Choroidal Structural Analysis in Alzheimer’s Disease, Mild Cognitive Impairment, and Cognitively Healthy Controls

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**Purpose:** To assess choroidal structural parameters in symptomatic Alzheimer’s disease (AD), mild cognitive impairment (MCI), and cognitively healthy controls.

**Design:** Prospective cross-sectional study.

**Methods:** *Setting:* Outpatient neurological disorders clinic. *Study Population:* One hundred and twelve eyes of 67 individuals with AD, 143 eyes of 74 individuals with MCI, and 248 eyes of 137 controls. Individuals with diabetes, glaucoma, or retinal pathology were excluded. *Observation Procedure:* High-definition EDI foveal scans were obtained using Zeiss Cirrus HD-5000 AngioPlex (Carl Zeiss Meditec, Dublin, CA). Subfoveal choroidal thickness (SFCT) was measured by two masked graders with a third adjudicator. Total choroidal area (TCA), luminal area (LA), and choroidal vascularity index (CVI) were calculated after image binarization. *Main Outcome Measures:* Association of choroidal parameters with AD, MCI, or controls using generalized estimating equations, adjusted for age and sex.

**Results:** After adjustment for age, sex, and visual acuity, TCA was significantly greater in AD (β 2.73, p = 0.001) and MCI (β 4.38, p < 0.001) compared to controls, LA was significantly greater in AD (β 1.68, p = 0.001) and MCI (β 2.69, p < 0.001) compared to controls, and CVI was significantly lower in MCI (β -0.58, p = 0.002) compared to controls. SFCT was similar among AD, MCI, and controls on multivariable analysis (p > 0.05).

**Conclusions:** TCA, LA, and CVI may differ between individuals with AD, MCI, and healthy cognition, whereas SFCT may not differ between these groups. TCA, LA, and CVI deserve further study in individuals along the Alzheimer’s continuum.
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Short Title: Choroidal Structural Analysis in Alzheimer’s Disease
Alzheimer’s disease (AD), a neurodegenerative condition that is a leading cause of death and disability worldwide, continues to increase in prevalence. Estimates show that from 2020 to 2050, the number of individuals aged 65 or older living with AD is expected to increase from 5.8 to 13.8 million. While there are currently no disease-modifying treatments for AD, an increasing focus has been placed on developing biomarkers for early detection of AD. Recent work has implicated the retina as a potential biomarker for neurodegeneration in a variety of conditions. Studies have suggested that a diagnosis of preclinical (i.e. asymptomatic but with known AD biomarkers) or clinically evident AD may be associated with characteristic microvascular and structural alterations of the retina. While this is still a relatively nascent area of research, there is the potential that retinal changes may eventually be used as a surrogate biomarker for the diagnosis and prognosis of AD, both in clinical practice and in drug development trials.

Optical coherence tomography (OCT) has been widely used as a non-invasive method of assessing retinal structure in ocular disease. Improvements in OCT technology have led to improved image resolution and enhanced depth imaging (EDI), which allow for visualization of deeper structures of the retina and choroid. In recent years, subfoveal choroidal thickness (SFCT) has been assessed as a surrogate marker for various retinal and systemic pathologies including central serous retinopathy (CSR) and obstructive sleep apnea. SFCT has also been shown to decrease with age and increasing axial length.

Notably, the choroid has been assessed as a potential biomarker for neurodegenerative conditions including AD. A recent meta-analysis found that SFCT is significantly decreased in individuals with AD compared to controls. A greater reduction in SFCT over a year in individuals with AD compared to controls has been reported. SFCT has also been shown to decrease in individuals with mild cognitive impairment (MCI), a neurologic condition associated with objective cognitive deficits that do not significantly impact quality of life yet are more pronounced than normal age-related cognitive changes. MCI often progresses to AD. Thus, characterizing retinal biomarkers in MCI may guide research for potential AD biomarkers, as these diseases exist along a clinical spectrum.

Recently, a new method for assessing the structure and vascularity of the choroid, known as the choroidal vascularity index (CVI), has been developed. CVI uses image binarization techniques to determine the ratio of luminal area (LA) to total choroidal area (TCA) within the choroid on a given OCT EDI scan. Unlike CT measurements, CVI is relatively unaffected by physiologic parameters. CVI has been validated as a marker of ocular and systemic conditions, as it is increased in CSR and decreased in individuals with neovascular age-related macular degeneration or diabetes, even without diabetic retinopathy. To date, there have not been any attempts to characterize choroidal angioarchitecture as a potential biomarker in neurologic disorders including AD and MCI.

In this study, we evaluate whether patients with a diagnosis of AD, MCI, or healthy cognition may differ in choroidal measurements, specifically TCA, LA, CVI, and SFCT.

**METHODS**
This cross-sectional study (Clinicaltrials.gov identifier NCT03233646) was approved by the Duke Health Institutional Review Board (Pro00082598), followed the tenets of the Declaration of Helsinki, and complied with the Health Insurance Portability and Accountability Act (HIPAA) of 1996. Written informed consent was obtained from all subjects or their legal representative/power of attorney before enrollment.

**Study Participants**

Individuals aged 50 years or older with a clinical diagnosis of AD or MCI were enrolled from the Duke Neurological Disorders Clinics. Each patient’s diagnosis was confirmed prior to study participation by an experienced memory disorders specialist (AL) in accordance with diagnostic guidelines and recommendations of the National Institute on Aging-Alzheimer’s Association. Healthy volunteers aged 50 years or older without subjective memory impairment or a history of neurological disease were enrolled from the Duke Neurological Disorders Clinics and the Duke Alzheimer’s Disease Prevention Registry of cognitively healthy, community-dwelling volunteers who had a Montreal Cognitive Assessment (MoCA) score of 23 or higher. All individuals with a known history of non-AD dementia, diabetes mellitus, glaucoma, retinal pathology, or refractive error ≥ +6.0 diopters (D) or -6.0 D were excluded from analysis. Clinical and ophthalmologic history was obtained from patient medical records (when available) or verbal report from patient and caregiver. All participants underwent testing for corrected Snellen visual acuity (VA) on the day of enrollment, and individuals with VA of 20/40 or worse were excluded from analysis. All enrolled participants also underwent cognitive testing using the Mini-Mental State Examination (MMSE) at the time of image acquisition. Years of education were tabulated from the first grade onward.

**Image Acquisition and Data Collection**

All subjects were imaged using the Zeiss Cirrus HD-5000 Spectral-Domain OCT with AngioPlex OCT Angiography (Carl Zeiss Meditec, Dublin, CA, Software Version 11.0.0.29946). A high-definition 21-lineEDI foveal scan was acquired for each participant. Images with poor signal strength (less than 7/10), motion artifact, or focal signal loss were excluded. SFCT was assessed as a measurement from the hyper-reflective line of the outer border of the retinal pigment epithelium perpendicularly to the hyper-reflective sclerochoroidal junction centered at the base of the fovea. Two independent, masked graders (BWP, JHP) measured the SFCT and these measurements were averaged to determine the final value. In cases of significant measurement differences between the two graders, as defined by a coefficient of variation greater than 5%, a third grader (DSG) adjudicated the SFCT measurement.

TCA, LA, and CVI were measured as previously described by Agrawal et al. Image binarization was performed using public domain software ImageJ (National Institutes of Health, Bethesda, USA). Polygon tool was used to select the TCA, which was added in the region of interest (ROI) manager. After converting the image into 8 bit, Niblack auto local thresholding was subsequently applied which gave the mean pixel value with standard deviation for all the points. On the EDI foveal scans, the LA was highlighted by applying the color threshold. In order to determine the LA within the selected polygon, both the areas in ROI manager were selected and merged by ‘AND’ operation of ImageJ. The composite third area was added to the
ROI manager. The first area represents the total of the choroid selected, and the third composite area is the vascular or LA. The CVI was calculated by dividing LA by TCA.

**Statistical Analysis**

Multivariable statistical analysis was performed using Stata (StataCorp, College Station, TX, Software Version 15.1). Demographic variables including age, sex, VA, years of education, and MMSE were compared between AD, MCI, and control participants using a two-tailed t-test for continuous variables, chi-square analysis for categorical variables, and tobit regression for MMSE scores. Snellen VA measurements were converted to logarithm of the minimum angle of resolution (logMAR) for statistical analysis. Differences in SFCT, TCA, LA, and CVI were compared between AD, MCI, and control participants using generalized estimating equations (GEE) in order to account for the correlation between eyes of the same subject. Univariable models were constructed for each parameter and demographic or clinical variable, and multivariable GEE models were then constructed to adjust for the potential confounders of age, sex, and logMAR VA. In order to further explore the effects of choroidal thickness on choroidal structure across diagnostic groups, the entire cohort was divided into tertiles by SFCT measurement and then TCA, LA, and CVI values were graphed by diagnostic category among eyes with relatively thin choroid (< 219 µm), moderately thick choroid (219-290 µm), and relatively thick choroid (> 290 µm). Correlations between choroidal structural parameters and MMSE score were assessed using Spearman’s rank-order testing. An alpha of 0.05 was used in all analyses to define statistical significance.

**RESULTS**

One hundred and twelve eyes of 67 AD participants, 143 eyes of 74 MCI participants, and 137 eyes of 248 healthy controls were analyzed. Twenty-two AD eyes, 5 MCI eyes, and 26 healthy control eyes were excluded prior to analysis due to poor scan quality or other exclusion criteria as detailed above in Methods. Of these 22 AD eyes, 16 were excluded due to confounding medical or ocular diagnoses (diabetes, glaucoma, retinal pathology) and 6 eyes were excluded due to imaging concerns (poor image quality). All 5 MCI eyes and 24 control eyes were excluded due to ocular pathology; 2 control eyes were excluded due to poor image quality. Demographic data for included patients is reported in Table 1. Mean age of participants was only significantly different between the AD vs. control groups (p < 0.001). Sex distribution was significantly different between AD vs. MCI (p = 0.017) and MCI vs. control (p < 0.001) groups. Years of education significantly differed between AD vs. controls (p < 0.001) and MCI vs. controls (p < 0.001). MMSE scores differed significantly between AD vs. controls (19.77 ± 7.09 AD vs. 28.96 ± 2.73 controls, p < 0.001), AD vs. MCI (19.77 ± 7.09 AD vs. 24.45 ± 5.85 MCI, p < 0.001), and MCI vs. controls (24.45 ± 5.85 MCI vs. 28.96 ± 2.73 controls, p < 0.001) after controlling for years of education. LogMAR VA differed significantly between AD vs. controls (p < 0.001), AD vs. MCI (p = 0.001), and MCI vs. controls (p < 0.001), but all included patients had VA of 20/40 (logMAR 0.3) or better at the time of image acquisition.

Representative EDI OCT images from an eye of one individual with AD, one individual with MCI, and one healthy control are shown in Figure 1, along with corresponding choroidal segmentation for TCA, LA, and CVI analyses. Results of univariable and multivariable GEE
analyses for choroidal structural parameters among groups are included in Table 2. In multivariable analysis, age, sex, and logMAR VA were included as covariates.

TCA was significantly higher in AD vs. controls (β 2.73, p = 0.001) and in MCI vs. controls (β 4.38, p < 0.001) in multivariable analysis. TCA was lower in AD when compared to MCI participants in both univariable (β -2.01, p = 0.033) and multivariable analysis (β -1.80, p = 0.055); however, in multivariable analysis, this association did not reach statistical significance.

LA was significantly higher in AD vs. controls (β 1.68, p = 0.001) and in MCI vs. controls (β 2.69, p < 0.001) in multivariable analysis. LA was lower in AD vs. MCI in univariable (β -1.22, p = 0.033) and in multivariable analysis (β -1.10, p = 0.053); however, the association was not statistically significant in multivariable analysis.

CVI did not differ between AD and controls; however, CVI was lower in MCI vs. controls in multivariable analysis (β -0.58, p = 0.002). CVI was greater in AD vs. MCI participants in univariable (β 0.50, p = 0.039) and in multivariable analysis (β 0.39, p = 0.097); this difference did not reach statistical significance in multivariable analysis.

Mean SFCT was thinnest in AD and thickest in controls, with AD having the lowest SFCT (AD 230.19 ± 86.38 vs. MCI 262.59 ± 72.88 vs. controls 274.12 ± 98.26). SFCT was thinner in AD vs. controls in univariable analysis (β -43.84, p = 0.001) and multivariable analysis (β -26.97, p = 0.054); however, this difference did not reach statistical significance in multivariable analysis. SFCT was not significantly different between MCI vs. controls; however, SFCT was significantly thinner in AD vs. MCI participants in multivariable analysis (β -29.00, p = 0.017).

No statistically significant correlation was found between any choroidal structural parameter (SFCT, TCA, LA, CVI) and MMSE score (all p > 0.05).

Results of choroidal parameter breakdown by SFCT tertile are shown in Figure 2. Results of GEE analysis among diagnostic categories, after further breakdown by SFCT tertiles, were determined to be invalid due to diverging model estimates; thus, we may draw no definitive conclusions regarding choroidal parameter differences among these subgroups.

**DISCUSSION**

In our study, we characterized differences in choroidal structure between individuals with AD, MCI, and cognitively healthy controls. We demonstrated that TCA and LA significantly differed between individuals with AD and controls, as well as between individuals with MCI and controls, after adjusting for age, sex, and logMAR VA. We also observed that CVI, a measurement of choroidal vascularity, was lower in MCI relative to controls but did not differ significantly between individuals with AD and controls or individuals with AD and MCI on multivariable analysis. Finally, SFCT measurement was significantly thinner in AD compared to MCI after adjusting for covariates; however, SFCT measurement did not differ between AD or MCI compared to controls on multivariable analysis. Notably, differences in choroidal parameters between diagnostic groups were small, and measurement overlap did exist between eyes of different diagnostic groups. Thus, while choroidal structure may significantly vary
between individuals with AD and MCI compared to controls, it is unclear whether these parameters may serve as discriminative, objective biomarkers of disease presence.

To our knowledge, this study is the first to utilize automated image binarization techniques to assess choroidal structure and vascularity in individuals with AD, MCI, and normal cognitive health. By utilizing EDI foveal scans, we were able to provide holistic measurements of choroidal vascularity that may be more reliable than manual measurements of SFCT alone. Prior research by Kakiuchi and colleagues has shown that choroidal thickness may vary regionally, which suggests that accounting for the whole choroid in analyses may yield more reproducible results. In our study, we sought to minimize variation in manual measurements of SFCT by using two independent graders and a third adjudicator in the case of significant measurement variation. Using this method, we observed decreased SFCT in AD, but we found that SFCT may not significantly differ between AD and control eyes after adjustment for age, sex, and logMAR VA. Inclusion of age, sex, and logMAR VA as covariates in a model characterizing associations between SFCT and AD may also be warranted.

We analyzed LA, TCA, and CVI by SFCT tertile in order to determine whether eyes with thin or thick choroids had notably different choroidal structures by diagnostic group; however, our GEE analysis for these parameters had diverging parameter estimates and thus was interpreted to be invalid. We thus cannot conclude that eyes with thin or thick choroids have significantly different TCA, LA, or CVI among diagnostic groups when analyzed as subgroups.

In contrast to our hypothesis that CVI may be an objective biomarker for AD, we did not observe a difference in CVI between AD and controls. However, individuals with MCI did have decreased CVI relative to controls; this suggests a complexity to choroidal vascular changes in MCI and AD, as the increase in TCA outpaces the increase in LA (CVI is calculated as the ratio of LA to TCA) in individuals with MCI. It is possible that amyloid-beta (Aβ) deposition in the choroid increases TCA, with a subsequent compensatory increase in LA as the disease progresses across the continuum. Further work in individuals with MCI who have known biomarkers of AD pathology, in cerebrospinal fluid or on positron emission tomography imaging, may clarify the longitudinal changes of the choroidal vasculature in individuals with MCI and AD compared to cognitively healthy controls.

In our study, we observed increased TCA and LA in individuals with MCI relative to those with AD. This finding is surprising, as previously hypothesized mechanisms for choroidal vascular alteration have implicated Aβ accumulation and subsequent neurotoxicity as the mechanisms for decreased cerebral, and concomitantly retinal/choroidal, blood flow in AD. It is unlikely that all individuals with MCI in our study had a significant Aβ load, relative to those with AD, leading to increased choroidal area. A recent study by Lad et al demonstrated that inner retinal layers show a pattern of regional thickening and thinning as individuals progress from MCI to AD. Their group hypothesized that this regional pattern of thickening and thinning may be due to the dynamic process of neuroinflammation that accompanies Aβ deposition and eventually leads to neurotoxicity, retinal ganglion cell loss, and subsequent retinal thinning. A similar process may reflect choroidal changes along the clinical spectrum of MCI and AD – as the retinal vasculature is disrupted by Aβ deposition, neuroinflammation, and neurotoxicity. Subclinical ischemia may lead to increased choroidal vessel counts in earlier disease (i.e. MCI, early AD), while vessel
count/area may decrease as the disease progresses to AD. Our results also corroborate a recent histopathological study by Asanad et al. that showed that TCA and choroidal vascularity may differ between eyes with AD and controls.\textsuperscript{25} Notably, Asanad and colleagues observed that choroidal thinning and thickening may differ regionally in individuals with AD, and that choroidal thickening was correlated with increased vessel counts (represented by increased LA in our analyses).\textsuperscript{25} These prior studies support our finding that AD eyes had a greater TCA and LA than controls but less than those with MCI.

Our findings support the conclusion that TCA, LA, and CVI may be more appropriate \textit{in vivo} parameters when compared to SFCT to differentiate individuals with AD from those with MCI and from those who are cognitively healthy using retinal imaging. Additionally, our findings suggest that individuals with MCI may differ from cognitively healthy controls in their choroidal structure. It is possible that choroidal analysis may be able to track disease progression in individuals as they develop progressive cognitive impairment. Future research may determine whether individuals with MCI who eventually develop AD or individuals with preclinical AD (i.e. biomarker-confirmed) have different choroidal structural parameters compared to those who do not go on to develop AD and how these parameters may change over time.

This study has several limitations. First, we attempted to mitigate sex, age, and logMAR differences across groups by adjusting for these parameters as covariates in a multivariable GEE analysis. Second, while individuals in our study cohorts were diagnosed by expert neurologists in accordance with international clinical guidelines, we were not able to obtain either amyloid PET scans on participants due to high out-of-pocket costs as it is not currently part of routine clinical care or cerebrospinal fluid due to its invasive nature. Correlation of choroidal structural parameters with other established neurologic biomarkers of AD or MCI would be of interest. Study exclusion criteria such as diabetes, glaucoma, and refractive error relied on information in the patient medical record and verbal history from both the patient and caregiver. Since high axial length may influence choroidal thickness measurements, it would be important to obtain axial length values in future work.\textsuperscript{26,27} Axial length measurement was not routinely performed as part of this study given the absence of an A-scan unit at our primary imaging site (a neurological disorders clinic). We recognize that studies assessing choroidal structure may be limited by exclusion of axial length measurements; as such, this is a limitation of our work. Future studies should seek to include axial length as a covariate in multivariable analysis, particularly if it is found that axial length differs among diagnostic categories. Finally, we were not able to definitively prove a mechanistic explanation for changes in choroidal structure in this study due to its cross-sectional design.

This study has several strengths. The sample size was relatively large, we had strict exclusion criteria, and we only retained high-quality images for analysis. We also included two independent, trained, and masked SFCT graders and a third adjudicator to decrease variations in individual measurements. In addition, we utilized image binarization techniques on EDI foveal scans to report TCA, LA, and CVI, which may be more holistic measurements of choroidal vascularity than SFCT alone. Finally, we used GEE analysis adjusting for potential confounders such as age, sex, and logMAR VA and also accounting for the correlation between eyes in the same subject.
In conclusion, this study demonstrated that choroidal structural parameters may differ between eyes of individuals with a diagnosis of AD or MCI when compared to cognitively healthy controls. Specifically, TCA, LA, and CVI may differ between MCI and healthy controls, whereas SFCT appears to be relatively similar between the three disease groups. TCA, LA, and CVI deserve further study in individuals along the Alzheimer’s continuum. Longitudinal data may help better characterize these imaging parameters as potential biomarkers for the diagnosis and prognosis of these and other neurodegenerative disorders.

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Other Acknowledgments: None
REFERENCES


**FIGURE CAPTIONS**

**Figure 1:** Representative optical coherence tomography enhanced depth imaging foveal scans of three eyes of three individuals: one with Alzheimer’s disease, one with mild cognitive impairment, and one cognitively healthy control (A, B, and C, respectively). Manual subfoveal choroidal thickness measurements are shown in Panels A, B, and C. Measurements were taken from the hyper-reflective line of the outer border of the retinal pigment epithelium perpendicularly to the hyper-reflective sclerochoroidal junction centered at the base of the fovea. Images resulting from image binarization which were used in further choroidal structural analyses are shown below the corresponding foveal scans (D, E, F).

**Figure 2:** Box plots for total choroidal area (TCA) values (upper left panel), luminal area (LA) values (lower left panel), and choroidal vascularity index (CVI) values (right panel) across tertiles of subfoveal choroidal thickness (SFCT) and diagnostic category are shown. Groups with relatively thin choroid (< 219 µm), moderate choroid (219-290 µm), and thick choroid (> 290 µm) were analyzed. Sample sizes for each group are listed below each box-and-whisker plot. Lines inside boxes represent medians, ends of boxes represent 25th and 75th percentile values, and outer lines are equal to lower and upper adjacent values (defined as the largest observation less than or equal to the upper inner fence, which is the third quartile plus 1.5 times the interquartile range).
### Table 1: Demographic data for study participants.

<table>
<thead>
<tr>
<th></th>
<th>Alzheimer’s Disease (n = 67)</th>
<th>Mild Cognitive Impairment (n = 74)</th>
<th>Healthy Controls (n = 137)</th>
<th>AD vs Controls p-value</th>
<th>AD vs MCI p-value</th>
<th>MCI vs Controls p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean ± SD)</td>
<td>72.76 ± 8.07</td>
<td>70.04 ± 11.53</td>
<td>69.23 ± 7.71</td>
<td>&lt; 0.001</td>
<td>0.062</td>
<td>0.068</td>
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<td>Sex</td>
<td>66% female</td>
<td>55% female</td>
<td>72% female</td>
<td>0.52</td>
<td>0.017</td>
<td>0.001</td>
</tr>
<tr>
<td>Years of education (mean ± SD)</td>
<td>15.55 ± 2.79</td>
<td>15.58 ± 2.35</td>
<td>17.12 ± 2.28</td>
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<td>0.95</td>
<td>&lt; 0.001</td>
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<td>MMSE (mean ± SD)</td>
<td>19.77 ± 7.09</td>
<td>24.45 ± 5.85</td>
<td>28.96 ± 2.73</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
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<td>logMAR VA (mean ± SD)</td>
<td>0.22 ± 0.12 (n = 112)</td>
<td>0.16 ± 0.11 (n = 143)</td>
<td>0.099 ± 0.096 (n = 248)</td>
<td>&lt; 0.001</td>
<td>0.001</td>
<td>&lt; 0.001</td>
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</table>

SD = standard deviation; logMAR = logarithm of the minimum angle of resolution; VA = visual acuity; MMSE = Mini-Mental State Examination
Table 2: Results of choroidal structural analysis (mean ± standard deviation) and results of univariate and multivariate (controlling for age, sex, visual acuity) generalized estimating equations analysis.

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<td>Multivariate GEE</td>
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<td>β (95% CI)</td>
<td>p-value</td>
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<td>p-value</td>
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<tr>
<td>TCA (in²)</td>
<td>15.67 ± 5.76</td>
<td></td>
<td>17.56 ± 5.55</td>
<td>13.49 ± 3.32</td>
<td>-2.01 (3.86, -0.16)</td>
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<td>1.99 (0.51, 3.46)</td>
<td>0.008</td>
<td>2.73 (1.17, -4.29)</td>
<td>0.001</td>
<td>-1.80 (3.63, 0.036)</td>
<td>0.055</td>
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<td>-1.80 (3.63, 0.036)</td>
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<td>LA (in²)</td>
<td>9.92 ± 3.49</td>
<td>11.06 ± 3.37</td>
<td>8.58 ± 8.32</td>
<td>1.22 (0.33, 2.11)</td>
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<td>0.001</td>
<td>-1.10 (-2.21, 0.015)</td>
<td>0.053</td>
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<td>CVI (%)</td>
<td>63.8 ± 1.7</td>
<td>63.2 ± 1.24</td>
<td>63.8 ± 1.3</td>
<td>-0.074 (-0.52, 0.38)</td>
<td>0.50 (0.025, 0.98)</td>
<td>0.039</td>
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<tr>
<td></td>
<td>-0.17 (-0.63, 0.29)</td>
<td></td>
<td>0.50 (0.025, 0.98)</td>
<td>0.039</td>
<td>0.39 (-0.070, 0.84)</td>
<td>0.097</td>
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<td>0.097</td>
</tr>
<tr>
<td>SFCT (µm)</td>
<td>230.19 ± 86.38</td>
<td>262.59 ± 72.88</td>
<td>274.12 ± 98.26</td>
<td>-43.84 (-68.68, -18.99)</td>
<td>-26.97 (-54.43, 0.49)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>-33.03 (-57.91, -8.17)</td>
<td></td>
<td>-29.00 (-52.84, 5.17)</td>
<td>0.009</td>
<td>-10.73 (-32.66, 11.20)</td>
<td>0.338</td>
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</tr>
</tbody>
</table>

Journal Pre-proof
AD = Alzheimer’s disease; MCI = mild cognitive impairment; GEE = generalized estimating equations; TCA = total choroidal area; LA = luminal area; CVI = choroidal vascularity index; SFCT = subfoveal choroidal thickness; µm = micrometers; in = inches
Journal Pre-proof
Choroidal Structural Analysis in Alzheimer’s Disease, Mild Cognitive Impairment, and Cognitively Healthy Controls

Cason B. Robbins, BS – Biosketch

Cason Robbins received his B.S. from Mississippi College and is a current 4th year medical student at Duke University School of Medicine; he is applying for Ophthalmology residency. His research interests include endophthalmitis, interdisciplinary research in Ophthalmology and neurodegenerative disease, and optical coherence tomography angiography.
Choroidal Structural Analysis in Alzheimer’s Disease, Mild Cognitive Impairment, and Cognitively Healthy Controls


TABLE OF CONTENTS STATEMENT

In this cross-sectional comparative study of 112 eyes of 67 individuals with symptomatic Alzheimer’s disease (AD), 143 eyes of 74 individuals with mild cognitive impairment (MCI), and 248 eyes of 137 cognitively healthy controls, choroidal structural parameters including total choroidal area, luminal area, and choroidal vascularity index significantly differed between groups after adjustment for age, sex, and visual acuity. These parameters deserve further study in individuals along the Alzheimer’s continuum.
Choroidal Structural Analysis in Alzheimer’s Disease, Mild Cognitive Impairment, and Cognitively Healthy Controls


CRediT Author Statement:

Cason B. Robbins – Conceptualization; Investigation; Data Curation; Writing – Original Draft; Writing – Review and Editing; Visualization

Dilraj S. Grewal – Conceptualization; Methodology; Validation; Investigation; Data Curation; Writing – Review and Editing; Visualization

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James H. Powers – Investigation; Data Curation; Writing – Review and Editing

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