 18-85years having :

- Best corrected visual acuity of 20/40 or better
- Refractive error within +/- 6.0 Diopters
- No media opacity that interferes with fundus imaging
- No evidence of retinal or ONH pathologies
- Normal 24-2 standard algorithm perimetry with less than 30% fixation losses and false positive and false negative responses

EXCLUSION CRITERIA

- On any medications which were known to have any effect on RNFL Thickness, eg. Anti glaucoma, ethambutol, isoniazid, cholroquine, aminoglycosides, NSAIDS etc.
- Any systemic disease that might affect retina or visual field, eg. Hypertension, diabetes, leukemia, anemia, connective tissue disorders etc.
- Previous intraocular operations other than uneventful cataract extraction

Macular Thickness Measurement

3D Radial module was used covering an area of 6×6 mm in the macular region. A false colour topographic image is displayed as defined by the ETDRS[7].

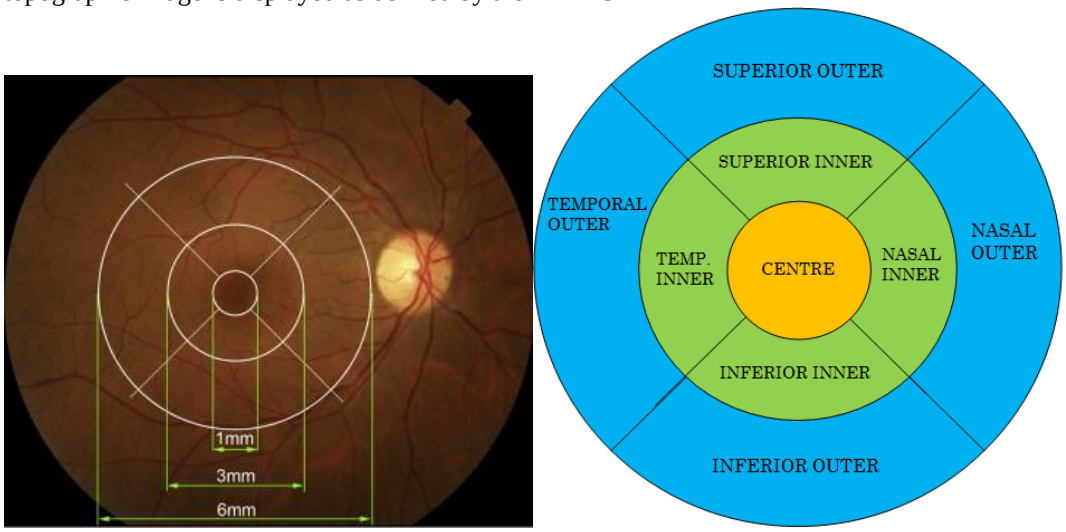
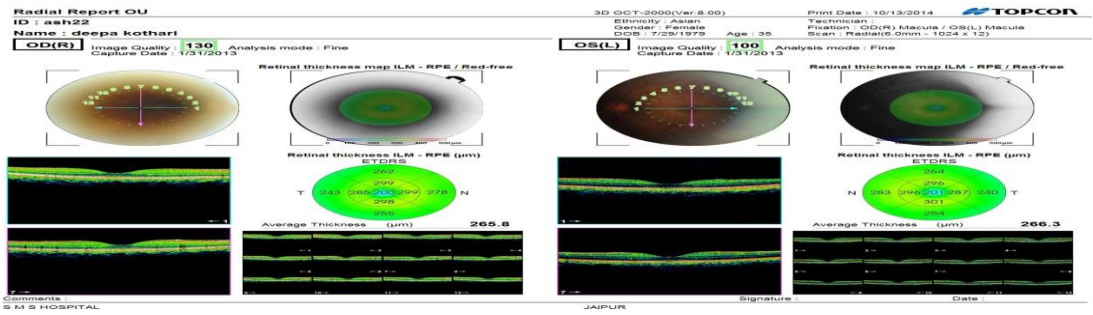


Figure 4: ETDRS Regions

Statistical analysis was performed using t test for comparative study and Pearson's co-efficient for correlation. Where indicated, linear regression was used to describe parametric association and to generate graphic representations of the same.



IV. Results

A cross-sectional, prospective study was done including 446 eyes of healthy individuals and data was recorded on the macular thickness. However, 46 eyes were excluded from the study due to poor scan quality (n = 26), poor centration (n = 10), non-clinically detectable small pigment epithelial detachments (n = 6) and early epiretinal membranes (n = 4). 400 eyes of 200 subjects aged 18 to years were evaluated.

The macular thickness was recorded in 9 ETDRS regions. The mean standard deviation are shown in Table. Looking at the macular scan, fovea was the thinnest area (222.01 ± 19.55µm), inner macular circle was thicker than the outer macula in all four regions superior, inferior, temporal and nasal ($p < 0.001$), nasal macular thickness was found to be significantly thicker (295.21 ± 17.93 µm), $p < 0.001$ than the temporal macular thickness. Nasal quadrant was the thickest among all four 9 ETDRS regions, followed by superior, inferior and temporal quadrant.

Age group		Quadrant											
	N	superior outer	inferior outer	nasal outer	temporal outer	superior inner	inferior inner	temporal inner	nasal inner	centre	centre min	centre max	overall
<30	90	262.07±14.85	258.41±14.31	280.3±18.58	249.39±16.05	304.98±14.55	299.42±16.58	287.48±17.47	303.72±16.96	230.38±21.38	163	276	270±20.56
30-40	82	262.67±14	257.93±14.8	278.62±18.18	253.04±13.98	299.73±17.28	294.1±14.39	287.24±19.77	299.99±14.7	227.6±17.86	182	265	270±23.43
40-50	86	262.42±13.31	255.41±14.72	276.23±13.84	251.98±13.67	294.12±15.31	290.87±16.33	284.27±22.56	296.15±16.68	227.58±18.05	182	264	267±25.12
50-60	78	255.22±11.17	251.31±13.87	272.28±11.53	247.97±13.22	289.64±14.48	287.59±14.39	280±17.56	291.13±18.67	226.15±15.44	184	257	261±25.69
>60	64	247.36±12.03	244.92±10.29	264.34±11.96	240.17±12.26	278.59±11.5	274.78±13.61	268.64±14.44	280.84±13.65	222.1±15.41	191	241	255±25.81
Total	400	258.58±14.42	254.12±14.59	274.97±16.19	248.94±14.57	294.36±17.17	290.24±17.07	282.27±19.58	295.21±17.93	227.08±16.48	163	276	264.6±24.122

All the regions plotted above show a decline in the thickness with age which was statistically significant,p<0.001. However, the superior outer and temporal outer, show a lower thickness between the age group of <30 years as compared to the 30 – 40 years, in the study which is not significant. The overall correlation of the thickness with increasing age had significantly decreased. The central macular thickness show a lower thickness in the 30 – 40 years age group than the 40 – 50 years age group and further decrease in the central macular thickness with the increasing age which is statistically significant.

V. Discussion

The macular thickness was recorded in 9 ETDRS regions. Fovea was the thinnest, inferior, temporal and nasal ($p < 0.001$). The nasal macular thickness was found to be significantly thicker (295.21 ± 17.93 µm), $p < 0.001$ than the temporal macular thickness. Nasal quadrant was the thickest among all four 9 ETDRS regions, followed by superior, inferior and temporal quadrant. This result is in accordance as stated by the previous studies by X R Duan et al and Bindu Appukuttan et al.[8,9]

In a study done using Topcon OCT by Mehreen Adhi et al[10] on subjects from Pakistan, mean macular thickness of 262.80 ± 13.342 µm and foveal thickness of 229.01 ± 24 µm was found. Giani et al[11]recently reported foveal thickness of 229 ± 24 µm, while Sull Ac et al[12] reported a foveal thickness of 231 ± 16 µm in healthy subjects using Topcon OCT system which are also in accordance to the results shown by our study i.e mean overall macular thickness 264.6 ± 24.12and foveal thickness 227.08 ± 16.48 µm . This shows that Indian population has a slightly thinner macular thickness as compared to what reported as above, but a little higher than reported by Hyang et al[13] (foveal thickness of 221.76 ± 15.95 µm,) and thinner than what was reported by Bruce et al[14] (foveal thickness of 244.83 ± 17.84 µm) in healthy subjects using Topcon OCT. This also explains the ethnic differences in macular thickness which have been described in a number of studies,[15-20] and the need for a different database according to the origin. A study by A. H. Kashani et al has also shown decreased retinal thickness in African Americans and a significantly greater retinal thickness in Hispancis .[21] . Previous studies on Indian eyes using Straus OCT by Tewari et al,[22] showed a thinner central foveal thickness of 149.16 ± 21.15 µm. He also stated that age was positively correlated with the mean thickness of central macula but negatively correlated with the inner and outer macular thickness. This difference in the measurements was due to the fact that time domain (TD-OCT) measures retinal thickness as the distance between internal limiting membrane (ILM) and the third hyper- reflective band, whereas SD OCT measures the distance between ILM and the retinal pigment epithelium (RPE) resulting in higher SD OCT readings compared to those obtained by TD-OCT.[23] Nevertheless, macular thickness in our subjects decreased from the center towards the periphery of retina, and was found to be thickest nasally and thinned out temporally. This was consistent with finding reported elsewhere.[12-13]

The overall macular thickness was found to slightly decrease with age in all the quadrants, similar findings in other previous studies of Tewari et al,[22] X R Duan et al,[25] Guedes V et al.[26] Kyung R Sung[24] which showed overall macular thickness statistically significantly decreased by -0.42 µm/year. But in contrast to previous studies we did not find any positive correlation with the central macular thickness which was found to be 227.08± 16.48 µm, which did not decrease significantly with advancing age. This may be related to the thickening of the internal limiting membrane and the centripetal force of the posterior vitreous resulting in the elevation of fovea, thus preventing its thinning.[190] Study by Amir H. Kashani et al,showed significant increase in centre 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.[27]

In contrast the studies by Grover et al,[28] Huang et al,[13] A. C. Sull et al,[12] Adhi M et al,[10] P.J. Kelty et al[29] failed to show a statistically association between retinal thickness with age, which may be due to the small sample size and the age distribution.

VI. Conclusion

Knowledge of normal anatomical values ofMacular thickness is essential to differentiate the abnormal changes from what is attributed to normal due course of ageing. Also ethnicity play a role in various studies,[16-20] therefore it is important to have a different database for each ethnic group.

Commercially available OCT systems, document variability in their measurements, likewise SD OCT gives a higher value of macular thickness than TD OCT. It is due to the different resolutions and difference in the retinal segmentation. Keeping in mind about the various aspects of these parameters, this is the first study to use SD OCT (TOPCON 3D OCT 2000) to establish the largest normative database for Macular thickness in Indian population and to determine the effect of age on them.

The inner sectors on ETDRS lost less thickness with age than the outer sectors. The central foveal area, which is devoid of the RNFL remains stable throughout life. Since the majority of the tissue thinning seen in the macula is most likely occurring due to ganglion cell and RNFL these changes are not reflected in the

central foveal measurements. All other regions showed statistically significant negative correlation with age, when analyzed using Pearson's coefficient of partial correlation.

There was statistically significant detectable loss of RNFL associated with age in most of the regional thicknesses of the macula, indicating that older individuals have a thinner RNFL than younger people. Histological studies have demonstrated that the number of retinal ganglion cell axons in the human eye decreases as one ages.

The superior, inferior and nasal sectors have shown a very similar rate of RNFL decline while the rate was comparatively slower in the temporal sector. Likewise, the rate of decline was similar in clock hours 12 – 7, however clock hours 8- 11 showed a slower rate of decline with increasing age. This may be due to the concentration of thinner nerve fibers in the papillomacular bundle at the temporal aspect of the ONH as has been reported in histology sections. The sectoral RNFL rate of thinning with age in our study were comparable to Sung et al[24] whereas were substantially different than those reported by Parikh et al.

The main limitation of our study was that it was based on cross sectional data rather than longitudinal data. It would be ideal if we could follow the change of retinal tissue in each individual longitudinally but for obvious reasons this is not feasible at this stage of the technology. Therefore, we acknowledge that we are not measuring true thickness changes but rather looking at differences among a large, broad population. This can cause some artifacts as can be observed in age group <30 years that had thinner RNFL thickness as compared to the 30-39 year old.

In conclusion, global and regional changes due to the effects of age on Macula thickness on OCT should be considered while assessments of these are undertaken.

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