Choroidal Thickness in Geographic Atrophy Secondary to Age-Related Macular Degeneration

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Submitted: June 2, 2014
Accepted: December 17, 2014

Purpose. To analyze choroidal thickness (CT) in eyes with geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Methods. A total of 72 eyes of 72 patients (mean age, 75.97 ± 7.09 years) with GA and 37 eyes of 37 healthy controls (73.89 ± 6.19 years) were examined by confocal scanning laser ophthalmoscopy and enhanced depth imaging (EDI) spectral-domain optical coherence tomography. Choroidal thickness was measured at 25 defined points in horizontal and vertical scans. Geographic atrophy size was determined in fundus autofluorescence (FAF) images and GA subtypes were classified based on abnormal FAF in the perilesional zone.

Results. In GA, subfoveal CT (mCT) was significantly thinner compared to controls (173.03 ± 90.22 vs. 253.95 ± 69.19 μm, P < 0.001). Analysis of averaged measurements of all 25 points obtained per patient (mCT) revealed similar results (162.07 ± 76.26 vs. 228.00 ± 66.24 μm, P < 0.001). Spatial differences in CT between both groups were largest superior to the fovea. Addressing “diffuse-trickling” (n = 15) and “non–diffuse-trickling” (n = 57) GA independently, mCT was 114.67 ± 43.32 and 188.39 ± 93.26 μm, respectively (P = 0.002), with both groups being significantly thinner than controls (P < 0.001 for “diffuse-trickling” and P < 0.001 for “non–diffuse-trickling”). Similar results were obtained for mCT, which was 110.21 ± 29.66 μm in “diffuse-trickling,” 175.72 ± 79.02 μm in “non–diffuse-trickling” and 228.00 ± 66.24 μm in controls. Differences were significant with P = 0.002 between both GA groups and P ≤ 0.001 toward controls for each GA group.

Conclusions. The results indicate that the choroid in eyes with GA is thinner compared to normal eyes of similar age. Hereby, the extent of thinning is most pronounced in a specific subtype of GA identified by FAF imaging (“diffuse-trickling”). Such GA subtype–related differences in choroidal thickness may reflect heterogeneity in the pathogenesis of disease. (ClinicalTrials.gov number, NCT02051998.)

Keywords: geographic atrophy, choroidal thickness, fundus autofluorescence

Geographic atrophy (GA) represents a common late stage manifestation of various retinal diseases, including advanced age-related macular degeneration (AMD). While choroidal neovascularization (CNV) is a common cause of severe acute visual loss in AMD, approximately 20% of AMD patients who are legally blind have lost central vision due to GA.1–5 Although the exact pathogenetic mechanisms leading to GA still are poorly understood, chronic inflammatory processes, excessive lipofuscin accumulation in the RPE lysosomal compartment, complement system dysregulation, and vascular factors have been implicated in the development of AMD (see prior review6).

Histologically, areas of GA are characterized by degeneration of the RPE, of outer layers of the neurosensory retina, and the choriocapillaris.7–8 In vivo visualization of cross-sectional morphology of the retina and the RPE/Bruch’s membrane complex has become possible by the advent of optical coherence tomography (OCT).3,10 Recently implication of enhanced depth imaging (EDI) in spectral-domain OCT (SD-OCT) devices enabled the evaluation of structures beyond Bruch’s membrane, in particular the entire choroid and the choriocapillaris interface, thereby reproducible measurement of choroidal thickness (CT) became possible.9,11

Several studies have assessed CT in AMD.12–21 Some investigators find that CT is generally thinned in patients with AMD.12,13,16 Results obtained by others additionally suggest that choroidal thinning is present already in early stages of AMD without GA or neovascularization.13–23 In contrast, the work of Jonas et al.21 with a remarkable high case number did not show significant difference in CT between patients with AMD without GA and controls, after correcting for known influence factors. Also, Lee et al.22 did not find significant thinning of CT in early AMD. Two recent studies have assessed CT in GA in particular and concordantly find that the choroid is thinned in eyes with this late stage manifestation of AMD.19,22

Recent developments in retinal imaging allow for refined phenotyping of patients with GA. Based on abnormal patterns of fundus autofluorescence (FAF) in the perilesional zone of GA, different phenotypes have been identified in the context of the "Fundus-Autofluorescence imaging in Age-related Macular
Degeneration” (FAM) study (NCT00393692). Preliminary observations by SD-OCT imaging suggest that the “diffuse-trickling” phenotype exhibits a significantly thinner subfoveal choroid compared to other GA subtypes. This phenotype is characterized by a lobular GA configuration and a significantly faster progression compared to other GA phenotypes. Recent data further suggest an association of cardiovascular diseases with this GA subtype.

In view of these findings, a more refined analysis of choroidal thickness in GA with a focus on this specific phenotype appears prudent. In the present study, we analyzed choroidal thickness at multiple locations in the macula and investigated topographic differences between “diffuse-trickling” GA, “non-diffuse-trickling” GA, and controls, respectively. Furthermore, we assessed the correlation between GA size and subfoveal choroidal thickness.

**METHODS**

**Patients**

Patients with GA secondary to AMD were recruited in the context of the “Directional Spread in Geographic Atrophy” (DSGA) study (NCT02051998), which represents an extension trial of the FAM study (NCT00393692). Patients without retinal disease (“controls”) of similar age were recruited at the Department of Ophthalmology, University of Bonn. The study protocol complied with the Declaration of Helsinki and was approved by the institutional review board (File No. 197/12). Informed consent was obtained from each participant after explanation of the study’s nature and possible consequences of participation.

Only patients above 55 years of age willing to undergo the examination procedure, and with clear ocular media that allowed FAF and OCT imaging were included into the study. For inclusion into the GA group, GA secondary to AMD had to be present in the study eye with no signs of exudation. For inclusion in the control group, the absence of any stage of AMD was required.

General exclusion criteria were the presence of retinal diseases that could possibly confound the observations (e.g., diabetic retinopathy, retinal dystrophy, present or past exudative AMD, idiopathic serous chorioretinopathy), glaucoma, or refractive error > ± 3 diopters (D) spherical equivalent (SE). In case of previous cataract surgery, SE before surgery must have fulfilled this criterion or, if SE was not available, axis length had to be within the limit of 22.5 ± 1 mm (determined by IOL Master; Carl Zeiss Meditec, Jena, Germany). If both eyes were eligible, the right eye was selected as study eye.

**Image Acquisition**

The FAF images were obtained using Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) with an excitation wavelength of 488 nm and an emission spectrum of 500 to 700 nm in high speed mode. The field of view was set to 30° × 30° with a minimum resolution of 768 × 768 pixels and centered to the macula. Single FAF images were automatically aligned and averaged to maximize the signal-to-noise ratio using the manufacturer’s software (ART-mode, Heidelberg Eye Explorer, Heidelberg Engineering). Horizontal and vertical SD-OCT scans through the fovea were performed with the same device using EDI mode. The OCT scans were averaged (up to 100 single images) by making advantage of the ART-mode to improve the signal-to-noise ratio.

Statistical Analysis

Data were analyzed using SPSS 22 (IBM SPSS Statistics, Chicago, IL). Age, SE, and sex were compared between control and GA group using t-test for independent samples or Fisher’s exact test, respectively. If only axis length, but not SE, was available, this eye was not included into the comparison of SE.

With the data obtained from CT measurements, three separate analyses were performed: First, only the values obtained directly subfoveal (fCT) were analyzed. Second, the mean CT (mCT) calculated as the average of all 25 points measured was evaluated analogously. Interobserver agreements for fCT and mCT were assessed using the interclass correlation coefficient (ICC). The ICC was 0.98 for fCT and 0.99 for mCT. Finally, the peripheral data points were analyzed separately. Further analyses of fCT, mCT, and of the peripheral data points were based on the average between the two readers. Inter-reader averages were compared between the different groups. Comparison between the two groups “GA” and “control” was done using an unpaired Student’s or Welch’s t-test, respectively. Together with the control group, subsequent splitting of the “GA” group into a “diffuse-trickling” and a “non-diffuse-trickling” group resulted in a total of three independent groups. Differences among these three groups were assessed using a 2-way ANOVA followed by a pairwise group comparison in case a difference among the groups was found. Significance was assigned for P < 0.05.

Finally, GA size was calculated as the average of the measurements of the two readers. In case the senior reader was called, it was calculated as the average between the senior reader and the reader with the closer results. The GA size then were controlled manually to be localized through the fovea (Fig. IA).

**Image Grading**

Image grading included measurements of choroidal thickness and of atrophy size. Furthermore, the GA phenotype was classified based on the perilesional FAF patterns according to Holz et al. All measurements were performed by two independent readers.

**Measurement of Choroidal Thickness.** In horizontal and vertical OCT scans, choroidal thickness was measured as the distance between the outer border of OCT band 4 (corresponding to the RPE/Bruch’s membrane complex) to the inner scleral border using the Heidelberg Eye Explorer “distance tool” (Heidelberg Engineering). Measurements were performed subfoveally and in an interval of 500 μm up to 3 mm superior, inferior, nasal, and temporal of the fovea, respectively, resulting in 25 data points for each patient and eye. Points were measured and included into the analysis regardless of if the point was located right under an atrophic area or outside. If a reader considered a measurement to be impossible at one data point (e.g., due to insufficient imaging quality), this point was excluded from the analysis. When quality of the whole scan was considered insufficient for grading by at least one reader the whole eye was excluded.

**Measurement of Atrophy Size.** Semiautomated atrophy detection and quantification were performed based on FAF images using the RegionFinder software (version 1.7.1; Heidelberg Engineering). In case of discrepancy between the two readers (≥ 0.15 mm²), a senior reader was asked for arbitration. If atrophy exceeded the image frame, making proper determination of GA area impossible, the eye was excluded from the subanalyses correlating GA size and CT.

**Statistical Analysis**

Data were analyzed using SPSS 22 (IBM SPSS Statistics, Chicago, IL). Age, SE, and sex were compared between control and GA group using t-test for independent samples or Fisher’s exact test, respectively. If only axis length, but not SE, was available, this eye was not included into the comparison of SE.

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diffuse-trickling GA” groups by an unpaired t-test. Cases where GA size could not be measured were excluded from this analysis. Pearson’s correlation coefficient was calculated to test if CT correlated with GA size in the GA-group in general, and in the “diffuse-trickling” and “non-diffuse-trickling” groups independently.

All obtained values are given as mean ± SD in the text. Median and interquartile range (IQR) are given where indicated. When represented in a box-and-whiskers plot, the upper and the lower edge of the box represent the 25th and the 75th percentiles, respectively. The black horizontal bar in each box represents the median, and upper and lower ends of the whiskers represent the 1.5-fold IQR below or above the 25th and 75th percentiles, respectively. Outliers are given as either circles (moderate outliers between 1.5 and 3 IQR) or asterisks (>3 IQR).

RESULTS
A total of 72 eyes of 72 patients with GA (22 men, 50 women) and 37 eyes of 37 patients without retinal diseases (“controls,” 15 men, 22 women) were included into the analysis. Two eyes of control participants had to be excluded before the analysis due to insufficient quality of the EDI SD-OCT scans.

There was no significant difference in the mean age of the two groups (75.97 ± 7.09 vs. 73.89 ± 6.19 years, \( P = 0.14 \)). Mean SE (recorded at the date of examination or, in pseudophakic eyes, before cataract surgery) in eyes with GA was 0.12 ± 1.56 and 1.10 ± 1.59 D in control eyes (\( P = 0.003 \)).

Of the 72 patients with GA, 36 were pseudophakic, while 12 of 37 control patients had undergone cataract surgery before their inclusion into the study. Table 1 gives an overview of the patients’ characteristics.

Comparison of Choroidal Thickness Between Total GA Cohort and Controls
Measurement of CT at the 25 defined locations in all 109 eyes included into the analysis resulted in a total of 2725 points for which data were available from both readers. No data from both readers were available for 133 points (4.8% of total, 5.7% of control samples). Measurement of fCT was possible in all 109 patients. In eyes with GA, mean fCT was significantly thinner compared to eyes without retinal diseases (173.03 ± 90.22 vs. 253.95 ± 69.19 \( \mu \)m, \( P < 0.001 \)). Correspondingly, median fCT was 154.25 \( \mu \)m (IQR 115.63–199.63 \( \mu \)m) for eyes with GA and 260.00 \( \mu \)m (205.00–297.00 \( \mu \)m) for controls (Fig. 1B).

There was no significant difference in fCT between male and female neither in the GA (162.47 ± 79.62 vs. 177.68 ± 94.89 \( \mu \)m, \( P = 0.51 \)), nor in the control group (238.70 ± 66.44 vs. 264.34 ± 70.60 \( \mu \)m, \( P = 0.27 \)).

Analysis of averaged measurements in horizontal and vertical scans revealed that the choroid in eyes with GA was overall thinner compared to controls (mean mCT, 162.07 ± 76.26 vs. 228.00 ± 66.24 \( \mu \)m, \( P < 0.001 \)). Median mCT was 147.87 \( \mu \)m (IQR, 119.70–196.19 \( \mu \)m) for eyes with GA and 230.28 \( \mu \)m (IQR, 179.72–271.56 \( \mu \)m) for controls (Fig. 1C).

The mCT was 152.66 ± 62.06 \( \mu \)m for males and 166.22 ± 81.97 \( \mu \)m for females in the GA group (\( P = 0.49 \)), and 209.37 ± 60.61 and 240.70 ± 68.24 \( \mu \)m in the control group (\( P = 0.16 \)), respectively. In respect to location, largest differences in CT between both groups were seen superiorly of the fovea, while inferior and nasally from the fovea, the differences were smallest. The CT at all 25 data points obtained for both groups and their difference are given in Tables 2 and 3.
Comparison of Choroidal Thickness Between “Diffuse-Trickling” GA, “Non-Diffuse-Trickling” GA and Controls, Respectively

Mean subfoveal CT (i.e., fCT) in eyes with “diffuse-trickling” GA (n = 15) was thinner compared to eyes with “non-diffuse-trickling” GA (n = 57, 114.67 ± 43.32 vs. 188.39 ± 93.26 μm, P = 0.002). Comparison with control eyes revealed a significantly thinner subfoveal choroid for both groups (“diffuse-trickling” GA versus controls, P < 0.001; “non-diffuse-trickling” GA versus controls, P < 0.001). As illustrated in Figure 2A, median fCT for “diffuse-trickling” GA was 105.50 μm (IQR 86.50–150.50 μm) and 174.50 μm (IQR, 133.25–235.00 μm) for “non-diffuse-trickling” GA.

Analysis of averaged measurements in horizontal and vertical scans (i.e., mCT) revealed that in “diffuse-trickling” GA the choroid was overall thinner compared to “non-diffuse-trickling” GA (110.22 ± 29.66 vs. 175.72 ± 90.22 μm, P = 0.002) and controls (110.41 ± 30.10 vs. 228.00 ± 66.24 μm, P = 0.001), respectively. The difference between “non-diffuse-trickling” GA and controls was less pronounced, but also significant (P = 0.001). As given in Figure 2B, the median mCT of eyes with “diffuse-trickling” GA was 108.80 μm (IQR, 88.30–127.26 μm) while the median of eyes with “non-diffuse-trickling” GA was 156.45 μm (IQR, 130.85–204.08 μm).

Analysis of the single CT measurements performed in the peripheral macula showed that differences in CT between controls and “non-diffuse-trickling” and “diffuse-trickling,” respectively, were most evident in the superior direction (Tables 2–5).

Correlation Between GA Size and Choroidal Thickness

For 68 eyes with GA, lesion size could be determined (four eyes were not included into this subanalysis; in two eyes with “non-diffuse-trickling” GA, the lesion exceeded the image frame; in two “diffuse-trickling” GA eyes, FAF images were not available at the day of EDI SD-OCT imaging).

Mean GA size at time of CT measurements was 6.84 ± 5.80 mm², regardless of the GA subtype. In eyes with “diffuse-trickling” GA (n = 13, 12.69 ± 8.35 mm²), the atrophic lesions were significantly larger than in eyes with “non-diffuse-trickling” GA (n = 55, 5.45 ± 4.42 mm², P < 0.001).

Plotting fCT and mCT against GA size revealed a ρ of −0.226 for fCT (P = 0.06) and −0.222 (P = 0.07) for mCT, respectively (Figs. 3A, 3B). In the “diffuse-trickling” GA group ρ = −0.225 (P = 0.460) for fCT and −0.268 (P = 0.376) for mCT (Figs. 3A, 3B, open squares). In the “non-diffuse-trickling” GA group, ρ was −0.060 (P = 0.66) for fCT and −0.054 (P = 0.75) for mCT (Figs. 3A, 3B, black circles).

DISCUSSION

The present analysis reveals that CT in eyes with GA is thinner compared to control eyes without retinal disease and, therefore, is in concordance with previous studies. However, the current study indicated that choroidal thinning is related to the phenotypic variations of GA. Herein, “diffuse-trickling” GA shows a significantly thinner choroid compared to other GA subtypes. The fact that significance was achieved despite the relatively small number of participants illustrates the apparent strength of the effect.
To assess whether choroidal thinning was a phenomenon equally distributed over the macula or was predominant only in certain regions of the macula, CT was analyzed at multiple locations superior, inferior, nasally, and temporally of the fovea. Analysis revealed that differences were most pronounced in the superior direction.

The present analysis, in contrast with another recent study on 16 eyes that suggested a dependency between GA size and CT, did not reveal a clear correlation between those two parameters despite the considerably larger sample size in the current analysis.

While choriocapillaris atrophy in GA has been shown by pathohistological studies, a more generalized involvement of the choroid is subject to ongoing debates. Thinning of the choroid by 19% in AMD eyes compared to normal age-adjusted eyes, though not significant, has been observed histologically, and Spraul et al. disclosed a rarefaction of large chorial vessels underneath GA. The present study supports the hypothesis of a thinning of the choroid in GA in general, and not just of the choriocapillaris. The choroid is considered to account for only <5% to 10% of the whole choroidal depth. In contrast, the mean loss of CT observed here was 3.2% (mCT) and 29% (mCT), respectively, for all GA and was even more pronounced in the “diffuse-trickling” phenotype. Thus, the loss of CT does not appear to be attributable to choriocapillary thinning only.

The pronounced thinning of CT in “diffuse-trickling” GA indicated that impairment of large chorial vessel layer is a feature predominant in this GA phenotype. Indeed, there is resemblance with funduscopic characteristics of “diffuse-trickling” to that described in a recently reported entity called “age-related choroidal atrophy.” An impaired blood supply due to an atrophic choroid in the elderly was assumed as source of the funduscopic changes. Compared to patients with “age-related choroidal atrophy,” patients of the FAM cohort with “diffuse-trickling” were considerably younger (mean age at the time of CT measurement was 68.2 ± 10.9 years). Therefore, ageing alone would unlikely be the reason for such changes in this phenotype that may manifest relatively early in life as reported in the original cohort. However, in the elderly patients there might be a continuum between “diffuse-trickling” GA and “age-related choroidal atrophy.”

Assessing CT in any disease requires careful control for possible confounders. Several influence factors on CT have been described. These include nutritive, environmental, and constitutional conditions. In the present study, we controlled for age and myopia, two remarkably strong influencing factors. Concerning myopia, the GA patients in our collective were by 0.91 D more myopic than controls. The CT has been found to decrease by 8.7 to 15 μm per D myopia; therefore, the effect observed in the current study is unlikely to be explained by differences in refraction. In analog, per year of age, CT has been shown to decrease by 4.1 μm. Again, the effect expected by the difference in mean age between the groups can possibly not explain the remarkable thinner choroid in GA patients. Furthermore, in cohorts of younger patients recent studies found that CT was thinner in females than in males (though not significant), while other studies did not find differences. To investigate for a possible confounding effect of distinct sex distributions between the groups, we compared CT between males and females in the control and GA groups separately. In both groups, females exhibited a marginally thicker choroid than men, suggesting that the present findings will likely not have been biased by influences of different sex distribution.

Influence of IOP or blood pressure on CT has been discussed previously. A recent study, however, showed that in a multivariate analysis no association between blood pressure or IOP in general to CT was found. Patients with glaucoma had been excluded from the current analysis because choroidal thickness changes are under debate in this disease.

Furthermore, changes in CT in a circadian fashion have been reported. In the present study, patients underwent OCT exams at various times of the day. However, time of examination mainly depended on the availability of a trained examiner and, thus, should not be systematically different between the groups. Also water, coffee, or nicotine administration has been reported to influence CT. However, we did not control for these factors.

Sympathetic nerve stimulation has been shown to reduce choroidal flow. However, little consensus has been achieved on the influence of the sympathetic and parasympathetic
TABLE 4. Mean Values of the “Diffuse-Trickling” GA and the “Non–Diffuse-Trickling” GA Groups as Obtained From Measurements at Each of the 13 Locations (Including Subfoveally, fCT) Measured in the Horizontal EDI OCT Scans

<table>
<thead>
<tr>
<th></th>
<th>CT “Diffuse-Trickling”</th>
<th></th>
<th>CT “Non–Diffuse-Trickling”</th>
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<tbody>
<tr>
<td></td>
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</tr>
<tr>
<td>T 3000</td>
<td>163.81 ± 29.60</td>
<td>&lt; 0.001</td>
<td>207.08 ± 60.98</td>
<td>0.29</td>
</tr>
<tr>
<td>T 2500</td>
<td>145.90 ± 26.81</td>
<td>&lt; 0.001</td>
<td>195.15 ± 64.67</td>
<td>0.08</td>
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<tr>
<td>T 2000</td>
<td>145.47 ± 33.73</td>
<td>&lt; 0.001</td>
<td>193.28 ± 63.17</td>
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</tr>
<tr>
<td>T 1500</td>
<td>129.17 ± 57.19</td>
<td>&lt; 0.001</td>
<td>190.88 ± 63.095</td>
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</tr>
<tr>
<td>T 1000</td>
<td>129.33 ± 46.21</td>
<td>&lt; 0.001</td>
<td>193.26 ± 84.95</td>
<td>0.03</td>
</tr>
<tr>
<td>T 500</td>
<td>129.63 ± 43.61</td>
<td>&lt; 0.001</td>
<td>191.61 ± 91.15</td>
<td>0.01</td>
</tr>
<tr>
<td>fCT</td>
<td>114.67 ± 43.32</td>
<td>&lt; 0.001</td>
<td>188.39 ± 93.26</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>N 500</td>
<td>98.53 ± 45.30</td>
<td>&lt; 0.001</td>
<td>182.44 ± 95.68</td>
<td>0.001</td>
</tr>
<tr>
<td>N 1000</td>
<td>89.13 ± 43.75</td>
<td>&lt; 0.001</td>
<td>169.75 ± 97.61</td>
<td>0.003</td>
</tr>
<tr>
<td>N 1500</td>
<td>80.17 ± 33.60</td>
<td>&lt; 0.001</td>
<td>152.13 ± 93.89</td>
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</tr>
<tr>
<td>N 2000</td>
<td>78.30 ± 35.15</td>
<td>&lt; 0.001</td>
<td>126.31 ± 64.94</td>
<td>&lt; 0.001</td>
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<tr>
<td>N 2500</td>
<td>72.87 ± 22.00</td>
<td>&lt; 0.001</td>
<td>108.50 ± 54.871</td>
<td>&lt; 0.001</td>
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<tr>
<td>N 3000</td>
<td>69.39 ± 19.57</td>
<td>&lt; 0.001</td>
<td>96.84 ± 46.30</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Associated values for the control group are given in Table 2. T, temporal; N, nasal; number, distance to fovea in µm.

TABLE 5. Mean Values of the “Diffuse-Trickling” GA and the “Non–Diffuse-Trickling” GA Groups as Obtained From Measurements at Each of the 12 Locations Measured in the Vertical EDI OCT Scans

<table>
<thead>
<tr>
<th></th>
<th>CT “Diffuse-Trickling”</th>
<th></th>
<th>CT “Non–Diffuse-Trickling”</th>
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<td></td>
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<td></td>
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<tr>
<td>S 3000</td>
<td>136.29 ± 38.18</td>
<td>&lt; 0.001</td>
<td>196.43 ± 74.25</td>
<td>&lt; 0.001</td>
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<tr>
<td>S 2500</td>
<td>127.10 ± 42.85</td>
<td>&lt; 0.001</td>
<td>189.32 ± 72.64</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>S 2000</td>
<td>113.50 ± 40.22</td>
<td>&lt; 0.001</td>
<td>187.02 ± 87.22</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>S 1500</td>
<td>109.57 ± 35.39</td>
<td>&lt; 0.001</td>
<td>179.91 ± 81.04</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>S 1000</td>
<td>103.20 ± 42.62</td>
<td>&lt; 0.001</td>
<td>177.95 ± 89.40</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>S 500</td>
<td>104.18 ± 46.00</td>
<td>&lt; 0.001</td>
<td>179.20 ± 89.59</td>
<td>&lt; 0.001</td>
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<td>I 500</td>
<td>110.82 ± 47.73</td>
<td>&lt; 0.001</td>
<td>177.12 ± 93.98</td>
<td>0.001</td>
</tr>
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<td>I 1000</td>
<td>99.23 ± 34.14</td>
<td>&lt; 0.001</td>
<td>174.44 ± 95.56</td>
<td>0.01</td>
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<td>I 1500</td>
<td>95.70 ± 27.72</td>
<td>&lt; 0.001</td>
<td>166.46 ± 70.35</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>I 2000</td>
<td>97.47 ± 28.65</td>
<td>&lt; 0.001</td>
<td>163.60 ± 61.09</td>
<td>0.001</td>
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<tr>
<td>I 2500</td>
<td>108.37 ± 36.71</td>
<td>&lt; 0.001</td>
<td>172.11 ± 62.83</td>
<td>0.03</td>
</tr>
<tr>
<td>I 3000</td>
<td>108.11 ± 25.02</td>
<td>&lt; 0.001</td>
<td>167.13 ± 61.66</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Associated values for the control group are given in Table 3. S, superior; I, inferior; number, distance to fovea in µm.

FIGURE 3. Subfoveal CT (A) and mean CT (B) are plotted against GA size. “Diffuse-trickling” and “non–diffuse-trickling” GA data points are depicted as open squares and filled circles, respectively.
nervous system and data from humans, in particular OCT data are still missing.

In view of the variety of factors potentially influencing CT, it is noteworthy that the variance within the group of “diffuse-trickling” GA was lower than the variance in the control group and in the “non-diffuse-trickling” group as well, which additionally points toward a particular role of the choroid in this group.

Limitations of this study include that only 25 single loci of the choroid in the horizontal and vertical axes have been analyzed. Although we consider measurements at these points to be good estimates to reveal local changes in CT, analysis of choroidal thickness maps based on SD-OCT volume scans might be more significant. This is planned to be investigated in the ongoing study. Furthermore, only 15 eyes with the “diffuse-trickling” phenotype were included into the analysis. However, in a recent study, we have reported on a frequency of this phenotype of approximately 5% among eyes with GA. Therefore, the frequency of “diffuse-trickling” might even be overrepresented in the current analysis.

Yet, the evidence for a correlation between CT and choroidal blood flow still has not been established to our knowledge (see review). Hence, the pathophysiological relevance of “reduced choroidal thickness” is unclear. Application of new imaging devices, for example, Angio-OCT, may highly contribute to assess CT and choroidal blood flow correlation to elucidate the impact of choroidal thickness.

Patients with GA, in particular if the fovea is involved, may have instable fixation. Despite the eye-tracking algorithm implemented in the Spectralis HRA+OCT device, instable fixation may lead to reduced imaging quality. The possible bias to exclude patients with a thick choroid as the choroidal/sclera interface cannot be identified in low quality SD-OCT images cannot be eliminated completely. However, measurement of fCT was possible in all eyes and the portion of peripheral points that were not measurable did not vary considerably between both groups. Therefore, systematically distinct imaging quality is unlikely to have had a strong impact on the data presented here.

Finally, the present analysis represents a cross-sectional approach. In the ongoing study, we will assess the spatiotemporal relationship between GA development and choroidal thinning.

In conclusion, the results herein indicated that the choroid in eyes with GA is thinner compared to controls. However, choroidal thickness appears to differ between certain GA subtypes based on abnormal FAF patterns in the perilesional zone. The “diffuse-trickling” phenotype is associated with extensive choroidal thinning. Refined phenotyping in GA including fundus-autofluorescence appears prudent in future studies in patients with AMD to further explore discriminating features.

Acknowledgments

Supported by research grants from DFG (German Research Council): Ho 1926/1-3, FL 658/4-1; BONFOR 0-137-0012 (MF). The authors alone are responsible for the content and writing of the paper.

Disclosure: M. Lindner, Heidelberg Engineering (F), Carl Zeiss Meditec (F), Optos (F), Genentech (F), Novartis (R); A. Bezatis, Heidelberg Engineering (F), Carl Zeiss Meditec (F), Optos (F); J. Czauderna, Heidelberg Engineering (F); Carl Zeiss Meditec (F), Optos (F); E. Becker, Heidelberg Engineering (F), Carl Zeiss Meditec (F), Optos (F); C.K. Brinkmann, Heidelberg Engineering (F), Carl Zeiss Meditec (F), Optos (F); S. Schmitz-Valckenberg, Heidelberg Engineering (F), Carl Zeiss Meditec (F), Optos (F), Genentech (F), Novartis (F, C, R), Bayer (F, R), Allergan (F), Merz (F), Roche (F), Quintiles Commercial (R); R. Fimmners, None; F.G. Holz, Heidelberg Engineering (F, C, R), Carl Zeiss Meditec (F), Optos (F, C), Genentech (F, C, R), Novartis (F, C, R), Bayer (F, C, R), Acucela (C), Allergan (C), Boehringer Ingelheim (C), Merz (C); M. Fleckenstein, Heidelberg Engineering (F, R), Carl Zeiss Meditec (F), Optos (F), Genentech (F, R), Merz (C), Novartis (R), Bayer (R), P.

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