Objective: To evaluate characteristics of small choroidal melanoma using enhanced depth imaging spectral-domain optical coherence tomography (EDI-OCT).

Design: Retrospective comparative analysis.

Results: Of 37 eyes with small choroidal melanoma imaged using EDI-OCT, the mean tumor thickness was 1025 µm by EDI-OCT compared with 2300 µm by ultrasonography. By EDI-OCT, choroidal features included optical shadowing in 36 (100%) and overlying choriocapillaris thinning in 37 (100%). Outer retinal features included shaggy photoreceptors in 18 (49%), as well as absence (structural loss) of photoreceptors in 9 (24%), inner segment–outer segment junction in 24 (65%), external limiting membrane in 16 (43%), outer nuclear layer in 6 (16%), and outer plexiform layer in 4 (11%). Inner retinal features included irregularity of inner nuclear layer in 3 (8%), inner plexiform layer in 3 (8%), ganglion cell layer in 3 (8%), and nerve fiber layer in 2 (5%). Also identified were subretinal fluid in 34 (92%), subretinal lipofuscin deposition in 35 (95%), and intraretinal edema in 6 (16%). Using EDI-OCT, a comparison with similarly sized choroidal nevus revealed that small choroidal melanoma showed increased tumor thickness, subretinal fluid, subretinal lipofuscin deposition, and retinal pigment epithelium atrophy. Statistically significant EDI-OCT features for small choroidal melanoma included intraretinal edema ($P = .003$), shaggy photoreceptors or loss of photoreceptors ($P = .005$), loss of external limiting membrane ($P = .008$), loss of inner segment–outer segment junction ($P = .02$), irregularity of inner plexiform layer ($P = .04$), and irregularity of ganglion cell layer ($P = .04$) ($t$ test and $\chi^2$ test). Shaggy photoreceptors were found overlying small choroidal melanoma in 18 (49%) but were not observed overlying choroidal nevus ($P < .001$).

Conclusions: Small choroidal melanoma tumor thickness was overestimated by 55% on ultrasonography compared with EDI-OCT. The EDI-OCT features of small choroidal melanoma compared with choroidal nevus include increased tumor thickness, subretinal fluid, subretinal lipofuscin deposition, and retinal irregularities, including shaggy photoreceptors.

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OCT (EDI-OCT) allow for better imaging of choroidal detail. For tumors, EDI-OCT provides in vivo quantification of tumor dimensions and cross-sectional detail of the tumor and surrounding choroidal tissues that previously were not depicted. Herein, we report our experience with EDI-OCT in the assessment of small choroidal melanoma. We explored the imaging features and tumor thickness in 54 consecutive eyes with small choroidal melanoma and compared our results with the findings in similarly sized choroidal nevus.

METHODS

A retrospective comparative study was designed to evaluate the imaging characteristics of small choroidal melanoma vs choroidal nevus using EDI-OCT. All the patients who were diagnosed as having small choroidal melanoma (≤3-mm thickness on ultrasonography) during a 1-year period between August 1, 2010, and August 1, 2011, on the Ocular Oncology Service, Wills Eye Institute, Philadelphia, Pennsylvania, and who were imaged with EDI-OCT were included in this study. Clinical and imaging features of the small choroidal melanoma were evaluated. Wills Eye Institutional Review Board approval was obtained.

The EDI-OCT was performed through a dilated pupil (Heidelberg Spectralis HRA + OCT; Heidelberg Engineering) using accompanying acquisition and analysis software (version 5.3.3.0 with automated EDI). The axial resolution was 3.5 µm, with an imaging speed of 40,000 A-scans per second. The images were captured using a custom image acquisition protocol of up to 13 raster lines of 9-mm image length, with 1536 A-scans per line. Real-time eye tracking (TruTrack Active Eye Tracking; Heidelberg Engineering) was used, and automatic real-time image averaging was set at 100 images. The EDI-OCT was performed using a technique similar to that described by Spaide et al, whereby the instrument is displaced closer to the eye to obtain an inverted image, which is adjusted by software to visualize the choroidal detail in the upright position. An EDI-OCT image was considered optimal and suitable for study when both the anterior and posterior margins of the tumor and the overlying retina were visualized. Images were classified as suboptimal when a portion of the tumor or the overlying retina could not be visualized, and these were excluded from the study.

Patient demographic data included age, sex, and race/ethnicity. Clinical tumor data included quadrantic location of the tumor epicenter, tumor basal diameter (in millimeters), tumor margin to the fovea and optic disc (in millimeters), color (pigmented, nonpigmented, or mixed), and related alterations in subretinal fluid, subretinal lipofuscin deposition, intraretinal edema, and RPE. The tumor thickness was measured by ultrasonography (in millimeters) and by EDI-OCT (in micrometers).

Risk factors for growth of 37 small choroidal melanomas included tumor thickness greater than 2 mm in 28 (76%), subretinal fluid in 34 (92%), symptoms of photopsia or visual loss in 27 (73%), orange pigment in 36 (97%), tumor margin within 3 mm of the optic disc in 32 (86%), hollowness on ultrasonography in 34 (92%), and the absence of overlying drusen in 33 (89%). Tumor growth (before referral) was documented in 6 (16%).

The EDI-OCT features included optical qualities of the melanoma and the status of surrounding tissues, including the choriocapillaris and large choroidal vessels, overlying RPE or Bruch membrane, and retina. The retinal layers were evaluated for abnormalities from outer to inner retina. The presence of subretinal fluid, subretinal lipofuscin deposition, and intraretinal edema was noted.

The method for measurement of the tumor thickness on EDI-OCT involved the placement of a parabolic curve on the anterior (curve 1) and posterior (curve 2) tumor margins, with caliber cross-sectional measurement between the apex of the 2 curves (Figure 1). Curve 1 was produced by auto-segmentation using OCT software automatically connecting positioned points at the base of the RPE. Curve 2 was produced by manual segmentation using manually positioned points at the tumor base judged to be at the junction of the hyperreflective inner sclera. If dense optical shadowing from the melanoma prohibited visualization of the tumor base for point selection and...
The mean basal diameter of the small choroidal melanoma was 6.7 mm, and the mean thickness using ultrasonography was 2.3 mm (median, 2.5 mm; range, 1.7-3.4 mm). The latter values were converted to 2300 µm (median, 2500 µm; range, 1700-3400 µm). Using EDI-OCT, the mean tumor thickness was 1025 µm (median, 1019 µm; range, 639-1410 µm) (Table 2). The mean difference of 1275 µm (a 55% reduction) between the tumor thickness measurement by ultrasonography vs EDI-OCT was statistically significant (P < .001).

The EDI-OCT features of the small choroidal melanoma showed homogeneous optical reflectivity along the anterior surface, with gradual shadowing more deeply. The internal characteristics of the tumor were unresolvable. Optical shadowing was partial in 27 eyes (73%) and complete in 10 eyes (27%). The overlying choriocapillaris was thinned in every eye. Bruch membrane showed rupture in 1 eye (3%) and drusen in 4 eyes (11%). The tumor, choroid, and Bruch membrane features did not significantly differ from those of choroidal nevus (Table 2).

Features that were more often found with small choroidal melanoma compared with choroidal nevus included increased tumor thickness, subretinal fluid, subretinal lipofuscin deposition, and RPE atrophy (Figure 2). Because these are established clinical features to classify melanoma vs nevus, they were excluded from the statistical evaluation. Features on EDI-OCT that were significantly more often found with small choroidal melanoma compared with choroidal nevus included increased shaggy photoreceptors (P < .001), abnormality of photoreceptors (P = .005), loss of external limiting membrane (P = .008), loss of inner segment–outer segment junction (P = .02), intraretinal edema (P = .003), irregularity of inner plexiform layer (P = .04), and irregularity of ganglion cell layer (P = .04).

Our understanding of normal choroidal anatomy and disease states continues to improve with EDI-OCT. In a seminal study, Spaide and coworkers14 found that the normal subfoveal choroidal thickness by EDI-OCT is approximately 320 to 330 µm. Subsequent studies15,17,18 disclosed that aging, refractive error, and disease could lead to changes in choroidal thickness, ranging from decreased thickness of 50 µm in age-related macular degeneration and myopia to increased thickness exceeding 500 µm in central serous chorioretinopathy. Margolis and Spaide15

Table 1. Enhanced Depth Imaging Spectral-Domain Optical Coherence Tomography of 37 Eyes With Small Choroidal Melanoma

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (n = 37)</th>
</tr>
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<tbody>
<tr>
<td>Age, y</td>
<td>56</td>
</tr>
<tr>
<td>Median (range)</td>
<td>60 (10-92)</td>
</tr>
<tr>
<td>Race/ethnicity, No. (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>37 (100)</td>
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<tr>
<td>Nonwhite</td>
<td>0</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (54)</td>
</tr>
<tr>
<td>Female</td>
<td>17 (46)</td>
</tr>
<tr>
<td>Presence of symptoms, No. (%)</td>
<td>27 (73)</td>
</tr>
<tr>
<td>Visual acuity, No. (%)</td>
<td></td>
</tr>
<tr>
<td>≥20/40</td>
<td>18 (49)</td>
</tr>
<tr>
<td>&lt;20/40</td>
<td>19 (51)</td>
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</table>

<table>
<thead>
<tr>
<th>Small Choroidal Melanoma Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color, No. (%)</td>
</tr>
<tr>
<td>Pigmented</td>
</tr>
<tr>
<td>Nonpigmented</td>
</tr>
<tr>
<td>Mixed</td>
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<tr>
<td>Location of melanoma epicenter, No. (%)</td>
</tr>
<tr>
<td>Macula</td>
</tr>
<tr>
<td>Extramacula</td>
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<tr>
<td>Distance from tumor margin to foveola, mm</td>
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<tr>
<td>Mean</td>
</tr>
<tr>
<td>Median (range)</td>
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<tr>
<td>Distance from tumor margin to optic disc, mm</td>
</tr>
<tr>
<td>Mean</td>
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<tr>
<td>Median (range)</td>
</tr>
<tr>
<td>Tumor basal diameter, mm</td>
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<tr>
<td>Median (range)</td>
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<tr>
<td>Ultrasonography findings</td>
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<tr>
<td>Tumor thickness, mm</td>
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<tr>
<td>Median (range)</td>
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<tr>
<td>Configuration, No. (%)</td>
</tr>
<tr>
<td>Plateau</td>
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<tr>
<td>Dome</td>
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<tr>
<td>Acoustic hollowness</td>
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<tr>
<td>Choroidal excavation</td>
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<tr>
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<tr>
<td>Tumor thickness, mm</td>
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<td>Mean</td>
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<td>Median (range)</td>
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<tr>
<td>Choroid Features</td>
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<td>Optical shadowing</td>
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<td>Partial</td>
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<tr>
<td>Complete</td>
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<td>Overlying choriocapillaris</td>
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<td>Drusen</td>
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<td>Retina Features</td>
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<tr>
<td>Photoreceptors</td>
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<tr>
<td>Irregular</td>
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<td>Absent</td>
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<tr>
<td>External limiting membrane</td>
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<tr>
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<td>Irregular</td>
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<tr>
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<tr>
<td>Irregular</td>
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<td>Irregular</td>
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<tr>
<td>Inner</td>
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<td>Abnormal</td>
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<tr>
<td>Abnormal</td>
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<tr>
<td>Subretinal fluid</td>
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<tr>
<td>Subretinal lipofuscin deposition</td>
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<tr>
<td>Subretinal edema</td>
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</tbody>
</table>

Abbreviation: NA, not applicable because these are established risk factors that select small choroidal melanoma from choroidal nevus and were excluded from the statistical analysis.

\(^a\) Data are from the study by Shah et al.\(^16\)

\(^b\) Comparing absent vs shaggy photoreceptors by \(\chi^2\) test. All other \(P\) values are by \(t\) test and \(\chi^2\) test.
few studies have reported on the use of EDI-OCT for choroidal tumors. Torres and coworkers evaluated 23 various choroidal tumors using EDI-OCT and were able to measure the base and thickness with this modality in only 10 cases (43%). They estimated that smaller tumors (<9-mm diameter and <1-mm thickness) were best for measurement. Most important, choroidal tumors that were too small for identification by ultrasonography were identified, imaged, and measured by EDI-OCT.

The technique of EDI-OCT is unsuitable for all patients. Shah and associates evaluated 104 eyes with choroidal nevus using EDI-OCT and found that approximately 50% of cases provided suboptimal images. The suboptimal images were related to older patient age (>60 years), female sex, extramacular location of the tumor (>3 mm from the foveola and >4 mm from the optic disc), and larger basal diameter of nevus (>5 mm). They concluded that patient cooperation was important and that EDI-OCT imaging was ideal only for smaller choroidal tumors (<3 mm), particularly those located in the macula.

Caliper measurement of choroidal tumors on EDI-OCT has consistently shown lesser thickness compared with ultrasonography. Shah and coworkers found that choroidal nevus was measured as approximately 54% less thick on EDI-OCT (mean, 685 µm) compared with ultrasonography (mean, 1500 µm). Similarly, herein we detected a 55% disparity between the measurement of small choroidal melanoma by EDI-OCT (mean, 1025 µm) vs ultrasonography (mean, 2300 µm). This discrepancy could be due to unintentional inclusion of a flat overlying retina with the anterior surface of the choroidal tumor measurement, as well as inadvertent inclusion of sclera in the often imprecise identification of the posterior tumor margin on ultrasonography. Axial resolution of EDI-OCT is

Figure 2. Enhanced depth imaging spectral-domain optical coherence tomography (EDI-OCT) of small choroidal melanoma compared with choroidal nevus. A through D. Comparison of juxtapapillary small choroidal melanoma vs choroidal nevus. The EDI-OCT shows shaggy photoreceptors, shallow subretinal fluid, and subretinal deposits (orange pigment) (A) overlying small choroidal melanoma (B) compared with choroidal nevus (C and D), with no subretinal fluid or with moderate retinal pigment epithelial (RPE) alterations. E through H. Temporal macular small choroidal melanoma vs choroidal nevus. The EDI-OCT shows subretinal fluid and shaggy photoreceptors (E) over small choroidal melanoma (F), with overlying minor RPE alterations (H). I through L. Macular small choroidal melanoma vs choroidal nevus. The EDI-OCT shows shaggy photoreceptors and subretinal fluid (I) overlying small choroidal melanoma (J) vs choroidal nevus (K), with choriocapillaris compression, no subretinal fluid, and intact retina (L). M through P. Amelanotic small choroidal melanoma vs amelanotic choroidal nevus. The EDI-OCT shows shallow subretinal fluid (M) and subretinal deposits (orange pigment) overlying small choroidal melanoma (N) compared with choroidal nevus (O), with lack of subretinal fluid, chronic retinal thinning with photoreceptor atrophy, and small RPE detachment (P).
approximately 3 to 4 μm compared with 10 μm for time-domain OCT and approximately 50 to 200 μm for ultrasonography. With thin choroidal tumors, a small misjudgment in caliper placement on EDI-OCT could lead to a 5- to 10-μm error, while caliper misplacement on ultrasonography might lead to a 200- to 400-μm error. As tumors increase in thickness, ultrasonography has a more important role in measurement because current EDI-OCT technology cannot accurately image thick choroidal melanoma.

In the present study, we had the opportunity to compare the features of small choroidal melanoma vs similar-sized choroidal nevus. We found EDI-OCT abnormalities at all levels of the retina, RPE, Bruch membrane, and choroid. Compared with choroidal nevus, small choroidal melanoma more often showed increased tumor thickness, subretinal fluid, subretinal lipofuscin deposition, and RPE atrophy. These clinical features were excluded from the statistical analysis because they are established selection criteria for melanoma. Using EDI-OCT, the statistical analysis revealed that small choroidal melanoma compared with choroidal nevus more often showed shaggy photoreceptors (P < .001), loss of external limiting membrane (P = .008), loss of inner segment–outer segment junction (P = .02), irregularity of inner plexiform layer (P = .04), intraretinal edema (P = .003), and irregularity of ganglion cell layer (P = .04). The term shaggy photoreceptors describes the irregular, elongated, and presumed swollen photoreceptors from fresh subretinal fluid; in this series, shaggy photoreceptors were found on EDI-OCT in 18 eyes (49%) with small choroidal melanoma and in no eye with choroidal nevus (Table 2). We believe that this important feature reflects an estimate of the duration of retinal detachment because with time, the photoreceptors become atrophic and the outer retina becomes thinned; structural loss of photoreceptors was found in 9 eyes (24%) with small choroidal melanoma and in 22 eyes (43%) with choroidal nevus.

Shaggy or elongated photoreceptors have been found with other conditions that produce subretinal fluid. Matsumoto and colleagues studied central serous choroidal retinopathy and calculated that the outer segments of the photoreceptors increase from a normal 30 μm in attached foveolar retina to an elongated 50 μm in detached foveolar retina. They further speculated that the elongated photoreceptor outer segments contain autofluorescent fluorophores that accumulate in the subretinal space and can settle into the fornix of the detachment, leading to the slight hyperautofluorescence of fresh subretinal fluid.

Limitations to our study include the few patients with small choroidal melanoma. A larger cohort could provide more robust information. In addition, tumor measurement and EDI-OCT analysis were subject to individual interpretation similar to ultrasonography thickness measurement. Another drawback is the reality that not all EDI-OCT images were of identical quality, which could have affected interpretation. Last, the diagnosis of small choroidal melanoma in these eyes was established by experienced ocular oncologists (C.L.S. and J.A.S.) based on suspicious clinical features, evidence of growth, and needle biopsy specimen evidence of related genetic mutations. Diagnostic bias could be present in our assessment of small choroidal melanoma vs choroidal nevus. The EDI-OCT data are descriptive and do not necessarily predict the ability to diagnose a small choroidal melanoma vs a choroidal nevus. Future studies could reduce bias with prospective interpretation of EDI-OCT findings masked to diagnosis.

In conclusion, EDI-OCT is an exciting technology for imaging small choroidal tumors, allowing visualization of detail not previously seen with other imaging modalities. Small choroidal melanoma expands the choroid, compresses the choiioi, and is associated with numerous changes in the overlying retina, including the presence of subretinal fluid with suggestive shaggy photoreceptors and disruption of the inner segment–outer segment junction. Compared with similar-sized choroidal nevus, small choroidal melanoma is thicker and more often demonstrates subretinal fluid, subretinal lipofuscin deposition, and shagginess to the photoreceptor layer.

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Author Contributions: Dr C. L. Shields had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Role of the Sponsors: The Eye Tumor Research Foundation had no role in the design or conduct of the study; in the collection, analysis, or interpretation of the data; or in the preparation, review, or approval of the manuscript.

REFERENCES


**Correction**

**Error in Figure.** In the Clinical Sciences article titled “Outer Retinal Tubulation: A Novel Optical Coherence Tomography Finding” by Zweifel et al, published in the December 2009 issue of the *Archives* (2009;127[12]:1596-1602), an error occurred in Figure 3E on page 1599. In that figure, the top portion of the schematic should have been labeled (from top to bottom) ONL, ELM, and IS/Os. In addition, the last 2 sentences of the figure legend should have read as follows: “A schematic (E) demonstrates focal disruption of the photoreceptor layer, invagination of remaining cells, and establishment of lateral contact by the outermost photoreceptors leading to complete tubule formation. ELM indicates external limiting membrane; ONL outer nuclear layer.”