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Variability in Spectral-Domain Optical Coherence Tomography Over Four Weeks by Age

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Abstract

Purpose—To quantify variation in spectral-domain optical coherence tomography (SD-OCT) measures of total retinal thickness (top of inner limiting membrane to top of retinal pigment epithelium, RPE) and RPE thickness measures over a 4-week period and by age.

Methods—76 volunteers aged 40–85 years were seen at 3 visits over 4 weeks. 2 Topcon SD-OCT scans were taken at each visit. Following grid re-centration, total retinal and RPE thickness were determined in 9 subfields. Multilevel modeling was used to quantify variance between scans and by age.

Results—In the central circle, mean total retinal thickness was 237.9 μ m (standard deviation, SD, 23.5 μ m) and RPE thickness was 46.0 μ m (SD 5.3 μ m). Intraclass correlation coefficient in the central circle was 0.988 for total retinal thickness and 0.714 for RPE thickness. Pairwise measures taken within 4 weeks were strongly correlated ($P>0.95$). Within-subject variation of total retinal thickness increased significantly with age. Subjects in the oldest age group had significantly increased among- and within-subject variability in measures of RPE thickness.

Conclusions—Correlation between retinal thickness measures was very high (>0.95) over a period of 4 weeks with small changes likely due to variation in measurement. Increasing variability in total retinal and RPE thickness measures with age suggest that the use of more and/or higher quality images to calculate mean thickness to reduce variability may benefit the study of these measures in older persons. This may also impact sample size calculations for future studies of SD-OCT measures in older adults.

Keywords

retinal thickness; retinal pigment epithelium thickness; spectral-domain optical coherence tomography; age; aging

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INTRODUCTION

Spectral domain optical coherence tomography (SD-OCT) is widely used in research and clinical care to evaluate retinal and optic nerve morphology.¹ This is useful in quantifying retinal layer thickness and in identifying the presence of retinal thickening (eg, in eyes with diabetic macular edema) and presence of retinal thinning (eg, in eyes with geographic atrophy). Retinal thickness is measured to determine the efficacy of and responsiveness to various treatments, such as intravitreal use of anti-vascular endothelial growth factor for diabetic macular edema.² The reproducibility of SD-OCT measurements has been well established.^{3,4} However, less is known about the natural change in retinal measurements that occur over a short time in healthy eyes and how natural variation in these measurements might lead to false conclusions regarding true change in retinal thickness and treatment efficacy. For this reason, it is important to quantify these variance measures to differentiate a true change in retinal thickness from normal variation in measurement.

While long-term anatomic and physiologic changes in retinal thickness measures would be expected, we hypothesized that short-term change in retinal thickness measures in persons without retinal disease would most likely be due to measurement error or variability rather than true changes in retinal thickness. We also sought to understand how age impacts the amount of variance in SD-OCT retinal thickness measures. Studies have focused on the effect of aging on mean retinal thickness measures^{5,6}, however, to our knowledge, no study has focused on how participant age affects the normal amount of variance between 2 scans. We hypothesized that there would be greater variability among individuals in older age groups due to differences in morphology of individuals' eyes as they age. Also, we expected more within-subject variability due to an aging participant's inability to focus or be positioned in the machine properly and/or lower signal strength that may decrease accuracy of the retinal thickness segmentation.

Thus, the purpose of the current investigation was to determine the amount of variability that occurs among subjects (variation among persons due to differences in true underlying thickness measure) and within subjects (variation among multiple measurements of the same retinal area from the same subject) between scans over a short period of up to 4 weeks. A secondary goal was to determine the amount of among- and within-subject variation for subjects of older age.

MATERIALS AND METHODS

Volunteer recruitment

Volunteer participants were recruited in Beaver Dam, Wisconsin but were not participants of the Beaver Dam Eye Study. Eligibility screening for this study took place at the time of a recruitment telephone call. Criteria for participation in the study required that the subject; 1) be aged 40 years or older; 2) have no history of refractive surgery for near- or far-sightedness; 3) have no known condition which would interfere with pupil dilation; 4) have a best-corrected visual acuity better than 20/200 in the eye to be studied; 5) be willing to be examined and have their pupil dilated on 3 separate dates over a 4-week period; 6) be mobile enough to be positioned repeatedly to obtain measures; and, 7) if there was a positive history

of cataract surgery in the eye to be studied, the surgery must have been performed more than 6 weeks prior to examination.

Study design

Participants were seen at 3 visits; baseline, 7 or 21 days after baseline, and 28 days after baseline. All examinations for a given participant were performed at the same time of day by the same trained examiner. All procedures were performed in the same order. 1 eye from each participant was chosen for examination. When both eyes met eligibility criteria, the right eye was chosen if the person's birthday was on an odd-numbered day, and the left eye was chosen if the participant's birthday was on an even-numbered day. The examination included measures of ocular biometry, pachymetry, intraocular pressure, refraction, height, weight, blood pressure, pulse, systemic oxygen saturation, and pupil size after dilation. Participants also underwent fundus photography using a Zeiss FF4 fundus camera (Carl Zeiss, [AU: city and country?]) as well as a slit-lamp examination. Self-reported medical and social histories were recorded.

All data were collected with Institutional Review Board approval from the University of Wisconsin-Madison in conformity with all federal and state laws, the work was compliant with the Health Insurance Portability and Accountability Act, and the study was performed in adherence to the tenets of the Declaration of Helsinki. Informed consent was obtained from each participant after explanation of the nature and possible consequences of the study.

Retinal image acquisition and grading

2 macular SD-OCT scans (Topcon SD-OCT 1000 Mark II, Topcon Corporation, Tokyo, Japan; 6mm × 6mm scan with 512 A scan × 128 B scan resolution) were completed on the chosen eye of each participant at each of the 3 visits. The first macular scan was completed for the selected eye, and then the participant moved to other equipment for completion of other examination components before returning to the SD-OCT equipment for a second macular scan of the same eye. The scans were processed with Topcon 3D-OCT software version 3.01 and were viewed for grading in Universal OCT software version 1.02.01, a program created by one of the authors of this report (YH).

For each scan, a trained grader determined the center of the fovea based on anatomic features and re-centered the Early Treatment Diabetic Retinopathy Study grid accordingly. The grader was masked to the grid placement from previous scans of the same eye. The scan's layer boundaries (top of the inner limiting membrane, top of the retinal pigment epithelium, RPE, and Bruch's membrane) were determined by the Topcon 3D-OCT software. The grader then assessed reliability of the retinal thickness measurements in 3 regions; the central circle, the inner circle, and the outer circle. The inner and outer circles each have 4 subfields (superior, inferior, temporal, and nasal; Figure 1).⁷ Each of the 9 subfields (central circle, 4 inner circle and 4 outer circle) were graded as "acceptable", "unacceptable", or "cannot grade". Any region with a subfield that was graded as "unacceptable" or "cannot grade" was excluded from analysis for all subfields within the region (eg, if a subfield in the inner circle was graded as "unacceptable," then all 4 subfields within the inner circle were excluded from analysis). Reasons for a subfield or region to be

deemed unreliable included but were not limited to segmentation errors, poor illumination, or a decentered scan (ie, when the scan is re-centered by the grader, a portion of the outer circle may lie outside of the segmented region which would cause the outer circle to be graded as “unacceptable” and therefore excluded). Total retinal thickness was defined as the distance from the top of the inner limiting membrane to the top of the RPE. RPE thickness was defined as the distance between the top of the RPE layer and Bruch’s membrane. The Manufacturer’s Signal Index or Q Score was obtained directly from the Topcon software, and the Tissue Contrast Index,⁸ an independent measure of signal quality, was calculated by the Universal OCT software.

Presence of early age-related macular degeneration, macular edema, and epiretinal membrane were assessed by a trained grader using a combination of stereo color photographs of the macula and SD-OCT scans. Cataract surgery (presence of an intraocular lens) and presence of cortical or posterior subcapsular cataract were assessed by a trained examiner during the baseline visit during the slit-lamp examination.

Statistical analysis

Mean differences and 95% limits of agreement (LOA) were used to examine the difference between 2 measures of total retinal and RPE thickness measures within visits and at visits 1 and 4 weeks apart. Data from 2 scans at the baseline visit were used for evaluation of variability within a visit. Thickness measures from the first SD-OCT scans of the 2 separate visits were used to evaluate the mean and difference between scans at visits 1 week and 4 weeks apart. To establish the base variance components model, multilevel mixed modeling was used to estimate the variance among and within subjects for the overall population.⁹ To estimate the variance of retinal thickness measurements over a short time period at unequally spaced intervals, an autoregressive correlation structure was used to model dependence between scans over the number of weeks between examinations.¹⁰ The beta estimate from this model represents the mean change in total retinal thickness or RPE thickness over 1 week as estimated from our study.

Grouped variance parameters were added to the base model to quantify variation among and within subjects in various age groups. Likelihood ratio tests were used to determine whether observed differences in among- and within-subject variation estimates across age groups were statistically significant.¹¹ The intraclass correlation coefficient in all models was calculated as the ratio of the among-subject variation to the total variation. SAS version 9.3 (SAS Institute, Cary, NC, USA) was used for all analyses.

RESULTS

Subject characteristics

77 volunteers were recruited and 76 (57 women and 19 men) participated in the study, completed at least 1 visit, and contributed data to analyses. Participants’ ages ranged from 40 to 85 years with a mean of 62.3 years (standard deviation, SD, 10.6 years). 96% of participants completed 4–6 SD-OCT scans, and 4% completed fewer than 4 scans. 57% of eyes included in analysis were right eyes and 43% were left eyes. Because each region of the

retinal scan was independently graded for reliability, the outer circle and its subfields were excluded more often than the central circle or inner circle. A total of 425 central circle, 428 inner circle, and 409 outer circle measurements contributed to these analyses.

Few persons in the analyses had prevalent early age-related macular degeneration, eye trauma, cataract, or cataract surgery (Table 1). Older persons tended to have a higher frequency of cataract, cataract surgery, and history of diabetes than younger persons. Younger persons tended to have a higher frequency of eye trauma and were more likely to be current smokers than older persons. Intraocular pressure increased marginally ($P=0.06$) and systolic blood pressure increased significantly ($P<0.001$) with age. Older persons tended to have lower retinal scan reliability scores as measured by the Topcon SD-OCT scanner (Manufacturer's Signal Index, $P<0.001$) and Universal OCT software (Tissue Contrast Index, $P<0.001$). No difference by age group was found for axial length, diastolic blood pressure, or total retinal thickness ($P>0.05$ for all measures). A difference by age group was found for RPE thickness in the outer nasal subfield ($P=0.03$), but was not significantly different in any of the other 8 subfields ($P>0.05$ for all subfields).

Variability of retinal thickness measures within and across visits

The mean difference and 95% LOA for total retinal thickness and RPE thickness are given for each of the 9 retinal subfields within and across visits in Supplementary Table S1 and Figure 2. The 95% LOA was similar between measures taken within a visit and taken 1 and 4 weeks apart. The 95% LOA were also similar between measures of total retinal thickness and measures of RPE thickness.

Mean, SD and results of the spatial correlation model for total retinal and RPE thickness are shown in Table 2. The mean total retinal thickness in the central circle was $237.9\mu\text{m}$ (SD $23.5\mu\text{m}$) and ranged from $282.3\mu\text{m}$ (SD $16.1\mu\text{m}$) to $299.4\mu\text{m}$ (SD $17.7\mu\text{m}$) in the 4 inner subfields and from $232.4\mu\text{m}$ (SD $13.5\mu\text{m}$) to $267.4\mu\text{m}$ (SD $18.7\mu\text{m}$) in the 4 outer subfields. For RPE thickness, the mean in the central circle was $46.0\mu\text{m}$ (SD $5.3\mu\text{m}$) and ranged from $43.5\mu\text{m}$ (SD $4.4\mu\text{m}$) to $46.4\mu\text{m}$ (SD $5.3\mu\text{m}$) in the 4 inner subfields, and $42.0\mu\text{m}$ (SD $3.7\mu\text{m}$) to $49.2\mu\text{m}$ (SD $6.3\mu\text{m}$) in the 4 outer subfields. The beta estimate for mean change in total retinal thickness ranged from $-0.01\mu\text{m}/\text{week}$ to $0.16\mu\text{m}/\text{week}$. The estimate for change in RPE thickness ranged from 0.002 to $0.14\mu\text{m}/\text{week}$. No estimated mean change per week in total retinal or RPE thickness was statistically significant ($P>0.05$), with the exception of total retinal thickness in the outer temporal region ($P=0.04$). The within-subject variance for each measure of total retinal thickness and RPE thickness was much larger than the model-estimated change in thickness over this short time period.

For each of the 9 subfields, the within-subject variance was less than the among-subject variance in measurements of total retinal and RPE thickness. The intraclass correlation coefficient (ICC) for total retinal thickness was very high. In the central circle, the ICC for total retinal thickness was 0.988 and ranged from 0.920 to 0.991 in the 4 inner and 4 outer subfields. For RPE thickness, the ICC was lower than that for total retinal thickness as within-subject variance accounted for a greater proportion of the total variance. The ICC for RPE thickness was 0.714 in the central circle and ranged from 0.667 to 0.761 in the 4 inner and 4 outer subfields (Table 2).

Variability of retinal thickness measures by age

Grouped variance parameters were added to the variance components model to quantify the variance of the retinal thickness measures among and within subjects across 3 age groups; 40–59, 60–69, and 70–85 years. There were 29 participants aged 40–59 years, 29 participants aged 60–69 years, and 18 participants aged 70–85 years. The ICC for measures of total retinal thickness remained high in each age group, ranging from 0.957 to 0.994 in persons aged 40–59 years, 0.916 to 0.988 in persons aged 60–69 years, and 0.784 to 0.991 in persons aged 70–85 years in the 9 retinal subfields. Among-subject variance of total retinal thickness was not significantly different across age groups in any subfield ($P>0.05$) with the exception of the outer inferior subfield ($P=0.04$). Within-subject variance for total retinal thickness was significantly different among the age groups, showing a trend of increased variance in the oldest age group for most subfields ($P<0.05$) with the exception of the central circle ($P=0.14$), inner nasal ($P=0.32$), and outer nasal ($P=0.13$) subfields. The lower ICC in measures of total retinal thickness for persons in the oldest age group is a reflection of the increased within-subject variance (more variation between 2 scans on the same person), rather than a change in among-subject variance (Table 3).

The ICC for RPE thickness tended to be lower for younger persons (40–59 and 60–69 years) compared to persons in the oldest age group (70–85 years). Those in the oldest age group had significantly more variation in measures both among and within subjects ($P<0.05$), with the exception of among-subject variation in the inner superior ($P=0.08$) and outer superior ($P=0.41$) subfields. The lower ICC in younger persons reflects the among-subject variation making up a smaller portion of the total variation, rather than any increase in within-subject variability at younger ages. Persons in the older age groups had greater among- and within-subject variation in measures of RPE thickness (Table 3).

DISCUSSION

SD-OCT measures of retinal thickness have been shown in several studies to be highly reproducible.^{3,4,12–16} Variability has generally been quantified to compare the amount of variation in measures between diseased and non-diseased eyes,^{12,13} or to estimate variance in diseased eyes,¹⁴ and has usually been measured over a very short time period.¹⁵ Our study was designed to estimate the amount of natural variance in SD-OCT measures of RPE thickness and total retinal thickness in healthy eyes over a period of 1–4 weeks and to quantify and compare the amount of variation that occurs in persons of older age. It is important to know how variability in these measurements compares to the expected true underlying change in healthy eyes over this period. Furthermore, it is imperative to understand how variance could outweigh true change when using SD-OCT to determine treatment efficacy as well as when calculating sample size in the design of clinical trials.

Our data have shown that differences in retinal thickness measures may be due to natural variation or measurement error rather than true thickness change, especially if measures are taken over a relatively short period of time. The beta estimates for true change were relatively small in comparison to estimations of variance over this period of 1–4 weeks. We expected that within-subject variability would be lower than among-subject variability and this is reflected in our data. We observed a relatively high SD and among-subject variability

in the central circle as compared to other subfields. This may be due to the automated measure of thickness around the foveal pit, which may be easily influenced by small fluctuations in grid centration.¹⁷ While each scan underwent grid re-centration by a trained grader prior to automated segmentation, this task was performed independently of the other scans for a given participant; therefore, we did not analyze the effect of grid placement on variability between the scans. In addition, while we did not explore the effects of centration in this manuscript, we have done so elsewhere.¹⁸ Based on our observations, we believe that manual re-centration of the grid is important for improving accuracy of measurements of retinal and RPE thickness, especially in the central circle.

In this population, variations in measures taken up to 4 weeks apart were very similar to measures taken within the same visit. No significant change in the value of total retinal thickness or RPE thickness was observed over 4 weeks in our population of older adults with relatively healthy eyes. The only exception was total retinal thickness in the outer temporal region, which may be attributed to a chance finding. This may be an indication that natural change in thickness usually does not occur in healthy eyes over this short period of time, and any apparent change between 2 measurements may actually be a result of natural variation in the measurement. Although we know that age affects retinal thickness measures,^{19,20} it is unlikely that significant changes will occur in healthy eyes within 4 weeks. For this reason, longer follow-up and the impact of natural measurement variation in retinal thickness measures should be considered when quantifying change and estimating treatment efficacy.

Among-subject variability of total retinal thickness did not change with age, while among-subject variability of RPE thickness was significantly higher in persons aged 70–85 years compared to younger persons. This may be a result of total retinal thickness being a more robust measure since it is less affected by pathology in the eye than the thinner RPE layer. For example, drusen, which occur just below the RPE layer, are likely to cause more variation in the automated measurements of this layer alone than in the total retinal thickness measurement. Higher within-subject variability for total retinal thickness and RPE thickness measures may be a reflection of the decreased reliability scores in persons at older ages. The increase in among- and within-subject variability may also be due to the inability of older persons to properly position themselves in the SD-OCT machine because of conditions affecting movement (eg, arthritis) or the inability to fixate due to decreased cognition or increased fatigue. It has been shown that artifacts such as scan misplacement due to operator error or a patient's eye movement can create several types of artifacts (eg, decentration, Z-offset errors, mirror artifacts) that may affect the quantitative measurements in SD-OCT.^{18,21} Older persons are also more prone to conditions such as cataract which can affect image quality. Boundary line errors may be related to poor signal strength, inadequate dilation of the pupil, or scanning through focal lens opacities. Each region (central, inner, and outer circles) of each scan included in analysis was graded for acceptability, and scans that were considered ungradable for reasons such as those listed above were excluded from analysis; therefore we could not estimate the effects of these issues on scan variability. Although this paper does not attempt to explain reasons for the observed variance, it is important to consider these common issues when using retinal thickness as a diagnostic tool. For this reason, one may choose to specify a minimum value of the reliability score in order to ensure only high quality scans are used. Also, in persons with higher variability, it would be

beneficial to perform multiple scans to obtain average measurements in an effort to come closer to a more precise estimate of the ‘true’ underlying thickness as the increased sample size results in smaller confidence bands around the estimate.

It should also be noted that the within-subject variance in measurements of the RPE layer are similar to the within-subject variance of measurements of the total retinal thickness. This is also illustrated in the Bland-Altman plots which show that the 95% LOA for differences between 2 measures of total retinal thickness or RPE thickness are very similar. Given that the RPE layer is much thinner, and that it may be more common to use change in RPE thickness as a measure of disease progression, it is important to exercise caution in making decisions based on an observed change between 2 measures of RPE thickness that fall within the range of natural measurement variation, as they are proportionally larger to the RPE thickness compared to total retinal thickness.

While the current study has many strengths, it also has limitations. The number of study participants that were seen at all visits was relatively small resulting in limited power for some analyses. The average age of our participants (61.6 ± 9.5 years) limits our inferences to middle and older aged adults. It is quite possible characteristics other than age may have a large impact on variability in measures. It is also possible that a different sex distribution and racial/ethnic distribution would produce different results. We did not examine the effect of pathology on changes in the eye over this time, as our cohort is limited to persons with healthy eyes and therefore we cannot speculate on amount of change or variation expected in persons with diseased eyes.

In summary, we found that total retinal and RPE thickness changed little throughout intervals as long as 4 weeks. Variability of measurements increases with age and therefore efforts should be made to obtain more and/or higher quality scans to ensure a more accurate representation of the true underlying thickness measure, especially in persons of older age for whom variability is expected to be greater.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Early Treatment Diabetic Retinopathy Study grid; dark gray area indicates the central circle, medium gray area indicates the inner circle, and light gray area indicates the outer circle.

Figure 2.

Bland-Altman plots; mean difference and 95% limits of agreement for retinal pigment epithelium (RPE) in the central circle A) within a visit, B) at visits 1 week apart, C) at visits 4 weeks apart; and for total retinal thickness in the central circle D) within a visit, E) at 1 week apart, F) at 4 weeks apart

Table 1

Baseline participant characteristics by age, Wisconsin, USA

Variable	Age group, years			P value [†]
	40–59	60–69	70–85	
Sex, n (%)				0.19
Female	22 (75.9)	23 (79.3)	12 (66.7)	
Male	7 (24.1)	6 (20.7)	6 (33.3)	
Early AMD present, n (%)				NE
No	29 (100.0)	27 (93.1)	16 (88.9)	
Yes	0 (0.0)	2 (6.9)	2 (11.1)	
Macular edema present, n (%)				NE
No	29 (100.0)	29 (100.0)	18 (100.0)	
Epiretinal membrane present, n (%)				NE
No	28 (96.5)	28 (96.5)	15 (83.3)	
Yes	1 (3.5)	1 (3.5)	3 (16.7)	
History of cataract surgery, n (%)				NE
No	29 (100.0)	29 (100.0)	15 (83.3)	
Yes	0 (0.0)	0 (0.0)	3 (16.7)	
Cortical cataract or PSC present, n (%)				NE
No	27 (93.1)	23 (79.3)	6 (40.0)	
Yes – central	0 (0.0)	0 (0.0)	0 (0.0)	
Yes – peripheral	2 (6.9)	6 (20.7)	6 (40.0)	
Yes – central and peripheral	0 (0.0)	0 (0.0)	3 (20.0)	
Self-reported history of eye trauma, n (%)				
No	21 (72.4)	25 (86.2)	15 (83.3)	NE
Yes – in study eye	6 (20.7)	3 (10.3)	1 (5.6)	
Yes – unsure which eye	2 (6.9)	1 (3.4)	2 (11.1)	
Currently smoking, n (%)				NE
No	27 (93.1)	28 (96.6)	18 (100.0)	
Yes	2 (6.9)	1 (3.4)	0 (0.0)	

Variable	Age group, years			P value [†]
	40–59	60–69	70–85	
Diabetes present, n (%)				NE
No	28 (96.6)	25 (86.2)	13 (72.2)	
Yes	1 (3.4)	4 (13.8)	5 (27.8)	
Intraocular pressure, mean (SD) mmHg	14.9 (2.4)	15.3 (2.7)	16.6 (3.0)	0.06
Axial length, mean (SD) mm	24.1 (1.1)	23.8 (0.7)	23.6 (1.0)	0.34
Mean diastolic BP, mean (SD) mmHg	76.8 (9.5)	78.5 (7.7)	77.7 (9.0)	0.79
Mean systolic BP, mean (SD) mmHg	125.4 (17.9)	134.3 (16.2)	147.3 (19.9)	<0.001
Tissue contrast index, mean (SD)	6.3 (0.6)	6.1 (0.7)	5.5 (1.0)	<0.001
MSI or Q score, mean (SD)	81.2 (7.1)	78.4 (8.1)	72.9 (10.1)	<0.001
Total retinal thickness, mean (SD) μm [*]				
Central subfield	243.5 (24.2)	232.4 (18.3)	237.6 (27.8)	0.18
Inner subfields				
Inferior	292.9 (18.5)	291.4 (14.4)	285.0 (12.5)	0.45
Nasal	301.6 (17.8)	299.9 (17.1)	294.6 (17.9)	0.66
Superior	297.4 (17.5)	296.5 (18.8)	287.1 (12.1)	0.24
Temporal	285.2 (17.2)	283.1 (15.5)	275.7 (12.9)	0.30
Average	294.3 (17.3)	292.7 (15.4)	285.6 (12.5)	0.37
Outer subfields				
Inferior	240.1 (17.4)	237.4 (11.9)	238.1 (12.5)	0.74
Nasal	269.7 (20.7)	268.2 (17.2)	261.2 (15.4)	0.56
Superior	250.4 (16.7)	248.9 (17.4)	244.9 (11.6)	0.54
Temporal	233.3 (15.5)	232.1 (11.7)	231.1 (12.5)	0.92
Average	256.3 (15.9)	254.7 (12.8)	251.9 (11.2)	0.70
RPE thickness, mean (SD) μm				
Central subfield	45.4 (3.8)	45.9 (5.1)	47.0 (7.9)	0.59
Inner subfields				
Inferior	43.6 (3.8)	43.3 (4.3)	45.0 (6.6)	0.20
Nasal	45.3 (3.8)	44.0 (4.2)	46.6 (6.9)	0.87
Superior	43.6 (3.8)	43.0 (3.9)	44.1 (5.9)	0.65

Variable	Age group, years			P value [‡]
	40–59	60–69	70–85	
Temporal	46.0 (3.8)	46.4 (4.7)	47.2 (7.9)	0.57
Average	44.6 (3.4)	44.1 (3.9)	45.8 (6.2)	0.57
Outer subfields				
Inferior	42.4 (3.4)	42.3 (3.8)	44.5 (6.9)	0.49
Nasal	41.7 (3.9)	41.9 (3.2)	43.5 (6.3)	0.04
Superior	41.9 (3.5)	41.0 (6.4)	42.7 (5.1)	0.24
Temporal	48.0 (3.8)	48.7 (4.6)	52.0 (10.6)	0.18
Average	43.5 (2.9)	43.6 (3.1)	46.0 (6.5)	0.10

AMD, age-related macular degeneration; BP, blood pressure; MSI, manufacturer's signal index; NE, not estimable; PSC, posterior subcapsular cataract; RPE, retinal pigment epithelium; SD, standard deviation.

* Measured from the top of the inner limiting membrane to the top of the RPE.

[‡] P value for difference among age groups.

Variability of retinal thickness measurements in the overall study population, Wisconsin, USA

Table 2

	Total retinal thickness, μm^*	Mean (SD)	β estimate [†]	P value	Autoregressive correlation model			
					Among-subject variance	Within-subject variance	Correlation estimate	ICC
Central subfield	237.9 (23.5)		0.04	0.71	583.3	5.8	0.999	0.990
Inner subfields								
Inferior	290.6 (16.0)		-0.01	0.89	243.5	9.4	1.000	0.963
Nasal	299.4 (17.7)		0.09	0.31	307.6	4.3	0.999	0.986
Superior	294.8 (17.5)		0.16	0.08	297.2	5.6	0.998	0.981
Temporal	282.3 (16.1)		0.03	0.73	254.6	4.6	0.999	0.982
Average	291.8 (15.9)		0.06	0.38	248.5	3.4	0.999	0.987
Outer subfields								
Inferior	238.7 (14.5)		0.08	0.51	189.3	16.6	1.000	0.920
Nasal	267.4 (18.7)		0.06	0.32	357.9	3.1	1.000	0.991
Superior	248.7 (16.2)		0.08	0.35	259.1	6.3	0.999	0.976
Temporal	232.4 (13.5)		0.14	0.04	184.1	5.0	1.000	0.974
Average	254.8 (13.9)		0.10	0.15	188.4	3.4	0.999	0.982
RPE thickness, μm								
Central subfield	46.0 (5.3)		0.14	0.12	20.8	7.6	0.988	0.733
Inner subfields								
Inferior	43.8 (4.8)		0.07	0.42	15.8	6.7	0.994	0.701
Nasal	45.1 (4.9)		0.11	0.23	18.4	5.6	0.970	0.766
Superior	43.5 (4.4)		0.06	0.48	14.3	5.0	0.968	0.743
Temporal	46.4 (5.3)		0.07	0.49	19.1	8.7	0.984	0.686
Average	44.7 (4.4)		0.08	0.33	14.4	4.6	0.982	0.759
Outer subfields								
Inferior	42.8 (4.6)		0.03	0.74	16.7	4.0	0.963	0.808
Nasal	42.1 (4.4)		0.10	0.26	13.3	5.3	0.972	0.714
Superior	42.0 (3.7)		0.002	0.98	11.2	3.4	0.970	0.769
Temporal	49.2 (6.3)		0.03	0.84	31.4	6.7	0.953	0.824

Total retinal thickness, μm [*]	Autoregressive correlation model					
	Mean (SD)	β estimate [†]	P value	Among-subject variance	Within-subject variance	Correlation estimate ICC
Average	44.0 (4.1)	0.04	0.66	13.5	2.6	0.960 0.837

ICC, intraclass correlation coefficient; RPE, retinal pigment epithelium; SD, standard deviation.

^{*} Measured from the top of the inner limiting membrane to the top of the RPE.

[†] For change in retinal thickness over 1 week.

Table 3

Variability of retinal thickness measurements by age group, Wisconsin, USA

	Among-Subject Variance (μm)				Within-Subject Variance (μm)				ICC	
	40–59 years	60–69 years	70–85 years	P value	40–59 years	60–69 years	70–85 years	P value	40–59 years	60–69 years
Total retinal thickness										
Central subfield	624.4	351.5	896.3	0.09	5.7	7.2	8.4	0.14	0.991	0.980
Inner subfields										
Inferior	333.4	199.6	168.4	0.22	8.9	5.1	18.3	<0.001	0.974	0.975
Nasal	310.2	282.7	339.4	0.91	5.5	4.4	5.7	0.32	0.983	0.985
Superior	308.1	343.3	201.1	0.50	6.3	5.3	9.9	0.007	0.980	0.985
Temporal	294.8	231.3	225.7	0.76	5.7	3.9	6.3	0.02	0.981	0.984
Average	297.8	230.5	196.0	0.61	4.1	3.0	5.4	0.01	0.986	0.987
Outer subfields										
Inferior	290.7	126.4	123.0	0.04	13.2	11.5	33.9	<0.001	0.957	0.916
Nasal	436.2	310.9	305.4	0.59	2.7	3.6	3.9	0.13	0.994	0.988
Superior	283.3	314.9	128.7	0.14	5.4	5.5	11.6	<0.001	0.981	0.983
Temporal	236.7	130.2	184.6	0.28	4.5	4.3	7.5	0.02	0.981	0.968
Average	251.6	161.6	127.5	0.25	3.7	2.8	5.9	0.001	0.986	0.956
RPE thickness										
Central subfield	7.0	18.7	43.9	<0.001	7.5	5.8	13.3	<0.001	0.481	0.763
Inner subfields										
Inferior	10.7	11.9	29.6	0.05	4.4	6.5	12.6	<0.001	0.710	0.646
Nasal	8.4	13.6	36.8	0.004	6.6	4.8	10.5	<0.001	0.560	0.740
Superior	9.4	11.0	24.4	0.08	5.5	4.0	10.0	<0.001	0.629	0.736
Temporal	7.8	15.6	40.9	0.002	6.9	6.3	19.4	<0.001	0.529	0.712
Average	7.2	11.0	29.7	0.005	4.8	4.2	7.4	0.01	0.603	0.724
Outer subfields										
Inferior	8.8	8.7	40.1	<0.001	2.9	5.4	9.2	<0.001	0.756	0.619
Nasal	10.0	4.9	28.1	<0.001	5.0	4.8	10.9	<0.001	0.665	0.504
Superior	8.3	9.6	15.5	0.41	3.8	2.7	7.3	<0.001	0.686	0.781
Temporal	9.4	13.8	88.8	<0.001	5.1	7.0	23.6	<0.001	0.646	0.664

	Among-Subject Variance (µm)				Within-Subject Variance (µm)				ICC	
	40–59 years	60–69 years	70–85 years	P value	40–59 years	60–69 years	70–85 years	P value	40–59 years	60–69 years
Total retinal thickness										
Average	5.5	6.7	33.7	<0.001	2.8	3.3	6.0	<0.001	0.661	0.672
										0.848

ICC, intraclass correlation coefficient; RPE, retinal pigment epithelium.
* Measured from the top of the inner limiting membrane to the top of the RPE.