Choroidal Anatomic Alterations After Photodynamic Therapy for Chronic Central Serous Chorioretinopathy: A Multicenter Study

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• PURPOSE: To study the early anatomic choroidal alterations in eyes with chronic central serous chorioretinopathy (CSCR) undergoing photodynamic therapy (PDT).
• DESIGN: Multicenter retrospective cohort study.
• METHODS: A total of 77 patients and 81 eyes with chronic CSCR treated with PDT and 64 untreated fellow eyes were evaluated. Central macular thickness (CMT) and choroidal features including subfoveal choroidal thickness (SFCT), total choroidal area (TCA), luminal choroidal area (LCA), and stromal choroidal area (SCA) were analyzed. Choroidal vascularity index (CVI) was calculated in all study eyes at baseline and at 1- and 3-months post-PDT.
• RESULTS: In eyes receiving PDT, Snellen visual acuity (VA) significantly improved at months 1 and 3 ($P < .001$). CMT and SFCT showed a significant reduction from baseline at months 1 and 3 ($P < .001$), whereas TCA and LCA showed a significant decrease only at the 1-month follow-up visit. Baseline mean TCA and LCA were 2.30 ± 1.41 mm^2 and 1.23 ± 0.73 mm^2, respectively, and decreased to 2.07 ± 1.21 mm^2 and 1.08 ± 0.63 mm^2 at the 1-month follow-up visit, respectively ($P = .01$). No significant changes were recorded for SCA and CVI. In the fellow eye group, VA, CMT, and all choroidal parameters showed no differences between baseline and any follow-up visits (all $P > .05$).
• CONCLUSIONS: After PDT for chronic CSCR we observed sustained reductions in CMT and SFCT, while reductions in TCA and LCA were only noted at the 1-month follow-up interval. These choroidal parameters may provide additional quantitative biomarkers to evaluate the anatomic response to therapy but await further prospective validation. (Am J Ophthalmol 2020;217:104–113. © 2020 Elsevier Inc. All rights reserved.)

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CENTRAL SEROUS CHORIORETINOPATHY (CSCR) IS A common chorioretinal disorder that may present therapeutic challenges. A congested, hyperpermeable, and thickened choroid is associated with a dysfunctional retinal pigment epithelium (RPE), leading to the development of a pigment epithelial detachment (PED) and the accumulation of subretinal fluid (SRF).[1,2] In 5%-10% of patients, SRF may persist and RPE alterations may develop, resulting in chronic disease that may require treatment intervention.[3–5]

Photodynamic therapy (PDT) with verteporfin may be the most efficient treatment option in reducing fluid leakage in patients with chronic CSCR.[6,7] PDT has angio-occlusive properties leading to the constriction of congested choroidal vessels and vascular remodeling.[8,9] Most reports on post-PDT choroidal alterations have focused on subfoveal choroidal thickness (SFCT), which decreases after laser treatment.[10,11] More recently, the choriocapillaris and choroidal response have been evaluated by optical coherence tomography angiography (OCTA).[12,13]

To date, there has been limited investigation of the effect of PDT on the luminal choroidal area (LCA) and

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stromal choroidal area (SCA) and the correlation of these advanced anatomic metrics with functional outcomes. Dilation of choroidal vessels and leakage into the interstitial space are well known features of CSCR, and the choroidal vascularity index (CVI) may provide a novel method to more robustly quantify the choroidal anatomic components.[14,15]

The aim of the present study was to measure the CVI and its subcomponents, including total choroidal area (TCA), LCA, and SCA in eyes with chronic CSCR undergoing PDT and to correlate these choroidal parameters with both functional and anatomic outcomes.

METHODS

THIS WAS A RETROSPECTIVE, MULTICENTER, COHORT study comprising 11 study centers. Institutional review board approval was obtained at the respective referral centers, if required, for a retrospective consecutive chart review. The study adhered to the guidelines of the Health Insurance Portability and Accountability Act and was performed in accordance with the tenets of the Declaration of Helsinki.

• **STUDY POPULATION:** Medical records of patients with a diagnosis of chronic CSCR were retrospectively reviewed. Inclusion criteria were patients ≥18 years of age with a CSCR history of >6 months' duration. CSCR was defined by the following multimodal imaging findings including serous macular detachment, evidence of a thick choroid and mottled RPE alterations, typically in a gravitational pattern, as noted with color fundus photography, spectral-domain (SD) or swept source (SS) OCT, and fundus autofluorescence.

Study patients were required to have baseline (before PDT) and follow-up retinal examination and multimodal imaging including SD-OCT and SS-OCT. For eyes receiving >1 PDT session, only the first treatment was considered for the analysis. Patients with evidence of macular neovascularization (MNV) or polypoidal choroidal vasculopathy (PCV) secondary to CSCR were also included. MNV and PCV were diagnosed with fluorescein angiography (FA), indocyanine green angiography (ICGA), and when available, OCTA.

Patients <18 or >70 years of age were excluded from the study. Additional exclusion criteria included any history of intraocular surgery within the past 6 months, high refractive error (ie, >−6 diopters [D] or +3 D), and the presence of other retinal diseases.

Eyes receiving anti–vascular endothelial growth factor (VEGF) injections within 2 months before PDT were also excluded. All eyes with low-quality OCT volume scans because of poor compliance with testing or media opacities that prevented high-resolution imaging of the choroid were excluded. When available, the fellow eyes were analyzed as control eyes, only if there was no history of any previous treatment.

• **CLINICAL EXAMINATION:** For eligible patients, deidentified medical records and multimodal imaging findings were comprehensively reviewed. Data collected included patient demographics, medical history, and Snellen visual acuity (VA; converted to logarithm of minimal angle of resolution [logMAR] for statistical analysis). Multimodal imaging included SD-OCT (Heidelberg Spectralis, Heidelberg Engineering, Germany; Cirrus HD-OCT model 5000, Carl Zeiss Meditec, Dublin, California, USA), SS-OCT (DRI OCT Triton, Topcon Medical Systems, Oakland, New Jersey, USA), FA, and ICGA (Heidelberg Spectralis, Heidelberg Engineering, Germany; Optos PLC, Dunfermline, Scotland, United Kingdom). The mean change in VA, SFCT, and central macular thickness (CMT), and the presence or absence of SRF involving the fovea, and all choroidal parameters including TCA, LCA, SCA, and CVI were analyzed and recorded at baseline and at 1- and 3-months post-PDT in eyes receiving the treatment and in the fellow untreated control eyes.

Intravenous verteporfin was administered over a period of 10 minutes, and treatment was started at 15 minutes after the start of the verteporfirin infusion. Choice of full-dose/half-fluence vs half-dose/full-fluence PDT was determined by the treating provider. In each center, only 1 of these 2 PDT protocols was applied for all cases. The total light energy was set at 50 J/cm^2 for the full-fluence approach and at 25 J/cm^2 for the half-fluence approach. Patients were advised to avoid any direct sunlight exposure for 3 days after treatment. The maximum PDT spot diameter used to target FA-guided leaking spots or ICGA-guided choroidal hyperpermeability was recorded for the analysis.

• **OCT ANALYSIS:** For all patients, the horizontal 9- or 6-mm B-scan section through the central fovea was used for the analysis. The presence or absence of SRF was recorded at each follow-up. SFCT was manually determined by measuring the subfoveal vertical distance between the Bruch membrane interface and the sclerochoroidal junction on the OCT B scan. Only the eyes in which the entire choroid (from the Bruch membrane to the sclerochoroidal interface) was clearly visible were selected for the analysis.

The CVI was calculated using the previously reported automated algorithm[16] that included initial denoising with localization of the choroidal inner and outer boundary.[17–19] To allow computation of LCA and SCA, the OCT B-scan was binarized and the binarized choroidal components were segmented. Automated binarization included preprocessing, exponential and nonlinear enhancement, and thresholding. The bright regions were labeled as SCA and the dark regions as LCA. TCA was measured as the sum of the SCA and LCA and the CVI was calculated as the ratio of LCA over TCA. A further

TABLE 1. Functional and Anatomic Outcomes at Baseline, and at 1- and 3-Month Follow-up Post–Photodynamic Therapy in Treated Eyes

	Baseline (N = 81)	1-Month (N = 81)	*P* Value	3-Month (N = 61)	*P* Value
CMT, μm (avg ± SD)	350.0 ± 126.5	234.1 ± 80.5	<.001	246.9 ± 76.8	<.001
SFCT, μm (avg ± SD)	430.1 ± 124.4	395.1 ± 134.9	<.001	398.1 ± 126.2	<.001
TCA, mm^2 (avg ± SD)	2.30 ± 1.41	2.07 ± 1.21	.01	2.26 ± 1.58	.88
SCA, mm^2 (avg ± SD)	1.07 ± 0.73	0.99 ± 0.63	.07	1.07 ± 0.82	.67
LCA, mm^2 (avg ± SD)	1.23 ± 0.73	1.08 ± 0.63	.01	1.19 ± 0.81	.95
CVI, % (avg ± SD)	54 ± 8	52 ± 8	.05	53 ± 8	.28
VA, logMAR (Snellen, avg ± SD)	0.39 ± 0.35 (20/49)	0.29 ± 0.28 (20/39)	<.001	0.25 ± 0.35 (20/35)	<.001

CMT = central macular thickness; CVI = choroidal vascularity index; LCA = luminal choroidal area; logMAR = logarithm of minimal angle of resolution; SCA = stromal choroidal area; SD = standard deviation; SFCT = subfoveal choroidal thickness; TCA = total choroidal area; VA = visual acuity.

subanalysis was performed in the treated eyes comparing the group with secondary MNV/PCV vs the group without baseline diagnosis of CSCR; no eyes showed MNV or PCV before CSCR diagnosis).

• **STATISTICAL ANALYSIS:** Statistical analyses were performed using R software (version 3.5.0; www.r-project.org). Results of descriptive analyses are expressed as counts and percentages for categorical variables, and as means ± standard deviations (SDs) for quantitative continuous variables. A χ^2 test was performed with ordinal or categorical variables (eg, sex, eye) while a 2-sample Student *t* test was performed for interval variables (age, logMAR vision, CMT, SFCT, TCA, CVI, LCA, and SA). A paired Student *t* test was performed in cases where the same patient was evaluated (baseline, 1-month, and 3-month follow-up) or unpaired when comparing different groups. In cases where 3 time points were evaluated, Bonferroni correction was used to reduce the risk of false positives, with $P < .016$ (0.05/3) considered statistically significant. Otherwise, $P < .05$ was considered statistically significant.

RESULTS

A TOTAL OF 81 EYES (77 PATIENTS) WITH CHRONIC CSCR UNdergoing PDT were included in the study after 9 eyes were excluded because of poor-quality OCT images. In the group of 77 CSCR patients (77.7% male), the mean age was 51.4 ± 10.2 years. Four patients received the treatment bilaterally. Of 81 treated eyes, 64 fellow eyes were treatment naïve and were available for analysis. Twenty-four of these fellow eyes showed CSCR signs including RPE alterations or mild extrafoveal SRF not requiring treatment.

One-month follow-up was available for all 81 eyes and the 3-month follow-up was available for 61 eyes (75.3%). Among the treated eyes, 21 (25.9%) had received previous CSCR treatment, including micropulse laser treatment plus eplerenone (2 eyes), focal thermal argon laser (7 eyes), and intravitreal anti–VEGF therapy (12 eyes of which 8 exhibited secondary MNV or PCV identified after

The mean maximum PDT spot size diameter was 2833.1 ± 1599.7 μm. LogMAR VA in treated eyes at baseline was 0.39 ± 0.35 (~Snellen 20/49) and significantly improved to 0.29 ± 0.28 (~Snellen 20/39, $P < .001$) at month 1 and further improved to 0.25 ± 0.35 (~Snellen 20/35, $P < .001$) at month 3. Complete SRF resolution was noted in 36 of 81 eyes (44.4%) at month 1 and 37 of 61 eyes (60.7%) at month 3.

The anatomic outcomes at baseline and at the 1- and 3-month follow-ups in eyes undergoing PDT are summarized in Table 1 and Figure 1. CMT and SFCT showed a significant reduction from baseline vs months 1 and 3 ($P < .001$). For the choroidal parameters, TCA and LCA were significantly reduced at the first follow-up interval (Table 1, Figures 1 and 2, and Supplemental Figure S1; Supplemental Material available at AJO.com) from a mean value of 2.30 ± 1.41 and 1.23 ± 0.73 mm^2 to 2.07 ± 1.21 and 1.08 ± 0.63 mm^2, respectively ($P = .01$). These values however, increased at the third month with no statistically significant differences compared with baseline ($P = .88$ and $P = .95$, respectively). No significant changes were recorded for SCA and CVI over the course of follow-up. Specifically, CVI showed a reduction from 54% ± 8% at baseline to 52% ± 8% ($P = .05$) at month 1 and increased again to 53% ± 8% ($P = .28$) at month 3. When performing the analysis within the fellow eye group, Snellen VA and all quantitative retinal and choroidal parameters were not significantly different between baseline and both follow-up visits (all $P > .05$, Table 2).

Table 2 shows the comparison between functional and structural parameters over time between treated and contralateral control eyes. As expected, mean Snellen VA was better in the fellow eye group at baseline ($P < .001$), 1-month ($P < .001$), and 3-month follow up ($P = .003$), whereas CMT and SFCT were significantly increased in the treated group at baseline ($P < .001$) but were not significantly different at the 1- and 3-month follow-up intervals (all $P > .05$).

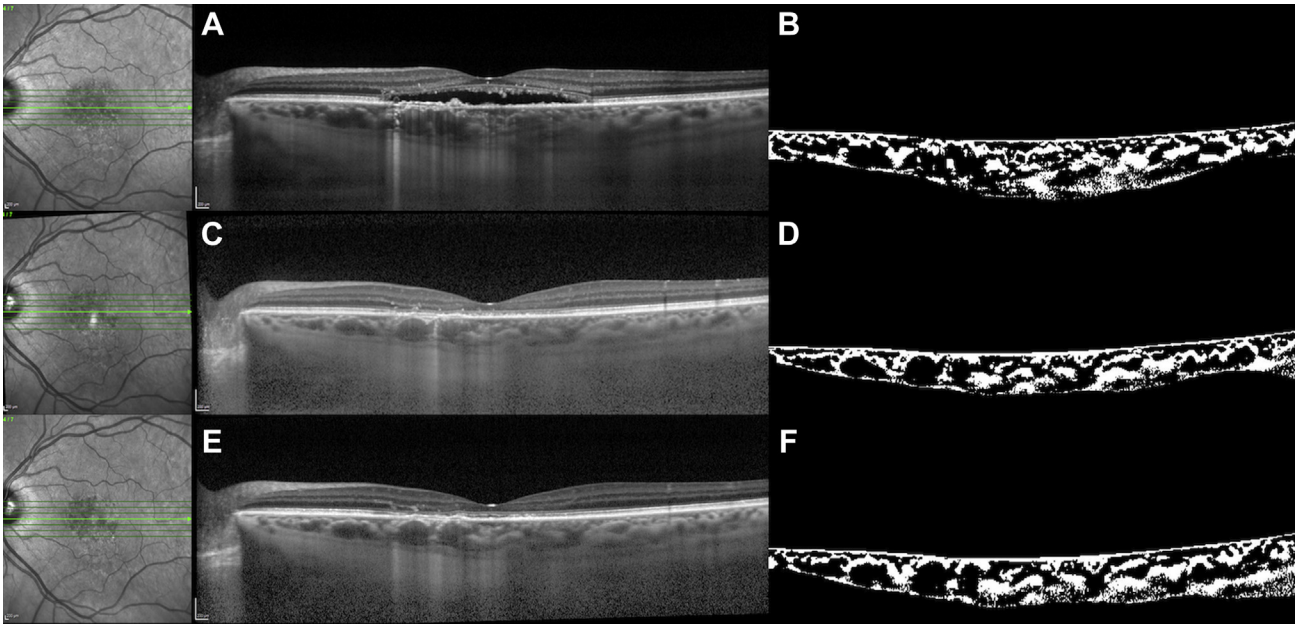

FIGURE 1. Spectral-domain optical coherence tomography (OCT) B scans (using enhanced depth imaging mode) and corresponding binarized OCT scans of the choroid from a 66-year-old man with chronic central serous chorioretinopathy (CSCR) before and after half dose full-fluence photodynamic therapy (PDT). Registered near-infrared reflectance images are also included to validate tracking of B scans from baseline to follow-up visits. (A and B) Baseline OCT B scan and binarized scan show central subretinal fluid (SRF) with increased subfoveal choroidal thickness (SFCT) of 370 μm. The total choroidal area (TCA) measured 2.53 mm^2, the stromal choroidal area (SCA) measured 0.93 mm^2, the luminal choroidal area (LCA) measured 1.60 mm^2, and the choroidal vascularity index (CVI) measured 63.2%. (C and D) At the 1-month follow-up after PDT, OCT B scan shows complete SRF resolution. Corresponding binarized OCT scan was analyzed. The SFCT decreased to 254 μm. The TCA, SCA, and LCA all decreased to 1.92 mm^2, 0.73 mm^2, and 1.19 mm^2, respectively. The CVI diminished to 61.9%. (E and F) At the 3-month follow-up, the OCT B scan shows continued SRF resolution. The binarized OCT scan shows an increase in all parameters: SFCT 333 μm, TCA 2.24 mm^2, SCA 0.86 mm^2, and LCA 1.37 mm^2. The CVI at the last follow-up was minimally changed at 61.1%.

In the treated group, 11 eyes (13.6%) showed evidence of type 1 MNV and 2 eyes (2.4%) were noted to have evidence of PCV. In the fellow eye group, only 2 eyes (3.1%) showed the presence of type 1 MNV and both lesions failed to exhibit signs of activity on multimodal imaging.

Subanalysis of functional and structural outcomes was performed in patients with secondary MNV/PCV (Table 3). Interestingly, Snellen VA did not significantly improve from baseline to months 1 and 3 ($P = .80$ and $P = .60$, respectively) and the reduction in CMT was not significant at both follow-up intervals ($P = .04$). In addition, eyes with secondary MNV/PCV did not show a significant reduction of SFCT at month 1 ($P = .11$) or at month 3 ($P = .03$). There was a decrease in both TCA and LCA at 1-month ($P = .19$ and $P = .24$, respectively) that persisted at the 3-month follow-up interval ($P = .54$ and $P = .48$, respectively), but these reductions were not statistically significant.

A total of 30 eyes (37.0%) received full-fluence, half dose PDT and 51 eyes (62.9%) received half-fluence, full dose PDT. There were significant differences at baseline for TCA and LCA between these 2 groups and therefore significant changes at follow-up may reflect baseline differences (Table 4). Snellen VA, CMT, SFCT, and CVI were not significantly different at baseline. Both half-fluence, full dose and full-fluence, half dose groups showed a significant decrease of CMT ($P < .001$) at 1-month follow-up, but in full-fluence, half dose group the reduction was significantly higher ($P < .001$). When comparing changes in choroidal parameters within each group, SFCT significantly decreased at the 1-month follow-up by 51.7 ± 81.1 μm in the full-fluence, half dose group ($P = .002$) and by 27.2 ± 47.2 μm in the half-fluence, full-dose group ($P < .001$), and this reduction persisted at 3 months. In the half dose PDT group, TCA, SCA, and LCA all significantly decreased at the one-month follow-up but returned to baseline at 3-months. The half-fluence PDT group showed a similar trend: TCA, SCA and LCA decreased at the one-month follow-up with an apparent rebound to baseline values at the 3-month follow-up, but these changes were not statistically significant. There was no correlation of spot size with change in vision or choroidal structural outcomes.

DISCUSSION

RECENT EVIDENCE SUGGESTS THAT EITHER HALF-DOSE OR half-fluence PDT should be the treatment of choice in

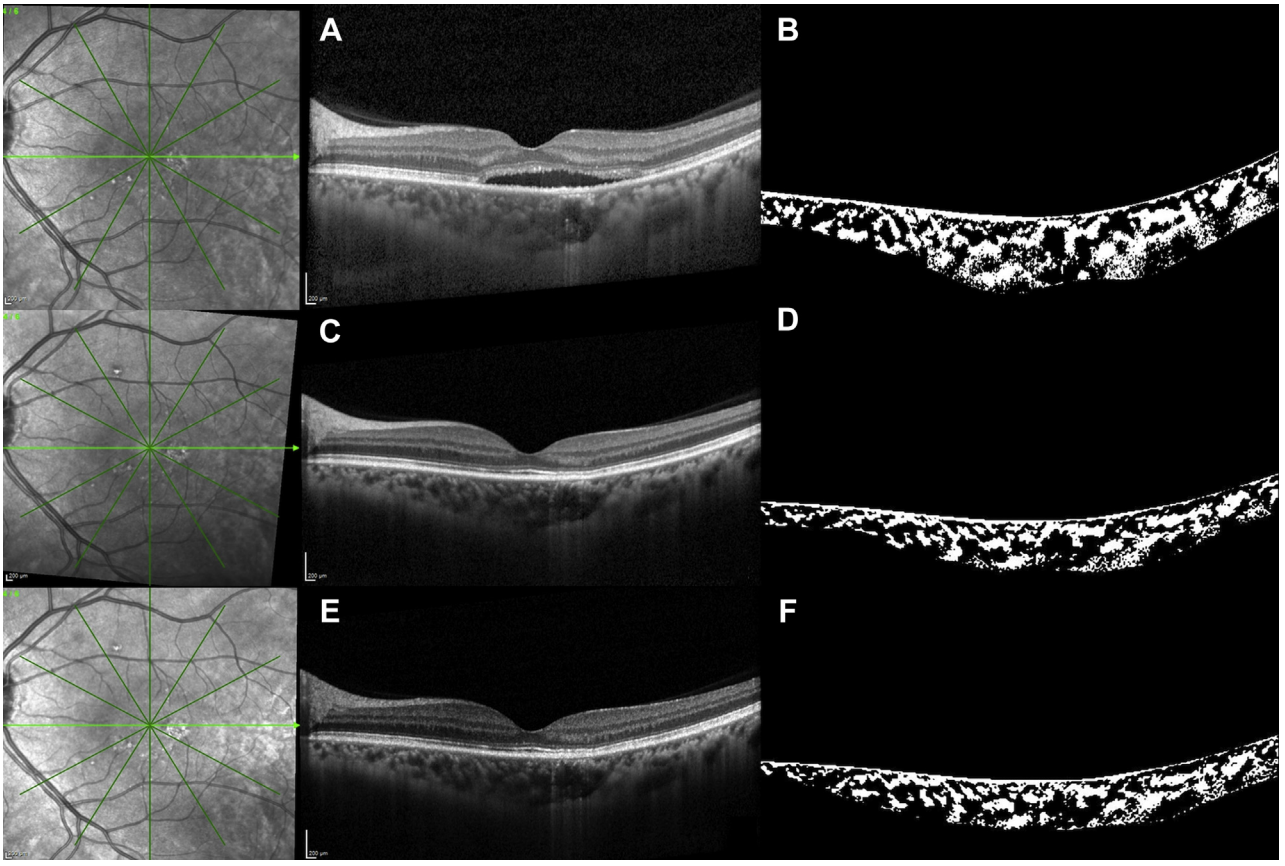

FIGURE 2. Spectral-domain optical coherence tomography (OCT) B scans (using enhanced depth imaging mode) and corresponding binarized OCT choroidal scans from a 48-year-old man with chronic central serous chorioretinopathy (CSCR) before and after full dose, half-fluence photodynamic therapy (PDT). Registered near-infrared reflectance images are also included to validate tracking of B scans from baseline to follow-up visits. (A and B) Baseline OCT B scan with corresponding binarized OCT scan shows central subretinal fluid (SRF) with an increased subfoveal choroidal thickness (SFCT) of 404 μm. The total choroidal area (TCA) measured 1.52 mm^2, the stromal choroidal area (SCA) measured 0.61 mm^2, the luminal choroidal area (LCA) measured 0.91 mm^2, and the choroidal vascularity index (CVI) measured 59.8%. (C and D) At the 1-month follow-up after PDT, the OCT B scan and corresponding binarized OCT scan show complete SRF resolution with a decreased SFCT to 344 μm. TCA, SCA, and LCA were all decreased to 0.88 mm^2, 0.38 mm^2, and 0.50 mm^2, respectively. The CVI diminished to 56.8%. (E and F) At the 3-month follow-up, the OCT B scan shows continued resolved SRF and the corresponding binarized scan shows an increase in all parameters: SFCT 353 μm, TCA 1.22 mm^2, SCA 0.51 mm^2, and LCA 0.71 mm^2. The CVI at the last follow-up increased to 58.1%.

patients with chronic CSCR.[7] In the present study, we evaluated the functional and anatomic outcomes occurring after PDT, focusing especially on the choroidal vasculature. Our results showed that Snellen VA improved at 1- and 3-month follow-up in treated eyes. Regarding the choroidal structural outcomes, SFCT was significantly decreased at both follow-up visits but TCA and LCA showed a significant reduction only at month 1 after treatment.

Of note, SCA and CVI slightly decreased after treatment, albeit not significantly. The CVI, a ratio of LCA over TCA, is a relatively novel parameter to quantitatively describe the choroidal vasculature, and has been applied to various chorioretinal diseases.[20–23] The automated algorithm used in this study measures CVI and provides the capability to stratify the stromal and vascular components. As shown in Table 1, both LCA and TCA were reduced after treatment with PDT, and this could explain why the CVI reduction did not reach significance during the follow-up visits. CVI only changes significantly if 1 of the 2 parameters varies more than the other.

The reduction of the TCA we found in our study may reflect the decrease in the SFCT. Izumi and associates[11] reported a significant reduction of the SFCT and of TCA, LCA and CVI at 3 months with no changes to the SCA after half dose full-fluence PDT treatment in a cohort of 22 eyes. However, the binarization process was applied only in the subfoveal 3-mm choroidal area and no choroidal analysis was performed at month 1. Manabe and associates[10] analyzed macular choroidal thickness in 22 eyes undergoing reduced-fluence PDT and reported a significant

TABLE 2. Comparison of Structural Outcomes and Visual Acuity at Baseline and at 1- and 3-Month Follow-up Between Eyes Receiving Photodynamic Therapy Versus Their Fellow Eyes

	PDT (N = 64)	Fellow Eye (N = 64)	*P* Value
CMT, μm (avg ± SD)			
Baseline	338.3 ± 106.5	242.8 ± 42.4	<.001
1-month	234.9 ± 80.5	241.7 ± 43.8	.50
3-month	246.7 ± 71.5	245.9 ± 50.2	.93
SFCT, μm (avg ± SD)			
Baseline	441.1 ± 124.1	396.5 ± 134.6	<.001
1-month	402.1 ± 129.9	388.9 ± 134.9	.23
3-month	409.3 ± 121.1	390.2 ± 137.2	.17
TCA, mm^2 (avg ± SD)			
Baseline	2.23 ± 1.45	2.04 ± 1.14	.44
1-month	2.02 ± 1.26	2.12 ± 1.40	.65
3-month	2.22 ± 1.72	1.94 ± 1.04	.37
SCA, mm^2 (avg ± SD)			
Baseline	1.05 ± 0.74	0.95 ± 0.57	.40
1-month	0.98 ± 0.68	1.13 ± 1.18	.37
3-month	1.06 ± 0.89	0.92 ± 0.50	.37
LCA, mm^2 (avg ± SD)			
Baseline	1.18 ± 0.75	1.10 ± 0.65	.52
1-month	1.03 ± 0.64	1.11 ± 0.78	.54
3-month	1.16 ± 0.89	1.02 ± 0.61	.39
CVI, % (avg ± SD)			
Baseline	53 ± 8	53 ± 8	.73
1-month	51 ± 9	52 ± 8	.66
3-month	52 ± 9	52 ± 8	.64
VA, logMAR (avg ± SD)			
Baseline	0.39 ± 0.34	0.10 ± 0.26	<.001
1-month	0.27 ± 0.27	0.10 ± 0.26	<.001
3-month	0.23 ± 0.36	0.04 ± 0.28	.003

CMT = central macular thickness; CVI = choroidal vascularity index; LCA = luminal choroidal area; logMAR = logarithm of minimal angle of resolution; PDT = photodynamic therapy; SCA = stromal choroidal area; SD = standard deviation; SFCT = subfoveal choroidal thickness; TCA = total choroidal area; VA = visual acuity.

reduction compared with normal control eyes at 1 and 3 months, but choroidal thickness gradually increased to baseline levels at 6 months.

CSCR is considered part of the pachychoroid disease spectrum.[24] SRF accumulation results from a chronically dysfunctional outer blood–retina barrier because of focal or diffuse choroidal thickening. Dilated outer choroidal veins (ie, "pachyvessels") represent an important "CSCR feature." The treatment effect of PDT is believed to be the result of remodeling of the choroidal vascular endothelium because of the formation of free radicals after photoactivation, resulting in thrombosis, occlusion, and choroidal hypoperfusion in the treated area. The significant reduction of the LCA of the choroid in this study supports the hypothesis that PDT targets large choroidal vessels, causing shrinkage and reduction of the total choroidal volume.

Previous OCTA studies reported that PDT may induce an early selective occlusion of the choriocapillaris.[12,25] By contrast, other studies have described an increase in choriocapillaris flow at 1 and 3 months after PDT.[13,26] Demirel and associates[13] showed that the LCA decreases as a result of the direct effect of half-fluence PDT on larger choroidal vessels while the choriocapillaris flow increases as a secondary reduction of focal compression from enlarged choroidal vessels. Our study did not include OCTA flow analysis of the choriocapillaris; however, the reduction in the choroidal LCA in the absence of associated choroidal stromal alterations seems to confirm the hypothesis that the large choroidal vessels are the main PDT target.

Subanalysis of CSCR eyes with MNV/PCV secondary to CSCR showed that there was only a slight (nonsignificant) improvement of VA after PDT. Moreover, the reduction of all choroidal parameters (SFCT, TCA, LCA, SCA, and CVI) after treatment was not significant at either follow-up interval. These findings would suggest that the presence of secondary MNV may represent a negative predictive factor for PDT success in patients with CSCR and that thinning of the choroid is not a sufficient index for good clinical response. As reported in the literature, the standard treatment for these patients with MNV secondary to CSCR is intravitreal anti–vascular endothelial growth factor (VEGF) therapy possibly supplemented by half dose or half-fluence PDT.[7,27]

Half dose, full-fluence PDT has been reported to be as effective as half-fluence, full dose PDT.[7] In our study, the half dose (full-fluence) regimen showed a more significant reduction of CMT at month 1 compared with the half-fluence (full dose) PDT, indicating a greater short-term effect, but this improvement was not significant at month 3. SFCT was significantly reduced at 1 month in both groups. In addition, statistically significant decreases in TCA, LCA, and SCA were noted in the half-dose group at 1 month, while the half-fluence group showed a similar trend that was not statistically significant. Analysis of the functional and structural choroidal changes in patients undergoing full vs half-dose PDT has been recently completed,[28] and the study found no significant differences between the 2 groups at month 3 after treatment, although the CVI and SFCT were significantly reduced and BCVA significantly increased in both groups.

Limitations of the present analysis include the retrospective nature of the study and the relatively short follow-up period. Although our study cohort was relatively large, subgroup analyses may not have been powered to identify statistically significant differences. The absence of statistical significance does not imply equivalence and therefore further studies are necessary. In addition, there were differences in the image acquisition protocol and the treatment modalities used between institutions and comparison

TABLE 3. Subanalysis of Structural Changes in Patients with Secondary Macular Neovascularization and Polypoidal Choroidal Vasculopathy

	Baseline (N = 13)	1-Month (N = 12)	*P* Value	3-Month (N = 13)	*P* Value
CMT, μm (avg ± SD)	368.8 ± 171.4	274.4 ± 70.8	.04	278.8 ± 84.0	.04
SFCT, μm (avg ± SD)	377.4 ± 97.5	354.2 ± 105.1	.11	354.2 ± 98.7	.03
TCA, mm^2 (avg ± SD)	2.42 ± 1.66	2.11 ± 1.86	.19	2.28 ± 2.04	.54
SCA, mm^2 (avg ± SD)	1.19 ± 0.96	1.07 ± 1.00	.16	1.16 ± 1.08	.69
LCA, mm^2 (avg ± SD)	1.23 ± 0.74	1.04 ± 0.90	.24	1.12 ± 0.98	.48
CVI, % (avg ± SD)	53 ± 7	50 ± 10	.25	50 ± 8	.19
VA, logMAR (Snellen, avg ± SD)	0.41 ± 0.43 (20/51)	0.42 ± 0.39 (20/52)	.80	0.43 ± 0.48 (20/53)	.60

CMT = central macular thickness; CVI = choroidal vascularity index; LCA = luminal choroidal area; logMAR = logarithm of minimal angle of resolution; SCA = stromal choroidal area; SD = standard deviation; SFCT = subfoveal choroidal thickness; TCA = total choroidal area; VA = visual acuity.

between PDT modalities may have been biased because of center-specific differences in therapeutic approach. Two different OCT technologies were used, SD-OCT vs SS-OCT. The latter may provide better choroidal visualization, however, as shown in a recent study the 2 systems are comparable for choroidal vascular and CVI measurements.[29] We excluded eyes with incomplete visualization of the choroid; however, it is possible that these eyes may

TABLE 4. Comparison of Structural Outcomes and Visual Acuity at Baseline, and at 1- and 3-Month Follow-up Between Full-Fluence, Half Dose Group Versus the Half-Fluence, Full Dose Group

	Full- Fluence, Half Dose (N = 30)	Half-Fluence, Full Dose (N = 51)	*P* Value
CMT, μm (avg ± SD)			
Baseline	364.6 ± 160.3	341.4 ± 102.5	.48
1-month	199.4 ± 60.0	256.3 ± 84.1	<.001
3-month	234.8 ± 105.9	249.2 ± 70.9	.69
SFCT, μm (avg ± SD)			
Baseline	420.4 ± 131.7	437.2 ± 120.9	.57
1-month	368.7 ± 134.1	410.9 ± 134.3	.18
3-month	367.2 ± 142.7	404.2 ± 123.3	.46
TCA, mm^2 (avg ± SD)			
Baseline	2.86 ± 1.07	1.96 ± 1.49	.002
1-month	2.53 ± 1.08	1.80 ± 1.20	.006
3-month	3.39 ± 1.83	2.03 ± 1.44	.05
SCA, mm^2 (avg ± SD)			
Baseline	1.28 ± 0.56	0.94 ± 0.79	.03
1-month	1.15 ± 0.53	0.89 ± 0.67	.06
3-month	1.44 ± 1.01	0.99 ± 0.77	.21
LCA, mm^2 (avg ± SD)			
Baseline	1.58 ± 0.61	1.02 ± 0.73	<.001
1-month	1.38 ± 0.63	0.91 ± 0.58	.002
3-month	1.94 ± 0.86	1.04 ± 0.72	.01
CVI, % (avg ± SD)			
Baseline	55 ± 8	53 ± 7	.35
1-month	54 ± 8	51 ± 9	.27
3-month	59 ± 4	52 ± 8	.33
VA, logMAR (Snellen, avg ± SD)			
Baseline	0.43 ± 0.28 (20/53)	0.37 ± 0.39 (20/47)	.45
1-month	0.28 ± 0.24 (20/38)	0.30 ± 0.30 (20/40)	.78
3-month	0.31 ± 0.46 (20/40)	0.23 ± 0.23 (20/34)	.62

CMT = central macular thickness; CVI = choroidal vascularity index; LCA = luminal choroidal area; logMAR = logarithm of minimal angle of resolution; SCA = stromal choroidal area; SD = standard deviation; SFCT = subfoveal choroidal thickness; TCA = total choroidal area; VA = visual acuity.

be associated with a thicker choroid and excluding such cases may represent an additional potential confounder. An additional study limitation relates to the exact location of the PDT laser spot administration; this information was not available for this study but may be partly accounted by the fact that choroidal alterations after PDT may occur remote from the treated area.[30,31] Finally, the presence of coexisting systemic illnesses was not recorded in this analysis and 25.9% of eyes received previous treatment that could potentially influence choroidal anatomic outcomes.

In conclusion, our study demonstrated a significant reduction of SFCT, LCA, and TCA in patients with chronic CSCR receiving PDT at 1-month follow-up with commensurate VA improvement. This analysis provides further evidence of the targeted effect of PDT on the remodeling of the large choroidal vessels. Half-dose and half-fluence protocols resulted in comparable choroidal anatomic outcomes and were both effective in resolving SRF with improved VA. However, patients with secondary MNV/PCV did not show significant functional and anatomic improvement after PDT. The results of our study suggest that quantification of TCA and LCA, in addition to SFCT, may provide additional quantitative biomarkers to evaluate the choroidal anatomic response to therapy, but this awaits further prospective validation.

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