Macular Telangiectasia Type 1: Capillary Density and Microvascular Abnormalities Assessed by Optical Coherence Tomography Angiography

ALEXANDRE MATET, ALEJANDRA DARUICH, ALI DIRANI, AUDE AMBRESIN, AND FRANCINE BEHAR-COHEN

- PURPOSE: To describe microvascular abnormalities and capillary density in macular telangiectasia type 1 (MT1) using optical coherence tomography angiography (OCTA), and correlate them with fluorescein angiography (FA).
- DESIGN: Observational case series.
- METHODS: Seven patients with MT1 and 12 age-matched controls were included. Focal microvascular dilations were identified on 3×3 mm OCTA and early-frame FA images. OCTA images were processed to determine the global capillary density after subtraction of larger vessels and cystoid edema cavities. Local capillary densities were calculated inside 100-μm circles around telangiectasias, projected over superficial (SCP) and deep capillary plexuses (DCP). They were compared to a random sample of 100-μm circles generated in each OCTA image. FA images were processed to measure mean perifoveal intercapillary areas (PIA), inversely reflecting capillary density.
- RESULTS: In MT1 eyes, fewer telangiectasias were identified with OCTA than with FA (P = .016), exclusively localized in the DCP (P = .016). Rarefaction of both capillary plexus and abnormal microvascular morphology were better identified by OCTA than by FA. The global capillary density on OCTA was significantly lower in MT1 eyes than in fellow and control eyes, respectively: SCP, 0.347 vs 0.513 (P = .004) and 0.560 (P = .0005); DCP, 0.357 vs 0.682 (P = .016) and 0.672 (P = .0005). Capillary density was significantly reduced around telangiectasias in both SCP (P = .021) and DCP (P = .042). Capillary density of the SCP correlated inversely with the mean PIA on FA (r = −0.94, P = .017). LogMAR visual acuity was inversely correlated with SCP (r = −0.88, P = .012) and DCP capillary densities (r = −0.79, P = .048).
- CONCLUSIONS: OCTA confirmed that global and focal capillary depletion is associated with MT1. (Am J Ophthalmol 2016;167:18–30. © 2016 Elsevier Inc. All rights reserved.)

MACULAR TELANGIECTASIA TYPE 1 (MT TYPE 1) IS a congenital or developmental vascular disorder affecting mostly male subjects and consisting of focal, exudative dilations of perifoveal retinal capillaries. It is usually unilateral, may extend beyond the macula, and therefore may be part of the larger spectrum of Coats disease. Historically, the condition has been termed “miliary aneurysms” by Leber, “idiopathic juxtafoveal telangiectasis” (group 1A-1B) by Gass and Blodi, “Type I aneurysmal telangiectasia” by Yannuzzi and associates, and finally MT type 1 in the recent classification by the MacTel Study Group.

In contrast with type 2 idiopathic macular telangiectasia or “MacTel2,” in which telangiectasias develop along with pathognomonic degenerative alterations of the retinal architecture linked to Müller cell depletion, MT type 1 is primarily a vascular disease, complicated by macular edema originating from the exudative telangiectasias. Fluorescein angiography (FA) allows the visualization of telangiectasias, but its ability to image the fine perifoveal capillaries at high resolution and to discriminate between the superficial and deep capillary plexuses is limited. Moreover, these lesions and the surrounding perifoveal capillaries are visible exclusively during the early frames of the sequence, since details are progressively submerged by dye diffusion from telangiectasias.

Optical coherence tomography angiography (OCTA) is a recent noninvasive imaging technology based on the detection of flows that provides a representation of the microvascular morphology. Absence of dye diffusion and higher resolution help to overcome limitations of FA to image the perifoveal capillary network. Moreover, the segmentation of volumes acquired by OCTA produces a separate visualization of the superficial and the deep retinal capillary plexuses. To date, several groups have employed OCTA to describe normal features of the...
macular microvasculature and to describe fine alterations involving both plexuses in several vascular disorders, such as retinal vein occlusion, diabetic retinopathy, and MT type 2. Furthermore, the recent adjunction of quantitative tools has expanded the ability of OCTA to investigate highly detailed abnormalities of the retinal microvasculature, such as vessel density or non-flow areas.

Imaging MT type 1 eyes with OCTA, we have described the vascular abnormalities ("telangiectasias") and their vascular microenvironment. We used a quantitative analysis of OCTA images to compare the macular capillary density of MT type 1 eyes with fellow eyes and with healthy control eyes. We then correlated OCTA findings with FA imaging.

METHODS

**SUBJECTS:** This observational case series adhered to the tenets of the Declaration of Helsinki and Swiss federal regulations and was approved by the local Ethics Committee of the Swiss Department of Health (CER-VD no. 19/15). The study was conducted from June 1 to October 1, 2015, at Jules-Gonin Eye Hospital, Lausanne, Switzerland.

Medical records, optical coherence tomography (OCT), OCTA, FA, and indocyanine green angiography (ICGA) images from 7 consecutive subjects presenting with MT type 1 were retrospectively analyzed. The diagnosis of MT type 1 was based on the presence of unilateral, exudative telangiectasia affecting the macular area, without any clinical sign or history suggestive of vascular occlusion, posterior segment inflammation, or other causes of secondary macular telangiectasia. Exclusion criteria were age <18 years and spherical equivalent <−2 diopter (D) or >+2 D.

Twelve eyes from 12 healthy subjects imaged by OCTA were selected from the local OCTA database based on age and sex to serve as a control group.

**IMAGE ACQUISITION AND SEGMENTATION:** The instrument used for en face OCT and OCTA images, Angiovue RTx 100, is based on the AngioVue Imaging System (Optovue, Inc, Fremont, California, USA) to obtain amplitude decorrelation angiography images. This instrument has an A-scan rate of 70 000 scans per second, using a low light source centered on 840 nm and a bandwidth of 50 nm. Each OCTA volume contains 304 \( \times \) 304 A-scans with 2 consecutive B-scans captured at each fixed position before proceeding to the next sampling location. Split-spectrum amplitude-decorrelation angiography (SSADA) was used to extract the OCT angiography information. Each OCTA volume is acquired in 3 seconds and 2 orthogonal OCTA volumes were acquired in order to perform motion correction to minimize motion artifacts arising from microsaccades and fixation changes. Angiography information displayed is the average of the decorrelation values when viewed perpendicularly through the thickness being evaluated.

In order to obtain comparable 3 \( \times \) 3-mm OCTA scans between subjects, volumes were automatically segmented by the software provided by the manufacturer to provide images of the superficial plexus (3 \( \mu \)m below the inner limiting membrane to 16 \( \mu \)m below the outer border of the inner plexiform layer) and deep plexus (16–69 \( \mu \)m below the outer border of the inner plexiform layer). We controlled the correct segmentation for each patient before reporting the data.

The central macular thickness was measured on the Angiovue RTx 100 OCT in the central subfield of an Early Treatment Diabetic Retinopathy Study (ETDRS) grid centered on the fovea.

FA and ICGA were performed on Spectralis (Heidelberg Engineering, Heidelberg, Germany). Early frames (\( \pm \)50 seconds after dye injection) were acquired with a 30-degree lens to visualize the macular microvasculature. Image quality was optimized using the "sharpen" tool of the Heidelberg Eye Explorer software (Version 1.9.10.0; Heidelberg Engineering). Angiograms were rotated and cropped to match the 3 \( \times \) 3-mm OCTA scans centered on the fovea, using ImageJ (Version 1.50c4, Wayne Rasband; National Institutes of Health, Bethesda, Maryland, USA).

**IDENTIFICATION OF MICROVASCULAR ABNORMALITIES:** OCTA images from normal and MT type 1 subjects and FA and ICGA images from MT type 1 eyes were presented randomly to 3 masked independent observers (A.A., A.Da., F.B.C.) during separate sessions for each imaging modality. Lesions identified as microvascular abnormalities were labeled by each observer, and those labeled by 2 observers or more were retained. The interobserver reliability was assessed using a 2-way, mixed-model intraclass correlation coefficient based on the number of lesions identified per OCTA, FA, or ICGA image. Numbers of lesions in the deep and superficial capillary plexuses on OCTA were compared using a Wilcoxon signed-rank paired test.

**QUANTITATIVE DETERMINATION OF CAPILLARY VESSEL DENSITY ON OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY:** The vascular densities of the capillary network in the superficial and deep plexuses were assessed by a custom semi-automated, intensity-based algorithm on Matlab (Mathworks, Natick, Massachusetts, USA).

First, original grayscale OCTA images were processed to detect pixels corresponding to vascular flow. In each image (Figure 1, Top and Bottom left), a region of interest (ROI) inside the foveal avascular zone that did not include dark areas corresponding to intraretinal cystoid cavities was manually outlined to define the background intensity of the intervascular retinal tissue. Using the threshold intensity \( I_{\text{threshold}} = \text{Mean (ROI pixels)} + 2 \times \)
Standard Deviation (ROI pixels), a binary transform of the OCTA image was performed, resulting in a “skeleton” of the vascular network (Figure 1, Top and Bottom middle left). In order to extract larger arterioles and venules that appear brighter owing to their higher flow, another binary transform was applied to the original OCTA images with a threshold set arbitrarily at 50% of the maximum pixel intensity value ($122.5 = 0.5 \times 255$) (Figure 1, Top middle right).

Second, pixels corresponding to the en face visualization of cystoid edema were identified on OCTA images. These areas appear slightly darker than the surrounding retinal tissue that is detected by the SSADA algorithm, most likely because of imperceptible retinal motion during acquisition originating from arterial pulsations, breathing, tremors, or microsaccades. Cystoid spaces were identified using a low threshold intensity value of 5% ($12.5 = 0.05 \times 255$) (Figure 1, Bottom middle left).

The capillary network density was calculated over an area defined by subtracting from the total OCTA binary image the areas corresponding to larger vessels and cystoid edema. A $12 \times 89$-pixel rectangle located in the lower left corner and corresponding to the “Angioflow” sign embedded in native OCTA images was also subtracted. Over this final binary image, the total capillary network density was defined as the ratio of 1-pixels to total pixels. For graphical purposes, vessel density maps were produced by plotting the local mean intensity values in a sliding $5 \times 5$-pixel square area (Figure 1, Top and Bottom right).

Total capillary vessel densities in the deep and superficial plexuses were compared between affected and fellow eyes of MT type 1 subjects and control eyes from healthy subjects, using Mann-Whitney test and Wilcoxon signed-rank paired test (for fellow eyes). Correlations of capillary densities with multimodal imaging findings and visual acuity were performed using the Spearman rank correlation coefficients.

**Quantitative Determination of Local Capillary Vessel Density Around Microvascular Lesions on Optical Coherence Tomography Angiography:** In MT type 1 eyes a local capillary vessel density was calculated inside $100$-$\mu$m-radius circles centered by each previously identified microvascular lesion, using a semi-automated algorithm on Matlab. These lesions were labeled manually on original OCTA images by a single operator (A.M.) and local capillary densities were computed automatically on the previously generated binary images where cystoid edema and larger vessels (and the “Angioflow” label) had been excluded. In each plexus, these local densities were computed around the microvascular lesions of both plexuses, whenever present.

In order to compare local densities to an analogous measurement reflecting the average density of OCTA images, a random distribution of 1000 local areas of similar size...
(100-µm-radius circles) was generated in each OCTA image. Areas overlapping a 100-µm-radius local region around a labeled microvascular lesion, another randomly generated area, or a central disc of 0.250 mm² (corresponding to the area of the foveal avascular zone reported by independent groups on OCTA14,25) were excluded (Supplemental Figure 1, available at AJO.com). The distributions of perilesional and randomly distributed local densities were compared within each plexus by a Kruskal-Wallis test and a multiple comparison post-test.

**QUANTITATIVE ESTIMATION OF CAPILLARY DENSITY ON FLUORESCEIN ANGIOGRAPHY:** To provide an estimate of the capillary density on FA, a quantification of perifoveal intercapillary areas was performed on Matlab by adapting a method previously described in detail26 and applied to digital FA.27 Briefly, after manual outlining of the foveal avascular zone border and automated intensity-based skeletonization of the perifoveal microvasculature, intercapillary spaces were automatically detected and their areas were measured over the 3 × 3-mm angiograms, which corresponds approximately to the perifoveal 5-degree region reported in the original method26 (Figure 2). For each angiogram, the mean perifoveal intercapillary area was calculated and was considered an inverse estimate of capillary density.

**STATISTICAL ANALYSES:** Comparative tests and correlation analyses were performed on GraphPad Prism (Version 5.0f; GraphPad Software, San Diego, California, USA). Intraclass correlation coefficients, Kruskal-Wallis test, and post-tests were calculated on R software (Version 3.2.2; R Foundation for Statistical Computing, R Core Team, 2015, Vienna, Austria; http://www.R-project.org/) using the “irr” package (Version 0.84, 2012, M. Gamer, J. Lemon, I. Fellows, P. Singh, http://CRAN.R-project.org/package=irr) and the “pgirmess” package (2015, Version 1.6.3, P. Giraudoux, http://CRAN.R-project.org/package=pgirmess). Visual acuities were converted to the logarithm of the minimal angle of resolution (logMAR) for calculations. P values inferior to .05 were considered statistically significant.

**RESULTS**

**THERE WAS NO DIFFERENCE BETWEEN THE 7 PATIENTS presenting MT type 1 and the 12 healthy controls in terms of age (57.1 ± 10.2 vs 57.8 ± 6.9 years, P > .99) and sex (all male subjects).**

**IDENTIFICATION OF MICROVASCULAR ABNORMALITIES:** In MT type 1 eyes imaged by OCTA, microvascular abnormalities consisting of focal capillary dilations were detected exclusively in the deep capillary plexus by the 3 independent observers. There was a mean of 6.9 (range, 2–14) lesions in the deep plexus and 0 lesions in the superficial plexus (P = .016) (Table 1). Microvascular abnormalities were not observed in fellow eyes of MT type 1 subjects or in control healthy eyes.

On early-frame 3 × 3-mm FA images, a higher number of lesions was identified by the 3 independent observers (mean: 21.8, range, 6–54) than on OCTA (P = .016). Early-frame confocal ICGA was obtained in 5 MT type 1 subjects. Lesions suggestive of telangiectasia were observed in all 5 subjects (mean: 13.2, range, 3–36), but their number was variably higher or lower than observed using OCTA or FA, with no difference in mean number (P = .13 and P = .31, respectively).

The resulting intraclass correlation coefficient was 0.97 (95% confidence interval [CI]: 0.89–0.99) for OCTA,
**TABLE 1. Clinical and Imaging Findings by Optical Coherence Tomography Angiography, Fluorescein Angiography, Indocyanine Green Angiography, and Optical Coherence Tomography in 7 Patients With Macular Telangiectasia Type 1**

<table>
<thead>
<tr>
<th>Case, Sex (Age, y)</th>
<th>Abnormal Microvascular Lesions, n</th>
<th>Observed Capillary Density of OCTA Image</th>
<th>Local Capillary Density in Random Regions</th>
<th>Abnormal Microvascular Lesions, n</th>
<th>Observed Capillary Density of OCTA Image</th>
<th>Local Capillary Density in Random Regions</th>
<th>Observed Perileisional Capillary Density</th>
<th>Abnormal Microvascular Lesions, n</th>
<th>Mean Perifoveal Intercapillary Area, 10⁻³ mm²</th>
<th>Abnormal Microvascular Lesions, n</th>
<th>Mean Central Macular Thickness, μm</th>
<th>Best-Corrected LogMAR (Snellen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, M (52)</td>
<td>0</td>
<td>0.377</td>
<td>0.379</td>
<td>0.302</td>
<td>9</td>
<td>0.542</td>
<td>0.564</td>
<td>0.396</td>
<td>54</td>
<td>3.75</td>
<td>36</td>
<td>343</td>
</tr>
<tr>
<td>2, M (51)</td>
<td>0</td>
<td>0.380</td>
<td>0.374</td>
<td>0.291</td>
<td>5</td>
<td>0.318</td>
<td>0.332</td>
<td>0.0978</td>
<td>7</td>
<td>3.59</td>
<td>3</td>
<td>402</td>
</tr>
<tr>
<td>3, M (68)</td>
<td>0</td>
<td>0.378</td>
<td>0.390</td>
<td>0.280</td>
<td>14</td>
<td>0.527</td>
<td>0.549</td>
<td>0.412</td>
<td>32</td>
<td>3.64</td>
<td>NA</td>
<td>377</td>
</tr>
<tr>
<td>4, M (56)</td>
<td>0</td>
<td>0.212</td>
<td>0.204</td>
<td>0.162</td>
<td>2</td>
<td>0.230</td>
<td>0.234</td>
<td>0.153</td>
<td>6</td>
<td>NA</td>
<td>4</td>
<td>305</td>
</tr>
<tr>
<td>5, M (54)</td>
<td>0</td>
<td>0.306</td>
<td>0.309</td>
<td>0.372</td>
<td>7</td>
<td>0.206</td>
<td>0.214</td>
<td>0.281</td>
<td>12</td>
<td>3.79</td>
<td>17</td>
<td>304</td>
</tr>
<tr>
<td>6, M (74)</td>
<td>0</td>
<td>0.319</td>
<td>0.311</td>
<td>0.310</td>
<td>8</td>
<td>0.235</td>
<td>0.251</td>
<td>0.267</td>
<td>28</td>
<td>4.99</td>
<td>NA</td>
<td>342</td>
</tr>
<tr>
<td>7, M (45)</td>
<td>0</td>
<td>0.455</td>
<td>0.430</td>
<td>0.400</td>
<td>3</td>
<td>0.441</td>
<td>0.461</td>
<td>0.355</td>
<td>13</td>
<td>2.15</td>
<td>6</td>
<td>282</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>0</td>
<td>0.347 ± 0.077</td>
<td>0.349 ± 0.077</td>
<td>0.302 ± 0.076</td>
<td>6.9 ± 4.1</td>
<td>0.357 ± 0.145</td>
<td>0.372 ± 0.232</td>
<td>0.280 ± 0.170</td>
<td>21.8 ± 17.4</td>
<td>3.65 ± 0.90</td>
<td>13.2 ± 13.9</td>
<td>326 ± 40</td>
</tr>
</tbody>
</table>

* FA = fluorescein angiography; ICGA = indocyanine green angiography; LogMAR = logarithm of the minimal angle of resolution; OCT = optical coherence tomography; OCTA = optical coherence tomography angiography.

*Kruskal-Wallis test with multiple comparison post-tests.
0.96 (95% CI: 0.81–0.99) for FA, and 0.99 (95% CI: 0.98–1.00) for ICGA, indicating excellent consistency between the 3 independent observers, with a greater agreement for OCTA and ICGA than for FA. The detailed number of lesions identified by each observer is given in Supplemental Table 1 (Supplemental Material available at AJO.com).

**QUALITATIVE DESCRIPTION OF CAPILLARY NETWORK CHANGES:** A qualitative visual assessment of OCTA images revealed a rarefied capillary network in the superficial and deep plexuses. Enlarged capillary-free areas along arterioles and exacerbated capillary loops were mostly observed in the superficial plexus (Figures 3–5). In 5 out of 7 patients, a proportion of focal microvascular dilations suggestive of telangiectasias were located close to a termination or branching of a venule or arteriole (Cases 1–3 and 5–6, Figures 3–5). In addition, the foveal avascular zone morphology was severely altered in OCTA images of the superficial plexus, and showed an abnormal capillary vessel crossing linearly this area in 4 out of 7 eyes (Cases 1–3 and 6, Figures 3–5). Similar abnormal features were partly visible on early-frame FA.

**FIGURE 3.** Multimodal imaging in a 52-year-old man with macular telangiectasia type 1 (Case 1) showing severe alterations of the perifoveal microvasculature. (Top left) Optical coherence tomography angiography of the superficial capillary plexus showed a rarefied capillary network with numerous patchy areas of severe capillary depletion (blue arrows), close to the localization of focal microvascular dilations in the deep plexus (green circles). Exacerbated capillary loops (yellow arrows), enlarged capillary-free areas along arterioles (orange arrows), and an abnormal capillary vessel crossing the foveal avascular zone (blue star) were also visible. (Top right) The deep capillary plexus harbored a number of focal microvascular dilations (green circles), diffuse capillary depletion with focal areas of severe depletion located in the vicinity of the microvascular dilations (blue arrows). Note that certain microvascular lesions in the deep plexus were close to the termination of an arteriole/venule in the superficial plexus (orange star). (Bottom left) Early-frame fluorescein angiography showed a higher number of telangiectasias than identified by optical coherence tomography angiography, diffuse and focal capillary depletion, an abnormal capillary vessel crossing the foveal avascular zone, capillary loops, and enlarged capillary-free areas along arterioles. (Bottom right) Early-frame indocyanine green angiography did not visualize details of the macular microvasculature, except for focal telangiectasia, but their number was lower than on fluorescein angiography and was comparable to optical coherence tomography angiography.
although it did not discriminate between superficial and deep plexus alterations (Figures 3–5). In addition, the definition of the perifoveal microvasculature on early FA images was variable and qualitatively lower than on OCTA. This discrepancy was caused by leakage from telangiectasias (Case 3, Figure 5), fluorescein filling of cystoid edema cavities (Case 2, Figure 4 and Cases 5–6, Figure 5), or long-standing retinal pigment epithelium alterations secondary to retinal edema and subretinal exudates (Case 4, Figure 5).

**CAPILLARY VESSEL DENSITY:** The capillary vessel density was estimated by a semi-automated method over the entire OCTA images after subtraction of areas corresponding to arterioles, venules, and cystoid edema spaces. The capillary density of the superficial plexus was $0.347 \pm 0.077$ in MT type 1 eyes, significantly lower than in corresponding fellow eyes ($0.513 \pm 0.080$, $P = .0041$) and control eyes ($0.560 \pm 0.065$, $P = .0005$). No difference was observed between MT type 1 fellow eyes and control eyes ($P = .22$). Similarly, the capillary density of the deep plexus...
FIGURE 5. Fluorescein angiography and optical coherence tomography angiography with corresponding capillary density maps in 4 eyes with macular telangiectasia type 1 (Cases 3–6), 1 fellow eye of a macular telangiectasia type 1 patient (Case 1), and 1 healthy control eye (Control 10). Each line displays the following images: (Left) early-frame fluorescein angiography; (Middle left) optical coherence tomography angiography of the superficial capillary plexus, with green circles indicating the locations of microvascular lesions identified as telangiectasias in the deep plexus; (Middle) capillary density map of the superficial capillary plexus after subtraction of areas corresponding to larger vessels and cystoid spaces; (Middle right) optical coherence tomography angiography of the deep capillary plexus, with green circles surrounding these microvascular lesions identified as telangiectasias; (Right) capillary density map of...
was 0.357 ± 0.145 in MT type 1 eyes, significantly lower than in MT type 1 fellow eyes (0.682 ± 0.054, P = .016) and control eyes (0.672 ± 0.064, P = .0005). No difference was observed between MT type 1 fellow eyes and control eyes (P = .83). Capillary density maps from 4 eyes with MT type 1, 1 MT type 1 fellow eye, and 1 normal eye are represented in Figure 5. Case-by-case capillary densities are graphically reported in Figure 6; values from MT type 1 subjects are detailed in Table 1 and values from control subjects are reported in Supplemental Table 2 (Supplemental Material available at AJO.com).

• LOCAL CAPILLARY VESSEL DENSITY AROUND MICROVASCULAR ABNORMALITIES: Owing to the exclusive localization of abnormalities in the deep plexus, their locations served as reference to assess the perilesional capillary density in both the deep and superficial plexuses (Figures 3–5). Among MT type 1 eyes, the mean perilesional capillary vessel density inside 100-μm-radius circles centered by the microvascular abnormalities (Figures 3–5, green circles) was 0.302 ± 0.076 in the superficial plexus and 0.280 ± 0.170 in the deep plexus. In order to compare these measures against the capillary density in each plexus, a random distribution of similar, nonoverlapping circular areas was generated over OCTA images, resulting in a mean of 124 areas per image (range, 104–196). Capillary density values were significantly lower in perilesional areas than in areas randomly distributed within the OCTA images, and this finding was observed in both superficial and deep plexuses (P = .021 and P = .042, respectively) (Table 1).

• CORRELATION OF MULTIMODAL IMAGING PARAMETERS AND VISUAL ACUITY: Among the 7 MT type 1 eyes, morphologic parameters from OCTA, OCT, FA, and visual acuity were evaluated for possible correlations. Exhaustive results are reported in Table 2. Regarding the microvascular density, there was an inverse correlation (r = −0.94) between the mean perifoveal intercapillary area on FA and the superficial capillary plexus capillary density on OCTA (P = .017), but not with the deep plexus (P = .42). There was a positive correlation (r = 0.86) in the number of identified telangiectasias between OCTA and FA (P = .24). LogMAR best-corrected visual acuity showed an inverse correlation with the capillary density of both superficial (r = −0.88) and deep plexuses (r = −0.79) on OCTA (P = .012 and P = .048, respectively), and did not correlate with any other imaging parameter.

**DISCUSSION**

WITH OCTA, TELANGIECTASIC MICROANEURYSMS TYPICAL of MT type 1 were identified as focal dilations of the microvasculature. Although OCTA detected fewer lesions than FA in each affected eye, OCTA showed that telangiectasias were exclusively located in the deep capillary plexus. Moreover, in MT type 1 eyes the density of the macular capillary network was reduced in both superficial and deep plexuses, as compared to fellow and healthy control eyes, and the capillary network density of both plexuses was the unique morphologic parameter correlated to the visual acuity of MT type 1 eyes. Finally, a focal decrease in capillary density was observed adjacent to telangiectasia in both plexuses as compared to other vascularized regions of the macula.

In fellow eyes of MT type 1 subjects, OCTA imaging showed no microvascular abnormalities, confirming the observation made by Gass and Blodi and by Yannuzzi and associates, who reported unilateral disease in 90%–95% of cases.1,4 Although stereoscopic and digital FA initially described telangiectasias as emerging from both the deep and superficial networks,1,4 OCTA data presented here tend to localize them preferentially in the deep plexus. Abnormal capillary loops, detected in the superficial plexus by OCTA and visible on early-frame FA, may produce dye leakage from incompetent vessels without the typical aspect of aneurysmal lesions, which could explain this discrepancy. Interestingly, early-frame confocal ICGA clearly captured the macular telangiectasias, but, in contrast to FA and OCTA, it failed to provide relevant information on the surrounding microvasculature in MT type 1 (Figures 3 and 4) or healthy eyes (Supplemental Figure 2, available at AJO.com). On OCTA, rarefaction of the capillary bed was systematically observed in eyes affected by MT type 1 but not in fellow or control eyes. Similarly, on FA Gass and Blodi identified “minimal evidence of capillary occlusion or loss” in “most eyes,” whereas Yannuzzi and associates observed “minimal, patchy nonperfusion or capillary ischemia” in “some patients,” clearly pointing to the presence of focal ischemic areas in the macula. These alterations of the macular microvasculature visualized on OCTA and FA may range from mild (Case 2, Figure 4) to severe (Case 1, Figure 3). OCTA images and capillary density maps in Figure 5 illustrate quantitatively the presence of patchy capillary loss in the perifoveal
microvasculature, involving both plexuses. In addition, the inverse correlation between superficial capillary plexus density on OCTA and mean perifoveal intercapillary area on FA (Table 2) is consistent with the dominant contribution of the superficial plexus to the FA signal. However, the deep plexus participates to the diffuse fluorescent backdrop on FA images classically attributed to choroidal flow, and becomes more visible when occupied by vascular abnormalities like telangiectasias. Finally, visual acuity was exclusively correlated, among all anatomic parameters, with the capillary density of both plexuses on OCTA, highlighting the relevance of OCTA for the clinical evaluation of macular disorders.

Different investigators have previously suggested an overlap between MT type 1 with extramacular extension and adult-onset Coats disease. In a report by Smithen and associates, 12 of 13 patients with adult-onset Coats disease had also perimacular telangiectasias with macular edema, and 11 of these patients presented areas of capillary nonperfusion often adjacent to areas of vascular abnormality and described as “a filigree-like network of capillaries.” The similarity of this description with features of MT type 1 observed on OCTA strengthens the hypothesis that retinal telangiectasias localize preferentially in microenvironments where the capillary density is reduced, as observed in the present study.

Telangiectasias could develop as a result of this focal capillary loss, via an excess of proangiogenic factors, such as vascular endothelial growth factor, secreted by surrounding hypoxic retinal cells. A similar mechanism of unbalanced capillary growth from the deep capillary plexus owing to the lack of regulation by depleted Müller cells in a hypoxic environment has been advanced recently by Spaide and associates to explain the deep localization of vascular telangiectasias observed by OCTA in MacTel2. Likewise, the repeated observation of an extra capillary vessel across the foveal avascular zone points to an imbalance in pro- or antiangiogenic factors in these MT type 1 patients. On the other hand, the decrease in capillary density may also occur secondarily to a local elevation in oxygen tension owing to its excessive diffusion from focally dilated capillaries. This is supported by the classical concepts that excessive oxygen tension is a potent inhibitor of retinal vessel growth, as long demonstrated in developmental disorders such as retinopathy of prematurity. The effect of higher oxygen tension is also visible along the walls of retinal arterioles, which are surrounded by a local decrease in capillary density. Noticeably, this phenomenon has been recently described on OCTA images of normal eyes, and is exacerbated in MT type 1 eyes, as reported in the present study. Although the absolute vascular flow in a given vascular structure cannot yet be accurately measured by current commercial OCTA devices, it is indirectly reflected by the gray pixel value and size of this structure on OCTA images, the SSADA algorithm output being a nonlinear function of several parameters, including flow speed. Therefore, the elevated brightness and caliber of microvascular lesions identified as telangiectasias on OCTA likely suggest a focal elevation in blood flow velocity. On the other hand, several telangiectasias that appeared on FA and ICGA were not visible on OCTA (as in Case 1, Figure 3). Similarly, Spaide has reported the variable detection of microaneurysms in diabetic retinopathy by OCTA and attributed this artifact to
a slower flow than the OCTA device detection threshold within some of the lesions. Here the number of lesions detected by OCTA was in all cases inferior to those observed by FA, but these counts were positively correlated. Unless OCTA segmentation failed to include all lesions, the most likely explanation is that all eyes harbor a subgroup of poorly perfused telangiectasias.

Several imaging technologies have been employed to evaluate in vivo the density of capillary vessels in the macula of healthy eyes, since fluorescein injection is not ethically permitted in healthy subjects. Using a prototype swept-source OCTA device, Kuehlewein and associates reported a mean vessel density of 0.74 in the superficial plexus and 0.72 in the deep plexus. These values are close to or within the range of our observations in normal eyes (0.47–0.65 and 0.57–0.81, respectively). This limited disparity may be explained by the fact that their measure was performed over a 500-μm annulus outside the foveal avascular zone, whereas we have included this area to take into account its variability and have averaged the capillary density over the whole 3 × 3-mm field of OCTA images. Using high-resolution, confocal adaptive optics–based FA, Pinhas and associates have determined that the relative vascular density of the superficial plexus in a 800-μm circle around the fovea was 0.51 (converted to arbitrary units), within the range of our observations. Other investigators have also shown that capillary densities obtained on a prototype speckle variance OCTA device did not differ significantly from those observed on histology of human donor eyes, but similar comparisons need to be repeated using the commercial OCTA system employed in the present study.

Furthermore, there is to date no standard quantitative method to assess the vascular density on OCTA. Most existing methods of vessel detection are based on pixel intensity level after a binary transform. Native OCTA images may also be first skeletonized, as proposed by Agemy and associates, but every additional step comes at the price of losing information. Complex indices based on vessel caliber, number of intersections, or intercapillary distances have also been proposed, but they require extra computational effort that will not fit easily into high-workflow clinical settings. Regarding the region of interest over which the density is assessed, several patterns have been advanced, such as using the fields of an ETDRS grid. In the present study we opted for a global density encompassing the whole 3 × 3-mm images after subtracting areas of cystoid edema and larger vessels, in order to obtain comparable values among subjects, and limit the influence of macular edema on capillary density. Also, the foveal avascular zone was not excluded from the region of interest because its variations were part of the capillary density changes observed in MT type 1 eyes. The concentration of values among normal subjects illustrated by the low standard deviation confirmed the relevance of this approach (Figure 6 and Supplemental Table 2). It is also supported by the correlation between the superficial capillary plexus density in MT type 1 eyes with an estimate of

| P Value (r) | Abnormal Microvascular Lesions (OCTA), n | Superficial Plexus Capillary Density (OCTA) | Deep Plexus Capillary Density (OCTA) | Abnormal Microvascular Lesions (FA), n | Mean Perifoveal Intercapillary Area (FA), 10⁻⁸ mm² | Abnormal Microvascular Lesions (ICGA), n | Central Macular Thickness, μm |
|------------|----------------------------------------|-------------------------------------------|------------------------------------|---------------------------------------|---------------------------------------------|--------------------------------)-|---------------------------------|
| Superficial plexus capillary density (OCTA) | .84 | | | | | | |
| Deep plexus capillary density (OCTA) | .24 | .14 | | | | | |
| Abnormal microvascular lesions (FA), n | .024 (r = 0.86) | .56 | .07 | | | | |
| Mean perifoveal intercapillary area (FA), 10⁻⁸ mm² | .36 | .017 (r = −0.94) | .42 | .66 | | | |
| Abnormal microvascular lesions (ICGA), n | .23 | .95 | .68 | .13 | .42 | | |
| Central macular thickness, μm | .91 | .78 | .96 | .66 | .66 | .68 | |
| Best-corrected visual acuity, logMAR | .40 | .012 (r = −0.88) | .048 (r = −0.79) | .24 | .06 | .68 | .40 |

FA = fluorescein angiography; ICGA = indocyanine green angiography; LogMAR = logarithm of the minimal angle of resolution; OCTA = optical coherence tomography angiography.

*Spearman rank correlation.
the capillary density extracted from early FA images (Table 2). Future software embedded in OCTA devices should provide quantitative tools that reproducibly extract vascular densities and other relevant information, and provide refined measures after removal of confounding areas such as intraretinal edema. Limitations of this study include the small number of subjects related to the low prevalence of MT type 1, and the absence of longitudinal follow-up of the vascular abnormalities detected on OCTA. Images have been interpreted by multiple observers to maximize the discrimination of true flow from artifacts, but this could not prevent smaller or lower-flow telangiectasias from being missed by the OCTA acquisition, as discussed above and elsewhere. To overcome this limitation owing to the variability in low-flow structure detection, several acquisitions should be performed on each eye and screened for these lesions. Finally, early-frame FA/ICGA images were not available, either for fellow eyes of MT type 1 subjects, because early acquisitions were focused on the diseased eye (except for Case 1, Figure 5), or for control subjects, because it was unethical to inject them with dye (except for Control 10, Figure 5, who presented a contralateral atypical choroidal nevus requiring retinal imaging). We are unaware of previous reports quantitatively assessing the capillary density changes of MT type 1 patients on OCTA, and could find no reference to it in a computerized search on PubMed.

To summarize, OCTA noninvasively identified focal capillary network abnormalities in better detail than FA and showed a global reduction of capillary network density in both superficial and deep plexuses of MT type 1 eyes, which was correlated to visual acuity levels. Telangiectasias were observed on OCTA exclusively in the deep capillary plexus and were localized in a microenvironment where the superficial and deep capillary densities were lower than in other vascularized regions of the macula. Whether this finding is a cause or consequence of the telangiectasia formation and whether it is present in other vascular disorders with macular telangiectasias remain to be explored.

FUNDING/SUPPORT: THIS STUDY WAS SUPPORTED BY A GRANT FROM THE LOWY MEDICAL RESEARCH INSTITUTE LTD (La Jolla, CA, USA). Financial disclosures: Alexandre Matet: travel expenses (Laboratoires Alcon S.A.S., Rueil-Malmaison, France; Laboratoires Thea, Clermont-Ferrand, France). The following authors have no financial disclosures: Alejandra Daruich, Ali Dirani, Aude Ambresin, and Francine Behar-Cohen. All authors attest that they meet the current ICMJE criteria for authorship. The authors thank Martine Elalouf, MD (Jules-Gonin Eye Hospital, Lausanne, Switzerland), Parmis Parvin, MD (Jules-Gonin Eye Hospital, Lausanne, Switzerland), Sarah Ferreira, optometrist (Jules-Gonin Eye Hospital, Lausanne, Switzerland), Luca Marchionno, optometrist (Jules-Gonin Eye Hospital, Lausanne, Switzerland), and Jean-Dominique de Azevedo, optometrist (Jules-Gonin Eye Hospital, Lausanne, Switzerland), for assistance in image acquisition.

REFERENCES


31. Michaelson IC, Campbell ACP. The anatomy of the finer retinal vessels, and some observations on their significance in certain retinal diseases. Trans Ophthalmol Soc UK 1940;60:71–112.


