

Optical Coherence Tomography-Measured Nerve Fiber Layer and Macular Thickness in Emmetropic, High-Myopic and High-Hyperopic Eyes

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Abstract

Purpose: To determine the nerve fiber layer and macular thickness by optical coherence tomography (OCT) in emmetropic, high-myopic and high-hyperopic eyes

Methods: One hundred five eyes of 55 randomly selected healthy subjects between 20 and 30 years old were included in this study. The eyes were categorized in three groups (high-myopic, emmetropic and high-hyperopic) according to their cycloplegic refraction and axial length (AL). The retinal nerve fiber layer (RNFL) and macular thickness was measured using three circumferential peripapillary scans and six radial scans of the macula by optical coherence tomography (OCT model 2010, Zeiss). Average RNFL thickness in the peripapillary region and macular thickness was measured and compared in these three groups.

Results: Mean age of participants was 24.3±2.6 years. Average RNFL thickness was 107.9±8.3 μ, 131.1±3.2 μ and 145.8±2.8 μ in high-myopic, emmetropic and high-hyperopic groups, respectively. There was a high correlation between RNFL thickness and AL ($r = -0.91$, $p < 0.001$). Average inner macular thickness was 221.6±13.2 μ, 246±10.5 μ and 255.9±15.0 μ and average outer macular thickness was 207.6±9.7 μ, 230.1±7.4 μ and 239.7±13.0 μ in high-myopic, emmetropic and high-hyperopic groups, respectively. The difference of RNFL thickness was statistically significant between these three groups.

Conclusion: High-hyperopic eyes had significantly thicker average RNFL thickness than emmetropic and high-myopic eyes; while emmetropic eyes had thicker average RNFL thickness than high-myopic eyes. There is a strong negative correlation between AL and average NFL thickness.

Keywords: optical coherence tomography, nerve fiber layer, macular thickness

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Introduction

Optical coherence tomography (OCT) is a new imaging technology with ophthalmic applications based on the principles of laser interferometry.^{1,2}

Its high depth resolution (10 microns) makes it possible to measure retinal thickness accurately.³ Comparison of histological and OCT images from prototype devices have shown a good correlation between the OCT estimates and real measurements of retinal nerve fiber layer (RNFL) thickness.^{4-8,13}

The RNFL thickness measurement could be invaluable to detect early stages of many ocular diseases such as glaucomatous changes and conditions like macular edema, central serous chorioretinopathy, epiretinal membrane, diabetic retinopathy and macular holes when the clinical judgment is equivocal.^{9,11,12}

It was shown that RNFL thickness was different in high-myopics and emmetrops.¹⁴ The aim of this study is to compare the average RNFL and macular thickness profiles by OCT in emmetropic, axial myopic and axial hyperopic cases.

To the best of our knowledge this is the first study comparing the average RNFL and macular thickness profiles by OCT in emmetropic, axial myopic and axial hyperopic cases.

Methods

One hundred five eyes of 55 randomly chosen healthy subjects between 20 and 30 years old were included in this study.

In a comparative uncontrolled case series study, a complete ocular examination including; visual acuity, slit-lamp examination with stereoscopic biomicroscopy of the optic nerve head (ONH) and nerve fiber layer (NFL), intraocular pressure (IOP) measurement (Goldman applanation tonometer), cycloplegic refraction, visual field testing (Humphrey 24-2, SITA standard) was performed. Axial length (AL) was measured using ultrasound biometry after dilation ≥ 5 mm with cyclopentolate (0.5%, for three times every 5 minutes). This study was approved by the ethics committee at Iran University of Medical Sciences and written informed consent was obtained from all participants before entering the study. Exclusion criteria were contraindications to dilation including

occludable chamber angles, intolerance or hypersensitivity to topical anesthetics or mydriatics, ocular hypertension (IOP > 22 mm Hg) or glaucoma in either eye, visual field abnormality in either eyes, history of any ocular or periocular surgery, systemic disease, best corrected visual acuity of worse than $20/40$, and optic nerve or RNFL abnormality.

Subjects underwent OCT testing of both macula and peripapillary NFL using the OCT unit (OCT 2000, version A 4.01; Carl Zeiss-Humphrey Systems, Dublin, CA).

Eyes were categorized into three groups based on the AL and cycloplegic refraction: AL > 26 and cycloplegic refraction > -6 D as high-myopia, $22 < AL < 24$ and cycloplegic refraction within ± 1 D as emmetropia and AL < 21 and cycloplegic refraction > 5 D as high-hyperopia.

Measurement of foveal retinal thickness and nerve fiber layer thickness

Following pupillary dilation at least 5mm with 0.5% cyclopentolate solution, optical coherence tomography was used to examine the eyes. Three circular scans were obtained at the peripapillary retina at a default radius of 1.74 mm from the center of the optic disc, and the measurements were averaged to provide the average peripapillary RNFL thickness. In addition, the peripapillary scan was divided into four equal 90 degree quadrants (superior, inferior, temporal, nasal) and RNFL thickness measurements in these four quadrants were also provided. Macular thickness was measured over the six linear scans (600 A) then averaged to provide an average for the macular thickness. All 6 mm radial scans consisted of 128 sampled locations along the radial line scan. Three concentric circles with radii of 0.5 mm, 1.5 mm, and 3 mm defined the central, inner, and outer subfields, respectively.

All imaging studies were performed on the same day of the ophthalmic examination for three times. An internal and external fixation point was used for acquisition of images.

Statistical analysis

Data were entered into an SPSS database (SPSS 11.5 for windows, Chicago, IL, USA). Each eye was considered as a subject in

analysis. Comparison between groups was performed using the analysis of variance (ANOVA) test. The groups were tested two by two using post hoc test (Tukey HSD test). Receiver operator characteristic (ROC) curve method was used to determine the best cut off point values in 3 groups. If the area under curve was significant, the best cut off point was extracted from the table of coordinates of the curve considering the values that correspond with highest sensitivity and specificity. P value of less than 0.05 was considered significant in the statistical analysis.

Results

There were 105 eyes included in the study. Mean age was 24.35 (SD: 2.6) years old. There were three different groups; high-myopic (40 eyes), emmetropic (41 eyes) and high-hyperopic (24 eyes) (Table 1).

RNFL thickness was significantly different between 3 groups. The difference in RNFL thickness in each of these regions was statistically significant between high-myopic and emmetropic groups ($P<0.001$) and also high-myopic and high-hyperopic groups ($P<0.001$). Except for inferior region ($P=0.188$), the difference in mean RNFL thickness of other parts of macula (superior, temporal and nasal region) of emmetropic and high-hyperopic eyes group

was also statistically significant ($P<0.001$) (Table 2).

There was a high negative and significant correlation between AL and RNFL thickness (ANOVA test, $r = -0.91$, $P<0.001$).

The average inner macular thickness was calculated $221.6\pm 13.2 \mu$, $246.4\pm 10.5 \mu$ and $255.9\pm 15.0 \mu$ in high-myopic, emmetropic and hyperopic groups (Table 3). The difference was statistically significant between high-myopic and emmetropic ($P<0.001$), high-myopic and high-hyperopic ($P<0.001$) and emmetropic and high-hyperopic groups ($P=0.012$). The average outer macular thickness was measured $207.6\pm 9.7 \mu$, $230.1\pm 7.4 \mu$ and $239.7\pm 13.0 \mu$ in high-myopic, emmetropic and hyperopic groups, respectively. The difference was statistically significant between high-myopic and emmetropic ($P<0.001$), high-myopic and high-hyperopic ($P<0.001$) and emmetropic and high-hyperopic groups ($P<0.001$). The correlation between AL and inner macular thickness ($r = -0.51$) and AL and outer macular thickness ($r = -0.60$) as analyzed by linear regression test was not as strong as correlation between AL and NFL thickness ($r = -0.91$). The macular and foveal volume was significantly different only between high-myopic and emmetropic ($P<0.001$) and high-myopic and high-hyperopic groups ($P<0.001$) (Table 4).

Table 1: Demographics, refraction and axial length (AL) of 105 eyes from 55 cases who underwent OCT nerve fiber layer and macular thickness measurements

	Total (105 eyes)	High-myopic (40 eyes)	Emmetropic (41 eyes)	High-hyperopic (24 eyes)	P value
Mean age (years)	24.35 (SD:2.6)	24.51 (SD:2.62)	24.48 (SD:2.65)	23.67 (SD:2.71)	0.623*
Males; n (%)	51 (92.7%)	22 (100%)	17 (81%)	12 (100%)	0.217**
Spherical equivalent Refraction (Diopter)	-1.44±5.9	-7.98±1.39	-0.055±0.72	7.08±1.17	<0.001*
AL (mm)	24.05±2.16	26.35±0.79	23.62±0.52	20.97±0.35	<0.001*

*: Kruskal-Wallis Test

** : Fisher's Exact Test

Note: for Age and sex the statistics were calculated considering the subjects as units of analysis and for the other ongoing parameters in the study eyes were considered as units of analysis. P values show the differences in each distribution between three comparison groups totally.

Table 2: Optical coherence tomography (OCT) nerve fiber layer thickness measurement in 105 eyes of 55 subjects

	Total (105 eyes)	High-myopic (40 eyes)	Emmetropic (41 eyes)	High-hyperopic (24 eyes)	P value ¹	P value ²	P value ³
Average NFLT (micrometer)	125.66 (SD:16.08)	107.94 (SD:8.366)	131.12 (SD:3.24)	145.86 (SD:2.83)	<0.001**	<0.001**	<0.001**
Sup. NFLT	151.02 (SD:17.74)	132.55 (SD:11.79)	156.90 (SD:6.36)	171.72 (SD:3.83)	<0.001**	<0.001**	<0.001**
Inf. NFLT	154.1 (SD:24.8)	133.02 (SD:11.25)	164.05 (SD:6.33)	172.33 (SD:34.66)	<0.001**	<0.001**	0.188**
Nasal NFLT	102.84 (SD:17.6)	84.19 (SD:13.56)	110.39 (SD:4.7)	121.04 (SD:2.83)	<0.001**	<0.001**	<0.001**
Temp. NFLT	96.56 (SD:16.14)	80.14 (SD:12.93)	102.82 (SD:4.96)	113.22 (SD:4.83)	<0.001**	<0.001**	<0.001**

** : Tukey Post Hoc test.

1. P values for comparing the emmetropic and high-myopic eyes.
2. P values for comparing the high-hyperopic and high-myopic eyes.
3. P values for comparing the high-hyperopic and emmetropic eyes.

Table 3: Macular thickness in 3 groups

	Total (105 eyes)	High-myopic (40 eyes)	Emmetropic (41 eyes)	High-hyperopic (24 eyes)	P value ¹	P value ²	P value ³
Average outer macula (microns)	223.78 (SD:16.4)	207.63 SD:(9.78)	230.18±7.49	239.76±13.09	<0.001	<0.001	<0.001
Temporal outer macula (microns)	207.65±23.5	189.72±21.51	211.80±14.29	230.45±14.99	<0.001	<0.001	<0.001
Superior outer macula (microns)	232.5±18.3	216.55±9.0	237.21±8.6	251.41±19.84	<0.001	<0.001	<0.001
Nasal outer macula (microns)	231.23±18.41	213.9±10.75	238.97±11.67	246.9±14.63	<0.001	<0.001	0.032**
Inferior outer macula (microns)	223.64±14.76	210.35±10.83	232.75±9.21	230.25±11.77	<0.001	<0.001	0.621**

*: ANOVA Test

** : Tukey HSD Post Hoc test

1. P values for comparing the emmetropic and high-myopic eyes.
2. P values for comparing the high-hyperopic and high-myopic eyes.
3. P values for comparing the high-hyperopic and emmetropic eyes.

Table 4: Optical coherence tomography (OCT) measurement of fovea thickness, macular total value and fovea volume in 105 eyes of 55 subjects

	Total (105 eyes)	High-myopic (40 eyes)	Emmetropic (41 eyes)	High-hyperopic (24 eyes)	P value ¹	P value ²	P value ³
Fovea thickness (microns)	224.38 (SD:20.68)	210.73 (SD:9.67)	228.07 (SD:25.16)	240.83 (SD:6.72)	<0.001	<0.001	0.013**
Macular Total Volume (square of millimeter)	2.48 (SD:0.16)	2.40 (SD:0.18)	2.54 (SD:0.09)	2.53 (SD:0.15)	<0.001	<0.001	0.987**
Fovea volume (cubic mm)	0.18 (SD:0.02)	0.16 (SD:0.01)	0.19 (SD:0.02)	0.19 (SD:0.004)	<0.001	<0.001	0.255**

** : Tukey HSD Post Hoc test.

1. P values for comparing the emmetropic and high-myopic eyes.
2. P values for comparing the high-hyperopic and high-myopic eyes.
3. P values for comparing the high-hyperopic and emmetropic eyes.

Discussion

Our study showed a mean RNFL thickness of 131.1 μm in emmetropic subjects. The RNFL was thickest in the inferior and superior quadrants, which is consistent with previous studies. Reported range of RNFL thickness in emmetropic subjects is 80 to 150 μm .⁷⁻¹⁰

In Schumann⁹ and Bowd¹¹ reports a difference was found between the nasal and temporal RNFL thickness, with the nasal quadrant thinner than the temporal quadrant. But in our study the temporal RNFL thickness was thinner than that of the nasal quadrant ($P < 0.0001$). These observations are supported by previous imaging and histological data. Indeed, histological measurements of the thickness of the RNFL in normal eyes demonstrate that superior, inferior, and nasal quadrant RNFL at the disc margin are significantly thicker than the temporal quadrant RNFL at the disc margin. It is possible that this results from subtle differences in axon trajectory away from the optic nerve head (ONH) and emphasizes the importance of eccentricity when comparing RNFL thickness around the ONH.^{11,12}

The difference between these two studies can be related to several factors, among which are population characteristics, and the measurement technique.¹¹ We used a circle around the optic disc (which is on average 3.4 mm in diameter, as used in the other studies), to avoid any contribution of disc size to our RNFL thickness measurements.

This finding is in normal eyes, but in high-myopic eyes, in study of Mrugacz¹⁴ the mean NFL thickness was 152 μm in eyes with low myopia (-1.0 to -4.0 D), 150 μm in eyes with medium myopia (-4.0 to -8.0 (D)) and 140 μm in eyes with high-myopia (> -8.0 D). Statistically significant differences were revealed between patients with high-myopia and the control group. But in study of Sek-Tien Hoh found mean peripapillary RNFL thickness did not correlate with SE in myopic eyes.¹⁵ We measured average NFL thickness in high-myopic groups 141.9 which was significantly different with emmetropic eyes. The difference of RNFL thickness values between Malgorzata Mrugacz¹⁴ study and ours can be explained by the fact that mean age in their study was 15 years old and in our study was 24.35. On the other hand, Alamouti¹⁶ et al,

found that older individuals had thinner RNFL than younger individuals, so the lower RNFL thickness values in our study may be attributed to older patients' age. In addition we showed that there is a high correlation between AL and peripapillary RNFL thickness. In Malgorzata Mrugacz¹⁴ series the different groups were categorized according to the subjects' refraction regardless of their AL. So the cases in high-myopic groups could be within normal AL with subsequent higher RNFL thickness.

Our study found significant differences in the peripapillary RNFL thickness in four quadrants and foveal thickness between normal and high-myopic eyes.

In general, high-hyperopic eyes had significantly thicker average RNFL thickness than emmetropic and high-myopic eyes; while emmetropic eyes had thicker average RNFL thickness than high-myopic eyes.

In our study there was a high correlation between RNFL thickness and AL. This could be explained by the fact that the number of axons which forms the RNFL is equal and not proportional to AL. On the other hand larger AL causes larger surface area and distribution of an equal amount of retinal nerves in larger area, causes a thinner layer.

An important limitation of the OCT is the lack of intersession image registration that allows images to be acquired and analyzed in a standardized manner and the slow scan speed of 1.3 seconds per scans. This may have reduced the accuracy of measurements.¹⁷ Another source of error maybe induced by the inability of the operator to center the scan accurately on the disc or macula.¹⁸ Pending the widespread availability of OCT registration and tracking systems, clinicians will need to be informed of the potentially important effect of scan centration on OCT based measurements.¹⁹⁻²¹ The presence of low anterior chamber (AC) was strongly associated with a higher rate of errors in RNFL thickness and the mean 10 mic difference between scans are within normal range.²⁰⁻²²

Conclusion

In summary, there are regional differences in RNFL thickness when measured with OCT. However, larger AL and more myopic eyes

have a thinner RNFL and macular thickness than shorter AL and more hyperopic eyes. Although the utility of OCT in the diagnosis and clinical management of glaucoma

requires further investigation, our results suggest that AL must be taken into consideration when determining optic nerve and macular disease with this instrument.

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