SUBCLINICAL MACULAR CHANGES AND DISEASE LATERALITY IN PEDIATRIC COATS DISEASE DETERMINED BY QUANTITATIVE OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

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Purpose: To determine vascular change at the macula in both eyes in unilateral pediatric Coats disease using optical coherence tomography angiography.

Methods: Retrospective case-series. Thirteen eyes of pediatric patients with a diagnosis of unilateral Coats disease of various stages were compared with 13 fellow eyes. Optical coherence tomography angiography images were acquired using the RTVue XR Avanti. Scans were analyzed with novel projection artifact removal software and improved segmentation. Vascular density and foveal avascular zone area were calculated.

Results: Vascular density was significantly decreased in eyes with Coats disease in comparison with fellow eyes in both the superficial capillary plexus and deep capillary plexus (43.7 ± 4.7 vs. 45.9 ± 4.4 [P = 0.000] and 43.0 ± 6.3 vs. 50.3 ± 2.2 [P = 0.001], respectively). The difference was also significant for most sectors of the macula. Foveal avascular zone area was significantly larger in eyes with Coats disease in comparison with fellow eyes (0.29 ± 0.1 vs. 0.24 ± 0.09 [P = 0.003]). These significant differences appeared as early as Stage 2A, preceding clinical findings.

Conclusion: The findings support the unilaterality of Coats disease and show that vascular changes on optical coherence tomography angiography precede clinical staging of the condition.

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Coats disease is a rare, predominantly unilateral retinal vascular developmental disorder characterized by retinal telangiectasia, areas of peripheral avascular retina, vascular leakage, and exudation resulting in visual impairment. It predominantly affects males, with an average age of onset of five years. The severity of the condition is classified based on funduscopic examination or color fundus photographs. Stage 1 is characterized by the presence of retinal telangiectasias only. In Stage 2, exudation accompanies telangiectasia, either extrafoveally (Stage 2A) or foveally (Stage 2B). In Stage 3, there is exudative retinal detachment, which can be subtotal (Stage 3A) or total (Stage 3B). In Stage 4, the condition advances to a total retinal detachment and glaucoma, whereas Stage 5 represents advanced end-stage disease. Recently, Daruich et al have suggested a change to the classification, further dividing Stage 2B into 2B1 and 2B2, with the latter including a subfoveal nodule and the former lacking this feature. Fluorescein angiography is the confirmatory diagnostic test used to confirm the diagnosis. Angiographic features include the presence of unilateral telangiectatic and light bulb aneurysmal vessels and peripheral retinal capillary nonperfusion, whereas macular findings include dilated capillaries, capillary closure, microaneurysms, and leakage.

Adult cases of Coats disease are similar in terms of unilateral clinical presentation and disease course, but generally have a more limited area of retinal involvement and slower disease progression. Indeed, it has been shown that an inverse relationship exists between age at presentation and the severity of disease. The exact mechanism of the disease is unknown. It is thought to be a nonhereditary disease and...
probably caused by a somatic mutation of the Norrie disease protein gene. However, with the advent of wide-field imaging, there have been reports that Coats disease may be a bilateral disease because of the presence of peripheral vascular changes in the fellow eyes. Such peripheral changes may also be seen in healthy eyes, further confounding the matter. Bilaterality also questions whether there is a hereditary element to the condition. Therefore, it is important to study the macula in Coats disease in more detail to better understand the laterality of the condition.

Optical coherence tomography angiography (OCTA) is a novel and noninvasive technique for demonstrating the microvascular blood flow within the macula. It produces depth-resolved evaluation of the reflectance data from retinal tissue, providing a three-dimensional volume of information. Its noninvasiveness and speed of use are advantageous in the pediatric population. In addition, development of handheld devices show promise for their use in neonates and in the setting of examination under anesthesia. A limited number of previous studies described qualitative OCTA findings in Coats disease, predominantly in the adult population, with no mention of disease stage.

Recently, different quantification algorithms have been used to extract angiographic data, including vascular density and the area of the foveal avascular zone (FAZ), from OCTA scans. The aim of this study was to quantify vascular density at the macula and FAZ area in a pediatric population with different stages of unilateral Coats disease and compare these parameters with those of the fellow eyes to determine whether there is any evidence to the laterality of the disease based on macular findings.

Methods

Institutional review board committee approval was obtained for the study. Pediatric patients with a diagnosis of Coats disease who underwent OCTA of both eyes at the pediatric clinic of Moorfields Eye Hospital between May 2016 and October 2017 were retrospectively evaluated. Data collected included findings of ophthalmologic examination, best-corrected visual acuity (in logarithm of the minimal angle of resolution) as measured by specialist orthoptists, and OCTA data.

Inclusion and Exclusion Criteria

Pediatric patients with the diagnosis of unilateral Coats disease based on clinical examination and confirmed on examination under anesthesia and fluorescein angiography (under anesthesia) were retrospectively enrolled. Patients were excluded if they had a systemic disease or another retinal pathology.

Optical Coherence Tomography Angiography Image Acquisition

Optical coherence tomography angiography images were acquired using the RTVue XR Avanti spectral domain OCT device with AngioVue software (Optovue, Fremont, CA). This system uses an SSADA software algorithm (version 2016.2.0.35) with a high speed of 70,000 axial scans per second, wavelength of 840 nm, and an axial resolution of 5 μm to acquire OCTA volumes consisting of 304 × 304 A-scans. The scanning area was captured in 3 × 3 mm sections centered on the fovea, capturing both eyes of each subject. Acquisition of scans was performed in clinic, after disease stabilization.

Optical Coherence Tomography Angiography Image Analysis

Image analysis was performed using a noncommercially available version of the AngioAnalytics software (version 2017.1.0.144), which was very similar to the future commercial version. This software uses a proprietary three-dimensional projection artifact removal algorithm (3D PAR), allowing for the removal of projection artifacts from deeper layers. The algorithm removes projection artifacts from the OCTA volume on a per voxel basis, using information from the OCT and OCTA volume to differentiate in situ OCTA signal from projection artifacts.

The software segments the macular vasculature into a superficial capillary plexus (SCP), extending from the internal limiting membrane to the inner plexiform
layer – 10 μm. Similarly, the deep capillary plexus (DCP) is segmented from the inner plexiform layer – 10 μm to the outer plexiform layer + 10 μm. The software allows for manual editing of segmentation lines and propagation of the change over the selected region of interest in areas where automated segmentation is incorrect. The segmentation was carefully examined for each case and corrected as needed to delineate the appropriate layers, including in cases of anatomical complications (i.e., edema or scarring) (Figure 1).

The software assigns a scan quality measure to each image, ranging from 1 to 10. Images with a scan quality <6 (due to motion or blink artifacts, lack of focus, etc.) or with otherwise poor image quality (i.e., due to vessel doubling, cropping, or low signal due to floaters) were excluded from the study.

Using the automated software, vascular density was measured using a partial Early Treatment Diabetic Retinopathy Study grid overlay that is superimposed on the automatically detected center of the fovea to generate vascular density in different areas of interest. The grid centration was adjusted manually when needed. It is composed of two circles: an inner circle with a diameter of 1 mm, covering the foveal region; and an outer circle with a diameter of 3 mm, corresponding to the parafovea. The outer circle is divided into sectors (nasal, temporal, superior, and inferior). For each predefined region, vascular density is calculated as percentage of the area occupied by vessels out of all region area (Figure 2).

The FAZ area parameter is calculated automatically by the software, and the detection boundary is based on inner plexiform layer to outer plexiform layer + 10 μm slab. In cases of incorrect automatic delineation, manual delineation adjustment was made.

**Statistical Analysis**

Continuous variables were tested for normality distribution (Shapiro–Wilk test). The paired t-test or Wilcoxon nonparametric test was used to compare the logarithm of the minimal angle of resolution visual acuity, vascular density, and FAZ area between eyes with Coats disease and fellow eyes. The Pearson or Spearman correlation coefficients were used to study the correlation between logarithm of the minimal angle of resolution visual acuity, vascular density, and FAZ.
Table 1. Patient Characteristics of the Study Population (N = 14)

| Measurement                  | Coats Eyes | Fellow Eyes | P    |
|------------------------------|------------|-------------|------|
| No. of Coats eyes            | 13         | 13          |      |
| No. of fellow eyes           | 13         | 13          |      |
| Sex (male)                   | 11         | 11          |      |
| Age (SD)                     | 11.6 ± 2.7 | 11.6 ± 2.7  |      |
| Disease stage                |            |             |      |
| 2A                           | 5          | 3           |      |
| 2B                           | 7          | 7           |      |
| 2B1                          | 6          | 6           |      |
| 2B2                          | 1          | 1           |      |
| 3A                           | 1          | 3           |      |
| Mean BCVA—Coats eyes (whole cohort) | 0.30 ± 0.19 (20/40) | 0.24 ± 0.09 (20/40) | 0.003 |
| Mean BCVA—Stage 2A           | 0.13 ± 0.13 (20/27) | 0.24 ± 0.09 (20/40) | 0.001 |
| Mean BCVA—Stage 2B           | 0.44 ± 0.12 (20/55) | 0.24 ± 0.09 (20/40) | 0.001 |
| Mean BCVA—Stage 3A           | 2 (20/2000) | 2 (20/2000) |      |
| Mean BCVA—Fellow eyes        | 0.03 ± 0.07 (20/21) | 0.24 ± 0.09 (20/40) | 0.001 |

BCVA, best-corrected visual acuity.

Table 2. Comparison of Vascular Density and Foveal Avascular Zone Area in all 13 Coats Eyes Versus 13 Unaffected Fellow Eyes

| Measurement            | Coats Eyes | Fellow Eyes | P    |
|------------------------|------------|-------------|------|
| Vascular density SCP (%) |            |             |      |
| Whole image            | 43.7 ± 4.7 | 45.9 ± 4.4  | 0.000 |
| Superior hemi          | 43.6 ± 4.8 | 45.7 ± 4.8  | 0.001 |
| Inferior hemi          | 43.7 ± 4.9 | 46.1 ± 4.3  | 0.002 |
| Fovea                  | 22.7 ± 5.8 | 22.6 ± 5.7  | 0.872 |
| Parafovea—total        | 45.7 ± 5.4 | 48.5 ± 4.7  | 0.000 |
| Parafovea—sup-hemi     | 45.6 ± 5.2 | 48.5 ± 5.3  | 0.001 |
| Parafovea—inf-hemi     | 45.7 ± 5.7 | 48.6 ± 4.5  | 0.002 |
| Parafovea—temporal     | 44.1 ± 5.1 | 48 ± 5.0    | 0.000 |
| Parafovea—superior     | 46.5 ± 5.3 | 49.3 ± 5.6  | 0.010 |
| Parafovea—nasal        | 45.5 ± 5.7 | 48.1 ± 4.7  | 0.004 |
| Parafovea—inferior     | 46.7 ± 6.2 | 49.1 ± 4.7  | 0.025 |
| Vascular density DCP (%) |            |             |      |
| Whole image            | 43.0 ± 6.3 | 50.3 ± 2.2  | 0.001 |
| Superior hemi          | 43.5 ± 5.7 | 50.4 ± 2.1  | 0.001 |
| Inferior hemi          | 42.5 ± 7.1 | 50.3 ± 2.3  | 0.002 |
| Fovea                  | 30.6 ± 6.2 | 36.3 ± 6.0  | 0.000 |
| Parafovea—total        | 44.5 ± 6.4 | 52.5 ± 2.0  | 0.001 |
| Parafovea—sup-hemi     | 44.8 ± 5.9 | 52.7 ± 2.1  | 0.001 |
| Parafovea—inf-hemi     | 44.1 ± 7.1 | 52.3 ± 2.1  | 0.001 |
| Parafovea—temporal     | 42.8 ± 7.1 | 52.7 ± 2.3  | 0.000 |
| Parafovea—superior     | 44.8 ± 5.7 | 52.6 ± 1.9  | 0.000 |
| Parafovea—nasal        | 45.5 ± 6.5 | 52.7 ± 2.3  | 0.004 |
| Parafovea—inferior     | 44.0 ± 7.5 | 52.0 ± 2.3  | 0.001 |
| FAZ area (μm²)          | 0.29 ± 0.1 | 0.24 ± 0.09 | 0.003 |

Data in boldface had significant values (p<0.05).

Results

Patient characteristics are listed in Table 1. A total of 26 eyes of 13 patients (11 male and 2 female) were included in the study. The mean age was 11.6 ± 2.7 (range 8–17) years. The mean age at time of diagnosis was 8.9 ± 4.0 years. Five patients had Stage 2A disease, 7 had Stage 2B, and 1 had Stage 3A. Two of the patients with Stage 2B disease had macular pathology that required manual segmentation of retinal layers due to cystoid macular edema and a macular scar (Figure 1). Notably, the patient with a macular scar had a nodule before development of the scar and was therefore Stage 2B2. The rest were Stage 2B1.

Vascular density and FAZ values are presented in Table 2. Vascular density was significantly decreased in eyes with Coats disease in comparison with fellow eyes in the whole SCP and DCP images (43.7 ± 4.7 vs. 45.9 ± 4.4 [P = 0.000] and 43.0 ± 6.3 vs. 50.3 ± 2.2 [P = 0.001], respectively). The difference was also significant for all sectors of the SCP and DCP except for the fovea in the SCP layer. The FAZ area was significantly larger in eyes with Coats disease in comparison with fellow eyes (0.29 ± 0.1 vs. 0.24 ± 0.09 [P = 0.003]).

Two patients with Stage 2B disease had macular edema or scarring, necessitating manipulation of the automatic segmentation performed by the OCTA algorithm. To rule out possible skewing of data due to these significant changes, data analysis was also performed for the other 11 patients only. For this group of patients, the statistical significance remained the same except for the inferior parafoveal region of the SCP layer, for which the difference between eyes with Coats disease and fellow eyes became borderline significant (P = 0.056).

Table 3 shows vascular density and FAZ data for the five patients with Stage 2A disease and Table 4 presents these data for the seven patients with Stage 2B disease. In the group of patients with Stage 2A disease, there were no significant differences in vascular density at the level of the SCP except for the temporal parafoveal area. However, most sections in the DCP layer (except for the inferior hemifovea, nasal, and temporal parafoveal areas) showed a significant decrease in vascular density in Coats eyes in comparison with fellow eyes. The FAZ area was also larger in the eyes with Coats disease (0.29 ± 0.1 vs. 0.25 ± 0.1, P = 0.012). In comparison, in the group of patients with Stage 2B disease, vascular density was decreased in both the SCP and DCP layers in almost all segments (except for the fovea and inferior parafovea in the SCP layer). The FAZ area was larger in eyes with Coats disease (0.31 ± 0.1 vs. 0.25 ± 0.1, P = 0.046).
This study provides quantitative data of the vessel density and FAZ in a pediatric population with Coats disease. We found that in all patients, vascular density was decreased in the eyes affected by Coats disease compared with the fellow eyes. The FAZ area was also significantly larger in eyes with Coats disease in comparison with fellow eyes. In a subgroup analysis, we found that in patients with Stage 2A there was a decrease in vascular density in the DCP layer in comparison with the fellow eyes, whereas in patients with Stage 2B, the decrease in vascular density involved both the SCP and DCP layers. The significant differences found in both vascular density and FAZ area between eyes with Coats disease and fellow eyes lends further evidence that Coats disease is a unilateral disease. However, larger studies are required to support these data.

Different studies quote different prevalence of unilaterality in Coats disease ranging from 80% to 95%.4,22,23 This study also reiterates that in patients with presumed bilateral Coats disease, one should investigate secondary bilateral Coats disease—like retinopathy with systemic conditions such as facioscapulohumeral dystrophy.24

Decreased vascular density has been reported in several retinal vascular diseases, including diabetic retinopathy (DR) (mostly in the DCP),25,26 retinal vein occlusion,27 and sickle cell retinopathy.28 It is not surprising then that according to our data, Coats disease exhibits the same changes to vascular density. In our group of patients, the decrease in vascular density was seen in both the superficial plexus and the deep plexus in patients with Stage 2B disease. According to the accepted clinical classification, Stage 2B disease involves the macula.2 However, we also found a significant decrease in the vascular density in patients with Stage 2A disease, which, according to the classification, should not involve the center. This is a new finding for this disease. Nevertheless, considering data from different vascular diseases, it is not a surprise. Optical coherence tomography angiography has proven to be a sensitive device for the detection of early subclinical changes in the macula. Vascular density changes are seen in diabetics even before the development of overt DR.26 Our data suggest that such subclinical changes also occur in Coats disease before the apparent involvement of the macula as seen by other imaging modalities and with biomicroscopy.

Interestingly, the DCP seems to be the first layer involved in the condition. This is consistent with

Table 3. Comparison of Vascular Density and Foveal Avascular Zone Area in 5 Coats Eyes With Stage 2A Disease Versus 5 Unaffected Fellow Eyes

| Measurement                   | Coats Eyes | Fellow Eyes | P       |
|-------------------------------|------------|-------------|---------|
| Vascular density SCP (%)      |            |             |         |
| Whole image                   | 45.6 ± 2.9 | 46.7 ± 2.3  | 0.158   |
| Superior hemi                 | 44.8 ± 3.9 | 46.4 ± 2.3  | 0.165   |
| Inferior hemi                 | 46.3 ± 2.0 | 47.1 ± 2.5  | 0.200   |
| Fovea                         | 21.4 ± 6.6 | 23.0 ± 5.8  | 0.228   |
| Parafovea—total               | 48.2 ± 2.8 | 49.6 ± 2.0  | 0.114   |
| Parafovea—sup-hemi            | 47.5 ± 4.0 | 49.5 ± 1.9  | 0.208   |
| Parafovea—inf-hemi            | 48.8 ± 1.9 | 49.7 ± 2.5  | 0.133   |
| Parafovea—temporal            | 46.2 ± 3.0 | 48.6 ± 2.9  | 0.035   |
| Parafovea—superior            | 48.7 ± 4.3 | 50.5 ± 2.2  | 0.406   |
| Parafovea—nasal               | 48.8 ± 1.6 | 49.3 ± 3.3  | 0.637   |
| Parafovea—inferior            | 48.9 ± 2.9 | 49.9 ± 2.3  | 0.538   |
| Vascular density DCP (%)      |            |             |         |
| Whole image                   | 46.7 ± 2.9 | 50.3 ± 2.2  | 0.023   |
| Superior hemi                 | 46.9 ± 3.1 | 50.5 ± 2.1  | 0.011   |
| Inferior hemi                 | 46.6 ± 3.1 | 50.1 ± 2.3  | 0.061   |
| Fovea                         | 30.9 ± 4.1 | 35.6 ± 4.0  | 0.001   |
| Parafovea—total               | 48.7 ± 2.7 | 52.5 ± 1.8  | 0.013   |
| Parafovea—sup-hemi            | 49.1 ± 3.3 | 52.9 ± 1.9  | 0.024   |
| Parafovea—inf-hemi            | 48.3 ± 2.3 | 52.2 ± 1.7  | 0.013   |
| Parafovea—temporal            | 49.5 ± 3.4 | 52.3 ± 2.2  | 0.054   |
| Parafovea—superior            | 47.9 ± 2.9 | 53.4 ± 1.6  | 0.007   |
| Parafovea—nasal               | 49.3 ± 3.0 | 52.4 ± 1.9  | 0.080   |
| Parafovea—inferior            | 48.1 ± 2.1 | 52.2 ± 1.7  | 0.004   |
| FAZ area (µm²)                | 0.29 ± 0.1 | 0.25 ± 0.1  | 0.012   |

Data in boldface had significant values (p<0.05).
Table 4. Comparison of Vascular Density and Foveal Avascular Zone Area in 7 Coats Eyes With Stage 2B Disease Versus 7 Unaffected Fellow Eyes

| Measurement        | Coats Eyes | Fellow Eyes | \( P \) |
|--------------------|------------|-------------|--------|
| Vascular density   |            |             |        |
| SCP (%)            |            |             |        |
| Whole image        | 42.1 ± 5.7 | 44.7 ± 5.5  | 0.002  |
| Superior hemi      | 42.4 ± 5.3 | 44.5 ± 6.1  | 0.002  |
| Inferior hemi      | 41.7 ± 5.8 | 44.8 ± 5.3  | 0.008  |
| Fovea              | 22.5 ± 5.3 | 20.6 ± 4.0  | 0.217  |
| Parafovea—total    | 43.8 ± 6.6 | 47.4 ± 6.3  | 0.001  |
| Parafovea—sup-hemi | 44.2 ± 6.2 | 47.3 ± 7.0  | 0.001  |
| Parafovea—in-hemi  | 43.5 ± 7.0 | 47.4 ± 5.7  | 0.007  |
| Parafovea—temporal | 42.2 ± 6.4 | 47.0 ± 6.7  | 0.000  |
| Parafovea—superior | 44.8 ± 6.0 | 48.1 ± 7.5  | 0.023  |
| Parafovea—nasal    | 43.2 ± 6.9 | 46.8 ± 5.7  | 0.003  |
| Parafovea—inferior | 45.0 ± 8.0 | 48.1 ± 6.1  | 0.065  |
| Vascular density   |            |             |        |
| DCP (%)            |            |             |        |
| Whole image        | 41.2 ± 7.2 | 49.9 ± 2.0  | 0.016  |
| Superior hemi      | 42.1 ± 6.1 | 50.0 ± 2.2  | 0.019  |
| Inferior hemi      | 40.4 ± 8.4 | 49.8 ± 2.1  | 0.015  |
| Fovea              | 29.4 ± 7.3 | 34.9 ± 5.2  | 0.034  |
| Parafovea—total    | 42.4 ± 7.1 | 52.1 ± 2.2  | 0.010  |
| Parafovea—sup-hemi | 43.0 ± 5.8 | 52.2 ± 2.3  | 0.008  |
| Parafovea—in-hemi  | 41.9 ± 8.5 | 52.0 ± 2.4  | 0.013  |
| Parafovea—temporal | 38.1 ± 4.8 | 52.9 ± 2.8  | 0.000  |
| Parafovea—superior | 43.7 ± 6.1 | 51.8 ± 1.9  | 0.012  |
| Parafovea—nasal    | 43.8 ± 7.4 | 52.5 ± 2.4  | 0.034  |
| Parafovea—inferior | 41.8 ± 9.2 | 51.6 ± 2.8  | 0.017  |
| FAZ area (\( \mu m^2 \)) | 0.31 ± 0.1 | 0.25 ± 0.1  | 0.046  |

Data in boldface had significant values (\( p < 0.05 \)).

previous studies that have shown more frequent and more pronounced changes to vascular perfusion in the DCP in both DR and retinal vein occlusion (RVO). Recent literature suggests that these findings are a result of this layer being the most likely to be confounded by projection artifacts and segmentation error. However, given the use of the 3D PAR algorithm in our study, designed to remove projection artifacts from deeper layers, it is possible that such findings may be true. Because the SCP is directly connected to the retinal arterioles, it may have greater perfusion pressure than the DCP. In addition, the DCP is located in a watershed-like area where oxygen saturation may be lower than in the inner and outer retina, suggesting higher vulnerability to ischemic or any other insults.

The FAZ area has been shown to be increased in different retinal vascular diseases. Optical coherence tomography angiography of 63 eyes of 64 patients with diabetes mellitus showed significant enlargement of FAZ from 0.25 mm\(^2\) in controls to 0.37 mm\(^2\) in diabetic eyes without DR, and to 0.38 mm\(^2\) in eyes with DR. A study of 23 subjects with RVO (15 central RVO and 8 branch RVO) and 8 eyes of 8 age-matched controls assessed FAZ size in both groups. Mean FAZ was larger in RVO eyes than in both fellow eyes and control eyes. In the above-mentioned study comparing patients with sickle cell disease to normal subjects, the FAZ area was significantly larger in affected eyes than in the control group.

As with vascular density, our data suggest that Coats disease also leads to FAZ enlargement similarly to other retinal vascular diseases, a finding that is seen as early as Stage 2A of the disease. The enlargement may represent macular vessel compromise and serves as an additional marker for central changes in this disease. Longitudinal studies exploring the change of FAZ and vessel density over time may provide a clue of the threshold of these parameters below which visible clinical findings occur.

Optical coherence tomography angiography has been limited by various image artifacts. Projection artifacts, in particular, pose a challenge, causing superficial vessels to be incorrectly detected as deeper vessels. This may lead to erroneous quantification at the level of the DCP. The current study used AngioAnalytics research software (Optovue), using the 3D PAR algorithm. This algorithm has been shown to effectively reduce projection artifacts. Studies have demonstrated a decreased two-dimensional correlation coefficient between plexuses (indicating that the plexuses are more dissimilar) and suppression of projection artifacts with reduced vascular density measurements in the deeper layers, which are mostly affected by projection artifacts.

In addition, the AngioAnalytics version used in this study includes a segmentation editing and propagation tool, allowing for correction of automatic segmentation errors. This was used in two patients in our study, one with a macular scar and the other with macular edema. The data from these patients were similar to that seen with the other patients not needing segmentation correction. This technique may improve the ability to analyze and follow-up on patients with significant macular changes, including Coats disease.

Our study was limited by a small sample size, resulting from the rarity of the condition and the elimination of patients with poor image quality. However, this group was sufficient to produce highly significant results, suggesting that the changes seen are indeed real and substantial.

In conclusion, this is the first study to provide quantitative data of the macular vascular density and FAZ area in a cohort of pediatric patients with Coats disease to lend evidence to the unilaterality of Coats disease and strengthen the evidence that a somatic mutation is a likely explanation for the disease. The findings in the eyes affected by Coats disease suggest that this vascular condition behaves similarly to other
retinal vascular diseases, with FAZ enlargement and reduction in vascular density. However, the study also provides evidence of overt macular changes at Stage 2A, which is currently classified clinically as a stage of nonmacular involvement. Given its noninvasiveness, OCTA may prove to be a valuable tool in the evaluation and follow-up of pediatric patients with Coats disease, including the potential impact of treatment on macular vascular density.

**Key words:** Coats disease, OCTA, OCTA, PAR, pediatric, unilateral.

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