Choroidal Imaging with Swept-Source Optical Coherence Tomography in Patients with Birdshot Chorioretinopathy

Choroidal Reflectivity and Thickness

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Purpose: To characterize choroidal thickness and choroidal reflectivity in the eyes of patients with birdshot chorioretinopathy (BSCR).

Design: Cross-sectional observational study.

Participants: Two hundred twenty BSCR patients and 59 healthy controls.

Methods: Patients with BSCR and healthy controls underwent imaging of the macula in both eyes with a swept-source optical coherence tomography device (DRI-OCT1 Atlantis; Topcon). Images were exported from the device, and analysis was performed by 2 graders in the Doheny Image Reading Center using Image J software. The choroidal thickness at the foveal center was measured. In addition, the inner and outer boundaries of the choroid and retinal pigment epithelium (RPE) as well as the inner retinal surface all were segmented to allow the brightness and reflectivity of the pixels in the choroid, RPE band, and overlying vitreous to be quantified. An adjusted or normalized choroidal reflectivity, with the RPE as the bright reference standard and the vitreous as the dark reference standard, was computed using the formula: normalized choroidal reflectivity = (choroidal reflectivity/choroidal thickness)/RPE reflectivity.

Main Outcome Measures: Choroidal reflectivity and choroidal thickness.

Results: Three hundred eighty-six eyes in the BSCR group and 59 eyes in the control group were included in this analysis. Higher choroidal reflectivity and lower choroidal thickness were documented in inactive BSCR patients compared with active BSCR and controls (P < 0.01). Active BSCR patients showed lower choroidal thickness compared with controls (P < 0.01). There was a negative correlation between choroidal reflectivity and choroidal thickness (r = −0.793; P < 0.001). On multiple regression analysis, choroidal thickness, age, and disease duration (all P < 0.01) all were significant predictors of choroidal reflectivity.

Conclusions: Choroidal reflectivity and choroidal thickness changes are evident in active and inactive BSCR patients. Novel choroidal parameters such as choroidal reflectivity may warrant further study in the setting of BSCR.


Birdshot chorioretinopathy (BSCR) is a chronic, bilateral, posterior uveitis characterized by multiple hypopigmented choroidal lesions radiating from the optic nerve, vitreitis, retinal vasculitis, and macular edema. It affects primarily white persons and has a strong association with the HLA-A29 allele, which is present in more than 96% of patients.

Visual acuity seems to be a poor indicator of the disease severity and other disease-monitoring activity typically requires the use of diagnostic tests such as visual field assessment, color vision testing, electroretinography, fluorescein angiography, indocyanine green angiography, and optical coherence tomography (OCT). However, the pathogenesis of the disease remains poorly understood. Histopathologic studies show multiple foci of lymphocytes at different levels of the choroid near the choroidal vessels and around retinal vessels. Comparisons of hypopigmented birdshot lesions using fluorescein angiography, indocyanine green angiography, and fundus autofluorescence have not demonstrated a good correspondence, suggesting that the choroid, retinal pigment epithelium (RPE), and retina may be affected independently.

Advances in OCT imaging have allowed the choroid to be accessed with unprecedented detail. Conventional spectral-domain OCT acquisition often does not allow visualization of the entire choroid because of loss of sensitivity with depth. However, Margolis and Spaide introduced the technique of enhanced depth imaging OCT whereby the point of maximum intensity (zero delay line) was oriented to the choroidal side, thereby enhancing signal in the choroid. However, enhanced depth imaging acquisition is not the only strategy to improve choroidal imaging. Swept-source (SS) OCT devices use a longer
wavelength light source that penetrates more deeply into the choroid. In addition, SS OCT features less sensitivity loss with depth. As a result, choroidal image quality is much better with SS OCT, allowing more accurate and consistent automated segmentation of the choroid to generate choroidal thickness maps.\footnote{11}

Recently, studies evaluating the choroid in the eyes of birdshot patients using enhanced depth imaging OCT have revealed a generalized choroidal thinning, discrete hyper-reflective foci, and the presence of suprachoroidal hyporeflective spaces.\footnote{12,13} Another study demonstrated that the presence of suprachoroidal fluid was correlated with photopsias,\footnote{14} vasculitis, and vitreous haze.\footnote{14}

In this study, we aimed to evaluate the choroid using SS OCT in a large cohort of BSCR patients and to quantify choroidal changes that occur with the disease. This was carried out as part of an ongoing longitudinal cohort study from a single institution, initiated at Hôpital Cochin, Paris, France, to characterize the clinical course of BSCR. To characterize changes in the choroid more fully and to build on studies that have reported qualitative changes in the choroid,\footnote{12,13} we introduce here a new metric, normalized choroidal reflectivity, to quantify the reflective properties of the choroid, normalized against the reflectivity of the RPE and the vitreous. We also quantified choroidal thickness and compared these choroidal parameters with those of a control group.

Methods

Study Design

Two hundred twenty patients with BSCR from our longitudinal cohort underwent a standardized, prospectively defined evaluation and were recruited at the Hôpital Cochin, Paris, France, between September and December 2014. In addition, we also enrolled a group of healthy control participants if they met the criteria of no systemic disease, normal ocular examination results including dilated ophthalmoscopy, no evidence of previous ocular disease or surgery, and refraction within \( \pm 3 \) and \( +2 \) diopters of refractive error.

Study Protocol

The research protocol for this longitudinal study of BSCR has been described in detail in our previous publications.\footnote{1-5} All BSCR patients met criteria for diagnosis as previously defined by an international group of investigators and had the HLA-A*29 allele.\footnote{13} All patients underwent a complete ophthalmologic examination on a single day, including medical and ophthalmic history, assessment of best-corrected visual acuity, anterior segment examination, intraocular pressure measurement, dilated fundus biomicroscopy, fluorescein angiography (60’ Fundus Camera; Canon, Tokyo, Japan), and SS OCT (DRI OCT; Topcon, Japan). Presence of hyalitis was quantified as described by Nussenblatt et al.\footnote{16} Visual field testing was performed using automated perimetry with the Humphrey visual field analyzer using the FastPac full-threshold 30-2 program (Zeiss-Humphrey, San Leandro, CA). Axial length was measured using noncontact optical biometry (IOLMaster; Carl Zeiss Meditec, Germany). Evidence of disease activity was defined as the presence of vitreitis, vasculitis, or cystoid macular edema.

Ethic Statement

Signed informed consent documentation was obtained from all participants, and all research adhered to the tenets set forth in the Declaration of Helsinki. All study-related data acquisitions were approved by the institutional review boards (CERB d’Ile de France, Paris, France, and the University of California, Los Angeles, Institutional Review Board).

Swept-Source Optical Coherence Tomography Protocol

The Topcon SS OCT uses a 1050-nm wavelength light source and has a scanning speed of 100,000 A-scans per second. A 6-line radial pattern scan (1024 A-scans) centered on the fovea was obtained from each eye of all participants.

Image Analysis

Images were exported from the DRI OCT device, and analysis was performed by 2 independent masked graders (A.I.D. and L.K.) in the Doheny Image Reading Center using Image J software (https://imagej.nih.gov/ij/). Images first were inspected for quality and suitability for segmentation and further analysis. Optical coherence tomography scans were rejected if they were decentered, if they were of low quality such that the RPE band and choroid could not be segmented reliably, or if there was significant disruption of the retinal architecture or RPE such that the RPE could not be segmented or the choroid demonstrated patchy areas of hyper-transmission (Fig 1) from overlying RPE–photoreceptor loss that could lead to artificial increases in choroidal reflectivity unrelated to intrinsic choroidal changes.

The choroid was segmented in the B-scans, after identification of the outer border of the RPE band and the choroid–scleral junction as the inner and outer boundaries of the choroid. The choroidal cross-sectional area was quantified in pixels. In addition, sections of the overlying RPE band (at least 300 pixels) and vitreous (at least 500 pixels) also were segmented (Fig 2). The vitreous segment was selected specifically from an optically clear area free of any visible vitreous opacities or hyperreflective structures. After segmentation of these structures, the reflectivity or mean brightness of the pixels of the choroid, RPE, and vitreous could be measured using Image J.

Because the brightness of structures on OCT may be impacted by overall image quality, which may be affected by media opacity (cata-ract, vitreitis, etc.), normalization of signal between scans, eyes, and patients is of importance. We and others previously have reported on the use of optical density ratios to normalize the signal between cases. In accordance with our previous methods, a normalized choroidal reflectivity was computed by using the RPE as a bright reference standard and the vitreous as a dark reference standard through the use of the formula:

\[
\text{normalized choroidal reflectivity} = (\text{choroidal reflectivity} - \text{vitreous reflectivity})/\text{RPE reflectivity}
\]

Both gradings were averaged and the mean was used as choroidal reflectivity. Automated segmentation by the instrument software was used to measure central choroidal thickness in each scan. Each scan was inspected visually by the graders to confirm correct segmentation; otherwise, manual adjustments were performed to calculate the central choroidal thickness.

Statistical Analysis

Choroidal thickness and reflectivity parameters were calculated as mean \( \pm \) standard deviation. Comparisons in variables between 2 groups were made using an unpaired Student \( t \) test. One-way analysis of variance with post hoc analysis was used in comparisons involving more than 2 groups. Pearson correlation coefficients were computed to test for associations between parameters.

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Multiple regression analysis was performed to identify the relationship between multiple variables. The level of significance was set at 0.05. The intergrader agreement was assessed by comparing the results of the 2 independent masked graders. Intraclass correlation coefficients (ICCs) with 95% confidence intervals (CI) testing for absolute agreement between graders were computed.

Results

Clinical Characteristics of the Participants with Birdshot Chorioretinopathy

Of the 220 patients recruited for this study, images could be obtained in both eyes from 186 participants, for a total of 406 eyes. In the remaining 34 eyes, dense media opacities precluded image acquisition. Of the 406 eyes, an additional 20 were excluded because of insufficient image quality or extensive retinal disruption, shadowing, or hypertransmission precluding accurate segmentation or grading. Thus, a total of 386 eyes from 220 participants were included in the final analysis cohort.

The mean age of the BSCR cohort was 61.5±11.0 years. Axial length was 23.43±1.16 mm, and the mean disease duration was 10.6±7.5 years (range, 0–40 years). Sixty-three patients (29%) were using systemic steroids and 83 patients (38%) were being managed with nonsteroidal immunosuppressants at the time of imaging. One hundred twenty-nine patients (59%) were not actively receiving any systemic treatment for BSCR, whereas 52 patients (24%) had never received systemic steroids or immunosuppressants. One hundred fifty-six eyes were receiving local steroid treatment, whereas 72 eyes were completely treatment naïve.

Imaging in Eyes of Participants with Birdshot Chorioretinopathy

Analysis of imaging data from the BSCR group showed a mean reflectivity of the choroid of 109.7±21.0 units, mean reflectivity of the vitreous of 30.1±2.1 units, and mean reflectivity of the RPE of 193.2±14.9 units. The mean normalized choroidal reflectivity score in that group was 0.413±0.107 units. The cross-sectional choroidal area on the central B-scan was estimated to be 78 266±35 226 pixels and the choroidal thickness was 210.0±90.9 μm.

Normative choroidal reflectivity was correlated negatively with the cross-sectional choroidal area (r = –0.795; P < 0.001) and central choroidal thickness (r = –0.793; P < 0.001; Fig 3). As expected, cross-sectional area and thickness were highly correlated (r = 0.835; P < 0.001). There was also a positive correlation between normalized choroidal reflectivity and age (r = 0.529; P < 0.001), indicating an increase in reflectivity scores with increasing age (Fig 4). Central choroidal thickness was correlated negatively with age (r = –0.439; P < 0.001). However, we did not observe a
significant correlation between axial length and these choroidal parameters (normalized choroidal reflectivity, $P = 0.063$; central choroidal thickness, $P = 0.377$).

**Comparison between the Birdshot Chorioretinopathy and Control Groups**

The control group consisted of 59 eyes from 59 participants. There was no difference in age ($P = 0.112$) or axial length ($P = 0.278$) between the BSCR and control groups. Normalized choroidal reflectivity was higher in the BSCR group compared with the control group ($0.413 \pm 0.107$ vs. $0.367 \pm 0.082$, respectively; $P = 0.008$; Table 1). Choroidal thickness was lower in the BSCR group compared with the control group ($210.0 \pm 90.9$ vs. $267.9 \pm 91.7$ μm; $P < 0.001$). Vitreous reflectivity also was higher in the BSCR group ($P = 0.002$).

One hundred twenty eyes were grouped as active BSCR based on the presence of any criteria, macular edema, vasculitis, or hyalitis. The inactive group consisted of eyes that showed no evidence of any of the above. Choroidal thickness was significantly lower in the inactive BSCR group ($197.5 \pm 88.5$ μm), followed by the active BSCR group ($236.7 \pm 93.5$ μm) and the controls ($271.6 \pm 88.4$ μm) that had the highest choroidal thickness (Table 2). Normalized choroidal reflectivity was significantly higher in the inactive BSCR group ($0.433 \pm 0.111$) compared with both the active BSCR group ($0.373 \pm 0.086$) and the control group ($0.371 \pm 0.084$), whereas the active BSCR and control groups showed no difference (Table 3).

In addition, we assessed whether choroidal thickness and normalized choroidal reflectivity were different in eyes with macular edema on OCT compared with those without edema. Overall, 47 eyes in the study had macular edema. The group of BSCR patients without macular edema demonstrated a lower choroidal thickness and a higher normalized choroidal reflectivity compared with the control group. The BSCR group with macular edema showed no statistically significant differences when compared with either the control group or the BSCR group without edema (Tables 2 and 3). Furthermore, we tested if retinal vasculitis was associated with differences in choroidal thickness and normalized choroidal reflectivity. Vasculitis was evident in 64 eyes. The BSCR group without evidence of vasculitis showed lower choroidal thickness and higher normalized choroidal reflectivity compared with either the BSCR group with vasculitis changes or the controls (Tables 2 and 3).

We also evaluated any association between choroidal parameters and clinical grades of inflammation, such as the presence of hyalitis at the time of OCT examination. Fifty-four of 386 eyes had hyalitis on the day of examination, with 47 eyes characterized as having grade 1 hyalitis and 7 eyes characterized as having grade 2 hyalitis. The BSCR group without hyalitis again showed thinner central choroidal thickness and higher normalized choroidal reflectivity compared with eyes with hyalitis and controls (Tables 2 and 3). There was no difference in choroidal thickness or choroidal reflectivity between grade 1 and grade 2 hyalitis eyes ($P > 0.3$ for both comparisons), although it should be noted that only 7 eyes had grade 2 hyalitis. Differences in measured cross-sectional area also were observed. Eyes without evident hyalitis had a lower total cross-sectional area compared with those with hyalitis and controls ($75.577 \pm 33.298$ vs. $93.707 \pm 38.994$ vs. $97.176 \pm 30.536$ pixels, respectively; $P < 0.001$). There was also no difference in vitreous reflectivity scores ($P = 0.632$) or in measured standard deviation of the vitreous reflectivity score within the measurement window ($P = 0.154$) between patients without clinical hyalitis, with hyalitis grade 1, or with hyalitis grade 2.
A significant relationship was found between normalized choroidal reflectivity and disease duration, suggesting that patients who have had the disease longer are more likely to have a higher normalized choroidal reflectivity score ($r = 0.409; P < 0.001$; Fig 5). A statistically significant negative correlation was observed between choroidal thickness and disease duration ($r = -0.267; P < 0.001$). To investigate the relative effect of different parameters on normalized choroidal reflectivity, multiple regression analysis

**Figure 4.** Scatterplots illustrating the relationship between age and (A) normalized choroidal reflectivity ($r = 0.529; P < 0.001$) and (B) choroidal thickness ($r = -0.439; P < 0.001$).

**Association between Clinical Parameters, Choroidal Thickness, and Normalized Choroidal Reflectivity in Birdshot Chorioretinopathy**

A significant relationship was found between normalized choroidal reflectivity and disease duration, suggesting that patients who have...
was performed and choroidal thickness (standardized β coefficient, −0.646; \( P < 0.001 \)), age (standardized β coefficient, 0.256; \( P = 0.003 \)), and disease duration (standardized β coefficient, −0.096; \( P < 0.001 \)) remained as independent significant predictors in the model (\( R^2 = 0.651 \)). There was a weak correlation between age and disease duration in this cohort (\( r = 0.172; P < 0.001 \)). In addition, foveal sensitivity and visual field mean deviation were not correlated with normalized choroidal reflectivity scores (\( P > 0.1 \)) or central choroidal thickness (\( P > 0.7 \)). Finally, the eyes of patients currently receiving therapy (corticosteroids, immunosuppressants, or both) had larger choroidal thickness (227.7±92.0 vs. 196.6±87.0 μm; \( P = 0.001 \)) and lower choroidal reflectivity values (0.389±0.099 vs. 0.430±0.111, respectively; \( P < 0.001 \)) compared with patients not receiving any therapy.

### Agreement between Observers

Excellent agreement was observed between graders for choroidal reflectivity with an ICC of 0.999 (95% CI, 0.986–0.993), with good agreement in reflectivity of the RPE (ICC, 0.784; 95% CI, 0.717–0.833) and the vitreous (ICC, 0.835; 95% CI, 0.758–0.882). Normalized choroidal reflectivity also showed good agreement between graders, with an ICC of 0.877 (95% CI, 0.852–0.899). Finally, agreement in measured cross-sectional area was excellent with an ICC of 0.939 (95% CI, 0.898–0.960).

### Discussion

In this analysis, we characterized and quantified choroidal parameters in eyes with BSCR using SS OCT and introduced the use of a new metric, normalized choroidal reflectivity. Because the choroid in BSCR is known to feature infiltration with inflammatory cells, one might expect the brightness or reflectivity of the choroidal stroma and the choroid overall to change in the setting of BSCR. Indeed, in this analysis, we observed that the normalized choroidal reflectivity was higher in BSCR patients compared with age-matched healthy controls. Moreover, the normalized choroidal reflectivity seemed to be lower in the setting of active disease (as determined by the presence of hyalitis, vasculitis, or macular edema) compared with inactive disease, suggesting that it could be a potential biomarker for disease activity. Choroidal reflectivity also showed a correlation with choroidal thickness, with lower reflectivity in the setting of greater choroidal thickness. The choroid overall was thinner in the inactive BSCR group compared with the active BSCR and healthy control groups.

Reflectivity, rather than thickness alone, has been proposed as a potentially useful quantitative metric that can be

### Table 1. Measured Parameters in the Birdshot Chorioretinopathy and Control Groups

<table>
<thead>
<tr>
<th>Birdshot Chorioretinopathy Group</th>
<th>Control Group</th>
<th>( P ) Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalized ChR</td>
<td>0.413±0.107</td>
<td>0.367±0.082</td>
</tr>
<tr>
<td>Reflectivity of the choroid</td>
<td>109.7±21.0</td>
<td>100.9±16.1</td>
</tr>
<tr>
<td>Reflectivity of the RPE</td>
<td>193.2±14.9</td>
<td>196.6±12.6</td>
</tr>
<tr>
<td>Reflectivity of the vitreous</td>
<td>30.1±2.1</td>
<td>28.9±3.0</td>
</tr>
<tr>
<td>Cross-sectional choroidal area</td>
<td>78 266±35 226</td>
<td>97 176±30 536</td>
</tr>
<tr>
<td>Central choroidal thickness (μm)</td>
<td>210.0±90.9</td>
<td>267.9±91.7</td>
</tr>
</tbody>
</table>

ChR = choroidal reflectivity; RPE = retinal pigment epithelium.

*Independent samples t test.

### Table 2. Choroidal Thickness in the Inactive and Active Birdshot Chorioretinopathy Groups and in the Control Group Based on the Presence of Macular Edema on Optical Coherence Tomography, Vasculitis, or Hyalitis or Based on the Presence of any of These 3 Criteria

<table>
<thead>
<tr>
<th>Inactive Birdshot Chorioretinopathy (Group A)</th>
<th>Active Birdshot Chorioretinopathy (Group B)</th>
<th>Control Group (Group C)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on OCT macular edema</td>
<td>207.3±91.0</td>
<td>229.5±89.4</td>
<td>Overall, &lt;0.001</td>
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<td></td>
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<td></td>
<td>A vs. B, 0.117</td>
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<td></td>
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<td></td>
<td>A vs. C, &lt;0.001</td>
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<td></td>
<td></td>
<td></td>
<td>B vs. C, 0.027</td>
</tr>
<tr>
<td>Based on presence of vasculitis</td>
<td>202.5±89.1</td>
<td>246.6±95.2</td>
<td>Overall, &lt;0.001</td>
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<td></td>
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<td>A vs. B, &lt;0.001</td>
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<td>A vs. C, &lt;0.001</td>
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<td>B vs. C, 0.200</td>
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<tr>
<td>Based on hyalitis</td>
<td>203.9±87.1</td>
<td>254.2±103.5</td>
<td>Overall, &lt;0.001</td>
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<td>A vs. B, &lt;0.001</td>
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<td>A vs. C, &lt;0.001</td>
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<td>B vs. C, 0.428</td>
</tr>
<tr>
<td>Based on any of the 3 criteria</td>
<td>197.5±88.5</td>
<td>236.7±93.5</td>
<td>Overall, &lt;0.001</td>
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<td></td>
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<td>A vs. B, &lt;0.001</td>
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<td>A vs. C, &lt;0.001</td>
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<td>B vs. C, 0.029</td>
</tr>
</tbody>
</table>

OCT = optical coherence tomography.
Table 3. Choroidal Reflectivity in the Inactive and Active Birdshot Chorioretinopathy Groups and in the Control Group Based on the Presence of Macular Edema on Optical Coherence Tomography, Vasculitis, or Hyalitis or Based on the Presence of Any of These 3 Criteria

<table>
<thead>
<tr>
<th></th>
<th>Inactive Birdshot Chorioretinopathy (Group A)</th>
<th>Active Birdshot Chorioretinopathy (Group B)</th>
<th>Control Group (Group C)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on OCT macular edema</td>
<td>0.417±0.107</td>
<td>0.387±0.107</td>
<td>0.371±0.084</td>
<td>Overall, 0.008</td>
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<td>A vs. B, 0.073</td>
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<td>A vs. C, 0.006</td>
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<td>B vs. C, 0.459</td>
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<tr>
<td>Based on presence of vasculitis</td>
<td>0.424±0.107</td>
<td>0.357±0.085</td>
<td>0.367±0.084</td>
<td>Overall, &lt;0.001</td>
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<td>A vs. B, &lt;0.001</td>
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<td></td>
<td>A vs. C, &lt;0.001</td>
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<td></td>
<td>B vs. C, 0.531</td>
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<tr>
<td>Based on hyalitis</td>
<td>0.422±0.108</td>
<td>0.361±0.088</td>
<td>0.367±0.084</td>
<td>Overall, &lt;0.001</td>
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<td>A vs. B, &lt;0.001</td>
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<td>A vs. C, &lt;0.001</td>
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<td>B vs. C, 0.695</td>
</tr>
<tr>
<td>Based on any of the three criteria</td>
<td>0.433±0.111</td>
<td>0.373±0.088</td>
<td>0.371±0.084</td>
<td>Overall, &lt;0.001</td>
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<td>A vs. B, &lt;0.001</td>
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<td>A vs. C, &lt;0.001</td>
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<td>B vs. C, 0.938</td>
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OCT = optical coherence tomography.

extracted from OCT data. Several studies have explored the potential value of reflectivity analysis to assess vitreitis, the retinal nerve fiber layer, the lamina cribrosa, and subretinal hyperreflective material in neovascular age-related macular degeneration. 17–20 Hu et al. 21 emphasized the importance and effectiveness of normalization of reflectivity in OCT data through the use of an internal bright and dark reference standard by demonstrating that normalization could be used to harmonize the intensity profiles of different retinal layers between different OCT devices. Given its vascular nature and complex structure, it may be difficult to characterize changes in the choroid; therefore, quantitative parameters can be useful to evaluate structural morphologic changes that occur in disease and are not readily detected qualitatively when viewing the OCT scans. Therefore, normalized choroidal reflectivity and choroidal thickness could characterize choroidal involvement by a disease process. In fact, these 2 parameters are shown to be correlated in the present study. Normalized choroidal reflectivity may be affected by the relative thinning of the choroid and the changes in the relative proportions of laminar and stromal areas in the choroid. However, it is possible that these 2 choroidal parameters also carry independent information. Longitudinal follow-up of these patients will be of importance to define better the relevance of choroidal reflectivity and choroidal thickness.

Our results highlight the choroidal changes that occur in patients with BSCR. In particular, patients with active BSCR manifest both higher normalized choroidal reflectivity and lower choroidal thickness compared with controls. Keane et al. 12 described characteristic choroidal changes in a cohort of BSCR patients using macular and extramacular OCT imaging. They reported thinning or absence of the Sattler layer, generalized thinning, discrete hyperreflective foci, focal depigmentation, and the presence of a suprachoroidal hyporeflective space. These hyperreflective foci were thought to represent lymphocytic aggregates, and it is possible that they contributed to the increased normalized choroidal reflectivity values seen in our BSCR group. 6,22,23

Our finding of a thinner central choroidal thickness agrees with previous reports by Keane et al. 12 and Silpa-Archa et al. 13 using spectral-domain OCT. In the study by Keane et al, 12 patients were scanned both in the macula and in extramacular locations with spectral-domain OCT, and the authors also reported significantly thinner foveal choroidal thickness compared with controls. In the study by Silpa-Archa et al in 8 BSCR patients, a thinner central choroidal thickness was observed in 8 inactive BSCR eyes compared with historical controls, whereas no difference was found between the 4 active BSCR eyes in the study and controls. 13 This is in agreement with the findings of this study, but now in a much larger cohort. In the study by Birnbaum et al. 14 in 14 BSCR patients, the authors did not measure choroidal thickness; however, they did report that the presence and thickness of the suprachoroidal fluid band correlated with vasculitis and haze, but not with the presence of macular edema.

Based on our data, clear changes were evident in both choroidal thickness and choroidal reflectivity in patients in the inactive BSCR group compared with either those with active BSCR or healthy controls. In fact, choroidal thickness also was able to discriminate between active BSCR patients and controls, whereas choroidal reflectivity did not differ in these groups. This suggests that choroidal reflectivity and choroidal thickness may provide independent and useful information in evaluating disease. Especially in the case of BSCR patients who were grouped based on the presence or absence of macular edema, only the patients without edema showed differences in both choroidal metrics compared with controls. In patients with macular edema, the choroid is thinner, but the reflectivity of the choroid is comparable with that of the control group. Interestingly, in the case of vasculitis, the group of patients without evidence
of vasculitis on fluorescein angiography showed clear changes in both choroidal thickness and reflectivity compared with either the group of BSCR patients with vasculitis or the control group. This was also the case with vitreitis.

Interestingly, higher normalized choroidal reflectivity and lower choroidal thickness were associated with longer disease duration. In fact, normalized choroidal reflectivity was shown to be related to choroidal thickness, age, and disease duration in multiple regression analysis, providing
Insight into the information that this parameter may carry. Further research in other inflammatory diseases may help to elucidate this. Of note, visual field indices (foveal sensitivity and mean deviation) did not demonstrate any association with the choroidal parameters. However, longitudinal data are required to determine whether alterations in choroidal reflectivity may influence subsequent changes in visual function.

In our cohort, normalized choroidal reflectivity also was shown to correlate with age, but not with axial length. Choroidal thickness and volume already have been reported to vary with age and axial length. In our set of data, the association with age was evident, with increasing age being associated with choroidal thinning. We also observed a negative correlation between the 2-dimensional choroidal area measured from individual 2-dimensional scans and age. The relationship between choroidal thickness and axial length did not reach the level of significance, and it is possible that the relationship that has already been reported to exist in healthy participants is blunted in patients with BSCR.

Our study is not without limitations, which should be considered when assessing our findings. First, our analysis is based on the grading of a single 6-mm horizontal line scan centered on the fovea and the selection of small portions of the RPE and choroid for normalization. Birdshot chorioretinopathy may have variable effects in different regions of the choroid. Future analyses of entire choroidal volumes or choroidal scans obtained outside the macula may help to address this issue. Second, although we were able to account for age and axial length, we were not able to control for the impact of diurnal variations in choroidal thickness in our assessments. However, the mean choroidal thicknesses in our cohorts were less than 300 μm, and for choroids in this thickness range, the amplitude of diurnal variation is relatively small and much lower than the differences between the controls and patients in our study. Third, although these assessments were performed as part of a longitudinal study of BCSR, thus far we have only SS OCT data at a single time point. As a result, it is difficult to assess the prognostic significance of these choroidal parameters at this time. Repeat assessment of these participants at a future date may allow this to be assessed. Finally, a small percent (<5%) of participants had OCT scans that could not be analyzed for choroidal reflectivity because they were confounded by extensive overlying RPE atrophy, thereby potentially introducing selection bias. However, this small excluded subgroup did not differ with the overall cohort with regard to any demographic or ocular variable.

Our study also has many strengths, including a relatively large sample size, the collection of data as a part of a large prospective longitudinal study of a carefully defined cohort, the use of certified reading center OCT graders, and the use of SS OCT technology, which provides excellent imaging of the vitreous and choroid. Importantly, compared with spectral-domain OCT, SS technology features much less sensitivity loss with depth, which is critical for assessing the reflectivity of deeper structures such as the choroid, especially when there is overlying retinal edema. As a result, we were able to identify the choroidal boundaries in 100% of our cases and the choroidal assessments seemed to be repeatable. We were able to generate our normalized choroidal reflectivity values using readily available free software, which we hope will facilitate replication of our results in future studies.

In summary, we report on quantitative alterations in the choroid, in terms of both thickness and reflectivity, in patients with BSCR. Normalized choroidal reflectivity and choroidal thickness may correlate with the status of the disease. Further investigation of this parameter in longitudinal studies of BCSR as well as in the setting of other diseases affecting the choroid seems warranted.

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Footnotes and Financial Disclosures

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Abbreviations and Acronyms:
BSCR = birdshot retinochoroidopathy; CI = confidence interval; ICC = intraclass correlation coefficient; OCT = optical coherence tomography; RPE = retinal pigment epithelium; SS = swept-source.

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