original article

# Retinal nerve fiber layer thickness in a healthy Turkish population measured by optical coherence tomography

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**BACKGROUND:** Normative optical coherence tomography (OCT) data is required for different subsets of the population as ethnic differences in retinal nerve fiber layer (RNFL) thickness have been reported.An OCT database for the normal Turkish population is not commercially available.
**OBJECTIVES:** Quantify peripapillary RNFL thickness in a Turkish population.
**DESIGN:** Cross-sectional, descriptive study.
**SETTING:** Numune Training and Research Hospital, Adana, Turkey.
**SUBJECTS AND METHODS:** RNFL measurements performed by Spectral OCT with a circular scan with 3.4 mm circle were centered around the optic disc of the right eye of each subject. Correlation of the effects of age and gender on RNFL thickness was analyzed.
**MAIN OUTCOME MEASURE(S):** Correlation and measurements of RNFL. Retinal nerve fiber layer thickness measurements were obtained for the entire circumference of the optic nerve head.
**RESULTS:** In 307 healthy subjects consisting of 135 (44%) males and 172 (56%) females, with a mean (SD) age of 35.1 (9.6) years (range, 20-50 years), RNFL was superior: 132.2 (16.63) µm, inferior: 139.1 (14.53) µm, nasal: 96.2 (14.23) µm, temporal: 79.8 (10.7) µm. The mean (SD) RNFL thickness for the group was 111.5 (9.3) µm. There was no significant difference between the average RNFL thicknesses of age groups nor between males and females ($P$=.1, $P$=.42), and no significant correlation with respect to age ($P$=.430, r=-.04). There was a statistically significant difference between the inferior quadrants of the two genders ($P$=.04).
**CONCLUSIONS:** RNFL thickness did not vary significantly with gender. A weak negative but statistically nonsignificant correlation between average RNFL thickness and age was found.
**LIMITATIONS:** The participants were young adults or at early middle age so age effects on RNFL thickness may not be explained. The data does not reflect the entire Turkish population, which is not homogeneous.

Glaucomatous optic neuropathy is associated with accelerated apoptosis of retinal ganglion cells (RGCs), manifesting as thinning of the retinal nerve fiber layer (RNFL) and increased cupping of the optic nerve head (ONH). The diagnosis of glaucoma is currently based on the appearance of the optic nerve head, RNFL, and standard achromatic perimetry. The deterioration of RNFL thickness is an early sign of glaucoma, and the degree of deterioration indicates the disease progression. It has been shown that 25% to 35% of RGC axons may be lost before any diagnostically characteristic defects appear under perimetry.[1-3] Various instruments have been developed to detect glaucomatous damage before actual functional field loss develops. Optical coherence tomography (OCT) is a non-contact medical imaging technology used to generate in vivo measurements of RNFL thickness. Detailed images of the eye are obtained by reflection of low coherence near infrared light (850 nm). An early version of OCT is time domain OCT, which is relatively slow due to the mechanical process limiting the amount and the quality of images. Spectral domain OCT is 100 times faster than TD-OCT.[4] The increased speed and number of scans translates into higher resolution and images of high quality.

A normal OCT database is required for different subsets of the population, as ethnic differences in RNFL thickness have been reported.[5,6] However, no normal OCT database is commercially available for the Turkish population. Thus, we aimed to study normal individuals to quantify peripapillary RNFL thickness in this population.

## SUBJECTS AND METHODS

This cross-sectional, descriptive study included healthy patients presenting for routine eye check-ups and staff members at the hospital who were able and willing to make the required study visits. The study protocol was approved by the local institutional review board and informed consent was obtained from all subjects. All procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. A complete ocular examination was carried out for each participant that included visual acuity, refractive error, anterior and posterior segment examination, intraocular pressure (IOP) using Goldmann applanation tonometry, gonioscopy, and Humphrey visual fields (SITA Standard 24-2).

Subjects were between 20 and 50 years of age, with refractive error ≤0.50D, IOP×20 mm Hg, a normal ONH, vertical CD ratio ≤ 0.6, without asymmetry >0.2, normal and reliable visual fields, and a good quality OCT scan (signal strength >7). An abnormal visual field was defined as the presence of any one of the following three criteria defined by Anderson:[7] (1) a glaucoma hemifield test outside normal limits, (2) P<5% for corrected pattern standard deviation, or (3) a cluster of at least three contiguous non-edge points with P<5%, including at least one of these with P<5% in the pattern-deviation plot. Patients with a history of diabetes mellitus, cardiac disease, ocular trauma, intraocular surgery, laser therapy, family history of glaucoma, neurological disease affecting the ONH, or best corrected visual acuity of less than 20/40 were excluded from the study. Inclusion and exclusion criterias of the participants were evaluated by ophthalmologists.

All subjects were tested with OCT (Spectral OCT/SLO, Opko/OTI, Inc., Miami, FL) following pupillary dilatation with 1% tropicamide and 5% phenylephrine. A single experienced observer captured images with the patient fixating at the internal fixation target (**Figures 1, 2**).

The MedCalc 12.7 software program (MedCalc, Belgium) was used for the statistical analysis, and data was reported as the mean (standard deviation) (SD). The chi square and Kolmogorov-Smirnov tests were used to compare the categorical measurements between the groups and to show the normal distribution of the quantitative measurements, respectively. The independent-groups *t* test was used for the comparison of the quantitative measurements between two groups, and the analysis of variance (ANOVA) or Kruskal-Wallis test was used to compare the quantitative measurements between three groups. A correlation coefficient was used to analyze the degree of association between two variables (Spearman or Pearson correlation coefficient r, with *P* value and 95% confidence interval CI for r). A log transformation was used for the variables that were not normally distributed. The level of statistical significance was .05 in all tests.

## RESULTS

Of 307 subjects, 135 (44%) were males and 172 (56%) females. The mean age of the subjects was 35.1 (9.6) years (range, 20–50). Subjects were divided by decade for analysis (**Table 1**). No statistically significant difference was found between average RNFL thicknesses of right and left eyes of the patients (111.5 [9.3], 111.4 [9.8], *P*=.97). The right eyes were used for analysis with an average RNFL thickness of 111.5 (9.3) (range: 84-140; 95% CI=110.4-112.5). The average RNFL thicknesses for the three age groups were 111.6 (9.1), 113.1 (9.3), and 110.2 (9.5), respectively. There was no statistically significant difference between the three groups (*P*=.100). The average RNFL thickness had no correlation with age (*P*=.430, r=-.04). Moreover, there was no correlation between age and RNFL thicknesses of the temporal, superior, inferior, or nasal quadrant (**Table 2**).

The maximum RNFL thickness was found in the inferior quadrant (139.1 [14.5] µm) followed by the superior (132.2 [16.6] µm), nasal (96.2 [14.2] µm), and temporal (79.8 [10.7] µm) quadrants. The differences between these four quadrants were statistically significant (*P*=.01) (**Table 3**). The average RNFL thickness was 111 (9.7) µm in men and 111.8 (9.1) µm in women. No significant differences were found in average RNFL thicknesses between the two genders (*P*=.42), however, there was a statistically significant difference between the inferior quadrants of the two genders (*P*=.04).

## DISCUSSION

Optical coherence tomography can provide detailed, high-resolution structural information on the retina and can also be used to assess retinal nerve fiber layer thickness with good reproducibility[8-11] and reliability.[12] Studies have shown that RNFL thickness can vary depending upon racial or ethnic differences.[5,6] The normative profile of various measurements has not been established for

the Turkish population.

This research on a healthy Turkish population revealed that the average RNFL thickness measured by Spectral OCT was 111.5 µm. **Table 4** summarizes other studies reporting average RNFL thicknesses in normal populations from different parts of the world using OCT. The average RNFL thickness in these studies ranged from 100 to 138 µm. In the current study, the RNFL found to be thickest in the inferior quadrant, followed by the superior, nasal, and temporal quadrants.

In keeping with the wide range in the number of axons in the healthy optic nerve, there is large variation in normal RNFL thickness, as well as its topographical distribution, presumably related to genetic or developmental factors.[5] Age-related differences in RNFL thickness have been demonstrated using OCT in several studies.[5,13-16] The current study demonstrated a weak negative correlation between average RNFL thickness and age; when the quadrants were analyzed, our results indicated a negative correlation between RNFL thickness and age in all but the temporal quadrant. However, these results did not reach statistical significance. Several other studies have reported a significant negative correlation.[5,13,14,17-19] The small and statistically insignificant correlation we found between peripapillary RNFL and age may be due to the younger population in our study (mean age, 35; range, 20–50 years). In the studies by Repka and Quigly, Nilforoushan and Ahadi, and Pakravan et al, no significant correlations were observed between age and RNFL thickness.[20-23] In the current study, there was no significant difference in average RNFL thickness between male and female subjects, which is compatible with other reports.[5,13,14,20,24] Wong et al[25] reported significantly thicker RNFL values in men, and suggested that this finding was because of men's higher body mass index. We found a statistically significant difference between the inferior quadrants of the two genders, where the inferior quadrant was thinner in male subjects. This finding may be associated with the lower number of male subjects enrolled in the study.

The main limitation of our study is that the participants were young adults or at early middle age. Therefore, the study might not satisfactorily explain the age effect on RNFL thickness. Glaucoma usually occurs in older population. We aimed to evaluate the mean RNFL of the Turkish population who has no systemic disorders that affects the optic nerve blood supply. As another limitation, the Turkish population is not homogeneous in the current study; whereas we considered the population as having only one ethnicity. The latest study on Turkish genetics revealed that the genetic variation of the contemporary Turkish population is within the context of

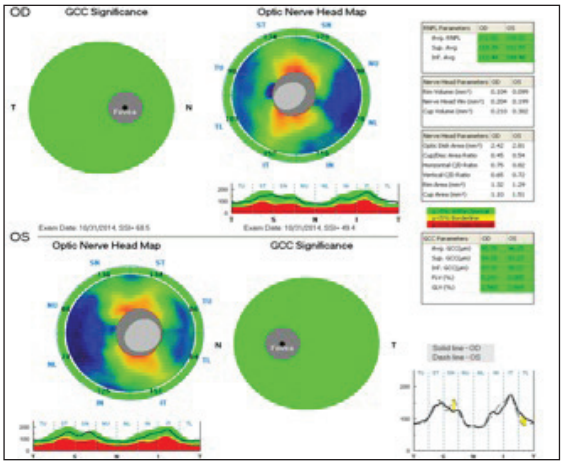


**Figure 1.** Spectral OCT scan of a peripapillary retinal nerve fiber layer of a normal patient.

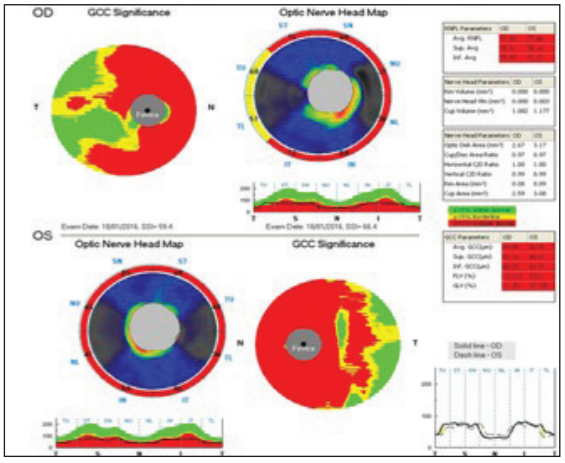


**Figure 2.** Spectral OCT scan of a peripapillary retinal nerve fiber layer of a patient who has advanced glaucoma in both eyes.

**Table 1.** Average RNFL thickness stratified by age category.

| Age category (years) | Number of subjects (%) | | Mean RNFL (µm) |
|---|---|---|---|
| | Female | Male | |
| 20-30 | 61 (35.4) | 43 (31.8) | 111.6 (9.1) |
| 31-40 | 43 (25) | 41 (30.3) | 113.1 (9.3) |
| 41-50 | 68 (39.5) | 51 (37.7) | 110.2 (9.5) |
| **Total** | **172** | **135** | **111.5 (9.3)** |

For the ANOVA, the difference between the average RNFL thickness stratified by age category was not statistically significant (*P*=.100 F-ratio=2.267). For the chi-square, differences between groups were not significant (*P*=.563). (*P*=.100)

RNFL: retinal nerve fiber layer

**Table 2.** Correlations between age and RNFL thickness by quadrant.

| Age (years) (n=307) | 20-30 (104) | 30-40 (84) | 40-50 (119) | *P* | r |
|---|---|---|---|---|---|
| Average | 111.6 | 113.1 | 110.2 | .313 | -.05 |
| Quadrant | | | | | |
| Temporal | 79.4 | 80 | 80.1 | .74 | .01 |
| Superior | 133.2 | 134.6 | 129.6 | .183 | -.07 |
| Nasal | 96.5 | 96.3 | 95.9 | .92 | -.005 |
| Inferior | 139.6 | 141 | 137.4 | .244 | -.06 |

Analysis by Pearson correlation test.

**Table 3.** RNFL thickness variations by gender.

| | All eyes (n=307) | Male (n=135) | Female (172) | *P* (2-tailed) |
|---|---|---|---|---|
| Mean | 111.5 (9.3) | 111 (9.7) | 111.8 (9.1) | .42 |
| Quadrants | | | | |
| Superior | 132.2 (16.6) | 131.2 (18.1) | 132.9 (15.2) | .36 |
| Nasal | 96.2 (14.2) | 97.4 (14.4) | 95.3 (14.1) | .18 |
| Inferior | 139.1 (14.5) | 137.3 (14.7) | 140.6 (14.2) | .04 |
| Temporal | 79.8 (10.7) | 79.3 (10.4) | 80.2 (11) | .43 |

Analysis by *t* test. For the mean, *t* statistic=-0.794, degree of freedom=305; Superior: *t* statistic=-0.899, degree of freedom=305; Nasal: *t* statistic=1.314, degree of freedom=305; Inferior: *t* statistic=-2.000, degree of freedom=305; Temporal: *t* statistic=-0.787, degree of freedom=305.

the Southern European/Mediterranean gene pool.[26] Indeed, the data from one center does not reflect the whole Turkish population.

In conclusion, the commercially available OCT databases do not provide information on ethnic difference within data groups. We have obtained estimated normal RNFL measurements in a Turkish population using Spectral OCT. These measurements may serve as a reference during screening for glaucoma with OCT in the Turkish population. To our knowledge this is the first study on normative data for the RNFL thicknesses of Turkish population. Additional normative data may need to be collected by multicentered studies evaluating RNFL thickness and macular ganglion cell complex which includes more subjects of Turkish population at a wider range of age and higher degrees of refractive error.

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**Table 4.** Comparison of mean RNFL thickness in normal subjects.

| Study | Number of eyes | Type of OCT | Mean (SD) RNFL thickness (μm) | Year of study | Country |
|---|---|---|---|---|---|
| Gramer et al[18] | 104 | Not mentioned | 107 (26) | 1998 | USA |
| Mok et al[19] | 129 | OCT2000 | 120 (28) | 2002 | Hong Kong |
| Kanamori et al[27] | 144 | OCT2000 | 123 (11.6) | 2003 | Japan |
| Varma et al[14] | 312 | OCT2000 | 132.7 (14.4) | 2003 | USA |
| Nilforoushan et al[20] | 45 | OCT II | 138 (17) | 2004 | Iran |
| Sony et al[28] | 146 | Stratus OCT | 104.3 (8.5) | 2004 | India |
| Leung et al[29] | 107 | OCT II | 105 (11) | 2004 | China |
| Yamada et al[30] | 100 | Stratus OCT | 108 (13.5) | 2006 | Japan |
| Ramakrishran et al[31] | 118 | Stratus OCT | 104.8 (38.8) | 2006 | India |
| Parikh et al[15] | 187 | Stratus OCT | 97.3 (11.3) | 2007 | India |
| Budenz et al[11]<br>Pakravan et al[22] | 328<br>96 | Stratus OCT<br>OCT II | 101.1 (11.6)<br>144.1 (33.3) | 2007<br>2009 | USA<br>Iran |
| Kanno et al[32]<br>Zeried et al[23] | 460<br>29 | EG-SCANNER<br>Stratus OCT | 111.8 (10)<br>101 | 2010<br>2013 | Japan<br>Saudi Arabia |

RNFL: retinal nerve fiber layer; OCT: optical coherence tomography.

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