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Retinal and choroidal thickness in early Age-related macular degeneration

("Retinal and choroidal thickness in early AMD")

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Introduction

Age-related macular degeneration (AMD) is the leading cause of blindness in the United Kingdom, with AMD responsible for more people being registered as 'sight impaired' or 'severely sight impaired' than all other ocular conditions combined.[1] The prevalence of AMD is expected to increase globally between 2005 and 2050 due to a predicted 3 fold increase in the number of people aged over 60 years.[2] Age-related macular degeneration manifests either as choroidal neovascularisation (wet AMD) or geographic atrophy (dry AMD), whilst early AMD, also known as age-related maculopathy (ARM), is characterised by soft drusen and focal pigmentary changes only.[3] Currently treatment is only available for the wet (neovascular) type of AMD, usually in the form of anti-angiogenic pharmacotherapy.[4] Although no treatment currently exists for dry AMD and early AMD there is some evidence to suggest that nutritional supplements may slow the progression of the disease.[5] The ability to accurately diagnose the onset of AMD and to monitor disease progression is vital in the early identification of patients suitable for therapy, and in evaluating the outcomes of the treatment.

Historically, the diagnosis and grading of AMD has largely been based on visual acuity and stereoscopic fundus photographs.[3] However, in recent years detailed analysis of retinal microscructure has become possible in the form of optical coherence tomography (OCT), and offers an extra dimension to the evaluation of age-related macular disease.[6] OCT is a technique which utilises the optical equivalent of the echo time delay in ultrasound to construct a cross-sectional image of the retina *in vivo*, analogous to a histological section.

Frequency domain OCT (FD-OCT) has traditionally used light sources with a bandwidth based around 800nm.[6] The limitation of this band of wavelengths is partly that ocular opacities can degrade the quality of the collected image (which is especially important in the assessment of elderly individuals), but also that the high level of scatter by retinal tissue and increased absorption by the retinal pigment epithelium (RPE) results in limited visualisation of sub RPE layers.[7-9] An alternative light source, with a bandwidth based around 1060nm, has been shown to allow deeper penetration into the choroidal tissue and better signal-to-noise ratio in the presence of media opacities.[7, 9-11]

Although the longer wavelength 1060nm OCT is the first system which allows a reliable assessment of *in vivo* choroidal thickness in all patients, it has only been used to date to assess outer retinal features and choroidal structure in patients with the neovascular form of AMD,[12] where the structural changes to the choroid/Bruch's membrane/RPE complex are already marked. There is substantial evidence to suggest that the dynamics of the choroidal circulation are affected earlier in the disease process (see Harris et al. 1999 for review [13]), and histological studies have found evidence of a difference in choroidal structure in eyes with early and advanced AMD compared to age-matched control eyes, such as reductions in choriocapillary density and choroid thickness.[14-16] However, histological evidence regarding choroidal thickness in AMD is mixed, with some evidence to suggest a reduction, particularly in the advanced stages of the disease,[15-16] whilst another study found no significant change in choroidal thickness, even in advanced AMD.[14]

The aim of this study was to use the 1060nm enhanced choroidal penetration OCT to investigate retinal and choroidal thickness as a function of eccentricity in patients with early AMD (drusen or pigmentary changes only). This will help determine the potential clinical value of the 1060nm OCT in assessing early macular disease, and provide an insight into the earliest structural changes occurring in AMD.

Methods

Participants

Control participants (n=16) and those with early AMD (n=16) were recruited for this study from staff, students and volunteers attending the Eye Clinic at the School of Optometry and Vision Sciences and the Eye Unit at the University Hospital of Wales. All participants had a corrected visual acuity (VA) of 0.3 logMAR (~20/40) or better assessed using an Early Treatment of Diabetic Retinopathy Study (ETDRS) sight chart and a refractive error of less than ±6D. Participants were excluded if they had secondary retinal disease, significant cataract (Lens Opacities Classification System III grade 4 or above for any criteria [17]) or narrow irido-corneal angles (Grade 1 or less assessed by Van Herick). Each participant was given a full explanation of the procedures involved and their written informed consent was obtained before participation in the study.

Participants were categorised into either a "Control" or "early AMD" group dependent on the assessment of 37° digital fundus images (CR-DGi Non mydriatic retinal camera, Canon, Inc. Lake Success, USA) and 20° 1060µm OCT images. Images were assessed for AMD related features located within a 6000µm diameter centred on the fovea. Definitions were based on the International [3] and the Age Related Eye Disease Study (AREDS) [18] AMD classification systems. Control participants exhibited no features associated with AMD, with any drusen present being less than 125µm in diameter (hard drusen). Early AMD was defined as the presence of soft drusen (>125µm diameter), pigment changes or drusenoid pigment epithelial detachment (PED) in the absence of any feature of advanced AMD (wet or dry) as defined by the AREDS grading system.[18] Classification was carried out by the author AW, and confirmed independently by AB and TM. One drop of Tropicamide 1.0% was instilled into the both eyes of each participant, ensuring pupil dilation of at least 7mm prior to obtaining fundus photographs and OCT images. Images were obtained from both eyes of all individuals, to determine their AMD status. One eye was selected for analysis from each participant; this was the eye with a diagnosis of early AMD or, in the case of bilateral early AMD or controls, the eye with the better VA, with the left eye used as default.

Three-dimensional OCT-imaging at 1060nm was performed with less than 2.5mW at the cornea, below the maximum power limit for a 10s exposure.[19-20] OCT volumes were acquired across a 20°×20° (5.76 x 5.76mm) field consisting of 512×512 A-scans obtained at a rate of 47,000 A-scans/second (~8µm axial resolution). OCT volumes were centred on the fovea, aligned by participant fixation. Axial length (cornea-RPE) measurements were acquired using optical biometry (IOL Master Zeiss, Jena, Germany), for each eye five measurements were averaged.

Image processing and analysis was undertaken using ImageJ software (ImageJ. Bethesda, Maryland, USA). Raw OCT images were digitally enhanced to improve the visibility of the retina and choroidal boundaries. Post-processing procedures were carried out subjectively and included: adjustments to brightness and contrast, b-scan registration, despeckling/noise removal and application of Gaussian or Convolving blur. Measurements were made using the calliper function in the axial plane of the images. The thickness represented by each pixel was calculated assuming a refractive index of 1.4.

Retinal thickness was measured from the most anterior hyper-reflective line, which corresponds to the inner limiting membrane (ILM), to the centre of the most posterior hyper-reflective line which corresponds to the RPE. Choroidal thickness

was measured from the RPE, to the choroid-sclera boundary. Thickness measurements were obtained for both retina and the choroid at the fovea, and then at 0.5mm intervals out to 2mm nasally (N), temporally (T), superiorly (S) and inferiorly (I) (see Figure 1). This produced thickness measurements at 17 individual retinal locations for each eye. At each location the distribution of thickness measurements was checked for normality and an independent t-test was conducted between the control and early AMD groups.

Additionally the fundus and OCT images were assessed subjectively, specifically the participants regarded at the highest risk of progression to advanced AMD (i.e. those with drusenoid PED, [21] confluent drusen or a fellow eye with advanced AMD [18]) were compared to those at lowest risk (i.e. those with normal fellow eyes and none of the high-risk features listed above).

Results

The study involved 32 participants consisting of a control (n=16) and early AMD (n=16) group. The control group (n=16) had a mean age of 67.6±5.4 years, and a mean axial length of 23.7±0.8 mm. The early AMD group (n=16) had a mean age of 71.6±8.5 years, and a mean axial length of 23.2±0.7 mm. The mean age (P=0.12, independent t-test) and axial length (P=0.09, independent t-test) of the two groups were not significantly different. The clinical features of the participants with early AMD are shown in Table 1.

The mean retinal thickness for participants in the control and early AMD groups was plotted for each retinal location and is shown in Figure 2 for the horizontal meridian and Figure 3 for the vertical meridian. The mean retinal thickness was found to be smallest at the fovea (F) for both groups, increasing with eccentricity in both vertical and horizontal meridians to reach a maximum at 1mm, before declining with further increase in eccentricity. Central retinal thickness, measured at the fovea (F), was 202±18µm for the control group, and 179±27µm for the early AMD group, this difference was significant (P=0.008). Table 2 shows mean retinal thickness at each retinal location and the P-value for the difference between the groups. The early AMD group was found to have significantly thinner retinal thickness values at the fovea and eccentricities out to 1 mm, extending to 1.5 mm temporally.

Mean choroidal thickness was plotted for each retinal location measured along horizontal and vertical meridians (Figures 4 and 5). In the horizontal meridian, choroidal thickness was found to be greatest at the fovea (F), decreasing to a minimum nasally, and showing a more modest reduction in thickness temporally. There was less variation in choroidal thickness in the vertical meridian. Central choroidal thickness, measured at the fovea (F), was 213±63 µm for the control group, and 231±70 µm for the early AMD group, this difference was not significant (P>0.05, independent t-test). Table 3 shows mean choroidal thickness at each retinal location and the P-value for the difference between each group, the difference between groups was not significant at any location for choroidal thickness.

OCT and macular photographs of those at most and least risk of progression to advanced AMD were compared subjectively to identify qualitative differences. Participant 1 (Figure 6), has a low risk of progression to advanced AMD[22] , whereas participant 14 is at high risk of progression.[21] A common feature identified on the OCT images of both participants was a localised thinning of the photoreceptor layer overlying drusen or pigment epithelial detachments, this is exemplified in Figure 6, although underlying choroidal thickness appears unaffected.

Discussion

This study used enhanced choroidal penetration (1060nm) OCT to assess the thickness of the choroid in patients with early AMD. It was found that retinal thickness differed significantly at the fovea, and at a number of extrafoveal points, between individuals with early AMD and age-matched controls. However, there were no significant differences in choroidal thickness at any eccentricity assessed.

The one previous study which used a 1060nm OCT system to evaluate the choroid in age-related macular disease recruited participants with the late, neovascular form of AMD (n=12).[12] Yasuno et al. compared images obtained using long wavelength OCT to the standard 830nm FD-OCT in visualising the morphology of structures beneath the RPE, such as choroidal neovascular membranes. They found a general improvement in the image contrast of sub-RPE structures in most eyes and, in 3 eyes, were able to see hyper-reflective structures beneath the choroidal neovascular membranes, not accessible using the 830nm OCT. However, the study did not evaluate disease-related changes in the thickness of the choroid.

This study provides *in vivo* evidence that choroidal thickness may not be affected by early AMD. Histological studies have been carried out to investigate the cross-sectional area and thickness of the choriocapillaris of donor eyes from individuals with early and advanced AMD. [14-16] Our data are in agreement with a study reporting a significant decrease in choriocapillary density in 25 eyes with features of AMD, but finding no significant decrease in the thickness of the choroid compared to age-matched controls.[14] Our data are also supported by a recent study by Chung et al. (2011) evaluating choroidal thickness in early AMD using the 870nm OCT with an enhanced depth imaging technique. They also found a small, but statistically non-significant reduction in subfoveal choroidal thickness in the individuals with early AMD, compared to age-matched controls.[23]

However, there is evidence to suggest that choroidal thinning may occur in end-stage AMD.[15-16, 23] McLeod et al. examined the post-mortem choroid in 3 aged control eyes, 5 with geographic atrophy, and 3 with neovascular AMD and reported a linear relationship between the loss of RPE and choriocapillaris in geographic atrophy, and a 50% reduction in choroidal vascular cross-sectional area in eyes with wet AMD, even in the absence of RPE atrophy.[15] Sarks carried out a histological study on 378 eyes from patients aged 43-97 years, who had either normal fundi or some degree of AMD.[16] They reported thinning of the choroid, resulting in a 'tigroid' fundus appearance. Thinning was associated with increasing age both in aged patients classified as clinically normal and in those with all stages of AMD, but it was particularly prevalent in those with advanced AMD. A significant reduction in *in vivo* subfoveal choroidal thickness has also been reported in individuals with exudative AMD, in a study which used 870nm enhanced depth imaging OCT.[23]

Although there is strong evidence for the occurrence of age-related thinning of the choroid,[14, 16, 24] and for changes in choroidal perfusion in early AMD,[13, 25-26] evidence for thinning of the choroid specific to early AMD is not apparent in the literature. Our findings would suggest that any changes in the perfusion and blood flow dynamics of the choriocapillaris associated with early AMD are independent of choroidal thickness.

Multiple studies have assessed choroidal thickness in healthy individuals using the OCT,[23-24, 27-30] however, only a few have used a 1060nm system.[27-28] A recent study using 1060nm OCT to investigate the correlation between axial length and choroidal thickness in 34 healthy subjects (64 eyes) aged 19-80 years, found a

mean central choroidal thickness of 315μm (SD 106μm), with the choroid thinnest in the nasal parafovea.[27] Other studies have also found choroidal thickness to be greatest at the fovea, with a greater reduction in thickness with eccentricity reported nasally than temporally,[23-24, 28, 30] a pattern reflected in our findings from both controls and individuals with early AMD. The mean subfoveal choroidal thickness reported has varied between studies from 225μm (SD 53μm),[23] to 354nm (SD 111μm).[28] The control group employed in our study was found to have a slightly lower mean subfoveal choroidal thickness of 213μm (SD 63μm), which may reflect the greater mean age of the participants than in most previous studies.

A manual technique was used to identify the boundaries and measure the retinal and choroidal thickness in this study. Although more time-consuming than automated systems, there is evidence to suggest that manual measurement is more accurate, especially in the presence of disruption caused by diseases such as AMD.[31-33] Using this strategy, the mean retinal thickness was found to be lower in individuals with early AMD than in controls at all eccentricities; this reached statistical significance at the fovea and at extra foveal locations up to 1 mm eccentricity in all meridians .

Multiple comparisons were carried out in this study (17 retinal locations were evaluated). If these were unrelated variables then one might expect the null hypothesis to be wrongly rejected in 1 comparison out of 20 through chance alone (i.e. multiple testing increases the risk of a type I error). However, in this study, the retinal thickness measurements at different retinal locations were highly correlated, (mean r=0.72 across all retinal locations, Pearson's correlation coefficient). When variables tested are correlated, the risk of a type I error decreases as the probability of the null hypothesis being rejected due to chance is not multiplicative of the probability of each individual comparison being found significant by chance alone.[34] However, even if a correction method such as that described by Sankoh et al. is used,[35] which factors in the correlation between variables, retinal thickness remains significantly reduced in individuals with early AMD at the fovea (P=0.019), 0.5mm inferiorly (P= 0.039) and 0.5mm temporally (P=0.023).

A number of studies have used OCT to evaluate retinal thickness in eyes with advanced dry or wet AMD,[36-40] but there is less evidence regarding retinal thickness assessed using OCT in early AMD.[41-43] One study using FD-OCT on 17 eyes with early AMD and 17 healthy control eyes reported that photoreceptor layer thickness is reduced over drusen in eyes with early AMD, but that there is no evidence of a generalised reduction in thickness across the macular region.[43] Similarly, Kaluzny et al.[41] used FD-OCT to identify focal changes in retinal thickness in 24 eyes with soft drusen, localised to the position of the drusen. They reported evidence of photoreceptor atrophy anterior to the drusen, but not diffusely present across the macula. Malamos et al.[42] used FD-OCT to evaluate macular changes in 12 individuals with early AMD, as well as 37 with choroidal neovascularisation. They also found that discrete thinning of the retina above underlying drusen was the only abnormality in retinal thickness in patients with early macular disease, and that this was not sufficient to influence mean thicknesses of annuli centred on the fovea. This localised reduction in retinal thickness has been ascribed to the outer retina, with Schuman et al.[43] finding inner retinal thickness to be almost unchanged over drusen.

It is possible that the finding of a reduced retinal thickness in individuals with early AMD in our study reflects the photoreceptor degeneration reported to occur overlying drusen.[41-43] Although drusen areas were not specifically targeted for our measurements, subjective assessment of the images showed localised thinning of

the photoreceptor layer overlying drusen and PED (Figure 6). Histological findings from human donor eyes have suggested that a loss of photoreceptors (with a predilection for rods over cones) occurs in non-exudative AMD, which may explain such a reduction in retinal thickness.[44] The difference in retinal thickness between individuals with early AMD and age-matched controls in this study extended out up to 1.5 mm (5.2°) eccentricity. Curcio et al. [44] also reported that the location of greatest cell loss in age-related macular disease occurs within the parafovea/perifoveal region, from 1.5-10° from fixation. Further investigation of the individual intraretinal layer thicknesses and their relationship to clinical features in early AMD patients may indicate the cause or location of the retinal thickness loss identified.

Legaretta et al.[45] and Kakinoki et al.[46] reported foveal retinal thickness in healthy subjects of 258.2µm (SD 23.5µm) and 257.6µm (SD 19.6µm) respectively; thicker than the 202 µm (SD 18µm) found in this study. Both of these studies used the Cirrus OCT, [45-46] which utilised the same retinal boundaries as this study but measured the foveal thickness as an average over 500 µm centred on the fovea rather than at the foveola as in this study. The values found in this study are comparable to myopic foveal thickness measurements using a similar methodology to our own,[29] and to minimum foveal thickness in normal eyes found using a stratus OCT.[45-47]

Our overall approach to the analysis was conservative because we adopted an independent samples rather than a paired approach, despite having matched our groups for age and axial length. Based on the standard deviation of the foveal thickness measurements and the sample size, the smallest difference between groups detectable in this study was 24.8 and 64.7 µm for retinal and choroidal thickness respectively (with a power of 80% and a significance level of 0.05).[48] Intraobserver reliability has previously been assessed for retinal and choroidal thickness measurements by observer AW using the manual measurement technique employed in this study. Using the Bland and Altman technique,[49] the intraobserver coefficient of repeatability for measurement of foveal retinal thickness on two separate occasions was 18.9 µm for individuals with early AMD (n=17) and 15.7 µm for healthy control participants (n=24). For choroidal thickness measurements, an intraobserver coefficient of repeatability of 58.7 and 35.6 µm was obtained for early AMD and control participants respectively. This study was therefore powered to detect any difference which was greater than the measurement error of the technique.

Whilst a modest, but significant, reduction in retinal thickness in early AMD was shown, no significant change in choroidal thickness was found during this study. These findings suggest that measurement of choroidal thickness using OCT is not diagnostic for early age-related macular disease.

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Figure Captions

FIGURE 1: Optical coherence tomography (OCT) layer boundaries and measurement locations used in this study. (Left) A cross sectional 1060nm OCT b-scan, the superior row of arrows indicating the location of the inner limiting membrane (ILM), middle row the retinal pigmented epithelium (RPE) and the inferior row choroid-sclera boundary. These features were used to delineate the boundaries of the retina and choroid for thickness measurements. (Right) A fundus photograph with retinal locations overlaid (solid dots) at which each retinal and choroid thickness measurement was obtained. Retinal direction is indicated by S (Superior), I (Inferior), N (Nasal), and T (Temporal) as labelled.

FIGURE 2: Retinal thickness in early age related macular degeneration (AMD) along the horizontal meridian. Retinal thickness for normal (black squares) and early AMD (open circles) participants from 2mm nasal (left) to 2mm temporal (right) of the fovea. A * indicates retinal locations where a difference between groups is significant at the P=0.05 level. Error bars indicate standard error at each point. Measurement locations identified as fovea (F), nasal (N) and temporal (T) with eccentricity of 0.5, 1.0, 1.5 or 2.0 mm.

FIGURE 3: Retinal thickness in early age related macular degeneration (AMD) along the vertical meridian. Retinal thickness for normal (black squares) and early AMD (open circles) participants from 2mm inferior (left) to 2mm superior (right) of the fovea. A * indicates retinal locations where a difference between groups is significant at the P=0.05 level. Error bars indicate standard error at each point. Measurement locations identified as fovea (F), superior (S) or inferior (I) with eccentricity of 0.5, 1.0, 1.5 or 2.0 mm.

FIGURE 4: Choroidal thickness in early age related macular degeneration (AMD) along the horizontal meridian. Choroidal thickness for normal (black squares) and early AMD (open circles) participants from 2mm nasal (left) to 2mm temporal (right) of the fovea. Error bars indicate standard error at each point. Measurement locations identified as fovea (F), nasal (N) and temporal (T) with eccentricity of 0.5, 1.0, 1.5 or 2.0 mm.

FIGURE 5: Choroidal thickness in early age related macular degeneration (AMD) along the vertical meridian. Choroidal thickness for normal (black squares) and early AMD (open circles) participants from 2mm inferior (left) to 2mm superior (right) of the fovea. Error bars indicate standard error at each point. Measurement locations identified as fovea (F), superior (S) or inferior (I) with eccentricity of 0.5, 1.0, 1.5 or 2.0 mm.

FIGURE 6: Retinal and optical coherence tomography (OCT) images for two study participants. Macular photographs and corresponding OCT sections (scan locations indicated by arrow) for participants 1 (Top) and 14 (Bottom). Participant 1: (Top Left) photograph of localised pigmentary disturbance, with few drusen present, (Top Right) OCT image of a drusen. Participant 14: (Bottom Left) photograph of multiple large soft drusen, pigmentary disturbances and drusenoid pigment epithelial detachments (PED), (Bottom Right) OCT image of a drusenoid PED and soft drusen.

TABLE 1. Clinical features of participants with early age-related macular degeneration

Participant			Presence of Clinical Feature[2]				Contralateral Eye Status[4]
Number	Age (years)	Tested Eye[1]	Drusen >125µm (diameter)	Drusen >10 (number)	Hyper/Hypo Pigmentation	Drusenoid PED[3]	
1	56	R	N	N	Y	N	Normal
2	64	R	Y	N	N	N	Normal
3	80	L	Y	N	Y	N	Normal
4	79	L	N	N	Y	N	Early
5	70	L	Y	Y	N	N	Early
6	67	L	Y	N	N	N	Early
7	58	L	Y	N	Y	N	Early
8	87	L	Y	N	N	N	Early
9	73	L	Y	Y	N	N	Early
10	65	L	N	N	Y	N	Wet
11	74	L	N	N	Y	N	Wet
12	65	L	Y	Y	Y	N	Wet
13	75	R	Y	Y	N	N	Wet
14	78	R	Y	Y	Y	Y	Wet
15	79	R	Y	N	N	Y	Wet
16	75	L	Y	Y	N	Y	Wet

[1]. Tested eye denoted by R (right eye) and L (left eye).
[2]. Presence of clinical features denoted by Y (yes) and N (no).
[3]. Pigment Epithelial Detachment (PED).
[4]. “Early” or “Wet” denotes the subtype of age-related macular degeneration.

TABLE 2. Mean retinal thickness values at each location for both the control and early age-related macular degeneration groups

	Control Retinal Thickness (µm)		Early AMD[2] Retinal Thickness (µm)		T-test[3]
Location[1]	**Mean**	**±SD**	**Mean**	**±SD**	**(* P<0.05)**
F	202	18	179	27	0.008*
T0.5	274	24	247	31	0.011*
T1.0	299	23	278	27	0.030*
T1.5	282	22	267	20	0.038*
T2.0	255	22	241	18	0.055
N0.5	278	24	255	35	0.040*
N1.0	313	19	292	30	0.028*
N1.5	302	15	289	27	0.092
N2.0	276	20	271	22	0.480
S0.5	288	22	265	37	0.039*
S1.0	306	23	288	25	0.045*
S1.5	277	23	263	24	0.090
S2.0	252	19	239	21	0.083
I0.5	287	24	261	33	0.018*
I1.0	306	15	292	22	0.036*
I1.5	279	21	267	19	0.104
I2.0	253	23	244	15	0.205

[1]. Measurement locations identified as fovea (F), nasal (N), temporal (T), superior (S) or inferior (I) with eccentricity of 0.5, 1.0, 1.5 or 2.0 mm.
[2]. Age-related macular degeneration (AMD)
[3]. Independent t-test; p-values for differences between groups at each location are denoted by a star (*) where a difference is significant at the P=0.05 level.

TABLE 3. Mean choroidal thickness values at each location for both the control and early age-related macular degeneration groups

	Control Choroid Thickness (µm)		Early AMD[2] Choroid Thickness (µm)		T-test[3]
Location[1]	**Mean**	**±SD**	**Mean**	**±SD**	**(* P<0.05)**
F	213	63	231	70	0.429
T0.5	219	60	220	72	0.974
T1.0	213	65	211	71	0.940
T1.5	203	62	203	54	0.982
T2.0	195	54	204	47	0.593
N0.5	219	71	229	71	0.710
N1.0	199	74	218	80	0.505
N1.5	188	77	200	85	0.678
N2.0	162	70	162	80	1.000
S0.5	207	62	207	65	0.973
S1.0	210	75	208	79	0.952
S1.5	209	76	203	86	0.830
S2.0	195	63	207	83	0.640
I0.5	218	62	240	74	0.360
I1.0	215	64	230	69	0.529
I1.5	206	72	218	65	0.624
I2.0	196	54	212	73	0.487

[1]. Measurement locations identified as fovea (F), nasal (N), temporal (T), superior (S) or inferior (I) with eccentricity of 0.5, 1.0, 1.5 or 2.0 mm.
[2]. Age-related macular degeneration (AMD)
[3]. Independent t-test; p-values for differences between groups at each location did not exceed the P=0.05 significance level.