

Effect of age and sex on retinal layer thickness and volume in normal eyes

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Abstract

The aim of the study was to evaluate the effect of sex and age on the thickness of the retinal layer in normal eyes using spectral-domain optical coherence tomography (SD-OCT).

Fifty healthy subjects between the ages of 20 and 80 had their retinal layers measured using SD-OCT at Seoul St. Mary's Hospital. Mean thickness and volume were measured for 9 retinal layers in the fovea, the pericentral ring, and the peripheral ring. The differences of sex- and age-related thickness and volume in each retinal layer were analyzed.

The retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), and outer plexiform layer (OPL) were thinnest in the fovea area, whereas the outer nuclear layer (ONL), photoreceptor layer (PHL), and retinal pigment epithelium (RPE) were thickest at similar locations. Mean thickness of the RNFL, GCL, IPL, and OPL was significantly greater in men than women. However, mean thickness of the ONL was greater in women than in men. When compared between patients < 30 years and > 60 years of age, the thickness and volume of peripheral RNFL, GCL, and pericentral and peripheral IPL were significantly larger in the younger group than the older group. Conversely, the thickness and volume of foveal INL and IR were larger in the older group than in the younger group.

The thickness and volume of the retinal layer in normal eyes significantly vary depending on age and sex. These results should be considered when evaluating layer analysis in retinal disease.

Abbreviations: BCVA = best-corrected visual acuity, ETDRS = Early Treatment Diabetic Retinopathy Study, GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner plexiform layer, IR = inner retina, ONL = outer nuclear layer, OPL = outer plexiform layer, PHL = photoreceptor layer, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium, SD-OCT = spectral-domain optical coherence tomography.

Keywords: age, retinal layer thickness, retinal layer volume, sex, spectral-domain optical coherence tomography

1. Introduction

The analysis of individual retinal layers is important to diagnose retinal disease and verify therapeutic response. Several previous studies have demonstrated the thickness of retinal layers in normal eyes and revealed regional differences in macular thickness according to age, sex, and axial length changes.^[1–3] Optical coherence tomography (OCT) software development has enabled automatic segmentation of the retinal layers. Ooto et al^[4] have demonstrated changes in individual retinal layer thickness according to age in the eyes of a Japanese population by an automated layer segmentation algorithm. Because specific layers among the retina are affected in some retinal diseases, examining

the involved layers by OCT imaging allows clinicians to confirm improvement or progression of retinal disease. For example, previous studies using ultra-high resolution OCT showed that the severity of photoreceptor loss is associated with visual loss in retinitis pigmentosa.^[5,6] Other studies using spectral-domain (SD) OCT showed that the thickness of the outer nuclear layer in the fovea is associated with visual acuity in retinal diseases such as central serous chorioretinopathy, polypoidal choroidal vasculopathy, and epiretinal membrane.^[7–11]

Most recently, updated software for SD-OCT was introduced with a new transverse section analysis for positioning and quantifying retinal diseases with automated measurement of macular thickness, in addition to automated segmentation of the retina into individual layers. The retina could not be segmented into the 9 retinal layers in previous studies. Thus, this study is the first to report automated retinal segmentation, and measure the thickness and volume of 9 macular individual layers using the OCT program, especially distinguishing between the outer plexiform layer and outer nuclear layer. The purpose of this study is to evaluate sex-related differences and age-related changes in thickness and volume of the 9 individual retinal layers in the normal eye, using SD-OCT with HEYEX 6.0C software (Heidelberg Engineering, Heidelberg, Germany).

2. Methods

2.1. Subjects

The medical charts of 50 healthy Korean subjects enrolled at Seoul St. Mary's Hospital between January 2014 and October 2015 were reviewed. This study was conducted according to the

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guidelines of the Association for Research in Vision and Ophthalmology. It adheres to the tenets of the Declaration of Helsinki and all protocols were approved by the Institutional Review Board of the Catholic University of Korea. Ophthalmologically healthy Korean subjects between the ages of 20 and 80 were recruited for this study. Exclusion criteria included any ocular disease or systemic disease including diabetes, hypertension, autoimmune, multiple sclerosis, rheumatoid arthritis or infectious diseases, such as HIV. Initial ocular examinations included best-corrected visual acuity (BCVA), slit-lamp examination, intraocular pressure measurement, auto refractometry, keratometry, and funduscopy to rule out any glaucoma or retinal diseases.

Exclusion criteria included BCVA worse than 20/25, refractive error over +5.0 or over -6.0 diopters, intraocular pressure >21 mm Hg, abnormal fundus findings, significant media opacities, history of intraocular surgery, findings of vitreo-retinal disease, and systemic disease, including diabetes mellitus, that could affect the eye. All subjects received an eye drop consisting of 0.5% tropicamide combined with 0.5% phenylephrine (Mydrin-P, Santen, Osaka, Japan) for pupil dilation. SD-OCT images were obtained using a commercially available OCT instrument (SPECTRALIS, Heidelberg Engineering, Germany) operated by a single experienced examiner.

2.2. SD-OCT measurements

OCT images then underwent automated segmentation of individual retinal layers: retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), inner retina (IR, from internal limiting membrane to external limiting membrane), photoreceptor layer (PHL), and retinal pigment epithelium (RPE)^[12] (Fig. 1). In this study, 3 retinal areas were demonstrated according to this Early Treatment Diabetic Retinopathy Study (ETDRS) grid: the fovea, the central circle with a diameter of 1 mm; the pericentral ring, 1 to 3 mm from the center of the fovea; and the peripheral ring, 3 to 6 mm from the center of the fovea (Fig. 2). Automated measurement of their mean macular

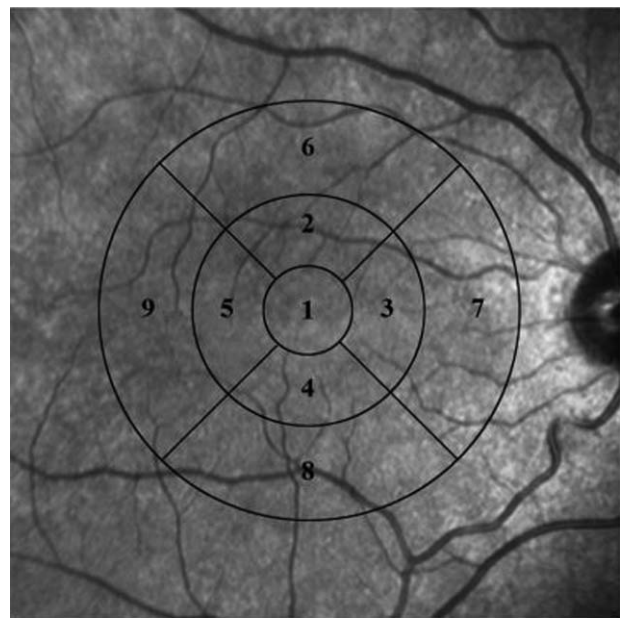


Figure 2. The 9 Early Treatment Diabetic Retinopathy Study (ETDRS) regions in OCT. Fovea (region 1 of the 9 Early Treatment Diabetic Retinopathy Study [ETDRS] regions); in the pericentral ring (ETDRS regions 2 to 5); and the peripheral ring (ETDRS regions 6 to 9). ETDRS = Early Treatment Diabetic Retinopathy Study.

thickness and volume was done in 9 separate areas based on ETDRS sectors. The mean macular thickness and volume of each retinal layer was measured at the fovea and 4 sectors (superior, inferior, nasal, and temporal) of the pericentral and peripheral rings. The mean thicknesses of the pericentral and peripheral rings were measured by averaging the thickness measurements of the 4 corresponding quadrant areas (segments 2 to 5 for the pericentral ring and segments 6 to 9 for the peripheral ring). Total macular thickness of all areas within the ETDRS grid was automatically calculated by summation of the 9 sectors.

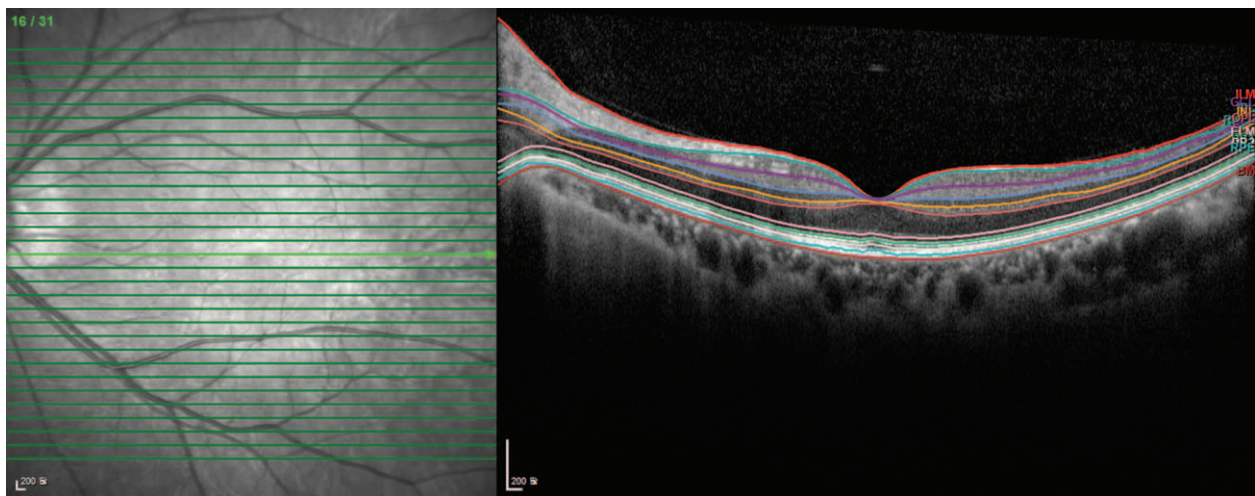


Figure 1. Normal retinal segmentation in SD-OCT. Nine retinal layers were identified by automatic segmentation: retinal nerve fiber layer (layer 1), ganglion cell layer (layer 2), inner plexiform layer (layer 3), inner nuclear layer (layer 4), outer plexiform layer (layer 5), outer nuclear layer (layer 6), inner retina layer (from internal limiting membrane to external limiting membrane) (layer 7), photoreceptor layer (layer 8), and retinal pigment epithelium (layer 9). SD-OCT = spectral-domain optical coherence tomography.

Table 1
Demographics and ocular features of subjects.

Characteristic	Mean ± SD
OD:OS, N	25:25
Men:women, N	24:26
Age, y	48.64 ± 14.9
Mean refractive error, dioptres	-2.17 ± 3.18
IOP, mm Hg	14.3 ± 3.0
BCVA, log MAR	0.0 ± 0.11

BCVA = best-corrected visual acuity, IOP = intraocular pressure, SD = standard deviation.

2.3. Statistical analysis

Statistical data were analyzed with a statistical software program (IBM SPSS 21; SPSS Inc. Chicago, IL). A *P*-value <0.05 was considered statistically significant.

An independent sample *t*-test was used for comparing macular layer thickness between the younger age group (<30 years) and the older age group (>60 years). For analyzing sex-associated differences and comparing retinal thicknesses among the sectors, an independent sample *t*-test was used.

3. Results

Demographic features of the subjects are shown in Table 1.

Mean thickness of the individual retinal layers in the 9 ETDRS sectors is shown in Table 2.

As shown in Table 2, the RNFL, GCL, IPL, INL, and OPL were thinnest in the foveal area, whereas the ONL, PHO, and RPE were thickest. In the pericentral and peripheral rings, the RNFL and GCL were thicker in the nasal quadrants than in the temporal quadrants. The RNFL was thickest in the peripheral retinal area, especially from nasal to the fovea and near the optic nerve head. The GCL was thickest in the pericentral area. The IPL was thicker in the pericentral ring than the peripheral ring, with a relatively similar thickness in the 4 pericentral sectors. The INL and OPL were thicker in the pericentral ring than the peripheral ring. The ONL was thickest in the central fovea area and decreased in peripheral retinal areas. The thicknesses of the PHL and RPE were increased in the central fovea area compared to the other sectors.

Mean thickness of the RNFL, GCL, IPL, IR in all ETDRS sectors, INL and OPL in the fovea, and OPL in the pericentral ring was significantly greater in men than in women, whereas mean thickness of the ONL was greater in women (Table 3). This

finding is quite different from the previous study by Ooto et al.^[14] They reported that the mean RNFL thickness was significantly greater in women than in men, especially at the peripheral macula.

When macular thickness was compared between <30 years and > 60 years of age, peripheral RNFL, peripheral GCL, and pericentral and peripheral IPL were significantly thicker in the younger age group than the older age group. On the other hand, fovea INL and fovea IR were thicker in the older age group than in the younger group (Table 4).

With regard to macular volume, peripheral RNFL and peripheral IPL were significantly greater in the younger age group than in the older age group. Conversely, peripheral GCL, fovea INL, and fovea IR were greater in the older age group than in the younger age group (Table 5).

4. Discussion

To date, there have been several previous studies about automated segmentation of individual retinal layers and measurement of macular thickness in the normal population. The automated retinal segmentation algorithm adopted by SD-OCT (SPECTRALIS, Heidelberg Engineering, Germany) has been used on mice.^[13] However, to our knowledge, this study is the first report to differentiate the OPL and ONL layers automatically by the OCT program itself, and carry out segmentation with thickness and volume into 9 retinal layers in human. In several previous studies, the thicknesses of the RNFL, GCL, IPL, and INL were so thin that they could not be reliably measured,^[14] and the segmentation of the macular layer into 6 or 7 retinal layers (OPL+ONL as 1 or lack of an RPE layer), rather than 9 individual layers, was performed.^[4]

The OCT-based mean thickness data of individual retinal layers in our study is similar to other previous reported SD-OCT studies, except for some differences that can be attributed to variances in the population of study, kind of OCT devices, and the differences in segmentation algorithms in detecting the posterior retinal boundary.^[15-17]

Several previous studies showed that total retinal thickness in the nasal quadrant is greater than in the temporal quadrant and is greater in the pericentral ring than the peripheral ring.^[15-25]

These results were also similar in our study. However, on closer examination, the GCL and INL were thinner in the temporal sector than in the nasal sector within the pericentral ring, but this difference was smaller within the peripheral ring. We also found that there may be a correlation between INL and

Table 2
Mean layer thickness measurements (μm) of the individual retinal layers of subjects in the 9 ETDRS sectors.

Retinal layer	Fovea	Pericentral ring				Peripheral ring			
		Superior	Temporal	Inferior	Nasal	Superior	Temporal	Inferior	Nasal
RNFL	11.5 ± 2.5	24.5 ± 2.5	17.4 ± 1.3	25.6 ± 2.6	20.6 ± 0.8	38.9 ± 4.9	20.2 ± 4.5	41.6 ± 6.9	46.4 ± 7.0
GCL	12.6 ± 3.2	52.1 ± 4.8	46.3 ± 5.6	51.7 ± 4.6	50.8 ± 4.8	36.2 ± 3.6	37.3 ± 5.3	33.2 ± 3.3	39.9 ± 3.1
IPL	19.2 ± 3.1	41.0 ± 2.9	40.1 ± 3.0	40.1 ± 2.8	42.1 ± 3.4	29.3 ± 2.6	33.5 ± 3.1	26.8 ± 2.4	30.8 ± 2.4
INL	16.4 ± 4.4	40.4 ± 3.2	37.8 ± 3.2	39.9 ± 3.1	39.6 ± 3.6	32.7 ± 2.5	34.1 ± 2.5	31.2 ± 2.7	34.7 ± 2.5
OPL	23.7 ± 7.9	38.0 ± 4.7	31.4 ± 4.7	34.3 ± 11.0	34.1 ± 7.3	28.2 ± 3.8	27.4 ± 2.1	26.9 ± 3.1	29.7 ± 3.0
ONL	96.1 ± 11.5	66.6 ± 14.0	74.3 ± 9.3	66.8 ± 12.8	73.7 ± 12.2	59.4 ± 7.2	59.0 ± 6.2	52.3 ± 6.5	58.6 ± 7.9
PHL	90.3 ± 4.8	82.9 ± 3.1	83.1 ± 2.9	80.9 ± 3.1	83.6 ± 3.0	79.7 ± 2.9	79.0 ± 3.0	77.6 ± 3.1	79.5 ± 2.6
RPE	16.8 ± 1.8	15.4 ± 2.0	14.6 ± 1.4	14.4 ± 1.9	15.2 ± 1.8	13.3 ± 1.7	12.9 ± 1.4	12.8 ± 1.6	13.4 ± 1.5
Total	268.6 ± 19.1	345.5 ± 12.6	330.3 ± 11.3	339.4 ± 0.9	344.4 ± 12.4	304.5 ± 12.0	290.8 ± 14.4	289.7 ± 12.6	319.4 ± 12.4

ETDRS = Early Treatment Diabetic Retinopathy Study, GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner plexiform layer, ONL = outer nuclear layer, OPL = outer plexiform layer, PHL = Photoreceptor layer, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium.

Table 3
Differences in mean macular layer thickness based on sex.

Macular layer	Male (n=24)	Female (n=26)	P*	Macular layer	Male (n=24)	Female (n=26)	P*
RNFL				OPL			
Fovea	13.2±2.0	10.0±2.0	0.000*	Fovea	26.6±8.3	21.3±6.8	0.028*
Pericentral ring	22.5±1.6	21.6±1.3	0.038*	Pericentral ring	36.9±5.5	32.5±4.9	0.01*
Peripheral ring	38.5±2.6	35.3±4.6	0.010*	Peripheral ring	28.4±2.3	27.8±1.9	0.351
GCL				ONL			
Fovea	14.8±2.1	10.8±2.9	0.000*	Fovea	96.7±12.9	95.7±10.4	0.765
Pericentral ring	53.3±2.9	47.7±4.1	0.000*	Pericentral ring	66.7±9.0	73.3±9.2	0.024*
Peripheral ring	38.5±3.2	35.2±3.0	0.001*	Peripheral ring	55.2±6.9	59.1±5.2	0.045*
IPL				PHL			
Fovea	21.1±2.8	17.7±2.5	0.000*	Fovea	90.7±3.8	89.9±5.5	0.608
Pericentral ring	42.4±1.9	39.5±2.5	0.000*	Pericentral ring	82.3±3.4	82.9±2.1	0.452
Peripheral ring	31.4±2.1	29.0±2.0	0.001*	Peripheral ring	78.3±3.2	79.5±2.2	0.148
INL				RPE			
Fovea	18.1±3.4	15.0±4.6	0.020*	Fovea	17.3±1.7	16.5±1.8	0.157
Pericentral ring	39.5±2.8	39.3±2.5	0.581	Pericentral ring	14.7±1.9	15.1±1.3	0.106
Peripheral ring	32.9±2.4	33.4±1.9	0.437	Peripheral ring	13.0±1.5	13.2±1.4	0.728
IR							
Fovea	190.3±15.2	168.6±15.3	0.000*				
Pericentral ring	261.2±10.5	254.1±9.2	0.023*				
Peripheral ring	224.9±11.5	219.7±9.6	0.124				

GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner plexiform layer, IR = inner retina, ONL = outer nuclear layer, OPL = outer plexiform layer, PHL = Photoreceptor layer, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium.
Unpaired t-test (*; significantly different, P<0.05).

GCL as the maximum thickness of INL and GCL both occurred in the same quadrant areas. Thus, we can assume that the densities of bipolar cells, amacrine cells, horizontal cells, and Muller cells are likely high in these areas.

In our study, mean macular thickness of the RNFL, GCL, IPL, and INL were thinnest in the central fovea area, as expected with normal anatomy. The RNFL thickness was highest in the peripheral retinal area near the optic nerve head, because of the high density of local nerve fiber bundles. Our study also presented

that the GCL thickness correlates with peripapillary RNFL thickness, as in other studies.^[26–28] The ONL and PHL displayed a maximum thickness in the central fovea area as expected in normal anatomy, partially because of the elongation of cone photoreceptors at the fovea.

Previous studies have shown sex-related differences in total macular thickness or in thicknesses of some sectors.^[2,19,20,29] In earlier work, the mean total retinal thickness at the central fovea was significantly greater in men than in women, and mean retinal

Table 4
Differences in mean macular layer thickness based on age.

Macular layer	<30 y	>60 y	P*	Macular layer	<30 y	>60 y	P*
RNFL				OPL			
Fovea	12.1±1.1	12.4±3.0	0.452	Fovea	25.0±5.0	27.8±9.1	0.346
Pericentral ring	22.2±1.6	22.1±1.4	0.922	Pericentral ring	34.7±5.5	35.7±4.9	0.649
Peripheral ring	39.0±3.4	35.2±2.8	0.007*	Peripheral ring	27.4±3.2	28.5±1.6	0.161
GCL				ONL			
Fovea	13.5±2.5	13.6±3.4	0.054	Fovea	91.2±11.8	97.2±11.0	0.218
Pericentral ring	51.8±3.4	50.0±2.6	0.172	Pericentral ring	68.7±8.7	68.4±10.8	0.951
Peripheral ring	37.7±3.6	35.0±2.1	0.037*	Peripheral ring	56.4±6.1	56.1±5.2	0.902
IPL				PHL			
Fovea	19.4±2.7	20.6±3.0	0.330	Fovea	91.8±5.0	89.8±5.2	0.357
Pericentral ring	42.1±2.3	40.8±1.5	0.006*	Pericentral ring	81.9±2.9	82.4±2.6	0.690
Peripheral ring	30.4±2.8	29.5±1.3	0.026*	Peripheral ring	77.8±3.1	78.8±2.7	0.443
INL				RPE			
Fovea	15.5±3.5	19.6±4.5	0.023*	Fovea	17.5±1.8	16.6±2.1	0.228
Pericentral ring	38.7±2.9	40.1±2.7	0.248	Pericentral ring	14.1±1.2	14.9±2.2	0.281
Peripheral ring	33.5±2.3	32.1±1.6	0.149	Peripheral ring	12.3±1.3	13.2±1.6	0.162
IR							
Fovea	176.9±10.0	189.9±19.5	0.021*				
Pericentral ring	258.0±6.5	257.1±11.0	0.824				
Peripheral ring	224.1±10.3	216.4±9.7	0.073				

GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner plexiform layer, IR = inner retina, ONL = outer nuclear layer, OPL = outer plexiform layer, PHL = Photoreceptor layer, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium.
Unpaired t-test (*; significantly different, P<0.05).

Table 5
Differences in mean macular layer volume based on age.

Macular layer	<30 y	>60 y	P*	Macular layer	<30 y	>60 y	P*
RNFL				OPL			
Fovea	0.01 ± 0	0.01 ± 0	1.0	Fovea	0.022 ± 0.006	0.022 ± 0.007	0.89
Pericentral ring	0.035 ± 0.003	0.035 ± 0.003	1.0	Pericentral ring	0.055 ± 0.1	0.056 ± 0.007	0.77
Peripheral ring	0.207 ± 0.018	0.187 ± 0.016	0.01*	Peripheral ring	0.145 ± 0.012	0.151 ± 0.008	0.15
GCL				ONL			
Fovea	0.01 ± 0	0.01 ± 0	1.0	Fovea	0.072 ± 0.009	0.075 ± 0.009	0.39
Pericentral ring	0.081 ± 0.005	0.079 ± 0.004	0.18	Pericentral ring	0.108 ± 0.014	0.108 ± 0.018	0.98
Peripheral ring	0.079 ± 0.019	0.186 ± 0.011	0.04*	Peripheral ring	0.292 ± 0.035	0.298 ± 0.028	0.64
IPL				PHL			
Fovea	0.015 ± 0.005	0.016 ± 0.005	0.70	Fovea	0.072 ± 0.004	0.07 ± 0.004	0.19
Pericentral ring	0.066 ± 0.005	0.064 ± 0.004	0.28	Pericentral ring	0.129 ± 0.005	0.129 ± 0.005	0.84
Peripheral ring	0.161 ± 0.015	0.156 ± 0.006	0.02*	Peripheral ring	0.413 ± 0.017	0.418 ± 0.014	0.43
INL				RPE			
Fovea	0.012 ± 0.004	0.014 ± 0.005	0.015*	Fovea	0.012 ± 0.004	0.011 ± 0.003	0.48
Pericentral ring	0.062 ± 0.005	0.062 ± 0.005	0.83	Pericentral ring	0.022 ± 0.003	0.023 ± 0.004	0.68
Peripheral ring	0.178 ± 0.011	0.170 ± 0.014	0.13	Peripheral ring	0.065 ± 0.007	0.070 ± 0.009	0.14
IR							
Fovea	0.134 ± 0.006	0.15 ± 0.015	0.03*				
Pericentral ring	0.406 ± 0.011	0.404 ± 0.017	0.78				
Peripheral ring	1.188 ± 0.056	1.147 ± 0.051	0.08				

GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner plexiform layer, IR = inner retina, ONL = outer nuclear layer, OPL = outer plexiform layer, PHL = Photoreceptor layer, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium.
Unpaired *t*-test (*; significantly different, *P* < 0.05).

thicknesses in all quadrants of the pericentral ring and in the temporal quadrant of the peripheral ring were significantly greater in men than in women.^[24] In another study, the mean thicknesses of the INL and OPL+ONL were significantly greater in men than in women, but the mean RNFL thickness was greater in women than in men, especially at the peripheral ring. Therefore, because the RNFL is relatively thin, the authors suggested that differences of thickness in the INL and OPL+ONL may be predominately responsible for the sex-related thickness difference of the total retina in the central sector, pericentral ring, and temporal quadrant of the peripheral ring.^[4] These results were partially similar with those in our study. However compared to previous studies, we were able to measure sex-related thickness differences in more individual retinal layers and found the mean thickness of the RNFL, GCL, IPL in all ETDRS sectors, foveal INL, foveal OPL, and OPL of pericentral ring was significantly greater in men than in women; conversely, the mean thickness of the ONL was greater in women (Table 3).

We found significant differences in thickness and volume of the retinal layer with age in a healthy population. When macular thickness was compared between < 30 years of age and >60 years of age, peripheral RNFL, peripheral GCL, and pericentral and peripheral IPL were significantly thicker in the younger age group than in the older age group (Table 4). Several previous histological studies support these results. The GCL and their axons (RNFL) are particularly prone to loss with age.^[30,31] Additionally, in a previous study by Ooto et al,^[8] the thicknesses in the RNFL, GCL, IPL, INL, and inner segment of the PHL were negatively correlated with age. However, the thickness of the OPL+ONL was unrelated with age, and the thickness of the outer segment of PHL had a positive correlation with age. Macular RNFL and GCL thickness also presented a linear correlation with negative slopes of -0.05 and -0.07 μm/year with age, respectively. And, like the results of our study, the decrease in thickness with age in other inner retinal layers (IPL and INL) suggests that aging is related to the loss of other neurons or glial cells in the INL. Indeed, several studies showed that aging was

related with loss of neurons in the inner retina.^[32,33] Also, histologic studies presented age-related losses of the retina as 0.3% to 0.6% per year, whereas the thickness of the RNFL decreases with age at a lower rate of 0.2% per year.^[32,33] According to a previous study, structural changes of the RPE occur with age, including loss of melanin granules, accumulation of lipofuscin, basal deposits, and thickened Bruch’s membrane. Because of these, fovea RPE thickness can increase significantly with age.^[12] In our study, however, foveal RPE thickness showed no significant differences with increasing age. This is likely due to differences in race and the type of OCT.

5. Conclusions

This study shows that there are differences in the thickness and volume of several retinal layers due to age and sex. Therefore, while analyzing retinal layer thickness associated with disease, these findings should be taken into consideration. Further research with more subjects would help shape these age-related changes and sex-related differences in thickness and volume of the retinal layer as more objective clinical parameters.

References

- [1] Neuvilte JM, Bronson-Castain K, Bearnse MAJr, et al. OCT reveals regional differences in macular thickness with age. *Optom Vis Sci* 2009;86:E810-6.
- [2] Song WK, Lee SC, Lee ES, et al. Macular thickness variations with sex, age, and axial length in healthy subjects: a spectral domain-optical coherence tomography study. *Invest Ophthalmol Vis Sci* 2010;51:3913-8.
- [3] Sung KR, Wollstein G, Bilonick RA, et al. Effects of age on optical coherence tomography measurements of healthy retinal nerve fiber layer, macula, and optic nerve head. *Ophthalmology* 2009;116:1119-24.
- [4] Ooto S, Hangai M, Tomidokoro A, et al. Effects of age, sex, and axial length on the three-dimensional profile of normal macular layer structures. *Invest Ophthalmol Vis Sci* 2011;52:8769-79.
- [5] Chan A, Duker JS, Ishikawa H, et al. Quantification of photoreceptor layer thickness in normal eyes using optical coherence tomography. *Retina* 2006;26:655-60.

- [6] Witkin AJ, Ko TH, Fujimoto JG, et al. Ultra-high resolution optical coherence tomography assessment of photoreceptors in retinitis pigmentosa and related diseases. *Am J Ophthalmol* 2006;142:945–52.
- [7] Matsumoto H, Sato T, Kishi S. Outer nuclear layer thickness at the fovea determines visual outcomes in resolved central serous chorioretinopathy. *Am J Ophthalmol* 2009;148:105.e1–10.e1.
- [8] Ooto S, Hangai M, Sakamoto A, et al. High-resolution imaging of resolved central serous chorioretinopathy using adaptive optics scanning laser ophthalmoscopy. *Ophthalmology* 2010;117:1800–9.e1-2.
- [9] Ooto S, Tsujikawa A, Mori S, et al. Thickness of photoreceptor layers in polypoidal choroidal vasculopathy and central serous chorioretinopathy. *Graefes Arch Clin Exp Ophthalmol* 2010;248:1077–86.
- [10] Arichika S, Hangai M, Yoshimura N. Correlation between thickening of the inner and outer retina and visual acuity in patients with epiretinal membrane. *Retina* 2010;30:503–8.
- [11] Ooto S, Hangai M, Takayama K, et al. High-resolution imaging of the photoreceptor layer in epiretinal membrane using adaptive optics scanning laser ophthalmoscopy. *Ophthalmology* 2011;118:873–81.
- [12] Staurengi G, Satta S, Chakravarthy U, et al. Proposed lexicon for anatomic landmarks in normal posterior segment spectral-domain optical coherence tomography: the IN•OCT consensus. *Ophthalmology* 2014;121:1572–8.
- [13] Dysli C, Enzmann V, Sznitman R, et al. Quantitative analysis of mouse retinal layers using automated segmentation of spectral domain optical coherence tomography images. *Trans Vis Sci Tech* 2015;4:9.
- [14] Demirkaya N, van Dijk HW, van Schuppen SM, et al. Effect of age on individual retinal layer thickness in normal eyes as measured with spectral-domain optical coherence tomography. *Invest Ophthalmol Vis Sci* 2013;54:4934–40.
- [15] Leung CK, Cheung CY, Weinreb RN, et al. Comparison of macular thickness measurements between time domain and spectral domain optical coherence tomography. *Invest Ophthalmol Vis Sci* 2008;49:4893–7.
- [16] Kakinoki M, Sawada O, Sawada T, et al. Comparison of macular thickness between Cirrus HD-OCT and Stratus OCT. *Ophthalmic Surg Lasers Imaging* 2009;40:135–40.
- [17] Sull AC, Vuong LN, Price LL, et al. Comparison of spectral/Fourier domain optical coherence tomography instruments for assessment of normal macular thickness. *Retina* 2010;30:235–45.
- [18] Chan A, Duker JS, Ko TH, et al. Normal macular thickness measurements in healthy eyes using Stratus optical coherence tomography. *Arch Ophthalmol* 2006;124:193–8.
- [19] Lam DS, Leung KS, Mohamed S, et al. Regional variations in the relationship between macular thickness measurements and myopia. *Invest Ophthalmol Vis Sci* 2007;48:376–82.
- [20] Kely PJ, Payne JF, Trivedi RH, et al. Macular thickness assessment in healthy eyes based on ethnicity using Stratus OCT optical coherence tomography. *Invest Ophthalmol Vis Sci* 2008;49:2668–72.
- [21] Eriksson U, Alm A. Macular thickness decreases with age in normal eyes: a study on the macular thickness map protocol in the Stratus OCT. *Br J Ophthalmol* 2009;93:1448–52.
- [22] Legarreta JE, Gregori G, Punjabi OS, et al. Macular thickness measurements in normal eyes using spectral domain optical coherence tomography. *Ophthalmic Surg Lasers Imaging* 2008;39:S43–9.
- [23] Grover S, Murthy RK, Brar VS, et al. Normative data for macular thickness by high-definition spectral-domain optical coherence tomography (spectralis). *Am J Ophthalmol* 2009;148:266–71.
- [24] Grover S, Murthy RK, Brar VS, et al. Comparison of retinal thickness in normal eyes using Stratus and Spectralis optical coherence tomography. *Invest Ophthalmol Vis Sci* 2010;51:2644–7.
- [25] Ooto S, Hangai M, Sakamoto A, et al. Three-dimensional profile of macular retinal thickness in normal Japanese eyes. *Invest Ophthalmol Vis Sci* 2010;51:465–73.
- [26] Koh VT, Tham YC, Cheung CY, et al. Determinants of ganglion cell-inner plexiform layer thickness measured by high-definition optical coherence tomography. *Invest Ophthalmol Vis Sci* 2012;53:5853–9.
- [27] Mwanza JC, Durbin MK, Budenz DL, et al. Profile and predictors of normal ganglion cell-inner plexiform layer thickness measured with frequency-domain optical coherence tomography. *Invest Ophthalmol Vis Sci* 2011;52:7872–9.
- [28] Lee K, Kwon YH, Garvin MK, et al. Distribution of damage to the entire retinal ganglion cell pathway: quantified using spectral-domain optical coherence tomography analysis in patients with glaucoma. *Arch Ophthalmol* 2012;130:1118–26.
- [29] Huang J, Liu X, Wu Z, et al. Macular thickness measurements in normal eyes with time-domain and Fourier-domain optical coherence tomography. *Retina* 2009;29:980–7.
- [30] Gao H, Hollyfield JG. Aging of the human retina. Differential loss of neurons and retinal pigment epithelial cells. *Invest Ophthalmol Vis Sci* 1992;33:1–7.
- [31] Nag TC, Wadhwa S. Ultrastructure of the human retina in aging and various pathological states. *Micron* 2012;43:759–81.
- [32] Kerrigan-Baumrind LA, Quigley HA, Pease ME, et al. Number of ganglion cells in glaucoma eyes compared with threshold visual field tests in the same persons. *Invest Ophthalmol Vis Sci* 2000;41:741–8.
- [33] Repka MX, Quigley HA. The effect of age on normal human optic nerve fiber number and diameter. *Ophthalmology* 1989;96:26–32.