

Study of effect of Age on Retinal Nerve Fibre Layer Thickness and Optic Nerve Head Parameters 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 tomography is of two types- Time domain OCT and Spectral- domain or Fourier Domain OCT. The time domain OCT 3000 became 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 retinal nerve fiber layer (RNFL) thickness around the optic nerve head (ONH) and optic nerve head parameters like disc size, cup size, are commonly seen in eyes with pathologies, like glaucoma, coloboma, age related macular degeneration, diabetic retinopathy etc., but can also be attributed to normal aging process. The knowledge of RNFL and ONH parameters 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 Retinal Nerve Fiber Layer Thickness and Optic nerve Head Parameters using spectral domain optical coherence tomography (OCT).
- To find out the effect of age on Retinal Nerve Fiber Layer Thickness and Optic nerve Head Parameters.

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.

Retinal Nerve Fiber Layer Thickness and Optic nerve Head Parameters were measured using SD OCT (TOPCON 3D OCT 2000). Glaucoma module 3D done for RNFL and ONH imaging. 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 Tonometry 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 18-85 years having :

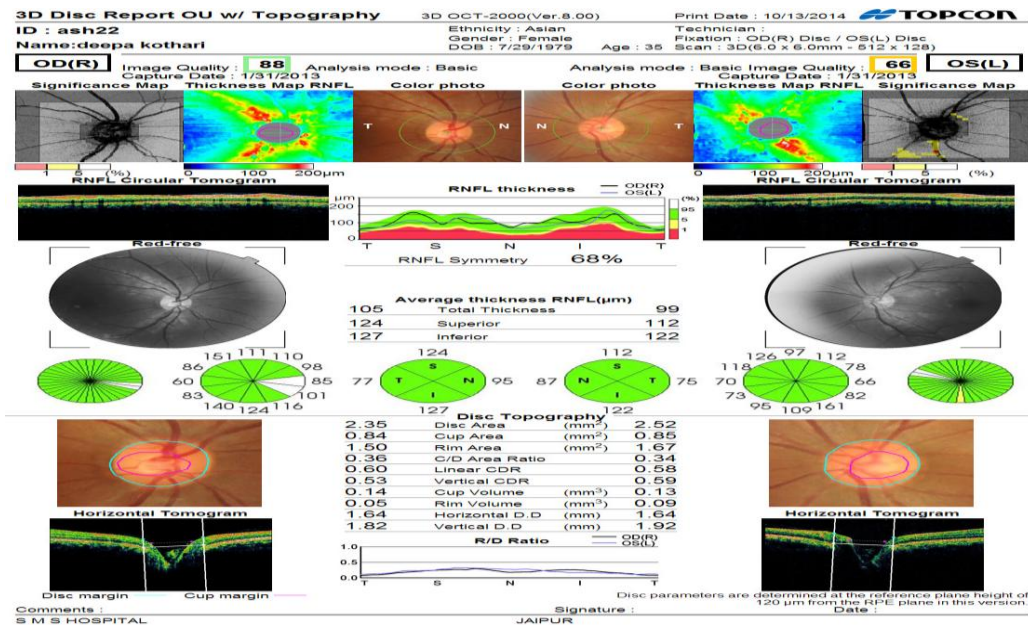
- Best corrected visual acuity of 20/40 or better
- Refractive error within +/- 6.0 Diopters
- No media opacity that interferes with fundus imaging
- No evidence of retinal or ONH pathologies
- Normal 24-2 standard algorithm perimetry with less than 30% fixation losses and false positive and false negative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

Retinal Nerve Fiber and Optic Nerve Head Parameters Analysis

The fast RNFL scan consists of three 3.4 mm diameter circumpapillary scans centered at the ONH, with each scan having 256 A-scans. The RNFL thickness parameters were calculated as the mean of three corresponding parameters measured independently on three individual circular scans. For RNFL scans, overall mean RNFL thickness and RNFL thickness measurements averaged within the 4 quadrants and 12 clock hours were used for analysis. P<0.05 was considered as statistically significant.



IV. Results

A cross-sectional, prospective study was done including 446 eyes of healthy individuals and data was recorded on the Retinal nerve fiber thickness and Optic nerve head parameters. 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.

Table 12: Parameters of RNFL thickness measurement

Parameters	N	MEAN	Std. Deviation	Minimum	Maximum	P-value
Overall	400	98.91	9.866	71	136	0.0001
Superior	400	114.30	13.200	70	158	
Inferior	400	120.29	12.954	83	156	
Temporal	400	69.83	10.223	37	101	
Nasal	400	81.43	13.629	40	125	
1 o'clock	400	116.36	16.635	59	159	
2 o'clock	400	98.19	17.245	52	171	
3 o'clock	400	69.98	14.861	34	120	
4 o'clock	400	79.03	15.929	35	130	
5 o'clock	400	109.03	17.836	61	149	
6 o'clock	400	128.05	16.426	83	189	
7 o'clock	400	119.33	20.069	60	180	
8 o'clock	400	70.86	12.969	38	119	
9 o'clock	400	60.79	10.223	36	97	
10 o'clock	400	81.97	13.424	36	127	
11 o'clock	400	116.36	19.108	55	182	
12 o'clock	400	115.56	15.003	63	164	

Table no 2: RNFL thickness

Age	N	RNFL THICKNESS				
		overall	superior	inferior	temporal	nasal
<30	90	102.96± 9.31	118.92±11.25	126.62±9.33	75.68±8.31	85.27±12.97
30-40	82	102.16±8.47	120.74±11.19	126.11±10.63	72.85±7.09	86.65±13.47
40-50	86	101.79± 8.93	118.21±11.03	123.93±9.57	71.34±8.91	83.05±13.35
50-60	78	94.77± 7.56	109.31±11.10	114.91±11.36	66.90±8.34	77.47±12.72
>60	64	90.22 ±8.08	100.36±10.74	105.59±11.77	59.30±10.97	72.02±9.89
Total	400	98.91± 9.87	114.30±13.2	120.29±12.95	69.83±10.22	81.43±13.63

RNFL thickness was found to decrease with the advancing age in the study population, however some clock hours exhibited a mild increase in the RNFL thickness in the 30 – 40 age group in comparison to the <30 years age group in the 1 o'clock, 2 o'clock, 3 o'clock, 4 o'clock and 12 o'clock region. The study also showed lesser degree of RNFL thickness decrease with advancing age from 7 o'clock to 11 o'clock region in comparison to the rest of the clock hours. There was significant decrease of RNFL thickness in all the regions between the first and the last decade of study population

Table no 3: optic disc parameters

Age	N	RNFL THICKNESS											
		1 o'clock	2 o'clock	3 o'clock	4 o'clock	5 o'clock	6 o'clock	7 o'clock	8 o'clock	9 o'clock	10 o'clock	11 o'clock	12 o'clock
<30	90	120.21±16.03	101.09±16.84	72.41±15.40	80.13±14.92	116.16±16.13	135.01±14.58	130.24±16.34	76.18±10.81	66.47±8.99	87.82±11.365	125.89±16.12	117.64±12.28
30-40	82	121.30±15.94	105.94±16.31	75.20±14.88	84.98±15.97	115.45±15.46	133.74±13.08	123.89±21.26	72.56±12.19	62.51±7.89	84.13±11.74	124.11±16.12	120.62±14.24
40-50	86	119.65±15.99	102.71±16.22	72.08±13.90	81.23±17.17	112.56±16.45	132.30±14.18	121.08±16.87	71.76±13.41	61.95±10.54	83.37±13.63	118.07±16.70	121.50±13.84
50-60	78	114.68±12.78	90.49±15.39	63.62±14.47	74.87±14.92	99.51±16.97	122.00±15.75	115.64±16.73	70.55±10.85	56.85±8.25	78.88±12.27	105.58±20.43	109.46±15.36
>60	64	102.23±15.64	87.48±13.73	64.78±11.61	71.98±12.96	97.61±15.32	112.64±13.84	100.25±16.66	60.42±12.90	53.84±10.71	72.86±13.90	103.88±14.52	105.61±13.07
Total	400	116.36±16.64	98.19±17.24	69.98±14.86	79.03±15.93	109.03±17.84	128.05±16.43	119.33±20.07	70.86±12.97	60.79±10.22	81.97±13.42	116.36±19.11	115.56±15.00

Table no 4: optic disc parameters

age	N	optic nerve head area	optic nerve head cup area	optic nerve head rim area	cup/disc ratio	linear c/d ratio	vertical c/d ratio	optic nerve head cup volume	optic nerve head rim volume	ONH hz diameter	ONH vt diameter
<30	90	2.47±0.41	0.67±0.38	1.77±0.46	0.27±0.13	0.49±0.15	0.51±0.16	0.12±0.11	0.27±0.39	1.67±0.15	1.88±0.19
30-40	82	2.51±0.38	0.77±0.43	1.74±0.45	0.30±0.15	0.53±0.15	0.53±0.16	0.16±0.14	0.18±0.15	1.72±0.16	1.87±0.13
40-50	86	2.54±0.30	0.83±0.41	1.71±0.37	0.32±0.15	0.55±0.14	0.56±0.15	0.18±0.17	0.16±0.19	1.70±0.14	1.88±0.12
50-60	78	2.52±0.36	0.99±0.46	1.54±0.39	0.38±0.15	0.59±0.14	0.60±0.14	0.21±0.17	0.13±0.9	1.72±0.17	1.89±0.14
>60	64	2.27±0.35	0.82±0.45	1.49±0.35	0.34±0.15	0.56±0.15	0.58±0.17	0.17±0.15	0.14±0.8	1.62±0.14	1.79±0.12
Total	400	2.47±0.37	0.81±0.43	1.66±0.42	0.32±0.15	0.54±0.15	0.55±0.16	0.17±0.15	0.18±0.23	1.69±0.15	1.87±0.15
p value		0	0.0001	0	0	0.0003	0.0018	0.0028	0.0002	0	0

There is increase of cup area, decrease in rim area, increase in cup/disc ratio, increase in cup volume ,decrease in rim volume with increase in age in the study population which is statistically significant as denoted by the p-value.

Meandisc area was 2.47 ± 0.37 mm² and optic cup area, rim area, and horizontal integrated rim width increased with disc size, whereas vertical integrated rim area did not. Vertical integrated rim area, horizontal integrated rim width, and rim area decreased and cup area, cup disc ratio increased with age. Sung et al and Marsh BC et al also have similar findings i.e cup area increased and rim area decreased with age, both of which were statistically significant.^{35,36} Disc size did not show significant change with age, but significant cup and rim area changes likely reflect neural tissue loss.

V. Discussion

The parameters analyzed are overall RNFL thickness which was $98.91 \pm 9.86 \mu\text{m}$, RNFL thickness for superior, inferior, nasal, and temporal quadrants were 114.30 ± 13.20 , 120.29 ± 12.95 , 81.43 ± 12.62 , and $69.83 \pm 10.22 \mu\text{m}$, respectively. Sung, Kyung Rim et al,¹⁵ reported overall RNFL thickness was $100.8 \pm 10.5 \mu\text{m}$, RNFL thickness for superior, inferior, nasal, and temporal quadrants were 138.2 ± 21.74 (95% CI: 134.3–142.1), 129.1 ± 25.67 (95% CI: 124.5–133.7), 85.71 ± 21 (95% CI: 81.9–89.5), and 66.38 ± 17.37 (95% CI: 63.3–69.5) μm , respectively in one study on Indian population. In the other, the average peripapillary RNFLT was $114.03 \pm 9.6 \mu\text{m}$ (range, 90–139). A study by Appukuttan B. et al,²⁰ showed the RNFL was thickest in the inferior quadrant followed by superior, nasal, and temporal quadrants which is also shown by our study. Results showed significantly higher values of RNFL thickness in Indian eyes when compared to White eyes,¹⁸ and lower value when compared to RNFLT in normal Latino population.¹⁹

The overall RNFL thickness was found to have negative correlation with age, which was statistically significant in all the four quadrants. This is in accordance with the study of Parikhet al. Appukuttan B. et al,²⁰ had also found the same but only in the superior and inferior quadrant. However, Sung, Kyung Rim et al,¹⁵ reported the slope change of RNFL over people of different ages was statistically significantly different from a slope of zero for overall, and in superior, inferior and nasal quadrants ($p \leq 0.01$) but not statistically significant in the temporal quadrant ($p = 0.46$). This is also in accordance with our study showing highly significant values in superior, inferior and nasal regions i.e. p value < 0.001 but only significant in temporal quadrant of lesser degree of RNFL thickness decrease with advancing age from 7 o'clock to 11 o'clock region in comparison to the rest of the clock hours. This difference in rate 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.²¹ Identical number of axonal loss will cause a shallower decline in locations predominantly composed by thinner fibers.

However some clock hours exhibited a mild increase in the RNFL thickness in the 30 – 40 age group in comparison to the < 30 years age group in the 1 o'clock, 2 o'clock, 3 o'clock, 4 o'clock and 12 o'clock region. The study also showed lesser degree of RNFL thickness decrease with advancing age from 7 o'clock to 11 o'clock region in comparison to the rest of the clock hours. There was significant decrease of RNFL thickness in all the regions between the first and the last decade of study population.

Recent reports have documented mean optic disc area in various normal populations between 1.60 mm^2 and 2.63 mm^2 ,²²⁻²⁹ mean optic cup area between 0.34 mm^2 and 0.93 mm^2 ^{2, 33, 35, 36, 37-42} and mean cup-to-disc area ratios between 0.16 and 0.45.²²⁻²⁹ Vertical optic disc diameter was documented in few reports and varied between 1.7 mm and 2.04 mm.²²⁻²⁹

The results shown by our study i.e. the mean optic disc area was $2.47 \pm 0.37 \text{ mm}^2$, mean rim area was $1.66 \pm 0.42 \text{ mm}^2$, and mean cup area was $0.81 \pm 0.43 \text{ mm}^2$. Vertical optic disk diameter 1.87 ± 0.15 , mean vertical cup-to-disc ratio of 0.55 ± 0.16 are compatible to the previous studies.

Girkin CA et al³³ suggested racial differences for optic nerve parameters, participants of European descent had significantly smaller optic disc area than other groups, and Indian participants had significantly smaller rim area than other groups which is also supported by the results of our study. However, the optic nerve parameters shown by an Indian study done in southern India by Mansoori et al were on the higher side as compared to our results indicating even a regional difference among the parameters and a different normative database for North Indian population with spectral OCT.³⁴

VI. Conclusion

Knowledge of normal anatomical values of Retinal Nerve Fiber Layer thickness and Optic Nerve Head parameter 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,⁷⁻¹¹ 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 Retinal Nerve Fiber Layer (RNFL) thickness and optic Nerve Head (ONH) parameters in Indian population and to determine the effect of age on them.

There was statistically significant detectable loss of RNFL associated with age in most of the regional thicknesses of the peripapillary RNFL and macula, indicating that older individuals have a thinner RNFL than younger people. Disc size did not show significant change with age, but significant cup and rim area changes, likely reflect neural tissue loss. 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 al¹⁵ whereas were substantially different than those reported by Parikh et al. Optic nerve head analysis showed that while the disc size remained stable there was a significant decrease in rim area and increase in the cup area. The rate of change varied substantially among the various parameters and differs from the rate in other locations. This might indicate preferential loss at the optic nerve head level that is less pronounced in the retina itself.

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, and some decline in the Disc area noted in the >60 years age group.

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

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