# ASSESSING THE ACTIVITY OF MYOPIC CHOROIDAL NEOVASCULARIZATION

## Comparison Between Optical Coherence Tomography Angiography and Dye Angiography

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**Purpose:** This study aims to suggest a novel strategy for assessing the activity of myopic choroidal neovascularization (mCNV) based on optical coherence tomography angiography (OCTA) and to compare it with traditional fundus fluorescein angiography as the gold standard.

**Methods:** Macular OCTA images were obtained using RTVue XR Avanti with AngioVue. Morphologic features of mCNV lesions were analyzed. Characteristics of OCTA in 41 eyes with active mCNV and 41 eyes with inactive mCNV were analyzed. Optical coherence tomography angiography parameters associated with mCNV activity and the clinical significance of their sensitivity and specificity were analyzed using fundus fluorescein angiography as the reference.

**Results:** Of the total 108 patients, 82 had OCTA images with good quality which were included in this study. Several anatomical features of the CNV lesions, including overall appearance, branching with tiny vessels, presence of anastomoses/loops, and choroidal dark halo, were considered the possible parameters associated with mCNV activity. The intra- and interobserver agreements were substantial. To evaluate the CNV activity, sensitivity of overall appearance, tiny vascular branching, and presence of anastomoses or loops were 65.9%, 82.9%, and 73.2%, respectively, whereas the specificity was 87.8%, 90.2%, and 92.7%, respectively. However, the choroidal dark halo showed low specificity (46.3%) and failed in terms of evaluating the activity of mCNV. A novel comprehensive procedure integrating branching as a major parameter and overall appearance and presence of anastomoses/loops as minor parameters was developed to evaluate mCNV activity with sensitivity of 95.1% and specificity of 85.4%.

**Conclusion:** In mCNV, the acquisition rate of clear OCTA images was 75.9%. A novel comprehensive diagnostic procedure combining mCNV appearance, vascular branching, and anastomoses/loops by OCTA may be a valuable strategy to evaluate neovascular activity in mCNV.

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Myopic choroidal neovascularization (mCNV) is one of the most common vision-threatening complications of pathologic myopia. It affects 5%–11% of patients with pathologic myopia and 0.04%–0.05% of the general population.[1] It is particularly prevalent among young and middle-aged Asians.[1,2] Without treatment, there have been very poor outcomes for mCNV. Visual acuity may drop to 20/200 or less within 5 years, with a tendency to progressively enlarge the lesion or CNV-related macular atrophy.[3–5] Anti–vascular endothelial growth factor (VEGF) treatment has become the first-line treatment for mCNV, leading to not only anatomical improvements but also functional improvements.[6] During anti-VEGF treatment, monitoring neovascular activity is essential for a re-treatment decision making.

Fundus fluorescein angiography (FFA) with dye injection is considered the gold standard for detecting mCNV and assessing its activity.[6,7] However, FFA is time consuming and invasive, resulting in varying degrees of patient discomfort, including anaphylactic reactions that can occur during and/or after FFA. A total of

4.8% patients were reported to have experienced adverse events after the FFA, including nausea (2.9%), vomiting (1.2%), and flushing/itching (0.5%).[8] Recently, optical coherence tomography angiography (OCTA) has been introduced in the clinical practice. Optical coherence tomography angiography provides depth-resolved visualization of the retinal and choroidal vasculature without the need for dye injection. The technology has been applied for the diagnosis and monitoring of CNV in age-related macular degeneration (AMD). A recent case series analyzed the morphologic characteristics of mCNV before and after anti-VEGF therapy by OCTA. Querques et al[9] described the OCTA features of mCNV and demonstrated its high sensitivity and specificity for neovascular detection. Nevertheless, studies of OCTA in monitoring mCNV activity remain very limited. The present study aims to evaluate the presence and structural features of mCNV on OCTA, to estimate the sensitivity and specificity of OCTA in assessing mCNV activity, and to compare it with FFA as the gold standard.

## Methods

### Patients

This retrospective case series was conducted in Zhongshan Ophthalmic Center with the permission of the Institutional Review Board of the Zhongshan Ophthalmic Center, Sun Yat-sen University. All investigations followed the tenets of the Declaration of Helsinki. A total of 82 eyes from 82 patients with active or quiescent mCNV were enrolled in this study from March 2014 to July 2018. The inclusion criteria were as follows: 1) aged ≥18 years; 2) diagnosis of pathologic myopia as defined by spherical equivalent

(SE) < −6.00 D or axial length (AL) >26.5 mm; 3) accompanied by characteristic degenerative changes in the choroid and retina or by myopic-related sclera changed, such as staphyloma. The exclusion criteria were as follows: 1) other secondary choroidal neovascular diseases, such as wet AMD or angioid streaks; 2) poor FFA or OCTA image quality due to severe vitreous hemorrhage; 3) poor FFA or OCTA image quality due to posterior staphyloma or cataract, the presence of other ocular diseases; 4) or evidence of any conditions other than CNV which may have affected the FFA and OCTA images. For patients with quiescent mCNV, the requirements included a history of active mCNV treated with anti-VEGF previously or confirmed with an image in the imaging bank.

A comprehensive ophthalmic examination, including measurement of best-corrected visual acuity, intraocular pressure, slit-lamp examination, FFA, and SD-OCT (Spectralis + HRA; Heidelberg Engineering, Heidelberg, Germany), was performed in each patient. Optical coherence tomography angiography was performed by the RTVue AngioVue System, XR Avanti SD-OCT device (Optovue, Inc, Fremont, CA), based on a high-speed SD-OCT platform that operates at 70,000 axial scans per second. A macula cube (3 × 3 mm) centered the fovea was acquired; in cases of partial visualization of the entire CNV network, a larger (6 × 6 mm) image was obtained. The image of the outer retina slab and choroid slab was collected and analyzed by the RTVue XR angio analytics software (2017.1.0.155). Manual adjustment was made by two expert retina specialists (S.L. and L.S.) to ensure accurate segmentation if necessary.

### Imaging

Typical active mCNV was subfoveal or juxtafoveal Type 2 neovascularization and "classic" on FFA, with well-defined hyperfluorescence on early frames and dye leakage on late frames. The dye leakage was identified by an increased area of hyperfluorescence in the late phase compared with the early phase. In addition, active mCNV lesions appeared as elevation of the, presenting subretinal or intraretinal hyporeflective or hyperreflective exudation, along with overlying fuzzy areas and absence of external limiting membrane visibility on structural SD-OCT. In quiescent mCNV, there are no signs of activity by FFA at the time of OCTA acquisition. The lesions present as staining of a CNV scar on FFA and a well-defined profile with hyperreflective borders on structural SD-OCT. The OCTA images were assessed for classification of several anatomical descriptors that were considered to be associated with the activity of the myopic neovascular

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lesion based on previous wAMD studies[10]: 1) overall appearance, a well-defined medusa or a sea-fan-shaped CNV lesion versus an irregular CNV lesion with linear vessels; 2) branching, numerous tiny capillaries versus rare, large, mature vessels; 3) the presence of anastomoses or loops; and 4) the presence of a perilesional dark halo. Two independent investigators (S.L. and L.S.) evaluated OCTA without visualization of the corresponding FFA or SD-OCT B-scan independently. Any discrepancies in the data were resolved through reassessment and discussion with a senior researcher (X.D.). Examples of overall appearance, branching, presence of anastomoses/loops and dark halo are represented in Figure 1.

### Statistical Analysis

Statistical analysis was performed using Graph Pad (GraphPad Software, CA) or SPSS (SPSS Inc, Chicago, IL). Kappa analysis was performed to examine the intra- and interobserver agreement between the two readers. Diagnostic sensitivity, specificity, positive predictive value (PPV), negative predictive value, agreement percentage, and Youden index were calculated for each OCTA parameter. The level of agreement was determined by Cohen κ-analysis. Kappa values were interpreted as follows: less than 0, poor agreement; 0 to 0.20, slight agreement; 0.21 to 0.40, fair agreement; 0.41 to 0.60, moderate agreement; 0.61 to 0.80, substantial agreement; and greater than 0.80, almost perfect agreement. The level of significance was set at $P = 0.05$.

## Results

### Study Population and Main Clinical Findings

A total of 108 OCTA and FFA examinations in 108 mCNV eyes were checked by two retinal specialists. Twenty-six were excluded because of unsatisfactory OCTA image quality. Of these 26 mCNVs, 15 could not be detected in OCTA and showed as small CNV (diameter of CNV <100 μm in OCT), 9 showed poor images due to staphyloma, 1 was excluded because of impaired eye fixation, and 1 was excluded due to refractive opacity. Finally, 82 eyes from 82 patients were included in this study. Of these, 42 patients (51.2%) were women; the mean age was 47.77 ± 13.09 years (range, 20–74 years). The average SE was −11.71 ± 4.80 D, and the mean AL was 28.99 ± 1.22 mm. Active mCNVs were found in 41 eyes of 41 patients (Group A), and quiescent mCNV was
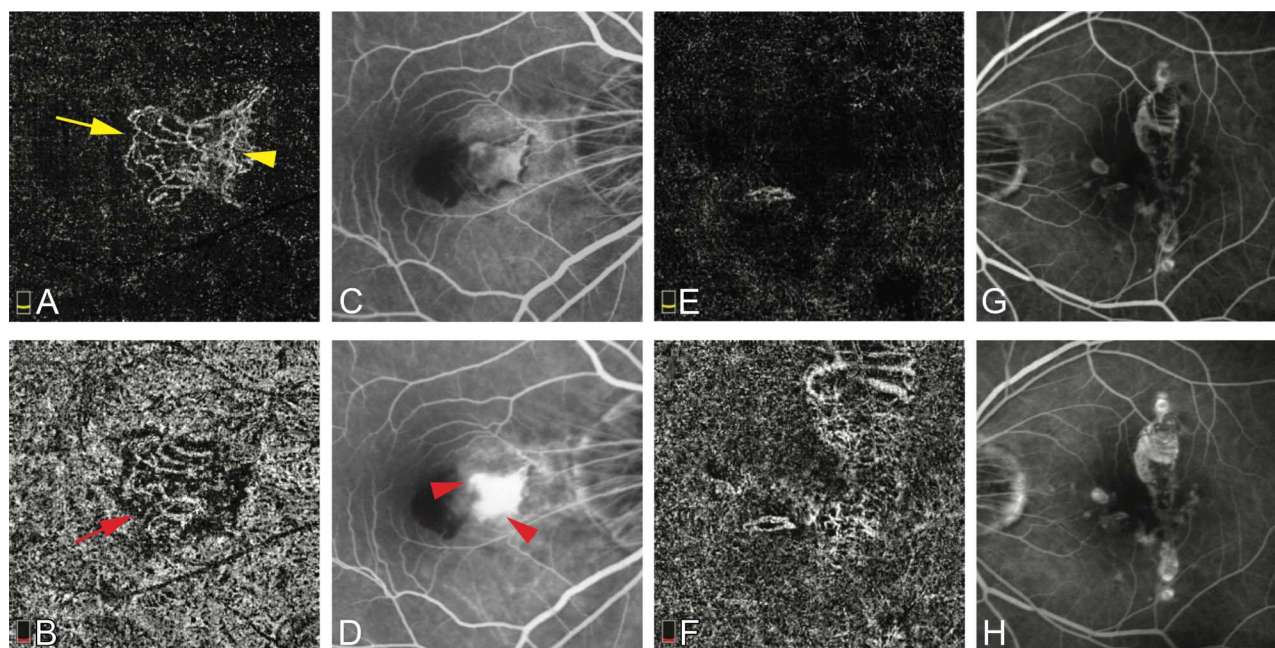


**Fig. 1.** OCTA images and FA images of (**A–D**) a recurrent active mCNV in a 26-year-old woman with AL of 28.78 mm and SE of −9.875 D and (**E–H**) a quiescent mCNV in a 54-year-old man with AL of 28.89 mm and SE of −11.375 D. **A.** The OCTA image shows the presence of neovascular structure in the outer retina layer. The lesion is composed by numerous tiny capillaries (arrowhead) with clear anastomoses and loops (arrow). **B.** The OCTA scan of the choroid layer under the mCNV shows a hyposignaling halo surrounding the lesion (arrow). **C.** Fluorescein angiography in the early phase reveals the neovascular structure, whose shape is similar to the one showed by OCTA. The shape of this mCNV is angular, which usually is a sign of previous treatment or shrunken lesion. **D.** The presence of mild leakage (arrowheads) of this lesion is observed in the late phase of FA. **E.** The OCTA image of a quiescent mCNV appears as an irregular shape and is composed by large, rare, mature vessels which lacks anastomose or loop. **F.** The choroid dark halo is absent in the choroid layer. **G.** On the early phase of fluorescein angiography, a hyperfluorescent vascular structure is clearly visible. **H.** No leakage is observed on the late phase in this inactive lesion.

identified in 41 eyes of 41 patients (Group Q). In Group A, 7 of the 41 patients received anti-VEGF treatment 3 months ago. In Group Q, all patients received anti-VEGF treatment previously. No statistical differences were found in terms of age, AL, and SE between the groups ($P = 0.17$, 0.52, and 0.34, respectively). Complete demographics are shown in Table 1.

*Intra- and Interobserver Agreement*

Four descriptive parameters, "A (appearance)—B (branching)—A (anastomoses/loops)—D (dark halo)," were used in this study: overall Appearance of the neovascular lesion, Branching of vasculature, presence of Anastomoses/loops, and presence of Dark halo. The intraobserver agreement of A-B-A-D was substantial to almost perfect, with kappa values of 0.955, 0.892, 0.876, and 0.937, respectively. Substantial to almost perfect interobserver agreement was also observed, with kappa values of 0.933, 0.783, 0.744, and 0.905, respectively (Table 2).

*Morphology Findings in Active and Quiescent Myopic Choroidal Neovascularization on Optical Coherence Tomography Angiography*

The overall appearance of the neovascular lesions was defined as medusa or sea fan in 32 eyes, including 27 in Group A (n = 41, 65.9%) and 5 in Group Q (n = 41, 12.2%) ($P < 0.0001$). Tiny vascular branching was found in 38 eyes, including 34 in Group A (n = 41, 82.9%) and 4 in Group Q (n = 41, 9.8%) ($P < 0.0001$). Multiple anastomoses and loops were identified in 33 eyes, with 30 in Group A (n = 41, 73.2%) and 3 in Group Q (n = 41, 7.3%) ($P < 0.0001$). Choroid dark halo, the hypointense perilesional halo at the choroid layer, was considered in 55 eyes, including 33 in Group A (n = 41, 80.5%) and 22 in Group Q (n = 41, 53.7%) ($P = 0.01$) (Table 3).

*Diagnostic Sensitivity and Specificity of Optical Coherence Tomography Angiography Parameters Compared With Fundus Fluorescein Angiography*

Four qualitative parameters, A (appearance)—B (branching)—A (anastomoses/loops)—D (dark halo), were used to evaluate mCNV activity. The overall appearance of medusa/sea fan on OCTA and leakage on FFA achieved a moderate agreement in 63 of the 82 cases (76.8%), with a κ-value of 0.537, sensitivity of 65.9%, specificity of 87.8%, and PPV of 84.4%. In 19 cases (23.2%), consensus was not reached; of these 19 cases, 14 presented leakage during FA but with an irregular shape in OCTA and 5 cases were shaped as medusa/sea fan on OCTA but without fluorescein leakage.

Lesions with tiny vascular branching also achieved good agreement in 71 of the 82 cases (86.6%), with a κ-value of 0.732, sensitivity of 82.9%, specificity of 90.2%, and PPV of 89.5%. Consensus was not reached in 11 cases (13.4%). In total, of these 11 cases, 4 were with tiny branching and capillaries on OCTA but no leakage on FFA, whereas 7 cases showing only rare, large, mature vessels on OCTA showed fluorescent leakage on FFA.

The presence of anastomoses and loops was noted with good agreement on OCTA compared with FFA in 68 of the 82 cases (82.8%), with a κ-value of 0.659, sensitivity of 73.2%, specificity of 92.7%, and PPV of 90.9%. A consensus was not reached in 14 cases (17.1%). A diagnosis of anastomoses and loops was made in 30 of the 41 active mCNV cases but only in 3 of the 41 silent mCNV lesions.

However, only fair agreement between choroid dark halo on OCTA and FFA leakage was reached in 52 of the 82 sessions (63.4%), with a κ-value of 0.268. The sensitivity was 80.5%, which is acceptable; however, the specificity was only 46.3%. A consensus was not reached in 30 cases (36.6%). Choroid dark halo was not identified in 8 of the 41

Table 1. Demographic Characteristics

| Characteristic | Active mCNV Group | Quiescent mCNV Group | P |
|---|---|---|---|
| No. of patients (no. of eyes) | 41 (41) | 41 (41) | |
| Male/Female (n) | 20/21 | 20/21 | 1.0 |
| OD/OS | 21/20 | 18/23 | 0.51 |
| Mean age ± SD, years (min to max) | 49.76 ± 13.64 (20 to 74) | 45.78 ± 12.37 (21 to 69) | 0.17 |
| Mean AL, mm (min to max) | 29.09 ± 1.20 (26.73 to 31.53) | 28.88 ± 1.25 (26.09 to 32.26) | 0.52 |
| Mean SE, D (min to max) | −12.35 ± 5.00 (−20.75 to −6) | −11.10 ± 4.62 (−20.25 to −6.5) | 0.34 |
| Mean BCVA, ETDRS letters (min to max) | 49.2 ± 14.3 (40 to 72) | 57.3 ± 13.3 (49 to 73) | 0.01* |
| Area of CNV, mm² (min to max) | 0.62 ± 0.58 (0.23 to 1.26) | 0.30 ± 0.43 (0.02 to 1.17) | 0.01* |
| Subfoveal lesion/parafoveal lesion (n) | 5/41 | 7/41 | 0.76 |

BCVA, best-corrected visual acuity.
* $P<0.05$.

Table 2. Interobserver Agreement Regarding the OCTA Characters

| Character | Observer 1 | Observer 2 | | % Agreement | Kappa ± SE | Strength of Agreement |
|---|---|---|---|---|---|---|
| | | + | − | | | |
| Medusa or sea-fan shape | + | 31 | 2 | 96.34 | 0.924 ± 0.043 | Very good |
| | − | 1 | 48 | | | |
| Tiny branching | + | 31 | 5 | 86.59 | 0.728 ± 0.076 | Good |
| | − | 6 | 40 | | | |
| Loop or anastomoses | + | 29 | 4 | 89.02 | 0.773 ± 0.071 | Good |
| | − | 5 | 44 | | | |
| Choroid dark halo | + | 54 | 1 | 96.34 | 0.916 ± 0.047 | Very good |
| | − | 2 | 25 | | | |

active mCNV lesions (19.5%) and 22 cases with dark halo did not leak on FFA.

*A Noninvasive Accessing Strategy for Myopic Choroidal Neovascularization Activity by Optical Coherence Tomography Angiography*

Considering the re-treatment requirement during anti-VEGF strategy and the poor prognosis of this disease if left untreated, a criterion with excellent sensitivity and good specificity is highly recommended to determine the treatment needed for active mCNV lesions to the greatest extent possible. Among the four OCTA parameters A-B-A-D, branching of tiny vasculature appeared to have the highest sensitivity (82.9%). Five of seven active lesions that appeared with no branching of vessels showed medusa/sea-fan shape and anastomoses/loops. In Group Q, only two lesions appeared as medusa/sea-fan shape and anastomoses/loops simultaneously. Therefore, we suggest branching could be used as the major parameter to assess the mCNV activity. In addition to branching, the presence of medusa or sea-fan shape and anastomoses/loops should also be considered as minor parameters in the evaluation of lesion activity.

We developed a novel comprehensive procedure intergrading the major (branching) and minor (appearance and anastomoses/loops) parameters. First, the major parameter (branching) is judged. If "yes" (38 eyes), the CNV lesion is likely active (n = 82) (Figure 2) and if "no" (44 eyes), the two minor parameters are evaluated. If the lesion appears as medusa or sea-fan shaped in the presence of anastomoses or loops simul-taneously, the CNV lesion is likely to be active (7 of the 44 eyes). If "no," the CNV lesion is likely to be inactive (Figures 3 and 4). In summary, an mCNV lesion with the major parameter (branching) positive or two minor parameters (appearance and anastomoses/loops) positive should be considered an active lesion. With this novel procedure to evaluate the lesion activity, the final sensitivity and specificity reached 95.1% and 85.4%, respectively. The final agreement was as high as 90.2% (74 of 82), with kappa value of 0.805, considered almost perfect agreement (Table 4).

## Discussion

Owing to the ability to visualize retinal and choroidal vasculature noninvasively with high resolution, several studies have reported on the potential value of OCTA in a variety of ocular diseases, including AMD, polypoidal choroidal vasculopathy (PCV), and mCNV. Several studies showed that the sensitivity (75.7–100.0%) and specificity (67.6–100.0%) appear to be high for detecting CNV in AMD by OCTA, especially for Type II CNV, compared with the gold standard FFA.[11–16] As most of the mCNVs appear as Type II CNV, located above the retina pigment epithelial layer and can be easily imaged, the detection of mCNV in OCTA showed high sensitivity (90.5–94.1%) in several studies as well as our own experience.[17–19] Nevertheless, some features of pathologic myopia such as posterior staphyloma may diminish OCTA image quality and may limit the interpretation of OCTA, especially for CNV located on the slope of staphyloma. As reported by

Table 3. OCTA Characters in Active mCNV and Inactive mCNV

| Character | Active mCNV (n = 41), n (%) | Inactive mCNV (n = 41), n (%) | P |
|---|---|---|---|
| Medusa or sea-fan shape | 27 (65.9) | 5 (12.2) | <0.0001 |
| Tiny branching | 34 (82.9) | 4 (9.8) | <0.0001 |
| Loop or anastomoses | 30 (73.2) | 3 (7.3) | <0.0001 |
| Choroid dark halo | 33 (80.5) | 22 (53.7) | 0.01 |
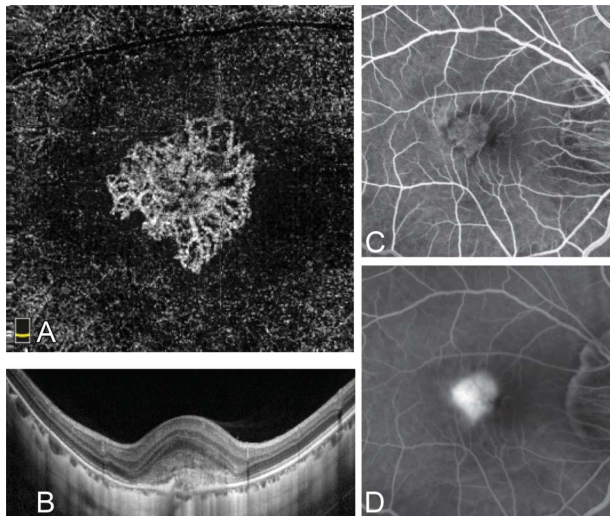
**Fig. 2.** Typical OCTA image and traditional multimodal images in a 55-year-old woman with active mCNV (AL: 29.47 mm; SE: −12.25 D). **A.** Typical medusa-shaped neovascular network with numerous tiny capillaries (branching) and anastomoses/loops in OCTA. **B–D.** Traditional multimodal images confirm the lesion is an active mCNV by the fuzzy shape around the hyperreflective CNV in OCT (**B**) and late-phase leakage of the neovascular lesion on FA (**C–D**).
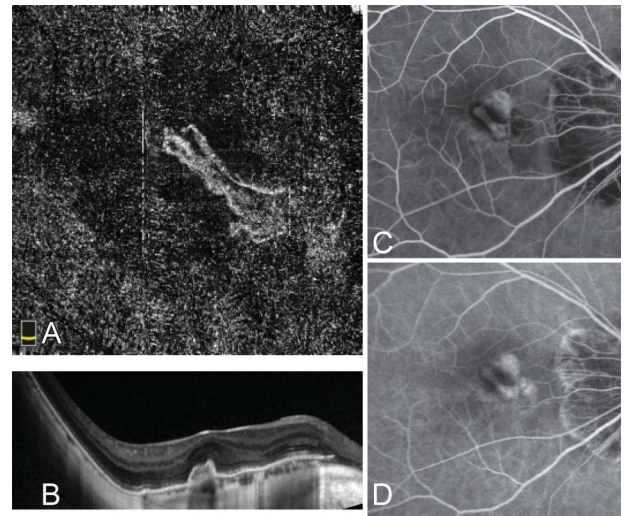


**Fig. 3.** Typical OCTA image and traditional multimodal images in a 43-year-old woman with inactive mCNV (AL: 29.70 mm; SE: −18.5 D). **A.** An irregular-shaped neovascular network with mature, large linear vessels and absent anastomoses/loops in OCTA. **B–D.** Traditional multimodal images confirm the lesion is an inactive mCNV by the well-defined boundary around the hyperreflective CNV in OCT (**B**) and absent late-phase leakage of the neovascular lesion on FA (**C–D**).

Miyata et al,[17] 75% of the patients (21 of 28) achieved OCTA images with sufficient quality, similar to the 75.9% (82 of the 108) achieved in the present study.

Several studies have assessed the ability of non-invasive methods, such as structure-OCT, in determining the activity of CNV in AMD. The results were quite positive for revealing the fuzzy border of the lesion; SRF and IRF were good indexes for activity checking in OCT.[7] In 2015, Coscas et al[10] also demonstrated that OCTA patterns with 1) a well-defined lacy-wheel or sea-fan shape, 2) tiny capillaries branching, 3) anastomoses and loops, and 4) perilesional hypointense choroid halo were more highly correlated with active CNV in wAMD than with FA. Thus, OCT and OCTA in patients with AMD could both serve as a noninvasive alternative for monitoring CNV and for making treatment decisions during follow-up. Nevertheless, according to previous studies and our previous investigation,[20] most mCNV cases feature less leakage on FFA and noteless SRF and IRF on OCT when compared with wAMD, limiting the application of structure-OCT in mCNV activity assessments. To date, very few studies have focused on OCTA characteristics in active and inactive mCNV lesions. In 2017, Querques et al[18] classified mCNV lesions as "interlacing" and "tangled" and proposed that the "interlacing" pattern may correspond to neovascular activity, suggesting that OCTA could be considered a potentially useful tool in characterizing CNV by its morphology and detecting CNV activity in eyes with pathologic myopia.

Coscas' study in wAMD reported that the PPV of shape, branching, anastomoses, and choroid dark halo was 59/59, 59/60, 59/60, and 53/65, respectively.[10] Here, in mCNV, all these characteristics were easily identified and are repeatable in clinical practice with good inter- and intraobserver agreement. The number of eyes with each of these four characters in the active mCNV group was significantly larger than that of the
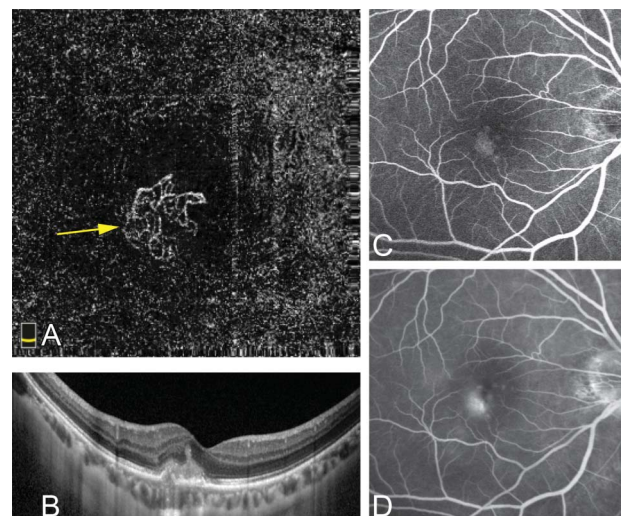


**Fig. 4.** A case of an active mCNV diagnosed by the presence of two minor characters in a 40-year-old man (AL: 28.49 mm; SE: −9.5 D). **A.** The lesion is barely seen tiny branching, but is medusa shaped and present with anastomoses/loops (arrow) in OCTA. **B–D.** Traditional multimodal images confirm the lesion is an active mCNV by the fuzzy shape around the hyperreflective CNV in OCT (**B**) and late-phase leakage of the neovascular lesion on FA (**C–D**).

Table 4. Diagnostic Performance of OCTA Characters Compared With FFA

| Character | % Sensitivity | % Specificity | % Positive Predictive Value | % Negative Predictive Value | Youden Index | Kappa ± SE |
|---|---|---|---|---|---|---|
| Medusa or sea-fan shape | 65.9 | 87.8 | 84.4 | 72.0 | 0.537 | 0.537 ± 0.091 |
| Tiny branching | 82.1 | 90.2 | 85.2 | 88.1 | 0.723 | 0.732 ± 0.075 |
| Loop or anastomoses | 75.0 | 92.7 | 87.5 | 84.4 | 0.677 | 0.659 ± 0.082 |
| Choroid dark halo | 80.5 | 46.3 | 50.0 | 76.0 | 0.249 | 0.268 ± 0.100 |
| One major criterion and two minor criteria | 95.1 | 85.4 | 86.7 | 94.6 | 0.805 | 0.805 ± 0.065 |

inactive mCNV group. Among these four characteristics, our study confirmed that branching with tiny vessels could help differentiate active mCNV with a sensitivity and specificity of 82.9% and 90.2%, respectively. Similar findings were also acquired in the analysis of appearance and anastomoses/loops, which may aid discrimination of active mCNV from quiescent ones. Furthermore, we demonstrated that the PPV of A (appearance), B (branching), and A (anastomoses) was 84.4%, 89.5% and 90.0%, respectively, similar to that in wAMD. Nevertheless, D (dark halo) failed to qualify for evaluating mCNV activity, with the specificity of 46.4% and PPV of 60%. In 2017, Al-Sheikh et al[21] reported the flow deficit in myopic eyes by OCTA, possibly explaining the presence of dark halo in both active and quiescent mCNV lesions. We supposed the possible reason could be decreased/injured choroid vascular perfusion.

This comparative analysis, focused on the potential correspondence between the OCTA pattern and gold standard FFA, was intended to evaluate the efficacy of OCTA in guiding treatment decisions. To identify every patient needing treatment, a diagnosis test with high sensitivity and appropriate specificity is preferred. Nevertheless, any one feature may not be sufficient to accurately demonstrate active mCNV. Similarly, Coscas et al[10] previously reported that these OCTA features could serve as biomarkers of CNV activity, not by any single one but by combining multiple markers on OCTA. Querques et al[18] roughly classified the mCNV lesion as "interlacing" and "tangled," also including several parameters such as branching and appearance. Based on our findings, we developed a novel comprehensive procedure to identify mCNV activity according to three image biomarkers: branching, overall appearance, and anastomoses/loops. Branching is considered the major sign and the other two are considered minor ones. An mCNV lesion with one major sign or two minor signs should be considered active by this criterion with the final agreement as 90.2% (74 of the 82) and the Kappa as 0.805, indicating an almost perfect agreement. We believe this novel procedure is easily conducted, noninvasive, and rapid

as a screen for mCNV lesions in terms of both diagnosis and monitoring.

Our study has a number of limitations. First, due to the long AL, posterior scleral staphyloma, and opacity of the refractive media, some OCTA data with low quality were excluded from the study, possibly weakening the findings. Furthermore, patients with poor fixation due to low vision and poorly perfused or small lesions could also limit the quality of the images and be excluded, possibly increasing the selection bias of the study. In addition, the mCNV detection rate and the image quality may limit the usefulness of OCTA in mCNV screening in assessing the CNV activity. Second, the sample of patients was limited, and the retrospective nature of the analysis restricts the integrality of the patient information. Further investigations with larger samples in various cohorts are warranted to confirm our observations. Third, another limitation of the current OCTA technology is the accuracy of segmentation algorithms. Manual segmentation to accurately locate the CNV lesion may induce inaccuracy, especially between observers.

In conclusion, the results of our study provided a detailed description and classification of OCTA characteristics in active and inactive mCNV lesions. As opposed to wAMD, choroid dark halo has low specificity for diagnosing active mCNV. Active mCNV primarily appears as medusa or sea-fan shaped, with tiny vascular branching and presence of loops/anastomoses. A novel comprehensive procedure includes one major parameter or two minor parameters, showing excellent sensitivity and good specificity in evaluating the mCNV activity based on noninvasive OCTA.

**Key words:** OCTA, OCT angiography, mCNV, myopic choroidal neovascularization, FFA, activity.

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