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Non-ICGA treatment criteria for Suboptimal Anti-VEGF Response for Polypoidal Choroidal Vasculopathy: APOIS PCV Workgroup Report 2

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Purpose: To develop and validate OCT and color fundus photography (CFP) criteria in differentiating polypoidal choroidal vasculopathy (PCV) from typical neovascular age-related macular degeneration (nAMD) in eyes with suboptimal response to anti−vascular endothelial growth factor (VEGF) monotherapy and to determine whether OCT alone can be used to guide photodynamic therapy (PDT) treatment.

Design: Clinical study evaluating diagnostic accuracy.

Participants: Patients with nAMD who received 3-month anti-VEGF monotherapy but had persistent activity defined as subretinal fluid or intraretinal fluid at month 3 assessments.

Methods: In phase 1, international retina experts evaluated OCT and CFP of eyes with nAMD to identify the presence or absence of features due to PCV. The performance of individual and combinations of these features were compared with ICGA. In phase 2, these criteria were applied to an independent image set to assess generalizability. In a separate exercise, retinal experts drew proposed PDT treatment spots using only OCT and near-infrared (NIR) images in eyes with PCV and persistent activity. The location and size of proposed spot were compared with ICGA to determine the extent of coverage of polypoidal lesions (PLs) and branching neovascular network (BNN).

Main Outcome Measures: Sensitivity and specificity of CFP and OCT criteria to differentiate PCV from nAMD and accuracy of coverage of OCT-guided PDT compared with ICGA.

Results: In eyes with persistent activity, the combination of 3 non−ICGA-based criteria (sharp-peaked pigment epithelial detachment [PED], subretinal pigment epithelium [RPE] ring-like lesion, and orange nodule) to detect PCV showed good agreement compared with ICGA, with an area under the receiver operating characteristic curve of 0.85. Validation using both an independent image set and assessors achieved an accuracy of 0.77. Compared with ICGA, the OCT-guided PDT treatment spot covered 100% of PL and 90% of the BNN.

Conclusions: In nAMD eyes with persistent activity, OCT and CFP can differentiate PCV from typical nAMD, which may allow the option of adjunct PDT treatment. Furthermore, OCT alone can be used to plan adjunct PDT treatment without the need for ICGA, with consistent and complete coverage of PL. *Ophthalmology Retina 2021;5:945-953 © 2021 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

See editorial on page 943.

Polypoidal choroidal vasculopathy (PCV) is a subtype of neovascular age-related macular degeneration (nAMD) characterized by nodular dilatations within type 1 neovascular networks that are best seen on indocyanine green angiography (ICGA).[1-6] Although dye angiography remains an important imaging modality in the assessment of nAMD lesions, there is an increasing reliance on OCT for management and diagnosis of nAMD because of its rapidity of image acquisition, localization of vascular structures to specific tissue layers, accessibility, and noninvasive nature. As a result, in current clinical practice, clinicians tend to perform fewer dye angiographies, leading to the possibility that PCV cases may be missed during management of nAMD. To address this, the Asia Pacific Ocular Imaging Society (APOIS) PCV workgroup recently reported that the combination of 3 OCT-based criteria (subretinal pigment epithelium [RPE] ring-like lesion, complex RPE outline on enface OCT, and a sharp-peaked pigment epithelial detachment [PED]) can differentiate PCV from typical nAMD in treatment-naïve eyes with a sensitivity of 0.75 and specificity of 0.91.[7] The APOIS Workgroup also

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recommended using the terms "polypoidal lesions" (PLs) and "branching neovascular network (BNN)" to describe the 2 lesion components of PCV.

Nevertheless, the initial differentiation of PCV from typical nAMD may not be essential when commencing treatment, because many clinicians will use intravitreal anti−vascular endothelial growth factor (VEGF) monotherapy as their first-line treatment modality for all subtypes of nAMD.[8] However, if disease activity remains persistent after the initial 3-month induction or loading phase, diagnosing possible PCV subtype becomes important, because a change in management plan, such as adding "rescue" photodynamic therapy (PDT), may be beneficial.[3,9-14] However, the need to perform ICGA to diagnose PCV may deter clinicians and potentially deny patients the opportunity to benefit from treatment options that are recognized as optimal for PCV.

In the current study, we aimed to develop and evaluate a set of non−ICGA-based OCT and color fundus photograph criteria to see if these can differentiate PCV from typical nAMD in eyes with persistent fluid after the initial 3-month induction phase of anti-VEGF monotherapy (which we term "suboptimal responders to anti-VEGF treatment" eyes, defined next). Furthermore, in keeping with the trend of using noninvasive non−dye-based imaging modalities, we further evaluated whether OCT alone can provide sufficient guidance for initiating PDT treatment in terms of spot location and size to reliably cover the PL and BNN as determined by the gold standard ICGA.

Methods

The APOIS PCV Workgroup was set up in 2019 to promote the application of ocular imaging in the understanding and management of PCV worldwide. Details of the selection of panel members have been described previously.[7] The study adhered to the Declaration of Helsinki, and all images and clinical data used in this study were obtained from the Phenotyping Asian AMD study, which is approved by the Institutional Ethics Board of SingHealth, which recruited consecutive patients presenting with treatment-naïve typical nAMD and PCV.[15,16] All participants gave written informed consent. Participants underwent clinical examination and multimodal imaging at baseline, month 3, and month 12, according to a standardized protocol.

Phase 1: Development and Validation of Non-ICGA Features to Differentiate PCV from Typical nAMD in Eyes with Suboptimal Response to Anti-VEGF Treatment

We included eyes that received an induction or loading phase of 3-month anti-VEGF monotherapy from baseline and had persistent subretinal fluid (SRF) or intraretinal fluid (IRF) at their month 3 (± 1 month) assessments based on reading center grading. For the purpose of this study, we define these eyes as "suboptimal responders to anti-VEGF treatment," although we recognize that there is no consistent definition of treatment responsiveness in the literature.

Test Set. Ten eyes (5 PCV and 5 typical nAMD) with persistent IRF/SRF at their month 3 assessment were selected. Graders from the Singapore National Eye Center Ocular Reading center determined the angiography subtype based on FA/ICGA and presence of SRF/IRF based on OCT. Baseline characteristics of the test set are summarized in Table 1. The test set was made available to a group of retina expert panel members who were masked to all baseline imaging and ICGA data. Each panel member assessed the following images taken at the month 3 assessment for each eye: color fundus photography (CFP), macular volume scan in enhanced depth imaging mode comprising 25-line scans covering 6 × 6-mm area centered on the fovea (Spectralis), and en face OCT fly-through video spanning the internal limiting membrane to the choroid (Triton). The en face scan was corrected and flattened to Bruch's membrane using inbuilt software (Imagenet v6, Topcon).

Panel members independently recorded in the test set the presence or absence of an orange nodule on CFP and each of the 6 prespecified features on OCT: (1) sharp peaked PED; (2) sub-RPE ring-like lesion; (3) pachychoroid; (4) double layer sign; (5) multilobular PED; (6) irregularly shaped lesion detected on en face RPE. Detailed definitions for each feature and reference images were provided before the grading exercise.[7] A set of diagnostic criteria based on CFP and OCT was constructed on the basis of the sensitivity and specificity of the features individually and in combination and subsequently applied to the next phase of validation on an independent set of images.

Phase 2: Validating OCT Criteria for PCV Diagnosis

Validation Set. To evaluate the wider applicability of these criteria, a group of independent assessors composed of 6 ophthalmology residents from Singapore and Milan masked to the angiographically determined nAMD subtype applied the set of criteria developed from the preceding step to an independently graded validation set of 80 eyes (40 PCV and 40 typical nAMD). To further increase the generalizability of the results, the validation set included eyes of patients recruited from Singapore and Italy. The gold standard diagnosis of nAMD subtype was established by the Singapore National Eye Centre ocular reading center and the Sacco reading center, Luigi Sacco Hospital, University of Milan for the cohorts, respectively.

Assessment of OCT Criteria to Guide PDT Treatment Spot Location and Size

In the next part of the study, retina expert panel members were invited to evaluate macular volume scans comprising 25 B-scans covering an area of 6 × 6-mm zone centered on the fovea (Spectralis, Heidelberg Engineering) from 10 eyes diagnosed with PCV and persistent fluid at month 3 and confirmed on ICGA and OCT by the reading center.

No specific instructions were provided on how to determine presence of polyps or the BVN on an OCT; however, all panel members had prior knowledge of the features used to diagnose PCV in the prior exercise. Panel members were asked to estimate the extent of the lesion based on OCT with its accompanying near-infrared (NIR) reflectance image only and place a spot of sufficient diameter on the IR enface image that would allow complete coverage of the PL(s) and BNN in a single circular spot in accordance with EVEREST study protocol.[17] Panel members were not given access to ICGA images.

To assess the accuracy of lesion coverage by OCT-guided PDT spots provided by the panel members, graders from the reading center outlined the area of the PL and any associated BNN on the en face ICGA using the free-form tool in ImageJ. Area of PL and BNN was derived from outlined ICGA images and expressed in μm^2. The ICGA images with lesion outline were subsequently registered with the NIR images that were marked with the OCT-guided PDT treatment spot (Fig 1). The proportion of PL and BNN covered by the OCT-guided PDT treatment spot was reported as a ratio of the lesion component size. The greatest linear

Table 1. Baseline Characteristics of Test Set

Subject	nAMD Subtype	Gender	Age, yrs	Agent	GLD	Type of Fluid at Month 3	
						IRF	*SRF*
1	PCV	M	61	aflibercept	3476	–	+
2	PCV	F	59	aflibercept	2835	–	+
3	PCV	M	69	ranibizumab	2906	+	+
4	PCV	F	60	aflibercept	3221	–	+
5	PCV	M	71	aflibercept	3052	+	+
6	Type I CNV	F	83	aflibercept	3479	+	+
7	Type II CNV	M	72	bevacizumab	2401	+	–
8	Type I + II CNV	F	78	bevacizumab	3968	–	+
9	Type I CNV	M	80	bevacizumab	3521	+	+
10	Type I CNV	M	76	bevacizumab	3738	+	–

CNV = choroidal neovascularization; GLD = greatest linear diameter; IRF = intraretinal fluid; nAMD = neovascular age-related macular degeneration; PCV = polypoidal choroidal vasculopathy; SRF = subretinal fluid.

dimension (GLD) of the entire lesion (PL + BNN) expressed in μm was measured by the reading center on ICGA.

Statistical Analysis

For the first objective, we analyzed the performance of non-ICGA features to differentiate PCV from typical nAMD and calculated the sensitivity, specificity, positive predictive value, negative predictive value, and predictive accuracy (area under the curve [AUC] and 95% confidence intervals [CIs]) for each individual feature against the reading center diagnosis as the gold standard. Combinations of individual criteria were also assembled for computation of AUC. Accuracy of the best combination was assessed in the validation exercise. Intergrader agreement for each feature was calculated using Fleiss' Kappa with slight, fair, moderate, and substantial agreement defined as a κ between 0.0–0.2, 0.21–0.4, 0.41–0.6, and 0.61–0.8, respectively.

For the second objective, where we evaluated whether OCT alone can guide PDT treatment, we calculated intergrader correlation coefficient (ICC) for the attributes of OCT-guided PDT treatment spot including size, location, and lesion component coverage.

Results

Characteristics of Study Participants

Patients with typical nAMD were older compared with patients with PCV (78 ± 4 vs. 64 ± 6 years, $P < 0.01$). There was no significant difference in gender, GLD of the lesion, and distribution of fluid within retina compartment between groups (Table 1).

Non-ICGA Diagnostic Criteria

Of the 21 panel experts, 16 responded to this exercise. The sensitivity, specificity, and AUC for each of the 7 individual features are summarized in Table 2. Sharp-peaked PED (AUC, 0.76), sub-RPE ring-like lesion (AUC, 0.73), and orange nodule (AUC, 0.67) were the highest performing individual features. Combination of these 3 features achieved an AUC of 0.85 (95% CI, 0.76–0.94), with sensitivity of 0.65, specificity of 0.82, positive predictive value of 0.68, and negative predictive value of 0.88. Examples of PCV and typical nAMD cases are shown in Figure 2. The top 3 permutations of all the features are shown in Figure 3. When this combination of 3 features was used by the additional group of assessors composed of ophthalmology residents in the independent validation set, an accuracy of 77% was achieved, based on ICGA as the gold standard diagnosis as graded by the reading centers.

OCT-Guided PDT Treatment Spot

On ICGA graded by the reading center, the mean ± standard deviation (SD) GLD of the whole lesion was 3617 ± 694 μm (range, 2681–4465 μm). The PL occupied a mean ± SD of 15% ± 5% (range, 2%–21%) of the total lesion area. The mean ± SD GLD of

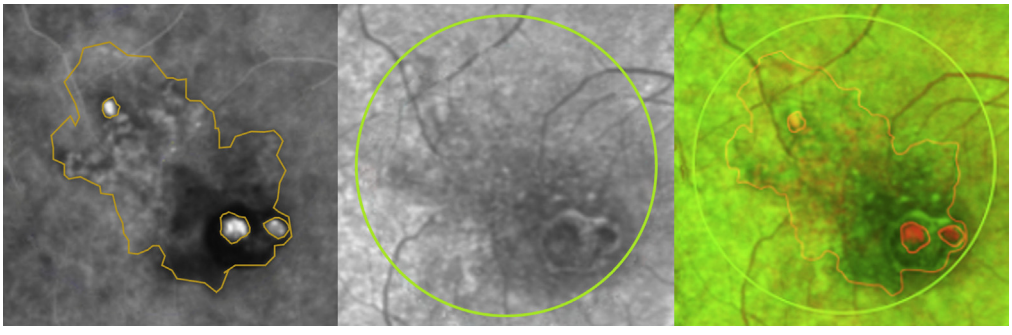

Figure 1. Outlines of polypoidal lesion (PL) and branching neovascular network (BNN) **(orange)** based on indocyanine green angiography (ICGA) **(left)** were registered onto near-infrared (NIR) image with OCT-guided photodynamic therapy (PDT) treatment spot marking **(green circle) (middle)**. Combined image is shown on the **right**.

Table 2. Area Under the Curve, Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value for Each Individual Feature

Feature	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	K	Agreement
Sharp-peaked PED	0.76 (0.64–0.88)	0.88	0.63	0.86	0.58	0.42	Moderate
Sub-RPE ring-like lesion	0.73 (0.60–0.87)	0.68	0.79	0.78	0.88	0.58	Moderate
Orange nodule	0.67 (0.51–0.84)	0.60	0.74	0.58	0.71	0.35	Fair
Thick choroid with dilated Haller's layer	0.63 (0.45–0.81)	0.52	0.75	0.56	0.68	0.53	Moderate
Double layer sign	0.60 (0.41–0.80)	0.37	0.83	0.42	0.85	0.48	Moderate
Complex/multilobular PED	0.63 (0.43–0.83)	0.56	0.63	0.60	0.66	0.38	Fair
En face OCT-complex RPE elevation	0.51 (0.29–0.73)	0.50	0.53	0.56	0.59	0.26	Fair

AUC = area under the curve; CI = confidence interval; K = Fleiss multi-rater Kappa; NPV = negative predictive value; PED = pigment epithelial detachment; PPV = positive predictive value; RPE = retinal pigment epithelium.

the OCT-guided PDT spot was 3263 ± 966 μm with good agreement between retinal expert panel members (n = 6) (ICC, 0.75; 95% CI, 0.56–0.90; $P < 0.01$). Among the 10 eyes evaluated, the OCT-guided GLD was larger than the ICGA lesion GLD in 6 eyes (mean ± SD, 13.6% ± 5.8% larger) and smaller in 4 eyes (mean ± SD, 6.8% ± 4.2% smaller). When we compared the OCT-guided PDT spot drawn by the retina panel experts to the ICGA lesion, 100% of PL area and mean ± SD 91% ± 12% of BNN area were found to be covered with the proposed spot. The agreement between panel experts for the area covered was moderate (ICC, 0.69; 95% CI, 0.47–0.88; $P < 0.01$) (Table 3).

An example in which the OCT spots covered all lesion components with good agreement among 6 panel experts is shown in Figure 4. An example in which a portion of the BNN was not covered in the proposed spot by the majority of panel experts is shown in Figure 5. The cross-sectional OCT through the "uncovered" BNN areas showed subtle undulating RPE with no overlying SRF or IRF.

Discussion

The APOIS PCV Workgroup recently developed and reported a set of non–ICGA-based imaging criteria that can differentiate treatment-naïve eyes with PCV from typical nAMD at initial presentation.[7] However, in many clinical practices, the first-line treatment for both subtypes is often anti-VEGF monotherapy.[9-14] Thus, in the current study, we developed and evaluated a further set of non–ICGA-based imaging features in differentiating eyes with PCV from

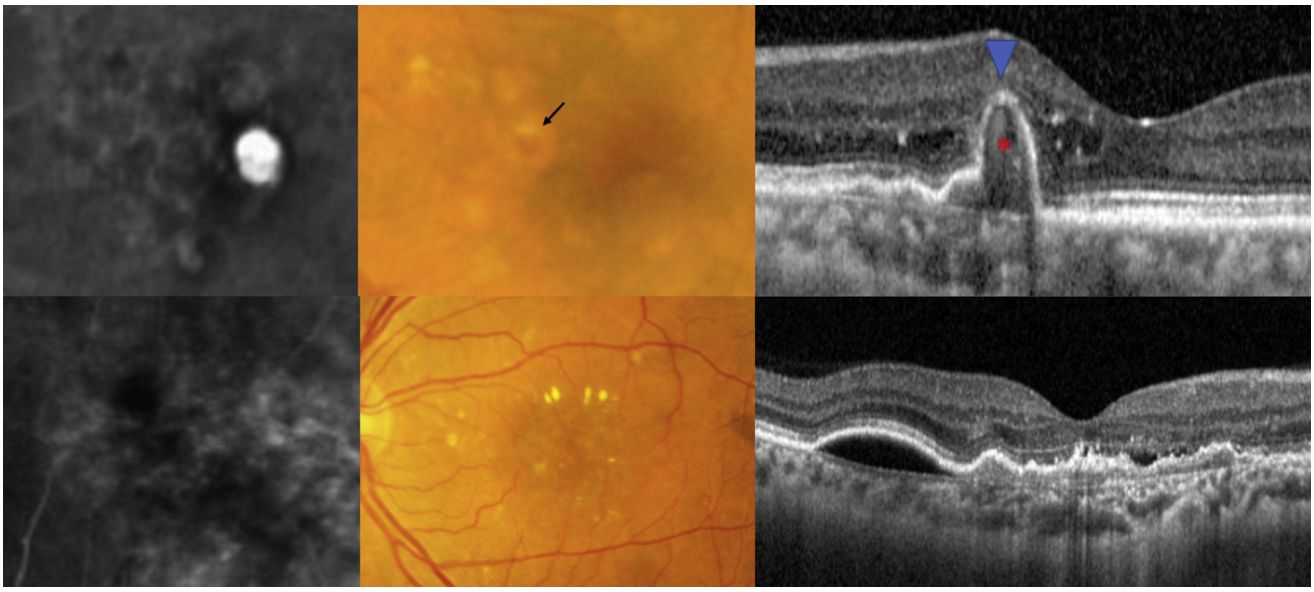

Figure 2. Examples of non-ICGA features in polypoidal choroidal vasculopathy (PCV) and typical neovascular age-related macular degeneration (nAMD). **Top:** An example of PCV with persistent intraretinal fluid (IRF) at month 3 visit despite having received 3 monthly anti-VEGF injections. Polypoidal lesion and BNN are confirmed on ICGA. In the corresponding color fundus photograph, an orange nodule **(arrow)** can be seen. In the OCT through the orange nodule, a sharp-peaked pigment epithelial detachment (PED) **(blue arrowhead)** and sub-retinal pigment epithelium (RPE) ring-like lesion occupying the full extent of the PED **(red asterisk)** can be seen. **Bottom:** An eye with typical nAMD with persistent subretinal fluid (SRF) despite having received anti-VEGF induction in which ICGA showed no PCV. None of the 3 features in the proposed set of diagnostic criteria are present. ICGA = indocyanine green angiography.

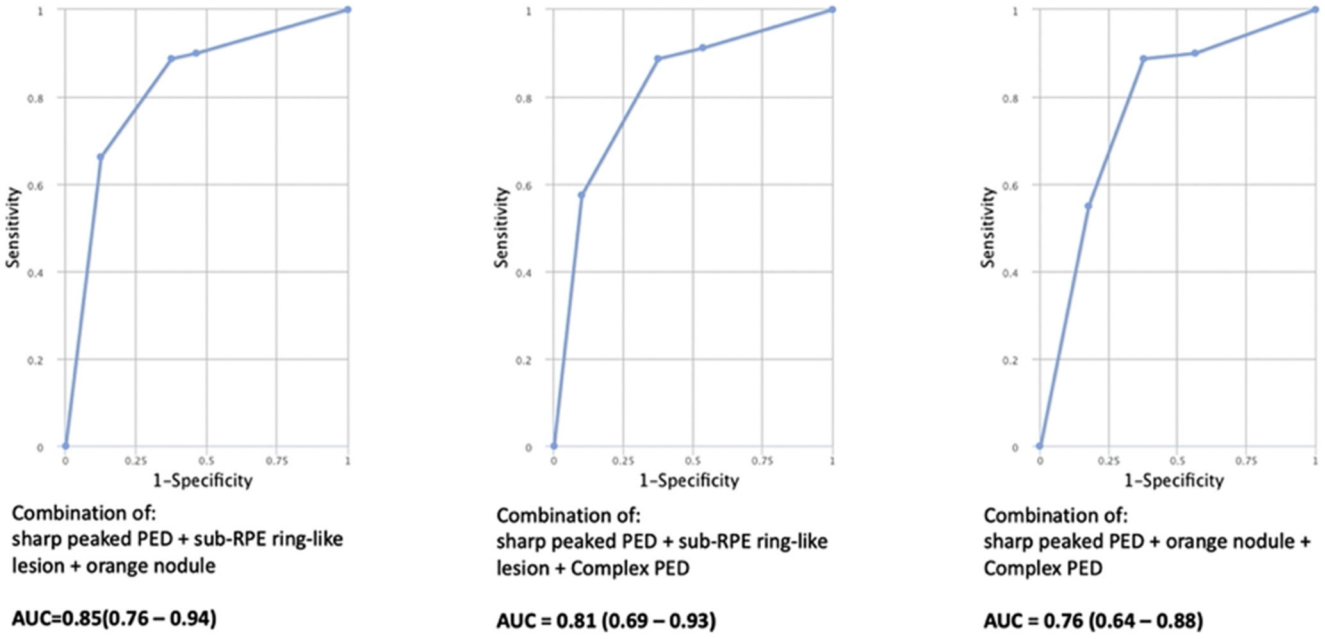

Figure 3. Receiver operating characteristic curves of the top 3 permutations of OCT features that were found to achieve the highest area under the curve (AUC) results for the detection of PCV in suboptimal responders. PCV = polypoidal choroidal vasculopathy; PED = pigment epithelial detachment; RPE = retinal pigment epithelium.

typical nAMD, which had a suboptimal response to anti-VEGF monotherapy after 3 monthly injections (which we termed "suboptimal responders" to anti-VEGF treatment for the purpose of this study). The combination of 3 criteria (sharp-peaked PED and sub-RPE ring-like structure on OCT and orange nodule on CFP) achieved an AUC of 0.85. The sensitivity of 0.65 suggest this set of OCT criteria may miss some PCV eyes, but this is mitigated by a relatively high specificity (0.85). When these features are detected, PCV is highly likely to be present, and therefore other alternative treatment options may be considered.[1,7,12,18]

Among the top 3 features recommended, both sharp-peaked PED and sub-RPE ring-like lesion were also features used for differentiating PCV and typical nAMD in treatment-naïve eyes. These signs on OCT represent the PL and are consistent with prior findings in which only 50% of PL achieve closure after the initial anti-VEGF loading. In contrast, the presence of orange nodule appears more useful as a differentiating factor in these suboptimal responders compared with treatment-naive eyes. This is in keeping with clinical observations because orange nodules can often be seen more clearly once fluid and blood decrease after initial anti-VEGF treatment. En face RPE elevations, which was one of the major criteria for non-ICGA diagnosis of PCV in treatment-naïve eyes, did not feature in the top 3 criteria in this study. This could be due to resolution of sub-RPE fluid from the BNN after initial anti-VEGF therapy. We observed a similar, moderate intergrader agreement for all the major criteria in this study compared with a study that described PCV diagnosis based on ICGA (K = 0.53).[3] Although the initial set of diagnostic characteristics and assessments were performed by retina specialists with expertise in imaging and management of PCV, we demonstrated that inclusion of ophthalmology residents yielded similar agreement and that they were also able to implement the recommended diagnostic criteria and in Singapore and Italy.

In the second part of this study, we evaluated whether it is possible to use OCT alone to guide the PDT treatment spot. Our

Table 3. Characteristics and Agreement of ICGA-Defined Lesions and OCT-Guided PDT

Features	Mean	SD	ICC	95% CI		P Value
				Lower	*Upper*	
GLD of OCT-guided PDT, μm	3263	966	0.76	0.56	0.9	< 0.01
GLD of total lesion on ICGA, μm	3617	694	–	–	–	–
Proportion of PL area covered, %	100	0	1	NA	NA	NA
Proportion of BNN area covered, %	91	12	0.69	0.47	0.88	< 0.01

BNN = branching neovascular network; CI = confidence interval; GLD = greatest linear diameter; ICC = intraclass correlation; ICGA = indocyanine green angiography; NA = not available; PDT = photodynamic therapy; PL = polypoidal lesion; SD = standard deviation.

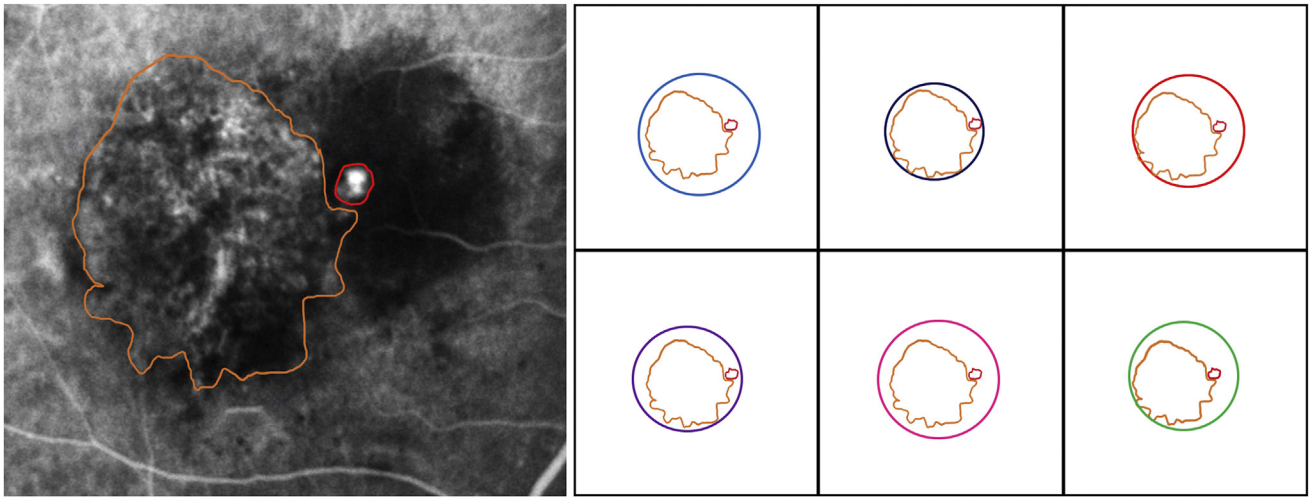

Figure 4. Comparison of OCT-guided PDT spot and lesions on ICGA. The PL **(red outline)** and BNN **(blue outline)** were outlined by reading center using ICGA **(left)**. The 6 small panels on the right showed the OCT-guided PDT spots by 6 retinal specialists, with lesion outline overlaid for comparison. Note that all lesion components were covered in all 6 panels, and the size and location of the OCT-guided treatment spots were similar among the 6 specialists. BNN = branching neovascular network; ICGA = indocyanine green angiography; PDT = photodynamic therapy; PL = polypoidal lesion.

results indicated that OCT-guided treatment spot can consistently cover 100% of the PL and 90% of the BNN. This result is encouraging because closure of PL is the main aim of combination therapy, whereas leakage from BNN may be controlled with anti-VEGF therapy. Agreement between the retinal specialists who performed this task was also good. The OCT-guided PDT spots were similar among the retinal specialists with very tight margins on many of the lesions with complete coverage. From the case examples, all 3 features in the diagnostic criteria are highly predictive of areas with PLs, whereas shallow irregular RPE elevation is useful in localizing the extent of the BNN. Overall, on reviewing the images from the panel, we found that the boundaries of the PDT spot corresponded to the PED, shallow separation of the RPE from Bruch's membrane (double layer sign), and sharp peaked PED on OCT. The double layer sign corresponded to the extent of the BNN and the sharp peaked PED to the PLs. Thus, the extent of the entire lesion can be estimated with reasonable accuracy on NIR images by identifying boundaries of these features on an OCT. However, approximately 10% of the area of BNN visible on ICGA was not covered by the proposed OCT-guided PDT spot. We noted that these areas are characterized by extremely shallow undulations of the RPE, with no overlying fluid. These areas of BNN may be visualized and supplemented with OCT angiography (OCTA) imaging.[19] Yet, this discrepancy between OCT- and ICGA-guided PDT spot may indicate an advantage rather than a limitation in the use of OCT, because the PDT spot size can be minimized by not including areas that are likely to be inactive, whereas traditional ICGA PDT planning is indiscriminate to exudative activity and may lead to unnecessarily large PDT spots. However, the effectiveness of OCT-guided PDT spots has not yet been evaluated in any study and remains a potential area of study.

Another advantage of OCT-guided treatment spot planning is that part of the lesion can be masked on ICGA in eyes with tall PED, but hyperreflective material under the PED can be discerned, suggesting the true extent of a BNN. Several groups have reported that BNN can be observed clearly with OCTA, whereas the appearance of PL is more variable.[20-22] Thus, addition of OCTA, where available, may further improve the accuracy of defining the extent of the lesion. OCTA was not assessed because the aim of this study was to use a widely accessible imaging modality, OCT, to ensure the generalizability of the methods described.

The results of this current study build on our previous work in treatment-naïve eyes, and we believe both sets of criteria can be easily adopted in clinical practices and are particularly important in settings where ICGA is not available or not routinely performed. In our previous work, we have recommended 3 OCT-based features that can distinguish PCV from typical nAMD in treatment-naïve cases.[7] Although anti-VEGF monotherapy is likely to be the preferred initial treatment regardless of nAMD subtype, a proportion of suboptimal responders may be due to PCV.[10-14,23] Identifying these eyes and considering alternative management such as PDT or switching anti-VEGF agents are important to avoid prolonged anti-VEGF treatment with suboptimal control. In the current study, we identified 3 non-ICGA features that can differentiate PCV from typical nAMD in eyes with suboptimal anti-VEGF response. Our validation exercise demonstrates that this set of criteria was easily adopted by ophthalmology trainees and therefore likely to be useful to most general ophthalmologists. Finally, planning of PDT may also be possible with OCT only with coverage of the entire PL in all eyes and a large proportion of BNN in most eyes.

Study Limitations

There are limitations that should be mentioned, including the relatively small number of cases evaluated. The quality of

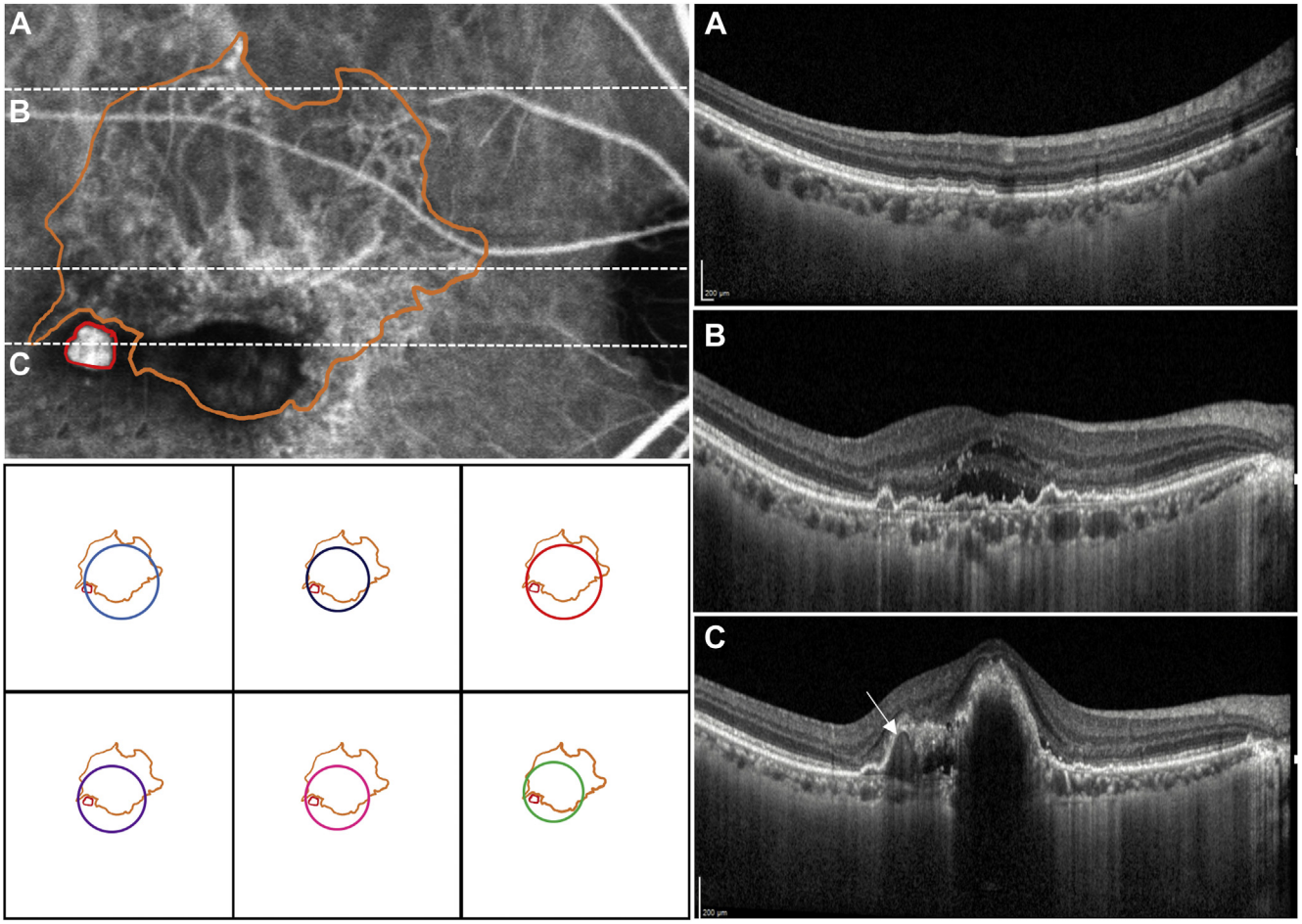

Figure 5. Comparison of OCT-guided PDT spot and lesions on ICGA. The PL **(red outline)** and BNN **(blue outline)** were outlined by reading center using ICGA **(left)**. The 6 small panels below showed the OCT-guided PDT spots by 6 retinal specialists, with lesion outline overlaid for comparison. In this case, the superior edge of the BNN **(A)** was not covered in the OCT spot. In the corresponding B-scan, this area showed subtle RPE undulation and no overlying fluid. The majority of the remaining BNN **(B)** and the entire PL **(C)** were covered in all 6 panels. The B-scan over the BNN that was covered by the proposed treatment spot showed more obvious irregular RPE detachment and presence of overlying fluid. The B-scan through the PL showed a sharp-peaked PED with sub-RPE ring-like lesion **(white arrow)**. The size and location of the PDT spot by the 6 specialists were similar. BNN = branching neovascular network; ICGA = indocyanine green angiography; PDT = photodynamic therapy; PED = pigment epithelial detachment; PL = polypoidal lesion; RPE = retinal pigment epithelium.

OCT scans, which may depend on various factors, such as the amount of averaging, media opacity, density of macular cube scan used, and segmentation of en face images, may affect the performance of the diagnostic criteria for individual cases. The location of PL at the termini of large BNN may be outside the area captured by OCT macular volume scan centered over the fovea. There are also limitations specific to the use of OCT-guided PDT spot placement. The ability to co-localize en face NIR and OCT B-scan is required to ensure accurate planning; nonetheless, this feature is available on the viewing platforms of most commercially available OCT instruments. However, this method of PDT spot derivation carries a risk that missing portions of the lesion may be missed or gratuitiously covering regions of normal retina because ICGA information will not be available. Finally, a clinical study using the non-ICGA criteria for detection of PCV in suboptimal responders to anti-VEGF treatment and OCT-guided determination of spots for PDT should be evaluated for its efficacy and safety before these criteria can be widely adopted.

Conclusions

The APOIS PCV Workgroup has proposed a set of simple, practical, easily adopted non-ICGA diagnostic criteria for differentiating PCV from typical nAMD among eyes with suboptimal response to anti-VEGF monotherapy. We have further demonstrated the feasibility of planning the PDT treatment spot using only OCT. The complete coverage of PL in this study is encouraging, although randomized studies are desirable to formally compare the effectiveness of OCT versus ICGA-guided PDT. These novel data will be useful to help further refine treatment outcomes for all clinicians managing nAMD, particularly in settings where ICGA is not available or routinely used.

Footnotes and Disclosures

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Abbreviations and Acronyms:
APOIS = Asia Pacific Ocular Imaging Society; **AUC** = area under the curve; **BNN** = branching neovascular network; **CFP** = color fundus photography; **CI** = confidence interval; **GLD** = greatest linear dimension;

ICC = intergrader correlation coefficient; **ICGA** = indocyanine green angiography; **IRF** = intraretinal fluid; **nAMD** = neovascular age-related macular degeneration; **NIR** = near-infrared; **OCTA** = OCT angiography; **PCV** = polypoidal choroidal vasculopathy; **PDT** = photodynamic therapy; **PED** = pigment epithelial detachment; **PL** = polypoidal lesion; **RPE** = retinal pigment epithelium; **SD** = standard deviation; **SRF** = subretinal fluid; **VEGF** = vascular endothelial growth factor.

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