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Study of Variation in Macular Thickness by OCT in Normal Eye

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Abstract: ***OCT has emerged as a useful imaging modality by providing new high resolution three-dimensional anatomic information about various features of macular pathology and allows clinicians to quantitatively measure macular thickness in a precise, reliable and highly reproducible manner. In our study, macular thickness in all quadrants have no significant correlation with age and sex and central macular thickness has no significant correlation with age and sex. In our study, average macular thickness decreases with age. Refractive error was not found to have any significant effect on macular thickness.***

Keywords: OCT, Macular thickness, Refractive error

1. Introduction

Macular thickness is important parameter inophthalmology. Macular thickness has been found to significantly correlated with visual acuity. Knowledge of normal population thickness would be essential for studying and evaluating macular thickening due to various ocular pathologies. Different studies have shown significant differences in macular thickness amongst subjects of different race, age, sex and refractive error in normal persons. These demographic variations may be important parameters when comparing macular thickness measurements and diagnosing ocular diseases of retina. Macular thickness for diagnostic function may differ with population. So it is desirable that normative value from population is available.

Macular thickness as determined by OCT. OCT is non-invasive and noncontact method giving a cross sectional image of macular thickness and its substructures in real time mode and in vivo. The resolution of OCT image is about 1-15 micrometer. It provides details 10 times superior to an ultrasound bscan. Change in macular thickness is very important parameter for early diagnosis of many retinal disorders and management (medical and surgical). It will provide a basis for ophthalmologist to screen for any macular thickness change due to race, age, sex and refractive error and not due to any abnormality. Recent advances in OCT technology have led to development of faster, more sensitive OCT scanning systems, known as spectral domain OCT (SD-OCT)and cirrus OCT.

Optical coherence tomography (OCT) is a new diagnostic tool that can perform tomography /cross sectional imaging of biologic tissues with <10 microns axial resolution using infra red waves. Since retina is easily accessible to the external light, it is especially suited for retinal disorders.

This imaging technique provides information regarding the retinal tomography and is akin to in vivo histopathology of the retina. The conventional imaging techniques including fundus photography and fluoresce in angiography yield diagnostic information about retinal topography. OCT yields information about retinal tomography that is complementary to conventional topographic techniques.

Macular edema is a common cause of visual loss. abnormal fluid accumulation within retina and a concomitant increase in retinal thickness usually result from the breakdown of the blood retinal barrier. This process can be found in those with diabetic retinopathy, retinal vein occlusion, uveitis and other ocular disorders. However, it has been observed repeatedly in clinical practice that the presence of macular edema dose not necessarily preclude good vision.

Traditional methods for evaluating macular edema such as slit lamp, stereoscopic photography are insensitive to small change in macular thickness and are qualitative at best. OCT has enabled clinicians to reliably detect and measure small change in macular thickness and to quantitatively evalute the efficacy of different therapeutic modalities.

The latest OCT model was made commercially available in 2019. It provides a4fold increase in imaging speed and better resolution (axial resolution<10micrometer) than earlier generations of the instrument. Based on our experience with OCT 3 and previous version of the system, we observe that themacular thickness measurement for healthy eyes are higher than the values obtained using earlier versions of the instrument, including the prototype OCT.As cirrus OCT has become more widely available and used, normative data will be important in interpreting pathological features of macula.

Aim and objectives of the study

- To see the variation of macular thickness in normal eyes.
- To determine normal values for macular thickness and volume byusing Cirrus OCT in healthy subjects in different age, sex and refractive error.

2. Materials and Methods

The study was done in according with ethical standards of institution with approval of institutional ethics committee of P.D.U. MEDICAL COLLEGE RAJKOT. This is a cross sectional hospital based observational study that was carried

out on 250 cases. The cases included were healthy patients attending the OPD of PDU MEDICAL COLLEGE RAJKOT and also volunteers.

Inclusion Criteria: healthy adult patients and volunteers coming to the OPD of PDU Hospital and Medical Collage, Rajkot for refractive error evaluation, Presbyopic correction and routine eye checkup etc.

Exclusion Criteria: healthy adult patients having any media opacity (glaucoma, cataract, RVO, corneal opacities, history of trauma) leading to poor OCT quality, history of intraocular surgery, posterior segment pathology and patients having best corrected visual acuity <6/6 and near vision N6.

All participants engaged in an informed consent document before study procedures were carried out. All subjects underwent a complete ophthalmologic examination like visual acuity, refraction, slit lamp examination, fundus examination and including a medical history, family history. Macular thickness map scan protocol on the cirrus OCT (Zeiss) was used to obtain 6 consecutive macular scans, 6mm in length, centered on the fovea, at equally spaced angular orientations and internal fixation. The data collected and software using Microsoft excel worksheet.

3. Methods

1) Number of cases: 250
2) Adult cases
3) Informed valid consent obtained from the healthy patient and volunteers.
4) Healthy patient and volunteers chosen according to inclusion and exclusion criteria.
5) Significant history like medical and family history
6) Study included following investigation
   - Visual acuity
   - Slit lamp examination
   - Fundus examination
   - Parameter to be analysed on OCT

Central macular thickness
Average macular thickness and volume. We obtained three OCT images from each subject as close to the fovea as possible, excluded images with obvious segmentation errors and adjusted for poor fixation if deemed necessary, with the understanding that slight differences in positioning, eye movement, blinking, poorfixation may affect the reliability of the macular thickness measurements.

4. Result and Analysis

In our study central macular thickness did not correlated significantly with sex but average macular thickness is more in female and in left eye.

In Dr Manushree Gautam et al JMSGR 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

OCT has emerged as a useful imaging modality by providing new high resolution three-dimensional anatomic information about various features of macular pathology and allows clinicians to quantitatively measure macular thickness in a precise, reliable and highly reproducible manner. Of the commercially available OCT systems, a documented variability in macular thickness measurements has been reported.

While Stratus OCT selects the inner segment/outer segment (IS/OS) junction as the outer retinal boundary for macular thickness measurements spectral domain OCT systems select RPE as the outer retinal boundary for thickness measurements, thus leading to an increase in macular thickness reported with these systems, when compared to the TD-OCT systems, while also a slight variability amongst the different SDOCT systems based on the various scanning protocols and differences in the segmentation algorithms. Therefore, macular thickness measurements using different OCT systems are not interchangeable.

Normative values for macular thickness in healthy population were obtained using commercially available OCT mapping software.

In our study mean+/-SD central macular thickness was 226+/-5, superior thickness was 265+/-5, inferior thickness was 264+/-5, nasal thickness was 260+/-5, temporal thickness was 257+/-5.

Macular thickness in our subjects decreased from the center towards the periphery of the retina, and was found to be thickest nasally and thinned out temporally. This was consistent with findings reported elsewhere. Demographic variations in macular thickness have been documented previously.

Asefzadeh et al found an overall trend towards a thinner retina in blacks compared to whites using Stratus OCT. Oshitari et al reported a thicker retina in Japanese population in comparison to the US population using Stratus OCT, while Tewari HK et al reported mean foveal thickness in healthy Indian subjects to be 149.16±21.15 µm using Stratus OCT, which was significantly lower than other populations..

In our study, macular thickness in all quadrants have no significant correlation with age and sex and central macular thickness has no significant correlation with age and sex.

In our study, average macular thickness decrease with age.

Refractive error was not found to have any significant effect on macular thickness.

5. Discussion

OCT has emerged as a useful imaging modality by providing new high resolution three-dimensional anatomic information about various features of macular pathology and allows clinicians to quantitatively measure macular thickness in a precise, reliable and highly reproducible manner.

Of the commercially available OCT systems, a documented variability inmacular thickness measurements has been reported .While Stratus OCT selects the inner segment/outer segment (IS/OS) junction as the outer retinal boundary for macular thickness measurements spectral domain OCT systems select RPE as the outer retinal boundary for thickness measurements, thus leading to an increase in macular thickness reported with these systems, when compared to the TD-OCT systems, while also a slight variability amongst the different SDOCT systems based on the various scanning protocols and differences in the segmentation algorithms. Therefore, macular thickness measurements using different OCT systems are not interchangeable

A study of Chan Annie et al, results show a mean macular thickness of262.80±13.342 µm and foveal thickness of 229.01±20.464 µm. Giani et al recently reported foveal thickness of 229±24 µm, while Sull AC et al reported a foveal thickness of 231±16 µm in healthy subjects using Topcon OCT system.

These values are comparable to our results. However, Hyang et al reported foveal thickness of 221.76±15.95, and Bruce et al reported foveal thickness of244.83±17.84 µm in healthy subjects using Topcon OCT, which varied significantly from our results.

Nevertheless, macular thickness in our subjects decreased from the center towards the periphery of the retina, and was found to be thickest nasally and thinned out temporally. This was consistent with findings reported elsewhere. Demographic variations in macular thickness have been documented previously. Kashani et al reported mean foveal thickness of 181.0±3.7 µm in African Americans and 200.27±2.7 µm in Caucasians using Stratus OCT.

Asefzadeh et al found an overall trend towards a thinner retina in blacks compared to whites using Stratus OCT. Oshitari et al reported a thicker retina in Japanese population in comparison to the US population using Stratus OCT, while Tewari HK et al reported mean foveal thickness in healthy Indian subjects to be 149.16±21.15 µm using Stratus OCT, which was significantly lower than other populations. Grover et al found a significant difference in mean foveal thickness between blacks and whites using Spectralis SD-OCT.

When compared to Caucasian and Hispanic subjects, African-American race has been shown to be a predictor of decreased mean foveal thickness and male sex to be a significant predictor of increased mean foveal thickness.

A decreasein macular thickness with age has also been reported.Other reports however, have shown no association of macular thickness with age and/or gender, suggesting that studies comparing macular thickness measurements should carefully control for age-based, race-based, and gender based variations.
A study of chan Annie et al, showed no association of macular thickness withage, but study of cha nannie et al, found male gender to be associated with greater foveal and mean macular thickness. Thus, demographic variations besides the type of OCT system in use may be important parameters when comparing macular thickness measurements, and diagnosing and monitoring macular pathologies.

Measurement reproducibility is an essential parameter when determining clinical usefulness of an OCT system, particularly when monitoring pathologies. Studies using cirrus OCT system have reported good reproducibility of the system for measuring macular thickness in normal and pathologic states.

As with other SD-OCT systems, reproducibility is better with cirrus OCT system, than with the conventional time-domain systems due to arapid speed of scan acquisition. We obtained three OCT images from each subject as close to the fovea as possible, excluded images with obvious segmentation errors and adjusted for poor fixation if deemed necessary, with the understanding that slight differences in positioning, eye movement, blinking artifacts and poor fixation may affect the reliability of the macular thickness measurements.

Male gender was associated with a greater macular thickness in all 9 regions of the ETDRS map compared to females. Foveal thickness in males was measured to be 232.68±21.07 µm, while in females it was 222.87±18.72 µm ($p<0.0001$). Mean macular thickness in males was 266±14.20 µm, while in females it was 258.21±10.03 µm ($p<0.0001$).

When adjusted for age, males were found to have an increase in mean macular and foveal thickness ($p = 0.005$ and $p = 0.0008$respectively) when compared to females.

By using linear regression analysis, there was no association of mean macular thickness ($r2 = 0.01$; $p>0.05$) and foveal thickness ($r2 = 0.00004$; $p>0.05$) with age. This was also true when adjusted for gender ($p>0.05$ and $p>0.05$ respectively).

Regression plots of foveal thickness and mean macular thickness vs. age.

There is no association of foveal thickness (A) [$r2 = 0.00004$; $p = 0.92$] and mean macular thickness (B) [$r2 = 0.01$; $p = 0.09$] with age previous study.

A study of chan annie et al, the fovea was the thinnest area (226.4025 ±22.5063µm). The inner macula was thicker in all four quadrants i.e. superior, inferiornasal 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 and chinese population.

Using the criteria of mean ± 2 SDs, which includes 95% of the population, we suggest that181 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 being226.4025 any patient with macular thickness of below 180 µm or above 270µm 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. Giani et al recently reported foveal thickness of 229±24 µm, while Sull AC et al reported a foveal thickness of 231±16 µm in healthy subjects from New England using Topcon OCT system. However, Hyang et al reported foveal thickness of 221.76±15.95, and Bruce et al reported foveal thickness of 244.83±17.84 µm in healthy subjects using Topcon OCT. However, in a study from Wisconsin, New Yorkthe CFT was found to be 274.3 ±72.4 µm using Topcon OCT. The same study showed CFT using stratus OCT as 249.8±72.4 µm. This difference in measurements can be explained on ethnic grounds.

In our study the temporal quadrants was thinnest of macula and superior quadrants was thickest. In our study normal range of macula is 220 to 270 micrometer. However we did not find any significant change in central macular thickness with age. In contrast, few studies 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.

In our study central macular thickness did not correlated significantly with age but average macular thickness is decrease with age. In Dr Manushree Gautam et al JMSGR study, showed that men had greater central foveal thickness as compared to women ($P<0.05$). Females were foundto 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 male vs females. In the study by Tewari et al. and Grover et al. no significant difference was seen in the average foveal thickness and minimum foveal thickness in men and women. However, other similar studies found males to have significantly higher average retinal thickness ascompared to females.

The presence of thinner foveas in females could probably explain the higher incidence of macular holes seen in them.

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