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Microstructural Remodeling of Type 1 MNV After hf-PDT in Pachychoroid Neovasculopathy: Image-Based Quantification Using OCT and OCTA

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Research Article

Keywords: Fractal dimension, pachychoroid neovasculopathy, photodynamic therapy, optical coherence tomography angiography, vascular remodeling

Posted Date: November 25th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11423084/v1

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Additional Declarations: No competing interests reported.

Abstract

Purpose

To assess microstructural remodeling after half-fluence photodynamic therapy (hf-PDT) in pachychoroid neovasculopathy (PNV) with type 1 macular neovascularization (MNV) and identify imaging features associated with response.

Methods

In this retrospective longitudinal observational study, 39 treatment-naïve eyes underwent OCT and 6×6-mm OCT angiography. MNV network metrics, including lesion area, vessel density (VD), fractal dimension (FD), lacunarity, skeletonized vessel length (VL), intersection points (IPs), and branch count were quantified after segmentation. Central choroidal thickness (CCT), choroidal vascularity index (CVI), central macular thickness (CMT), and flat irregular pigment epithelial detachment (FIPED) height were measured. Eyes were classified by 6-month subretinal fluid status and eyes achieving complete resolution were further evaluated for subsequent recurrence during extended follow-up.

Results

After hf-PDT, FD decreased significantly ($p = 0.006$), whereas MNV area and VD were unchanged ($p = 0.290$ and $p = 0.198$). CCT, CMT, and FIPED height decreased (all $p < 0.001$), while CVI remained stable ($p = 0.073$). At 6 months, 59% achieved complete resolution; 35% of these recurred. Subgroup analysis showed that recurrence was associated with higher baseline FIPED height ($p = 0.020$) and greater FIPED height at recurrence than at resolution ($p = 0.018$). Eyes with sustained resolution had higher baseline CCT ($p = 0.016$) with lower FIPED height ($p = 0.031$), IPs ($p = 0.006$), branch count ($p = 0.010$), and VL ($p = 0.016$).

Conclusion

hf-PDT was associated with neovascular simplification without reducing lesion size or VD, primarily reflected by reduced FD. Baseline CCT and FIPED height were associated with treatment response and recurrence risk, suggesting imaging features may be associated with anatomical response and warrant further validation.

Introduction

Pachychoroid spectrum diseases are characterized by increased choroidal thickness, dilated outer choroidal vessels (pachyvessels), and compression of the choriocapillaris. Within this spectrum, pachychoroid neovasculopathy (PNV) typically presents with type 1 macular neovascularization (MNV)—

vessels originating from the choriocapillaris and extending into the sub-retinal pigment epithelium (RPE) space—occurring in the absence of drusen or other features of classic neovascular age-related macular degeneration (AMD) 1.

Half-fluence photodynamic therapy (hf-PDT) has emerged as an effective treatment option for PNV, demonstrating fluid resolution and lesion regression comparable to anti–vascular endothelial growth factor (anti-VEGF) monotherapy 2–5. The therapeutic mechanism of hf-PDT involves selective closure of abnormal choroidal vessels, thereby preserving the outer retinal integrity while minimizing collateral choriocapillaris damage—particularly in treatment-naïve eyes or those refractory to anti-VEGF therapy. Moreover, eyes initially treated with PDT have been reported to require fewer anti-VEGF injections compared with anti-VEGF monotherapy alone 6. Despite these favorable outcomes, the mechanistic basis of post-treatment microstructural changes within the neovascular complex remains poorly understood.

Therapeutic response in PNV is still primarily evaluated using conventional choroidal parameters such as central macular thickness (CMT), central choroidal thickness (CCT), and choroidal vascularity index (CVI), or through qualitative assessment of MNV regression. While these parameters reflect global anatomic improvement, they may not fully capture the complex vascular remodeling that occurs within the lesion. The advent of optical coherence tomography angiography (OCTA) has enabled direct visualization of MNV, allowing for detailed morphological classification and longitudinal monitoring of structural changes.

Several studies have investigated the morphological characteristics of MNV in both AMD and pachychoroid-related diseases. Some have relied on conventional assessments or automated OCTA-derived metrics such as lesion area or vessel density (VD) 7–9, while others have conducted more refined quantitative analyses focusing on microstructural features 10, 11. Furthermore, mathematical descriptors—particularly fractal-based indices— have been introduced to characterize MNV morphology, demonstrating potential as biomarkers of neovascular activity and therapeutic response in AMD and polypoidal choroidal vasculopathy (PCV) 12–16. More recently, OCTA-based evaluations following PDT have been proposed to predict recurrent exudation by detecting post-treatment lesion enlargement in PNV 17

In AMD, it is well established that anti-VEGF therapy reduces retinal and subretinal fluid (SRF) primarily by suppressing vascular leakage from MNV. However, in PNV, it remains unclear whether retinal drying following treatment results predominantly from decreased choroidal thickness and permeability or from direct reduction of MNV leakage. The relative contribution of these mechanisms—and which one plays the dominant role—has yet to be determined. Evaluating treatment response from this perspective may therefore be crucial for guiding future therapeutic strategies and optimizing management of pachychoroid-related MNV. Although hf-PDT is known to reduce SRF and choroidal thickness in PNV, the accompanying structural response of the neovascular complex itself remains incompletely characterized. Conventional parameters such as lesion area or VD may not capture subtle changes in

vascular organization, and it remains unclear whether anatomical improvement after hf-PDT is accompanied by remodeling of the internal MNV network even when overall lesion size is preserved. Quantitative OCTA metrics may therefore provide additional insight into treatment-related vascular remodeling beyond conventional structural OCT measures.

We hypothesized that hf-PDT would induce microstructural simplification of type 1 MNV in PNV, reflected primarily by a reduction in FD, even in the absence of substantial change in overall lesion size or VD. Accordingly, the primary objective of this study was to evaluate the change in FD of the neovascular network from baseline to 6 months after hf-PDT. Secondary objectives were to assess accompanying changes in OCTA-derived metrics and structural OCT and choroidal parameters. Exploratory analyses evaluated whether baseline imaging features were associated with sustained fluid resolution or persistent/recurrent fluid after treatment.

Materials and Methods

Study Design and Participants

This retrospective longitudinal observational study included 39 eyes of 39 patients with treatment-naïve type 1 MNV secondary to pachychoroid disease who underwent hf-PDT at a tertiary

ophthalmology referral center between January 2016 and August 2025. All eyes had a minimum imaging follow-up of 6 months, which constituted the predefined time point for quantitative OCT/OCTA analysis. Recurrence was additionally assessed over the available extended clinical follow-up. The study adhered to the tenets of the Declaration of Helsinki, and ethical approval was obtained from the institutional ethics committee of the study center. The diagnosis of PNV was based on clinical evaluation and multimodal imaging, including spectral-domain OCT (Spectralis; Heidelberg Engineering, Heidelberg, Germany), fundus fluorescein angiography (FA), indocyanine green angiography (ICGA), fundus autofluorescence (FAF) imaging (Heidelberg Retina Angiograph 2; Heidelberg Engineering, Heidelberg, Germany), and optical coherence tomography angiography (OCTA) (AngioVue; RTVue XR Avanti, Optovue Inc., Fremont, CA, USA). PNV was defined as type 1 MNV in the presence of pachychoroid features—namely, focal or diffuse choroidal thickening (subfoveal choroidal thickness ≥ 200 μm or at least 50 μm greater than adjacent subfoveal measurements), attenuation of Sattler's layer and choriocapillaris overlying dilated outer choroidal vessels (pachyvessels) on enhanced depth imaging OCT (EDI-OCT), and choroidal vascular hyperpermeability or filling defects with associated RPE

abnormalities on ICGA. Exclusion criteria included previous retinal treatment (laser photocoagulation, PDT, intravitreal anti-VEGF, or corticosteroid injections), the presence of polypoidal lesions on ICGA, drusen or degenerative findings consistent with AMD, and any inflammatory or non-inflammatory chorioretinal disease. Eyes with refractive error exceeding ± 5 diopters (spherical equivalent) or OCTA images of insufficient quality (signal strength < 6/10 or with motion/projection artifacts) were also excluded. Given the diagnostic overlap between de novo PNV and MNV associated with central serous

chorioretinopathy (CSC), both entities—with or without a prior history of acute CSC—were included in the analysis. In cases of bilateral disease, the eye with the longer duration of MNV was selected for inclusion.

hf-PDT Protocol

hf-PDT Protocol
All patients underwent hf-PDT using the *Zeiss Visulas 690S PDT Laser System* (Carl Zeiss Meditec, Jena, Germany). Verteporfin (6 mg/m²) was administered intravenously over 10 minutes, followed—15 minutes after infusion onset—by laser irradiation at 689 nm for 83 seconds with a reduced light dose of 25 J/cm² and intensity of 300 mW/cm². The treatment spot size was determined based on the area of choroidal hyperpermeability on ICGA, ensuring complete coverage of the leakage plaque and/or hot spot. When multiple hyperfluorescent areas were present, the spot size was extended to encompass the entire leakage zone.

Patients were categorized according to their anatomical response at 6 months after hf-PDT based on the presence of subretinal fluid (SRF). A binary classification based on the presence or absence of subretinal fluid was used to ensure clinical clarity and avoid ambiguity related to percentage-based thresholds:

- Total resolution group: complete resorption of SRF
- Incomplete resolution group: persistence of SRF

In addition, a longitudinal analysis was performed among eyes achieving total resolution. These eyes were further classified as:

- Sustained resolution: no recurrence of SRF during follow-up
- Recurrence: reappearance of SRF after initial complete resolution

Imaging Acquisition and Analysis

Spectral-domain OCT and OCTA were performed at baseline and six months after hf-PDT. OCTA scans covered a 6 × 6 mm macular area centered on the fovea using the split-spectrum amplitude decorrelation angiography (SSADA) algorithm. Segmentation errors were manually corrected to ensure accurate delineation of the type 1 MNV between Bruch's membrane and the RPE. Conventional OCT parameters—including SRF height, CMT, CCT and flat-irregular pigment epithelial detachment (FIPED) height—were manually measured on horizontal EDI-OCT B-scans passing through the fovea using the built-in caliper tool (Heidelberg software). CCT was defined as the perpendicular distance between Bruch's membrane and the choroidoscleral interface.

Quantitative Choroidal Analysis

Quantitative analysis of the choroidal vasculature was performed using ImageJ (version 1.54p; National Institutes of Health, Bethesda, MD, USA). EDI-OCT images were cropped to a 3000 μm width (1500 μm nasal and 1500 μm temporal to the fovea) and vertically extended from the RPE to the choroidoscleral border. After converting to 8-bit format, images were binarized using the Niblack local thresholding method. The dark and light pixel areas were defined as the luminal area (LA) and stromal area (SA), respectively. The total choroidal area (TCA) was computed as the sum of LA and SA, and the CVI was computed as the ratio of LA to TCA.

Quantitative OCTA and Vascular Network Analysis

To analyze the topological organization of the MNV lesion, the exported outer-retinal angiogram slab was manually outlined in ImageJ using the freehand selection tool, and areas outside the region of interest were cleared. The image was then converted to 8-bit and binarized using the Otsu method, which automatically determines the optimal threshold to separate flow signals from background noise by maximizing interclass variance [18]. This global thresholding approach minimizes operator bias and ensures consistent segmentation across scans.

VD was defined as the percentage of the lesion area occupied by flow pixels. The binarized images were skeletonized to reduce vessels to single-pixel centerlines while preserving branching architecture. From the skeletonized image, total VL, branch count, and IPs were derived, with IPs representing junctions where three or more vessels converge. A higher number of IPs reflects a more complex and interconnected neovascular network, whereas a post-treatment decrease suggests microvascular pruning or remodeling rather than simple lesion contraction [19].

FD and lacunarity were computed using the box-counting algorithm (FracLac plugin, ImageJ) [20]. FD quantifies the complexity and space-filling capacity of the vascular network, where higher values correspond to dense, tortuous branching, whereas lower values indicate simplified structure. Lacunarity measures spatial heterogeneity with higher values indicating irregular, patchy distribution and lower values reflecting more homogeneous vascular organization.

Outcome Measures

The primary outcome was the change in FD of the type-1 MNV from baseline to 6 months after hf-PDT. Secondary OCTA outcomes included changes in lesion area, VD, lacunarity, VL, IPs, and branch count. Secondary structural outcomes included changes in CCT, CMT, CVI and FIPED height. Exploratory analyses assessed baseline imaging features associated with sustained fluid resolution versus persistent or recurrent SRF during follow-up.

Statistical Analysis

The statistical analyses were performed using the Statistical Package for Social Sciences; version 27.0. The variables were investigated using visual (histograms, probability plots) and analytical methods

(Shapiro–Wilk test) to test the distribution of the data. Continuous variables were expressed as the mean ± standard deviation (SD) or median (interquartile range) depending on the normality of the data. Categorical variables were expressed as the number of observations. For the comparison of pre- and post-treatment measurements, the paired sample *t*-test or Wilcoxon signed-rank test was applied, depending on the distribution of the data. The independent sample *T*-test or the Mann–Whitney *U* test was used for the comparisons of baseline parameters between groups, depending on the distribution of the data. The correlation between continuous variables was assessed using Spearman's rank correlation coefficient. The level of significance was defined at $p < 0.05$.

Results

A total of 39 eyes from 39 treatment-naïve patients (24 men, 15 women; mean age = 56.3 years) with PNV were analyzed. The mean follow-up duration was 34.7 months. Quantitative pre- and post-treatment parameters are summarized in Table 1. Six months after hf-PDT, mean FD ($p = 0.006$) and median VL ($p = 0.033$) decreased significantly, indicating post-treatment microvascular simplification. In contrast, mean VD ($p = 0.198$) and CVI ($p = 0.073$) showed no significant change. Median total MNV area, lacunarity, branch count, and IPs remained unchanged (all $p > 0.05$). Based on SD-OCT imaging, median CCT, median CMT and mean FIPED height all decreased significantly (all $p < 0.001$). Although the mean BCVA improved slightly from 0.30 (range, 0.0–0.9) to 0.20 (range, 0.0–0.8) logMAR after hf-PDT, the difference was not statistically significant ($p = 0.231$). When eyes were categorized by anatomical response at 6 months, 23 (59%) achieved total resolution and 16 (41%) had incomplete resolution. Baseline characteristics were similar between groups (all $p > 0.05$). Among eyes achieving total resolution (23/39), 8 eyes experienced subsequent recurrence. Compared with eyes that remained stable (15/23), those with recurrence (8/23) had higher baseline median FIPED height (71.5 μm vs 39.0 μm; $p = 0.020$). In eyes with recurrence, median FIPED height at the time of recurrence was significantly higher than at the time of total resolution (45 μm [range, 31–137] vs 37.5 μm [range, 23–102]; $p = 0.018$). Eyes that maintained complete resolution throughout follow-up (15/39) were compared with those exhibiting persistent or recurrent fluid (24/39) (Table 2). The sustained-resolution group showed higher baseline mean CCT ($p = 0.016$) and lower baseline median FIPED height ($p = 0.031$), number of IPs ($p = 0.006$), number of branches ($p = 0.010$), skeletonized VL ($p = 0.016$). No significant differences were found in FD, VD, MNV area, or lacunarity (all $p > 0.05$). Correlation analysis demonstrated that baseline total MNV area was strongly associated with FD ($r = 0.835$), IPs ($r = 0.911$), branch count ($r = 0.950$), and skeletonized VL ($r = 0.963$) (all $p < 0.001$), indicating a consistent relationship between lesion size and network complexity. Additionally, baseline total MNV area ($r = + 0.424$, $p = 0.034$) and VL ($r = + 0.412$, $p = 0.041$) showed moderate positive correlations with post-treatment BCVA in logMAR, suggesting that larger and more extensive lesions were associated with less favorable functional recovery. These findings further support the biological validity of the quantitative OCTA metrics used in this study, as lesion size was consistently associated with increasing vascular complexity.

Table 1

Paired Analysis of Pre- and Post-Treatment Quantitative Spectral-domain Optical Coherence Tomography (SD-OCT) and Optical Coherence Tomography Angiography (OCTA) Parameters in Eyes with Pachychoroid Neovasculopathy (n = 39)

Parameter	pre-treatment	post-treatment	p value
Quantitative MNV metrics (OCTA)			
Total MNV area (mm²)	0.708 (0.110–3.640)	0.666 (0.120–3.990)	0.290□
MNV Vessel Density (%)	56.28 ± 8.12	58.19 ± 10.12	0.198□
Skeletonized vessel length (mm)	14.07 (3.34-104.48)	13.62 (2.55–95.82)	**0.033**□
Intersection points (count)	36 (8-227)	36 (2-254)	0.776□
Branches (count)	120 (24–734)	86 (24–800)	0.194□
Fractal dimension	1.52 ± 0.11	1.50 ± 0.13	**0.006**□
Lacunarity	0.32 (0.22–0.41)	0.30 (0.11–0.44)	0.184□
SD-OCT & Choroidal Parameters			
CCT (μm)	425 (185–636)	362 (166–627)	< **0.001**□
FIPED height (μm)	51 ± 17	38 ± 21	**< 0.001**□
CMT (μm)	276 (164–522)	228 (157–402)	**< 0.001**□
CVI (%)	72.99 ± 2.50	72.21 ± 2.70	0.073□

All values are expressed as mean ± SD or median (range) as appropriate. Bold values indicate statistically significant *p* values.

MNV: Macular neovascularization; CCT: Central choroidal thickness; FIPED: Flat irregular pigment epithelial detachment; CMT: Central macular thickness; CVI: Choroidal vascularity index.

□ *Paired T-test.*

□ *Wilcoxon signed-rank test*.

Table 2
Baseline Comparison of Quantitative Spectral-domain Optical Coherence Tomography (SD-OCT) and Optical Coherence Tomography Angiography (OCTA) Parameters Between Sustained-Resolution and Recurrent/Persistent Groups

Parameter	Sustained resolution group (n = 15)	Recurrent/Persistent group (n = 24)	p value
Quantitative MNV metrics OCTA			
Total MNV area (mm²)	0.626 (0.150–3.640)	0.918 (0.110–3.230)	0.317
Vessel density (%)	56.16 (50.60–69.61)	53.60 (42.63–72.12)	0.296
Intersection points (count)	26 (8–227)	44 (14–197)	**0.006**
Branches (count)	75 (24–734)	138 (36–581)	**0.010**
Skeletonized vessel length (mm)	8.65 (3.34–104.48)	19.10 (4.27–75.87)	**0.016**
Fractal dimension	1.53 ± 0.11	1.51 ± 0.11	0.662
Lacunarity	0.31 ± 0.04	0.33 ± 0.05	0.140
SD-OCT measurements			
FIPED (μm)	39 (31–76)	56 (30–209)	**0.031**
CMT (μm)	347 (220–500)	253 (177–522)	0.146
CCT (μm)	439.64 ± 58.23	354.72 ± 118.64	**0.016**
CVI (%)	73.60 ± 2.08	72.62 ± 2.72	0.313

Bold values indicate statistically significant *p* values.

MNV: Macular neovascularization; FIPED: Flat irregular pigment epithelial detachment; CMT: Central macular thickness; CCT: Central choroidal thickness; CVI: Choroidal vascularity index.

 Independent Samples T-test.

 Mann–Whitney U test.

Discussion

In this study, we evaluated post-PDT alterations in the structure of type-1 MNV networks together with accompanying changes in choroidal morphology. Half-fluence PDT used as monotherapy has been reported to achieve favorable outcomes in treatment-naïve PNV eyes, with complete SRF resolution observed in approximately 75% of cases within three months and most maintaining remission up to one year [4]. In contrast, Lee et al. evaluated eyes with anti-VEGF–refractory PNV, where a single PDT session achieved complete fluid absorption in 85.7% of cases at three months and sustained dryness in about

60% at one year [2]. These findings support PDT as an effective treatment option in PNV, either as primary therapy or in eyes with suboptimal response to anti-VEGF treatment.

Recent studies suggest that qualitative assessment of vascular architecture—such as the presence of a central trunk or peripheral capillary formation and morphologic appearance of MNV —may provide insights into lesion activity or stability [14, 15]. However, predicting which lesions are more likely to recur remains challenging [21]. Beyond these subjective qualitative observations, quantitative and mathematical descriptors offer a more objective means of monitoring subtle topological and structural changes within the neovascular complex. Notably, while SRF often resolves completely following PDT, the neovascular membrane continues to undergo microstructural remodeling within its skeletonized framework. Certain imaging biomarkers may therefore help identify eyes that respond favorably to treatment and those more prone to resistance or recurrence [17].

Previous studies have reported that anti-VEGF therapy leads to a reduction in MNV lesion area or in VD [22, 23]. However, within shorter follow-up periods, this is not consistently observed—some lesions may not appear shrunken, and the main truncal vessels of the network often persist [22]. Instead, treatment primarily induces remodeling of peripheral capillary segments, which alters the overall vascular complexity rather than eliminating major structures [24]. Therefore, in our study, we evaluated lesion complexity using FD and lacunarity, quantitative parameters that respectively reflect the structural complexity and spatial heterogeneity (“gappiness”) of the neovascular network. The principal finding of this study was that hf-PDT induced significant microstructural simplification of type 1 MNV in PNV, as demonstrated by a reduction in OCTA-derived FD, the predefined primary outcome. This change occurred without significant reduction in overall MNV area or VD, suggesting that hf-PDT may preferentially alter the fine vascular architecture of the neovascular complex rather than causing simple lesion contraction.

Pre-treatment type-1 MNV lesions related to PNV exhibit distinct structural characteristics compared with type-1 MNV associated with neovascular AMD (nAMD). Yanık et al. reported that type-1 MNV in PNV tends to be smaller and less complex, potentially due to higher local VEGF concentrations that accelerate vascular maturation and promote earlier remodeling [11]. The lower frequency of a central trunk, the predominance of immature vascular patterns, and the reduced FD and branching complexity observed in PNV relative to nAMD further support this interpretation [7, 11]. In our cohort, larger type-1 MNV lesions exhibited a greater number of branches and IPs, indicating a more complex vascular network characterized by higher median FD values. This correlation, evident only before hf-PDT, likely reflects the structural interdependence between lesion size and vascular complexity, which becomes less pronounced after treatment as pruning and closure of peripheral capillary loops simplify the overall network architecture. Our baseline topological metrics were also consistent with those reported in previous OCTA-based studies. The mean FD in our treatment-naïve PNV eyes (1.52 ± 0.11) closely matched the values reported by the same group for PNV (1.56 ± 0.10) and was slightly lower than in nAMD (1.59 ± 0.11) [11]. These findings are consistent with previous reports describing lower vascular

complexity in PNV than in drusen-associated nAMD, although differences in OCTA acquisition and analysis methods limit direct comparisons across studies.

In our study, hf-PDT was associated with selective simplification of the neovascular network without significant changes in overall lesion area or vessel density. The reduction in FD together with the decrease in VL suggests remodeling predominantly affecting the finer vascular architecture rather than contraction of the entire neovascular complex. Therefore, OCTA-derived topological metrics may capture subtle treatment-related structural alterations that are not reflected by conventional size-based measurements. Interestingly, a remarkably similar OCTA pattern has previously been reported following anti-VEGF therapy. Al-Sheikh et al. demonstrated that lesion area and vessel density remained largely unchanged after treatment, whereas FD decreased significantly, indicating reduced vascular complexity despite preservation of the overall neovascular network [15]. Likewise, in the present study, hf-PDT resulted in a significant reduction in FD without measurable changes in lesion area or VD. These consistent findings across two distinct treatment modalities suggest that simplification of the fine vascular architecture may represent a common imaging feature of treatment-related vascular remodeling. Nevertheless, the underlying biological mechanisms are likely different. Anti-VEGF primarily suppresses VEGF-dependent neovascular proliferation, whereas hf-PDT induces selective photothrombotic occlusion of abnormal choroidal vessels together with reduction of choroidal congestion. Therefore, similar OCTA findings may reflect convergent vascular remodeling achieved through different biological pathways.

In parallel with OCTA-detected microvascular simplification, structural OCT parameters also improved after hf-PDT. CCT, CMT, and FIPED height decreased significantly, supporting the concept that PDT exerts part of its therapeutic effect through choroidal decongestion and efficient outer-retinal fluid clearance driven by its selective vaso-occlusive mechanism in pachychoroid disease. In contrast, CVI did not change significantly, suggesting that early anatomical improvement may occur before measurable proportional changes in the vascular and stromal components of the choroid. Similar observations have been reported in longer-term studies of PDT combined with anti-VEGF therapy, in which early reductions in choroidal thickness and CVI were followed by relative stabilization [25]. Therefore, the absence of a significant CVI change in our cohort may reflect the timing of imaging, the monotherapy design, or limited statistical power rather than absence of choroidal remodeling.

Previous OCTA studies in nAMD have suggested that MNV topology may provide information beyond lesion size alone. Peripheral loops, closed-circuit patterns, greater vessel length, and higher junction counts have been associated with persistent exudative activity or the need for continued anti-VEGF treatment [14]. Conversely, non-foveal, circular MNV configurations with fewer peripheral anastomoses tended to stabilize after initial therapy [26].

In PNV, however, evidence remains limited. Hikichi et al. reported that enlargement of the square root of the MNV area preceded recurrence after PDT, suggesting that early lesion expansion may be associated with renewed exudation [17]. Lee et al. investigated the relationship between MNV complexity and

treatment outcomes in both typical AMD and polypoidal choroidal vasculopathy (PCV). They found no significant association between changes in FD or lacunarity and either visual outcomes or anti-VEGF treatment response. The only morphologic feature linked to poorer outcomes was greater heterogeneity of branch vessel length, a finding that warrants further investigation to elucidate its mechanism [12]. In our study, lesion area itself was not significantly different between outcome groups, whereas eyes with sustained resolution showed lower baseline IPs, branch count, and VL. These findings may suggest that baseline vascular connectivity, rather than lesion size alone, may be relevant to post-PDT anatomical stability. Furthermore, Lee et al. noted that smaller choroidal vessel areas and diameters, accompanied by lower FD values of the choroidal vasculature, were correlated with visual acuity decline in both nAMD and nAMD + PCV eyes, before and after anti-VEGF treatment [12]. These observations align with the hemodynamic theory of AMD, which attributes disease progression to choroidal hypoperfusion and progressive vascular attenuation [27, 28]. A thinner choroidal vasculature may exacerbate ischemia, thereby impairing functional recovery [29, 30]. We found that structural OCT parameters also appeared clinically informative. Eyes with sustained resolution had greater baseline CCT and lower FIPED height, whereas recurrence was associated with higher baseline FIPED height and an increase in FIPED height at recurrence. These findings suggest that eyes with a thicker pachychoroid phenotype may be more responsive to PDT-mediated choroidal decongestion, while greater FIPED height may reflect a more active or treatment-resistant sub-RPE neovascular component. Because these subgroup analyses were exploratory and based on a limited sample, these parameters should be interpreted as candidate imaging markers rather than validated predictors.

Taken together, our findings indicate that hf-PDT induces OCTA-detectable simplification of type 1 MNV in PNV, primarily reflected by reduced FD, while structural OCT changes suggest concurrent improvement in the pachychoroid environment. The combination of OCTA-derived network metrics and conventional OCT parameters may therefore provide complementary information regarding treatment response. However, larger prospective studies are needed to determine whether these features can guide patient selection, recurrence monitoring, or the need for adjunctive anti-VEGF therapy.

The present study has several limitations. First, the retrospective design and relatively small sample size may limit statistical power, particularly for subgroup analyses. Second, although recurrence was assessed during extended follow-up, the primary imaging analysis was limited to baseline and 6 months after hf-PDT; therefore, longer-term vascular remodeling could not be evaluated. Third, OCTA measurements were obtained using a single device and segmentation protocol, and manual delineation of the neovascular complex may have introduced observer-dependent variability. Furthermore, reductions in OCTA-derived vascular complexity may reflect flow signals falling below the detection threshold rather than true anatomical loss of neovascular vessels. Finally, the absence of an anti-VEGF monotherapy control group precludes direct comparison between photothrombotic and pharmacologic mechanisms of vascular remodeling.

In conclusion, hf-PDT was associated with significant reduction in OCTA-derived FD, suggesting microstructural simplification of type 1 MNV in PNV without substantial lesion contraction. Structural

OCT findings, particularly CCT and FIPED height, may provide complementary information regarding anatomical response and recurrence risk, but their predictive value requires validation in larger prospective cohorts.

Declarations

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of conflicting interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Acknowledgements: Not applicable.

Ethical considerations: This study was approved by the institutional ethics committee of the study center and was conducted in accordance with the tenets of the Declaration of Helsinki. Full ethics committee details are provided on the title page.

Consent to participate: The requirement for informed consent was waived by the institutional ethics committee due to the retrospective nature of the study.

Consent for publication: Not applicable.

Data availability: The datasets generated and/or analyzed during the current study are not publicly available due to ethical and privacy restrictions but are available from the corresponding author on reasonable request.

Authors' Contributions

PGB**;** Investigation, data collection, OCT/OCTA image analysis, data curation, and writing – original draft. FS**;** Investigation, data collection, quantitative imaging analysis, and manuscript writing.
SD; Conceptualization, study design, methodology, interpretation of results, writing – review and editing, supervision, and project administration. FŞ; Conceptualization, methodology, interpretation of results, critical revision of the manuscript, and supervision.

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