Optical Tomography–Measured Retinal Nerve Fiber Layer Thickness in Normal Latinos

Robit Varma,1,2 Sheila Bazzaz,1 and Mei Lai2

PURPOSE. To measure retinal nerve fiber layer (RNFL) thickness in normal Latinos using optical coherence tomography (OCT).

METHODS. Three hundred twelve Latino participants, aged 40 years or more, underwent a detailed ophthalmic examination, including measurement of visual acuity, intraocular pressure, visual field perimetry, and stereoscopic optic disc photography. None of the participants had any evidence of ocular hypertension, glaucoma, or other ocular disease. Nine scans were performed on one eye of each participant by optical coherence tomography (OCT Model 2000; Carl Zeiss Meditec, Dublin, CA, software version A 6.1): three circumferential peripapillary scans and six radial scans of the macula. The average RNFL thicknesses in the peripapillary region and macula were measured. A paired t-test and linear regression analyses were used to analyze the data.

RESULTS. The mean age of the participants was 52 years (range, 40–79 years). The average peripapillary RNFL thickness 1.74 mm from the center of the disc was 132.7 ± 14.4 μm, and the average macular RNFL thickness was 44.8 ± 14.8 μm. The average macular retinal thickness was 173 ± 28.5 μm. The average peripapillary RNFL thickness in the four quadrants was as follows: superior 157.7 ± 17.8 μm, nasal 109.3 ± 19.1 μm, inferior 159.8 ± 18.9 μm, and temporal 102.5 ± 19.0 μm. There were no gender-related differences in macular or peripapillary RNFL thickness (P = 0.12 and P = 0.35, respectively). The average macular and peripapillary RNFL thickness was thinner in older Latinos than in younger Latinos (P = 0.04 and P = 0.0001, respectively).

CONCLUSIONS. Regional and age-related differences in the peripapillary and macular RNFL thickness should be considered when diagnosing and monitoring individuals with diseases that affect the RNFL. (Invest Ophthalmol Vis Sci. 2003;44:3369–3373) DOI:10.1167/iovs.02-0975

Optical coherence tomography (OCT) is a relatively new, noncontact imaging technique that has been developed to assess tissue thickness, such as that of the retinal nerve fiber layer (RNFL). The fundamentals of image acquisition and their interpretation have been described.1–5 Briefly, with OCT, a scanning interferometer is used to obtain a cross section of the retina based on the reflectivity of different layers within the retina. OCT has been shown to detect changes in tissue thickness with micrometer scale sensitivity.1,2 OCT has been applied to a multitude of ophthalmologic diseases, including epiretinal membranes,3 age-related macular degeneration,3 diabetic macular edema,4 and central serous chorioretinopathy.5 Direct cross-sectional imaging of the retina with OCT offers the potential for early diagnosis and more sensitive monitoring of various optic nerve and retinal diseases, such as glaucoma, macular degeneration, and macular edema.

In the past, evaluation of the RNFL has depended on good-quality photographs, which require clear media, a dilated pupil, a darkly pigmented fundus, a trained photographer, and most important, an experienced observer. Evaluation of RNFL photographs is subjective, and diffuse RNFL loss may be difficult to assess. Advancement in OCT technology has provided an objective and quantitative method to evaluate RNFL thickness. Previous studies have demonstrated a good correlation between histopathologic and OCT measurements of RNFL thickness.6 The OCT has been shown to localize focal RNFL defects accurately.8,9 In addition, the reproducibility10–13 and intersession repeatability14 of RNFL thickness measurements obtained with OCT have been established. The purpose of this study was to use OCT to measure RNFL thickness in various parts of the retina in Latinos with no evidence of retinal or optic nerve disease. In addition, we sought to evaluate differences in RNFL thickness related to age and gender.

METHODS

Three hundred twelve consecutive healthy Latino participants were included. Informed consent was obtained from all participants. The study protocol was approved by the Institutional Review Board at the University of Southern California and followed the recommendations of the Declaration of Helsinki.

Each participant received a detailed ophthalmologic examination, automated perimetry using the Swedish interactive test algorithm (SITA) standard test and/or the 24-2 full threshold test (Carl Zeiss Meditec, Dublin, CA, and simultaneous stereoscopic optic disc photography. The ophthalmologic examination included visual acuity measurement, slit lamp biomicroscopy, applanation tonometry, and dilated direct and indirect fundus examination. Participants were considered to have no evidence of retinal or optic nerve disease if they had no history of ocular disease or surgery, had a reliable SITA standard test or 24-2 full-threshold test with no visual field defect (the pattern standard deviation and the glaucoma hemifield test results were within normal limits), had intraocular pressures less than 21 mm Hg, and had no evidence of any optic nerve or retinal disease based on binocular direct and indirect fundus examination. A normal optic disc included cup-to-disc asymmetry of less than 0.2, a neural rim without generalized or localized thinning, and absence of retinal nerve fiber layer defects, disc hemorrhages, or optic disc pallor. One eye of each subject was selected for study.

OCT is an imaging technique that generates cross-sectional images of ocular microanatomy. Low-coherence light (820 nm wavelength) from a superluminescent diode is projected onto a beam splitter, creating two beams: one directed at the retina and one acting as a reference beam. The amplitude and delay of tissue reflection is determined by an interferometer that combines the electromagnetic beam of the two reflected light beams. The instrument has a tissue resolution

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of 10 to 20 μm. In the OCT model 2000 (Carl Zeiss Meditech, Dublin, CA, software version A 6.1), the retina is differentiated from other layers with an algorithm detecting the edge of the retinal pigment epithelium and the photoreceptor layer. Macular retinal thickness is calculated by obtaining the difference between the first signal from the vitreoretinal interface and the signal from the anterior boundary of the retinal pigment epithelium. The nerve fiber layer thickness is calculated as a multiple of the number of pixels between the anterior and posterior edges of the RNFL. The analysis yields a single mean RNFL thickness at the macular or peripapillary retina.

For macular measurements, the OCT generates six linear scans 30° apart, centered on the fovea, consisting of 100 A-scans each. Each scan acquisition time is 1 second. Each linear scan is 5.93 mm in length. The scan length is corrected for magnification based on the refractive error of the eye. The retinal nerve fiber thickness measured over the six linear scans (600 A-scans) is then averaged to provide an average for the macular RNFL thickness. Similarly, the retinal thickness over the six linear scans is averaged to provide the average macular retinal thickness. In the circular peripapillary scan around the optic nerve head circumference, the OCT generates 100 A-scans along a 360° circular path. 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 is divided into four

### Table 1. Demographic/Clinical Characteristics of the Study Group

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>312 (100)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>171 (55)</td>
<td></td>
</tr>
<tr>
<td>Age (Years)</td>
<td></td>
<td>51.9 ± 9.8</td>
</tr>
<tr>
<td>40–49</td>
<td>159 (51)</td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>86 (27)</td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>46 (15)</td>
<td></td>
</tr>
<tr>
<td>70+</td>
<td>21 (7)</td>
<td></td>
</tr>
<tr>
<td>IOP (mm Hg)</td>
<td></td>
<td>14.6 ± 2.76</td>
</tr>
<tr>
<td>Sph. Equiv. (D)</td>
<td></td>
<td>+0.35 ± 1.52</td>
</tr>
<tr>
<td>MD (dB)</td>
<td></td>
<td>−1.31 ± 4.7</td>
</tr>
</tbody>
</table>

IOP, intraocular pressure; Sph. Equiv., spherical equivalent; MD, mean deviation; dB, decibels; D, diopters.
DISCUSSION

Recent advances in technology have made it possible to measure the RNFL thickness in an objective, quantifiable, and reproducible fashion.\textsuperscript{2,10–14} OCT evaluates the reflectance of retinal tissue and provides a cross-sectional view of the retina. The RNFL is most accurately measured using OCT because it provides a detailed visualization of the retinal layers and allows for precise determination of the RNFL thickness. OCT has become a valuable tool in the assessment of glaucoma and other retinal disorders due to its ability to provide objective, non-invasive measurements of RNFL thickness.

The data in Table 2 demonstrate that there are differences in RNFL thickness across different age groups, with younger individuals having thicker RNFL than older individuals. This finding is consistent with previous studies and supports the theory that RNFL thickness decreases with age.

The intraobserver and interimage CoV for RNFL thickness measurements were both found to be low, indicating high reproducibility of the measurements. This suggests that OCT can provide reliable and consistent measurements of RNFL thickness, making it a valuable tool in the diagnosis and monitoring of glaucoma.

In conclusion, OCT is a useful tool for assessing RNFL thickness in normal eyes. The results of this study support the use of OCT in the diagnosis and monitoring of glaucoma and other retinal disorders. Further research is needed to investigate the relationship between RNFL thickness and disease progression, as well as the impact of other factors such as age and sex on RNFL thickness.
demonstrate that the superior, inferior, and nasal quadrant RNFL at the disc margin are significantly thicker than the temporal quadrant RNFL at the disc margin.\(^\text{18}\)

In the present study, there was no statistically significant difference in RNFL thickness (except in the inferior quadrant) between men and women at the macula, peripapillary circumference, and superior, temporal and nasal quadrants. Previously, Schuman et al.\(^\text{14}\) and Bowd et al.\(^\text{15}\) also found no significant gender-related differences in any RNFL parameters. Thus, our results agree with previous reports that have shown no significant gender-related differences in the optic disc and RNFL thickness.\(^\text{19,20}\)

Our study found a significant difference in the peripapillary RNFL thickness in the four quadrants and in the macula between older and younger Latinos. These age-related differences in RNFL thickness have been demonstrated previously, although in fewer participants. Using OCT in 35 subjects, Schuman et al.\(^\text{14}\) found that older individuals had thinner RNFL than younger individuals \((P = 0.03)\). However, the same study reported no age-related difference in the cup-to-disc ratio and neural rim area. These results are similar to our findings in this and previous studies.\(^\text{19}\) Histologic data regarding age-related differences in the number of optic nerve fibers are conflicting. In a histologic study of 19 eyes, Repka and Quigley\(^\text{21}\) found no statistically significant difference in the number of nerve fibers between younger and older individuals. On the other hand, histologic studies by Balazsi et al.\(^\text{22}\) (studying 16 eyes) and Johnson et al.\(^\text{23}\) (studying 13 eyes) have reported fewer axons in older individuals compared with younger individuals.

The present study is one of the largest to evaluate normal differences in RNFL thickness. We ensured that no participant had any ocular disease with a thorough ophthalmic examination. In addition, we reduced data collection variability by collecting data in a standardized manner, with only one technician performing all the scans on one instrument.

### Table 3. Comparison of OCT-Measured RNFL Thickness in Normal Eyes

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age Range (y)</th>
<th>Peripapillary Scan Diameter (mm)</th>
<th>Software Version</th>
<th>Peripapillary RNFL Thickness ((\mu m))</th>
<th>Temporal</th>
<th>Superior</th>
<th>Nasal</th>
<th>Inferior</th>
<th>Macular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schuman et al.(^\text{14})</td>
<td>11</td>
<td>23–33</td>
<td>3.4</td>
<td>NP</td>
<td>153</td>
<td>126</td>
<td>179</td>
<td>131</td>
<td>175</td>
<td>NP</td>
</tr>
<tr>
<td>Jones et al.(^\text{12})</td>
<td>15</td>
<td>20–53</td>
<td>3.4</td>
<td>A5.0</td>
<td>127.9</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
</tr>
<tr>
<td>Schuman et al.(^\text{14})</td>
<td>8</td>
<td>49–71</td>
<td>3.37</td>
<td>NP</td>
<td>110.7</td>
<td>91.5</td>
<td>133.5</td>
<td>89.2</td>
<td>128.7</td>
<td>NP</td>
</tr>
<tr>
<td>Bowd et al.(^\text{15})</td>
<td>30</td>
<td>53–73</td>
<td>3.4</td>
<td>A4X1</td>
<td>85.8</td>
<td>66.2</td>
<td>105.7</td>
<td>61.8</td>
<td>107.6</td>
<td>NP</td>
</tr>
<tr>
<td>Liu et al.(^\text{17})</td>
<td>150</td>
<td>10–69</td>
<td>3.4</td>
<td>A4</td>
<td>114.1</td>
<td>90.1</td>
<td>140.3</td>
<td>85.0</td>
<td>140.3</td>
<td>NP</td>
</tr>
<tr>
<td>Hoh et al.(^\text{16})</td>
<td>17</td>
<td>27–72</td>
<td>3.4</td>
<td>A4.1</td>
<td>90.8</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
</tr>
<tr>
<td>Varma et al.(^\text{18})</td>
<td>512</td>
<td>40–79</td>
<td>3.4</td>
<td>A6.1</td>
<td>132.7</td>
<td>102.5</td>
<td>157.7</td>
<td>109.3</td>
<td>159.8</td>
<td>44.8</td>
</tr>
</tbody>
</table>

The race/ethnicity of many of the participants in these studies is not published. In the current study all participants were Latino. NP, Not published.
Although this study was performed in Latinos, we believe that the general patterns of regional and age- and gender-related differences in RNFL thickness are generalizable to all racial and ethnic groups. However, caution should be exercised when generalizing the absolute measurements of RNFL thickness to other ethnic groups. Several studies have shown racial-ethnic differences in the absolute magnitude of optic disc parameters. Although absolute measurements of the RNFL thickness may be different across racial or ethnic groups, it is likely that the variation in the thickness of the normal RNFL overlaps among the different groups because of the large interindividual variation within each racial/ethnic group. Therefore, although it is important to establish average racial and ethnic subgroup norms, the value of these norms in distinguishing between normal and abnormal eyes may be limited.

An important limitation of the optical coherence tomodiagnosis is the lack of intersession image registration that would allow images to be acquired and analyzed in a standardized manner. Currently, the operator asks the patient to focus on an internal fixation light to stabilize the eye during image acquisition. However, some saccadic movement of the eye may still occur. A solution to this problem would be the use of an eye-tracking system during image acquisition. Although such a system usually adjusts for horizontal and vertical movements, a torsional shift in the eye due to either positioning of the head or to torsional movements of the eye can be adjusted during image acquisition and analysis by locating landmarks on the fundus to register images from multiple sessions. Furthermore, another source of error may be induced by the inability of the operator to center the scan accurately on the disc or the macula. Again, the use of landmarks to center the images would help decrease this source of error. In our study, we used trained operators who had extensive experience with OCT. However, given the limitations of the current hardware and software, we were unable to decrease further the variability in the RNFL measurement. Finally, despite the lack of these possible refinements, the CoV in our measurements was acceptably low (3.8%–10.6%).

In summary, there are regional differences in RNFL thickness when measured with OCT. Also, older individuals have a thinner RNFL than younger individuals. Although the utility of OCT in the diagnosis and clinical management of glaucoma requires further investigation, our results suggest that the regional and age-related differences in RNFL thickness must be taken into consideration when determining optic nerve and macular disease with this instrument.

References