Evidence and Consensus-Based Imaging Guidelines in Multifocal Choroiditis With Panuveitis and Punctate Inner Choroiditis—Multimodal Imaging in Uveitis (MUV) Taskforce Report 5

SAPNA GANGAPUTRA, ANIRUDDHA AGARWAL, JEANNETTE OSSEWAARDE-VAN NOREL, EDMUND TSUI, JENNIFER E. THORNE, ALEJANDRA DE-LA-TORRE, MICHAEL ALTAWEEL, JYOTIRMAY BISWAS, SRINIVAS SADDA, ALESSANDRO INVERNIZZI, RUPESH AGRAWAL, JESSICA G. SHANTHA, MASSIMO ACCORINTI, AMANI FAWZI, DOUGLAS A. JABS, DAVID SARRAF, AND VISHALI GUPTA, ON BEHALF OF THE MULTIMODAL IMAGING IN UVEITIS (MUV) TASK FORCE*

• PURPOSE: To develop imaging and consensus-based guidelines on the application of multimodal imaging in noninfectious multifocal choroiditis and panuveitis (MFCPU) and punctate inner choroiditis (PIC).

• DESIGN: Consensus agreement guided by the review of literature and an expert committee using nominal group technique (NGT).

• METHODS: An expert committee applied a timed structured nominal group technique (NGT) to achieve consensus-based recommendations on specific disease characteristics, biomarkers of activity, and complications for MFCPU and PIC. Representative cases with noninfectious active and inactive MFCPU and PIC with color fundus photographs (CFP), optical coherence tomography (OCT), fundus fluorescein angiography (FFA), OCT angiography (OCTA), indocyanine angiography (ICGA), and fundus autofluorescence images (FAF) were reviewed. These recommendations were voted upon by the entire task force.

• RESULTS: The experts agreed that lesions of MFCPU and PIC can be well characterized using CFP. OCT is the preferred modality for detecting active lesions. Both FAF and OCT are effective for monitoring disease recurrence. Late-phase ICGA is most valuable in recurrent disease when the lesions are not visible on FAF and CFP. While OCTA and ICGA can successfully identify lesions and complications such as choroidal neovascularization, no imaging biomarkers were found to reliably distinguish between active and inactive lesions on these two modalities.

• CONCLUSIONS: Incorporating imaging findings, particularly OCT, into the Standardization of Uveitis Nomenclature (SUN) classification criteria for MFCPU and PIC enables more precise assessment of disease activity. These consensus-based guidelines provide a framework for selecting optimal imaging modalities for diagnosis, monitoring and identification of complications of MFCPU and PIC. (Am J Ophthalmol 2025;276: 272–285. © 2025 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/))

Accepted for publication April 19, 2025.

Vanderbilt Eye Institute (S.G.), Vanderbilt University Medical Center, Nashville, Tennessee, USA; Eye Institute (A.A.), Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates; Cleveland Clinic Lerner College of Medicine (A.A.), Cleveland, Ohio, USA; University Medical Center Utrecht (J.O.N.), Utrecht, the Netherlands; Stein Eye Institute (E.T., D.S.), David Geffen School of Medicine at UCLA, Los Angeles, California, USA; Department of Ophthalmology (J.E.T., D.A.J.), Wilmer Eye Institute, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; The Department of Epidemiology (J.E.T.), The Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; Neuroscience Research Group (NEUROS) (A.D.T.), Neurovitae Center for Neuroscience, Institute of Translational Medicine (IMT), School of Medicine and Health Sciences, Universidad del Rosario, Bogotá, Colombia; Department of Ophthalmology and Visual Sciences (M.A.), University of Wisconsin, Madison, Wisconsin, USA; McPherson Eye Research Institute (M.A.), University of Wisconsin, Madison, Wisconsin, USA; Uveitis and Ocular Pathology Department (J.B.), Sankara Nethralaya, Chennai, India; Doheny Eye Institute (S.S.), University of California, Los Angeles, Pasadena, California, USA; Department of Biomedical and Clinical Science (A.I.), Eye Clinic, Luigi Sacco Hospital, University of Milan, Milan, Italy; Department of Ophthalmology (A.I.), Save Sight Institute, University of Sydney, Sydney, Australia; National Healthcare Group Eye institute (R.A.), Tan Tock Seng Hospital, Singapore; LKC School of Medicine (R.A.), Nanyang Technological University, Singapore; Duke NUS Medical School (R.A.), Singapore, Singapore; Ocular Infections and AntiMicrobials (R.A.), Singapore Eye Research Institute, Singapore, Singapore; Department of Ophthalmology (J.G.S.), Francis I. Proctor Foundation, University of California, San Francisco, USA; IRCSS Fondazione G. B. Bietti (M.A.), Rome, Italy; Northwestern University Feinberg School of Medicine (A.F.), Chicago, USA; Department of Epidemiology (D.A.J.), Center for Clinical Trials and Evidence Synthesis, The Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; Advanced Eye Centre (V.G.), Postgraduate Institute of Medical Education and Research, Chandigarh, India

Inquiries to Sapna Gangaputra, Vanderbilt Eye Institute, Nashville, Tennessee, USA.; e-mail: sapna.gangaputra@vumc.org

Inquiries to Vishali Gupta, Advanced Eye Center, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, 160012, India.; e-mail: vishalisara@gmail.com

* Full list of task force members in Appendix.

0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2025.04.018

Multifocal choroiditis (MFC) is a nonspecific descriptive term used to encompass a variety of posterior uveitic conditions, that exhibit multifocal choroidal inflammation, with or without inflammation in other anatomic layers of the eye.[1] Diseases included in this group may be infectious such as syphilis[2] or tuberculosis,[3] postinfectious such as presumed ocular histoplasmosis,[4] inflammatory such as sarcoidosis,[5] and isolated autoimmune or autoinflammatory entities such as punctate inner choroiditis (PIC) and multifocal choroiditis with panuveitis (MFCPU).[6] Malignancies such as primary intraocular lymphoma[7] and metastases[8] can also masquerade as a MFC, complicating diagnosis and management.

The Standardization of Uveitis Nomenclature (SUN) defined MFCPU according to the following criteria: (1) absence of an associated infectious or systemic disease and (2) presence of multiple lesions larger than 125 μm in diameter predominantly located outside the vascular arcades. Lesions may manifest as inactive punched-out atrophic chorioretinal scars or may be associated with signs of intraocular inflammation, such as anterior chamber cells or vitreous inflammation.[9]

Punctate inner choroiditis is a more specific term that is used to describe a noninfectious, nonsystemic, immune-mediated disease that targets the posterior pole. Whether PIC is on the same spectrum of MFCPU is disputed, but there is consensus that PIC lesions represent a more localized clinical phenotype compared to MFCPU.[10,11] As per the SUN classification criteria, PIC is defined according to the following criteria: (1) absence of appropriate infectious (eg, toxoplasmosis retinitis or syphilis) or associated systemic diseases (eg, sarcoidosis) and (2) multiple punctate lesions smaller than 250 μm in diameter, predominantly located in the posterior pole, with very little to no intraocular inflammation.[11]

The SUN classification criteria for both MFCPU and PIC were developed following image review to characterize phenotypes but did not explicitly identify or define multimodal imaging biomarkers of activity specific to these conditions. This represents a gap in current clinical guidelines and emphasizes the need for more defined imaging characteristics to aid in the diagnosis, management, and monitoring of these uveitic conditions.

The Multimodal Imaging in *Uv*eitis (MUV) task force is an international collaboration aimed at addressing this gap by developing imaging-based criteria to enhance the SUN classification framework. This effort is focused on five of the most common multifocal choroidopathies. This manuscript specifically focuses on imaging features of MFCPU and PIC.

METHODS

The Multimodal imaging in Uveitis (MUV) project is a research initiative of the International Uveitis Study Group (IUSG), an international group of uveitis specialists, to establish guidelines for the use of multimodal imaging in noninfectious posterior uveitis and to identify features characteristic of active and inactive disease for each entity. The study used previously collected, retrospectively reviewed, de-identified images and, as such, was considered "not human" research. The study was conducted under the tenets of the Declaration of Helsinki and received IRB exemption from the Vanderbilt University Medical Center (IRB # 240146).

• **SUBCOMMITTEE SELECTION:** The MUV task force is comprised of uveitis specialists, retina specialists and ocular imaging experts with clinical and research experience in posterior uveitis. The MFCPU/PIC subcommittee, formed using purposeful sampling strategy,[12] included geographically diverse specialists from India, Colombia, the Netherlands, and the United States to provide a broad range of expertise and perspectives, recognizing the regional variations in presentation and progression of MFCPU and PIC over time. This team was tasked with reviewing existing literature, analyzing multimodal image sets, and developing imaging guidelines and activity criteria with illustrative examples. We followed the principles of Standards for Reporting Qualitative Research: A Synthesis of Recommendations (SRQR).[13] for reporting the results of our study.

• **CASE SELECTION:** All task force members contributed deidentified high quality image sets that met SUN criteria[9,11] with clinical signs consistent with MFCPU and PIC, and exclusion of infectious causes. To be eligible for review, the image sets were required to include color fundus photographs (CFP), which were used as a surrogate for the clinical examination, optical coherence tomography (OCT), fundus fluorescein angiography (FFA), fundus autofluorescence (FAF), and indocyanine green angiography (ICGA) (if available) and OCT angiography (OCTA). No clinical information, patient identifiers or other patient demographics were shared to maintain confidentiality.

• **NOMINAL GROUP TECHNIQUE (NGT):** We employed a structured NGT approach, a formal consensus or brainstorming technique, in order to achieve agreement by the expert subcommittee.[14-16] The NGT discussions were conducted virtually and led by one neutral facilitator (SG). The discussions ensured that time-limited, uninterrupted comments were provided by each committee member followed by anonymous voting. The propositions were either accepted (>75% super majority vote), defeated, or revised and revisited.[14-16] The MFCPU/PIC subcommittee held multiple NGT discussions across time zones to ensure thorough review of all available image sets after excluding poor quality images. The subcommittee then determined the imaging biomarkers associated with active inflammation for each of the imaging modalities and devel-

oped consensus-based imaging guidelines in the diagnosis and management of MFCPU and PIC.

• **ESTABLISHMENT OF CONSENSUS:** The subcommittee guidelines were shared with the entire MUV task force listed in Supplement A. The task force members used anonymous voting on an online survey platform and assessed the recommendations. Any requested modifications were collaboratively discussed among the members. The consensus was developed by the taskforce as follows:

Unanimous consensus: 100% participants agree
Strong consensus: > 95% vote
Consensus: 75% to 95% vote
Majority agreement: > 50% to 75% vote
No consensus: < 50% vote (lack of agreement or divided votes)

The percentage thresholds for consensus derived by voting were reported as per the guidelines of various international associations. These included the Guidelines International Network (GIN),[17] European League Against Rheumatism (EULAR),[18] and Association of Scientific Medical Associations of Germany (AWMF).[19] When there was no consensus achieved (<50% vote), the guidelines were rejected.

Study data were collected and managed using REDCap electronic data capture tools hosted at Vanderbilt University Medical Center.[20,21] REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources.

RESULTS

• **IMAGING FEATURES OF MULTIFOCAL CHOROIDITIS AND PUNCTATE INNER CHOROIDOPATHY:**

Color fundus photography

The subcommittee agreed with the SUN.[9,11] classification criteria that PIC lesions were smaller and located in the posterior pole. In contrast, MFCPU lesions were larger and could be identified in the posterior pole, nasal peripapillary retina, and in the periphery (Figures 1 and 2). MFC and PIC are characterized by multifocal lesions which appear creamy and ill-defined when active. When inactive, the lesions are atrophic or punched out and clearly defined, often with a pigmented border. Peripapillary atrophy[22] may be present but can also be detected in myopic eyes. Since myopia is associated with both MFC and PIC,[23] as well as POHS,[24] the subcommittee considered peripapillary atrophy to be a nonspecific finding.

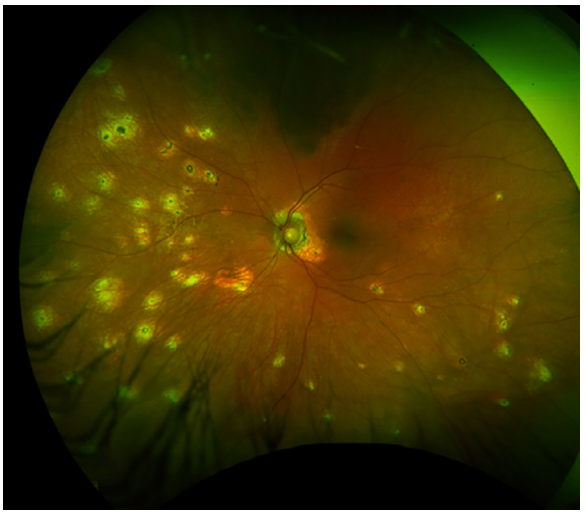

FIGURE 1. Ultrawide color photograph showing multifocal choroidal lesions scattered in the nasal and peripheral retina, representative of multifocal choroiditis.

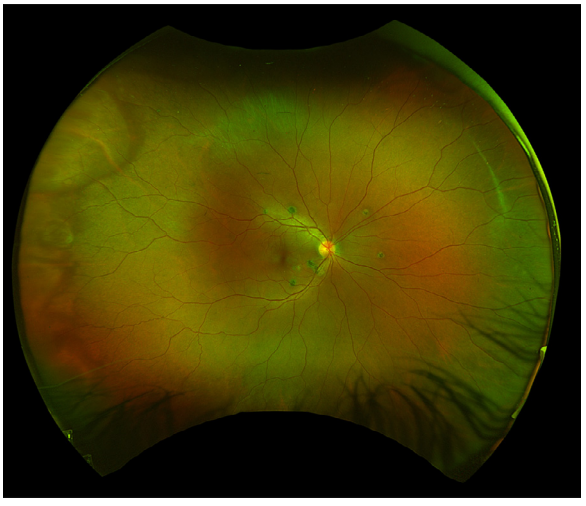

FIGURE 2. Ultrawide color photograph showing few small multifocal choroidal lesions, in the posterior pole, representative of punctate inner choroiditis.

Optical coherence tomography

The subcommittee unanimously agreed that OCT is the most reliable indicator of active inflammation in lesions associated with MFCPU and PIC. Active lesions demonstrated several characteristic features on OCT that the committee unanimously agreed represent classic indicators of disease activity. Fluffy subretinal hyper-reflective material (SHRM) (Figure 3) overlying the retinal pigment epithelium (RPE) is a sign of active inflammation, with ellipsoid zone (EZ) disruption extending beyond the borders of the lesion (Figure 4). There may be associated inflammatory pigment epithelial detachment (PED) or a discon-

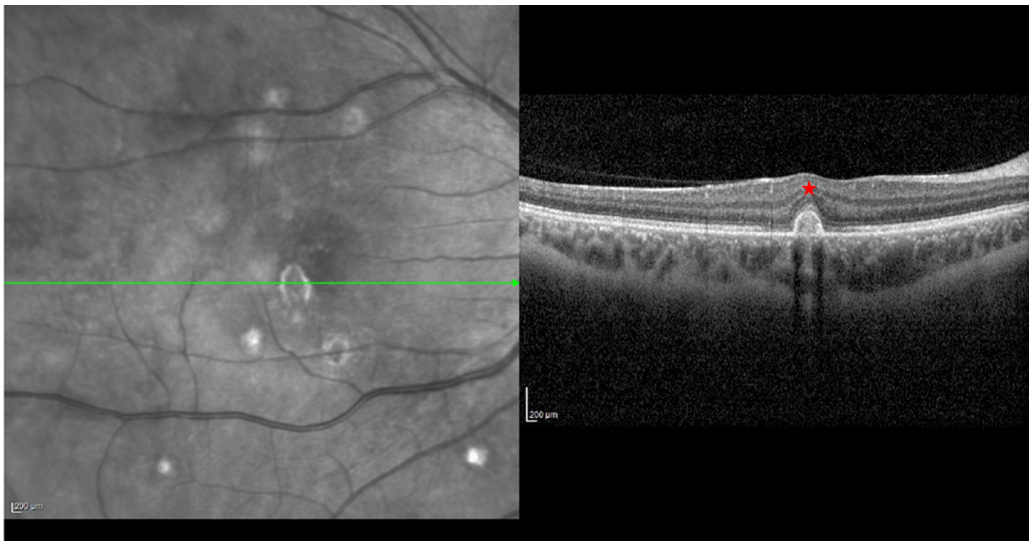

FIGURE 3. OCT B scan showing an active lesion with homogenous subretinal hyper-reflective material (SHRM) and splitting of the retinal pigment epithelium (red star). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

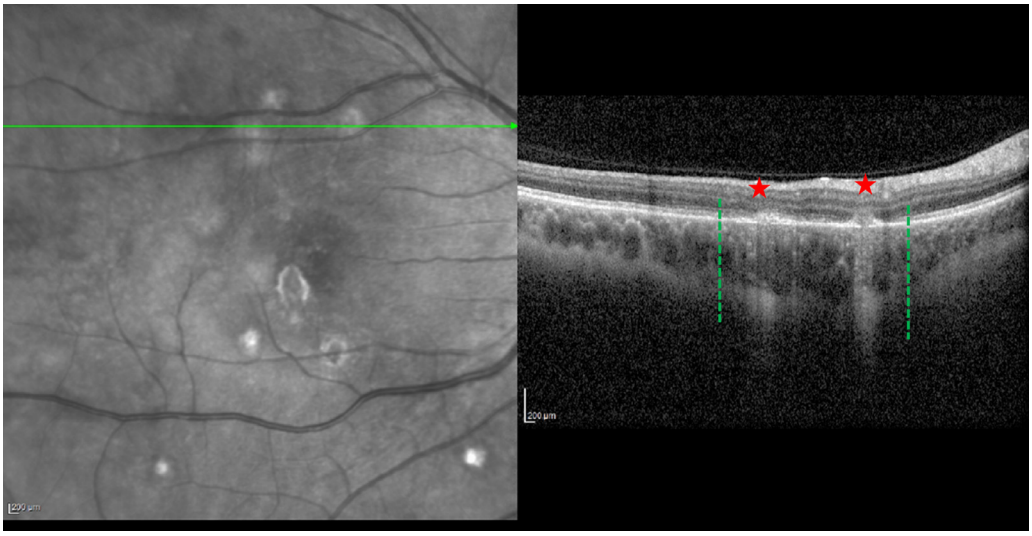

FIGURE 4. OCT B scan showing 2 active lesions with fluffy subretinal hyper-reflective material (SHRM) overlying the retinal pigment epithelium (red star). Note the disrupted ellipsoid zone (between the green dotted lines). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

tinuous RPE band with elevated edges. Except for larger size of the MFCPU lesions, no differences are evident in the OCT appearance of MFCPU and PIC lesions. Figures 5 and 6 present serial follow-up of cases of MFCPU with SHRM indicating active disease that subsequently became inactive following treatment, with possible resolution of SHRM and EZ disruption. Enhanced-depth imaging OCT (EDI-OCT) shows focal thickening of the choroid underlying active lesions (Figure 7). Inactive lesions are characterized by resolution of SHRM and reduction of the thickness of the inner choroid with clearer visualization of choroidal vessel landmarks. Focal disruption of EZ and RPE may remain (Figure 8). Focal choroidal excavation may represent a longstanding complication of acute disease, best visualized on EDI-OCT.

The subcommittee did not reach consensus on the OCT appearance of chrysanthemum lesions[25] or the pitchfork sign of MFCPU-associated choroidal neovascularization (CNV).[26]

Fundus autofluorescence

On FAF, active lesions appear as new crops of uniformly hyper-autofluorescent (hyper-FAF) spots (Figure 9). When the disease is reactivated, the new lesions are

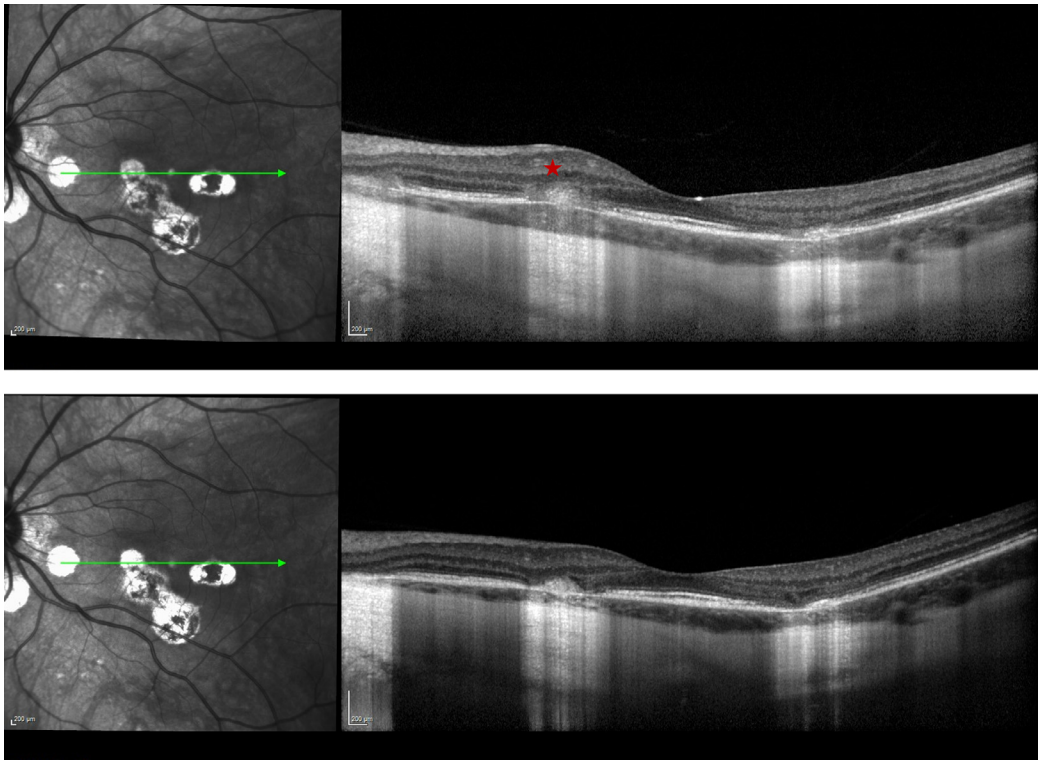

FIGURE 5. OCT B scan showing an active lesion with fluffy subretinal hyper-reflective material (SHRM) overlying the retinal pigment epithelium (red star) in the top panel and resolution of the same area in the bottom panel. Both scans are from the same eye and scanned through the same area. Note the choroidal thickening in the active phase. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

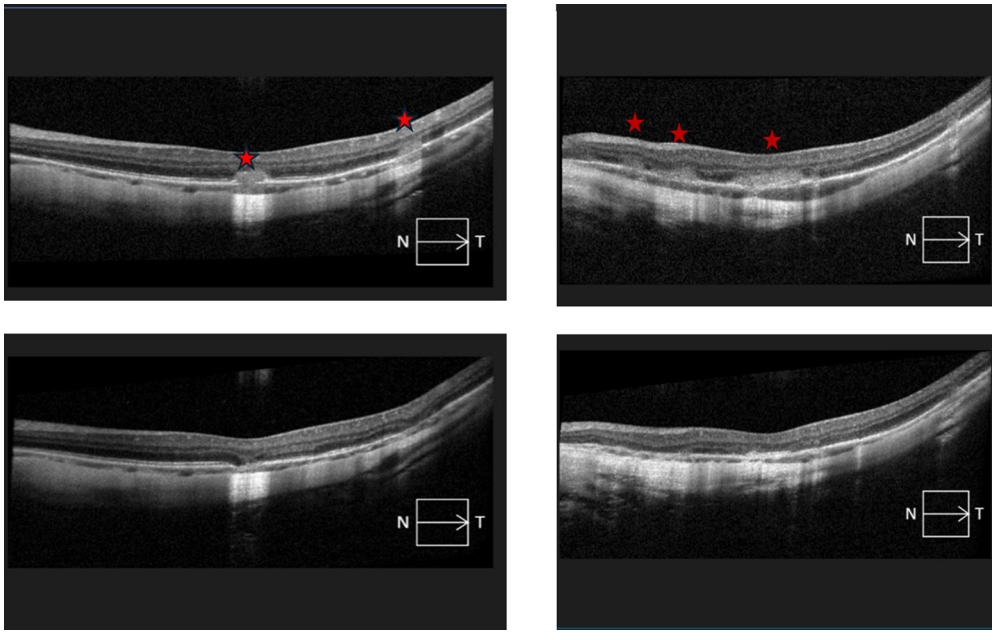

FIGURE 6. Examples of corresponding OCT B scans showing active subretinal hyperreflective material (red star) in top panel that have resolved in subsequent scans through the same area, as seen in bottom panel. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

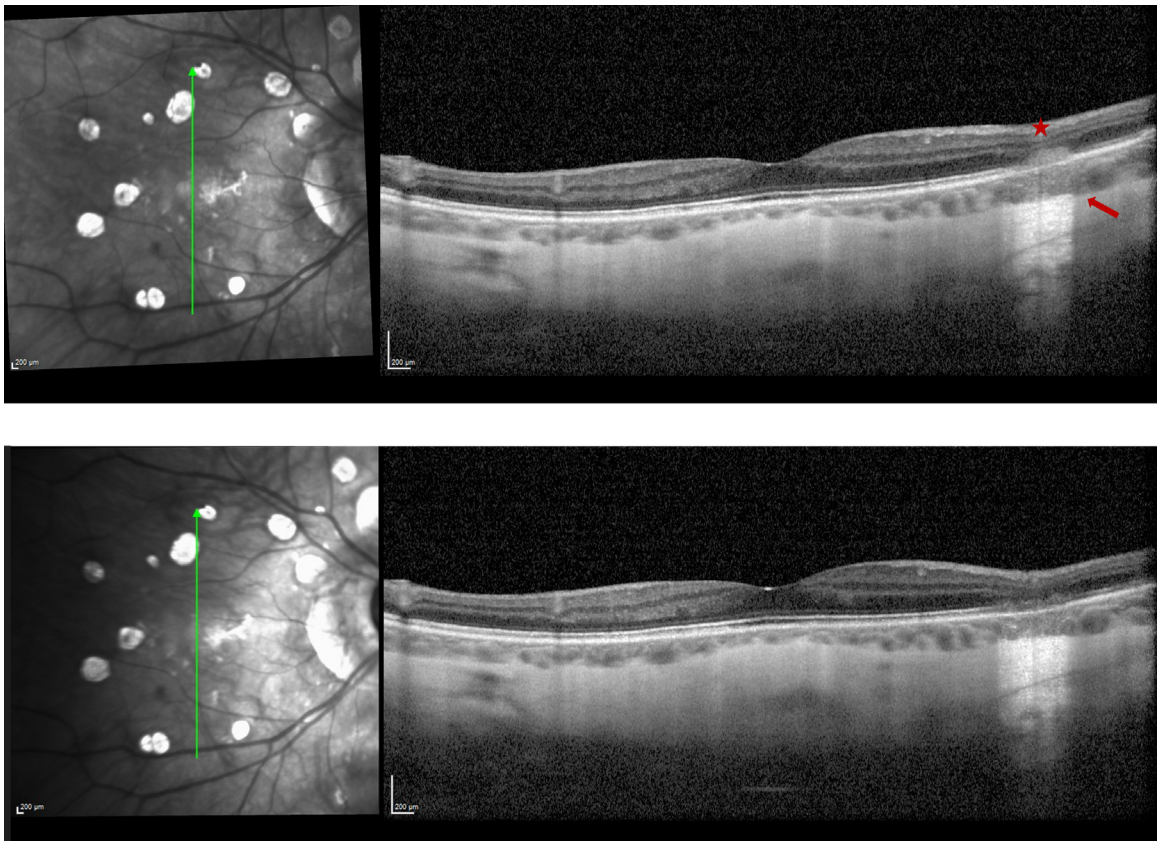

FIGURE 7. OCT B scan with choroidal thickening (red arrow) seen under the active subretinal hyperreflective material (red star) in active state (top panel) as compared to inactive in bottom panel. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

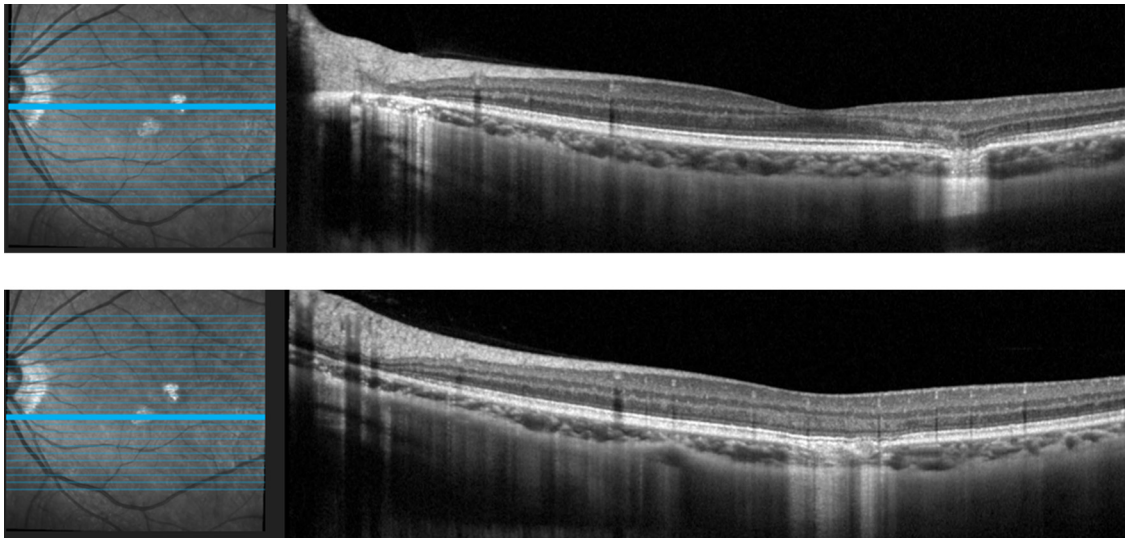

FIGURE 8. OCT B scans showing two unique inactive lesions with ellipsoid zone and RPE disruption with hyper-transmission.

also hyper-FAF. Inactive lesions typically evolve to hypo-autofluorescent (hypo-FAF) lesions corresponding to atrophy; however, some inactive lesions can present with a hyper-FAF cuff (Figure 10). The hyper-FAF cuff may be associated with subretinal fluid, scarring, or CNV. Such lesions can retain the hyper-FAF cuff and no longer indicate active disease. The areas of SHRM may resolve without RPE disruption, and hence may not necessarily be associated with hypo-FAF. The subcommittee agreed that ultra-wide field FAF is useful in determining lesion activity.

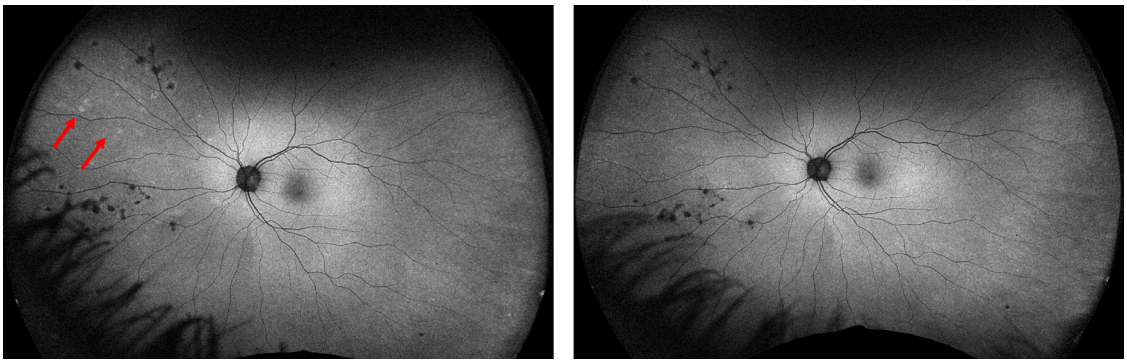

FIGURE 9. Ultrawide images showing a crop of active hyper autofluorescent spots in nasal periphery (red arrows) of the left panel. The same eye was imaged a few months earlier and only had the dark hypo-autofluorescent areas as seen in right panel. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

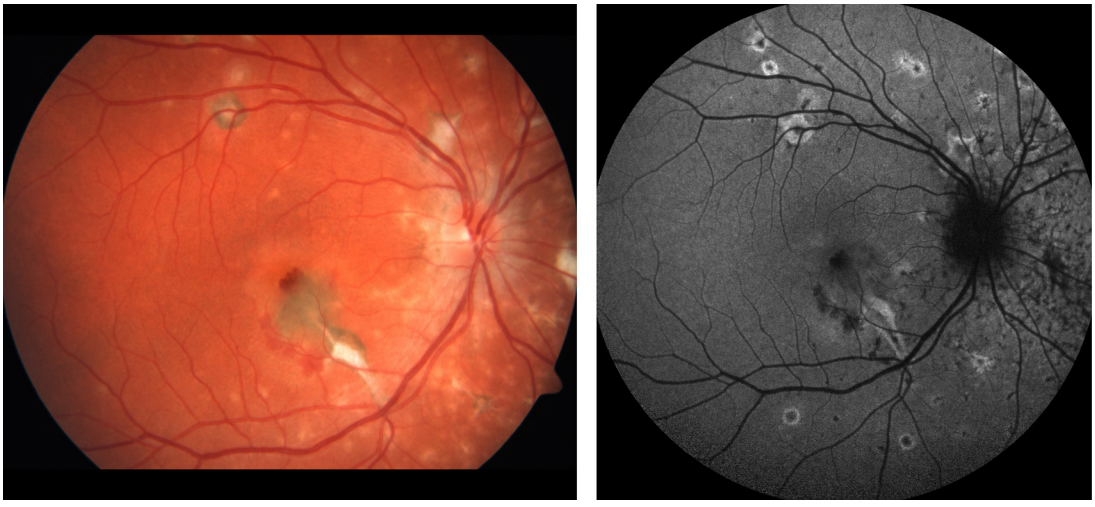

FIGURE 10. Left panel is a color photograph showing chorioretinal lesions nasally and along the arcades and CNV with hemorrhage at the fovea. On the right panel are seen several hypo-autofluorescent lesions with a cuff of hyper-autofluorescence. The macula has a fibrotic scar and choroidal neovascularization (CNV) with hemorrhage.

Fundus fluorescein angiography and optical coherence tomography angiography

The subcommittee determined that FFA did not offer any additional utility in the diagnosis or monitoring for reactivation of MFCPU and PIC lesions. Figure 11 shows leakage from the lesions when active. However, FFA is useful for detecting CNV which can display a hyperfluorescent lacy network with late leakage. Neovascular networks can also be captured with OCTA (Figure 12). The subcommittee did not arrive at any consensus criteria for the activity of CNV on OCTA.

Indocyanine green angiography

Late-phase ICGA were determined to be useful in detecting hypofluorescent choroidal lesions that are not easily visualized on clinical examination, FAF or CFP (Figure 13). ICGA is unable to reliably differentiate between active and inactive lesions, although blurry borders and larger area than FAF may suggest active lesions. The most reliable indicator of activity is the appearance of new lesions on late ICGA.

Consensus statements for the individual imaging modalities typically used to diagnose MFCPU and PIC are provided in Table 1 and the consensus statements for monitoring of complications is listed in Table 2.

• **CONSENSUS-BASED RECOMMENDATIONS:** The details of the recommendations drafted by the MFCPU/PIC subcommittee and voted upon by the entire MUV taskforce is presented in Table 3, along with the strength of the consensus.

DISCUSSION

The MUV project was launched by IUSG to build upon the existing classification criteria established by the SUN Working Group.[9,11] with the integration of modern mul-

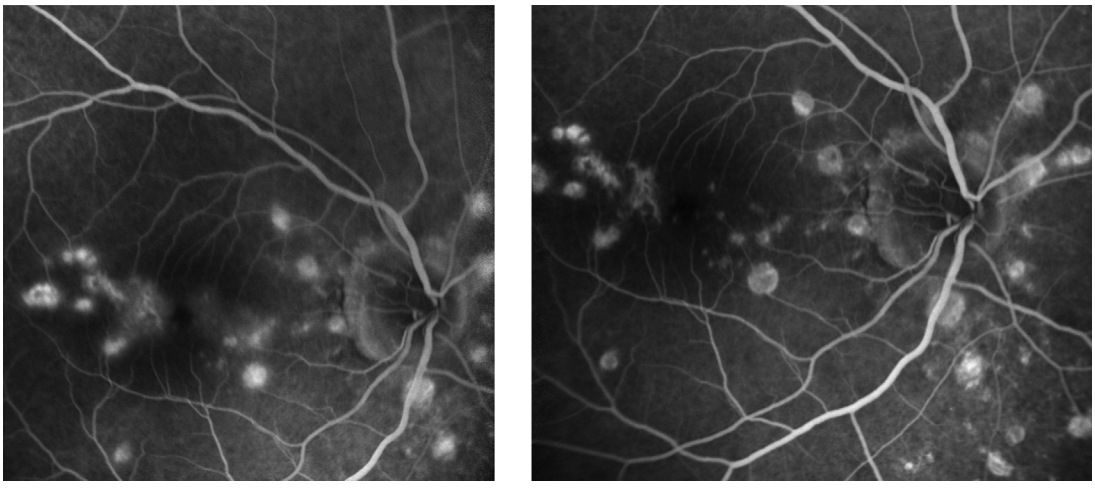

FIGURE 11. Fundus fluorescein angiography showing late leakage (26 minutes) from lesions in active phase in left panel, and 3 months later no leakage in late phase of the same eye (right panel).

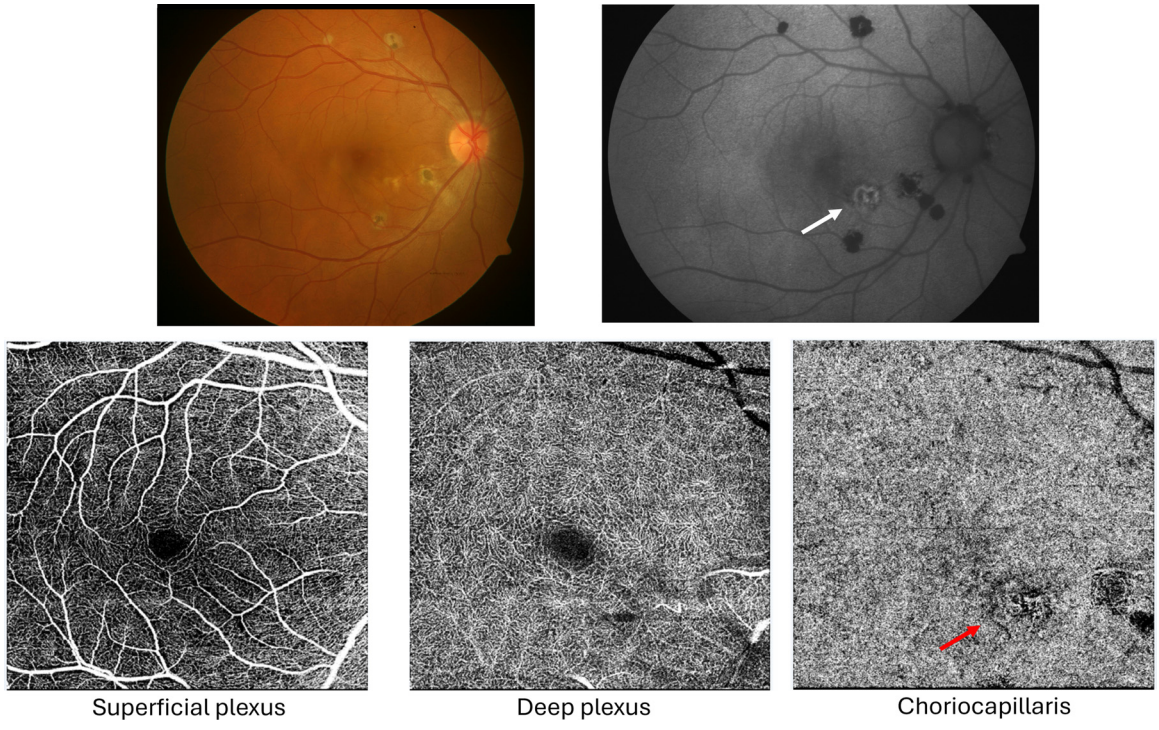

FIGURE 12. Color photograph and fundus autofluorescence showing inactive chorioretinal scars with pigmentation in the top panels. The lesions along the arcades are seen as uniformly hypo-autofluorescent but the lesion closest to the macula has a hyper-autofluorescent cuff secondary to choroidal neovascularization (white arrow).
Bottom panels show OCT angiography with a choroidal neovascularization net (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

timodal imaging technologies. The MUV project sought to establish guidelines for the use of imaging in diagnosing and managing these diseases and criteria/biomarkers for identifying active and inactive disease. Multimodal imaging is now widely integrated into clinical practice and has enhanced our comprehension of the pathoanatomy of the retina and allows for better characterization of diseases that affect the outer retina and choroid.[25,26] Our assessment of a well-characterized dataset of eyes with MFCPU and PIC, supported by extensive multimodal imaging, achieved consensus on defining active and inactive lesions across each imaging modality.

The guidelines developed by the MFCPU/PIC subcommittee underscore the significance of a standardized ap-

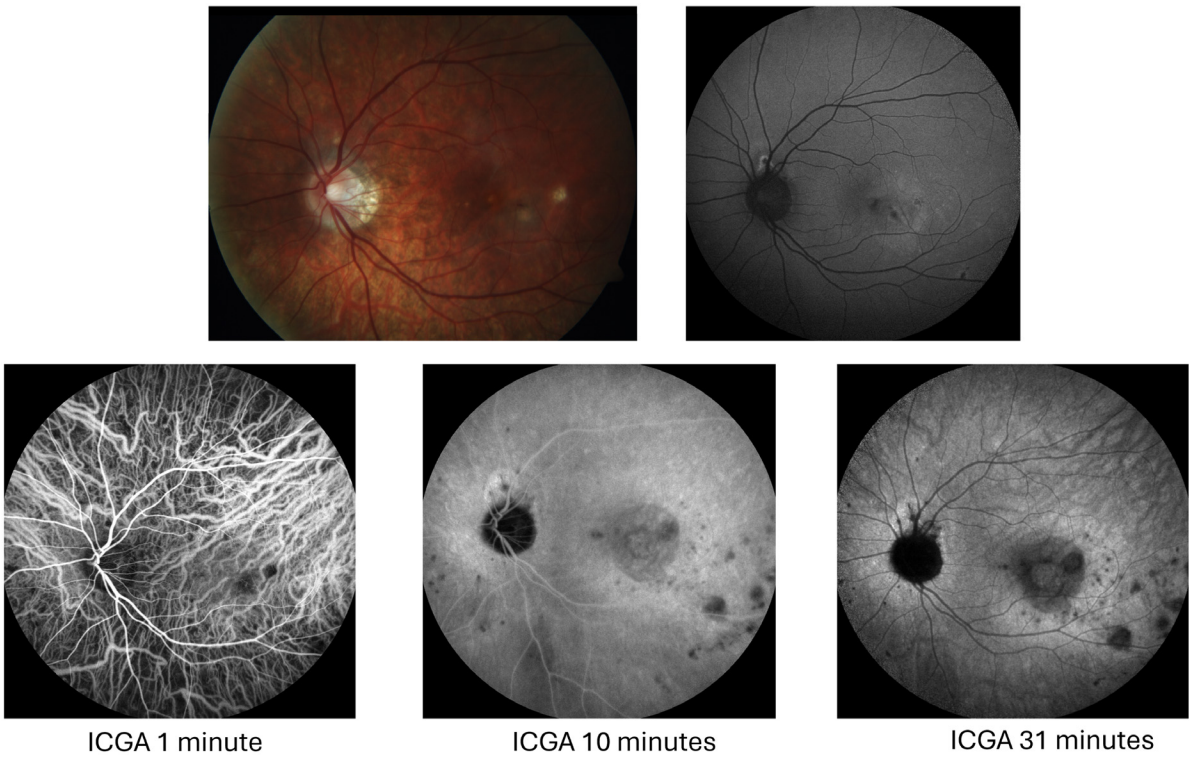

FIGURE 13. Top panels demonstrate color photographs and fundus autofluorescence images with chorioretinal scars. Bottom images show a larger number of choroidal lesions especially on the late indocyanine angiography image.

TABLE 1. Imaging-Based Consensus Criteria for Multifocal Choroiditis With Panuveitis (MFCPU) and Punctate Inner Choroiditis (PIC)

Imaging Modality	Consensus Criteria
Color Fundus Photography	Multiple discrete choroidal or chorioretinal lesions that are cream colored (active) or atrophic (inactive).
	MFCPU lesions are larger (>125 microns diameter) than PIC lesions (<250 microns diameter)
	Located in posterior pole (PIC) and midperiphery (MFCPU)
	Variable pigmentation
Optical Coherence Tomography	Active lesions of MFCPU and PIC present as fluffy subretinal homogenous material (SHRM) overlying the retinal pigment epithelium (RPE) or as inflammatory PED.
	Ellipsoid zone (EZ) disruption extends beyond the lesion edges.
	Focal thickening of the choroid is visible under the lesions
	Lesions disappear when inactive, with residual focal disruption of EZ and RPE.
	Choroidal excavation maybe seen.
Fundus Autofluorescence	Active lesions are hyper-autofluorescent
	Inactive lesions are hypo-autofluorescent, sometimes with a hyper-autofluorescent cuff.
Fluorescein Angiography	Disc hyperfluorescence may be seen.
	Choroidal neovascularization can be detected.
Indocyanine Green Angiography	Lesions are hypofluorescent and more extensive than clinical examination or fundus autofluorescence.
Optical Coherence Tomography Angiography	Confluent flow deficit areas in the choriocapillaris of active lesions.
	Detection of choroidal/subretinal neovascularization as an abnormal vascular network with flow signal.

proach to multimodal imaging in diagnosing and managing MFCPU and PIC. The subcommittee's consensus, ratified by the entire MUV taskforce, emphasizes the essential role of OCT as the primary imaging modality for assessing disease activity due to its reliability in visualizing inflammatory markers such as SHRM, inflammatory PED, and ellipsoid zone disruptions. OCTA holds particular value for the noninvasive detection of CNV, necessitating confirmation through OCT to guide treatment decisions. Furthermore, the taskforce highlighted the importance of ultra-wide field FAF and late-phase ICGA for monitoring lesion reactivation, particularly in the peripheral retina where changes

TABLE 2. Imaging Modalities for Monitoring the Activity and Detecting Complications in Multifocal Choroiditis and Panuveitis and Punctate Inner Choroiditis

Modality	Criteria/Utility
Optical Coherence Tomography	Shows the most characteristic signs of active inflammation. Relapse can present as new lesions or reactivation of previously inactive lesions. Choroidal neovascularization can be detected especially if associated with subretinal or intraretinal fluid.
Fundus Autofluorescence	Hypo-autofluorescence of the lesion uniformly or centrally with a hyper-autofluorescent cuff indicate inactivity. Ultrawide autofluorescence images help monitoring inactive lesions.
Indocyanine Green Angiography	Lesions are hypofluorescent and more extensive than clinical examination or fundus autofluorescence. Can identify new lesions which indicate overall disease activity. Best used for atypical cases when fundus autofluorescence is not sufficient.
Optical Coherence Tomography Angiography	Detection of choroidal neovascularization.

TABLE 3. Consensus-Based Guidelines for Imaging in Multifocal Choroiditis and Panuveitis and Punctate Inner Choroiditis[a]

No.	Guidelines	Strength of Consensus
1	CFP to document the location and size of choroidal lesions, which help distinguish MFCPU lesions from PIC lesions ***(consensus)***	90.5%
2	OCT through the lesions to assess the lesion activity in new and recurrent cases ***(unanimous consensus)***	100%
3	FAF (including ultra-wide) imaging for the determination of peripheral lesions ***(strong consensus)***	95.2%
4.	FFA to assess the activity of lesions of MFCPU/PIC ***(majority agreement)***	64.3%
5.	ICGA to assess the extent of the lesions at baseline ***(consensus)***	83.3%
6.	OCT serially through the lesions to determine the healing of lesions, disruption of outer retinal and inner choroidal layers ***(unanimous consensus)***	100%
7.	Ultra-wide field FAF or late-phase ICGA to detect activity of peripherally located lesions ***(consensus)***	88.1%
8.	OCT in detecting complications such as CNV with subretinal fluid ***(unanimous consensus)***	100%
9.	OCTA or FFA to determine the presence of underlying CNV in inflammatory lesions of MFCPU/PIC ***(strong consensus)***	95.2%

[a]The seven members of the expert subcommittee did not cast their votes.

CFP = color fundus photography; CNV = choroidal neovascularization; FA = fluorescein angiography; FAF = fundus autofluorescence; ICGA = indocyanine green angiography; MFC = multifocal choroiditis; OCT = optical coherence tomography; OCTA = optical coherence tomography angiography; PIC = punctate inner choroidopathy; RPE = retinal pigment epithelium.

Unanimous consensus: 100% participants agree.

Strong consensus: > 95% vote.

Consensus: 75% to 95% vote.

Majority agreement: > 50% to 75% vote.

No consensus: < 50% vote (lack of agreement or divided votes).

may not be evident through standard imaging or clinical examination. These consensus-based guidelines, detailed in Table 3, provide an evidence-backed framework that aids clinicians in making informed decisions and aligning diagnostic practices with standardized criteria. The incorporation of multimodal imaging findings into diagnostic protocols enhances early detection, precise assessment, and effective long-term management.

Our analysis of the study cohort aligned well with the findings from single center case series and expert opinion reports, particularly related to the description of active MFCPU and PIC lesions on OCT.[21,27-32] We observed that inactive lesions may have persistent loss of EZ but the linear extent may be smaller than the EZ loss identified when the lesions are active, presumably implying reconstitution of at least some portion of the EZ in the penumbra surrounding an active lesion.

A key observation from our study was the identification of a hyper-FAF cuff that surrounds some lesions and can persist long term without fading or becoming hypo-FAF. These have been reported more frequently in the PIC literature[33,34] than in the MFCPU literature.[35-38] The hyper-FAF cuff's persistence, without transitioning to iso- or hypo-FAF, may indicate underlying pathophysiological changes related to subretinal fluid or CNV[36,39] or more likely related to persistent EZ disruption[35,40] observed on OCT. It may also be from increased amount of hyper AF material in the adjacent RPE that persists, once formed during active

inflammation of the PIC lesions. Airaldi et al[38] reviewed the area of hypo-FAF annually over 4 years in 30 eyes with atrophic MFCPU. They reported that lesions that had relapses had 20% higher growth rate annually (mean difference in area between lesions that reactivated and those that did not reactivate was 0.051, SD 0.035, $P < .001$).[36] The decision to initiate or continue treatment based on hyper-FAF cuff should consider the possibility that certain lesions may remain hyper-FAF without progression to hypo-FAF, even in the absence of active inflammation.

In our study, FFA and OCTA were found to provide limited additional information on the inflammatory activity of specific lesions beyond what could be observed through color fundus photography, clinical examination, FAF, or structural OCT. We also evaluated the potential advantages of ICGA, given its superior ability to reveal choroidal lesions. However, due to the difficulty in differentiating between active and inactive lesions,[22-24,35] there was limited benefit to ICGA. However, late-phase ICGA demonstrated lesions that were not captured with color fundus photographs or autofluorescence,[28,35] thereby making it a useful tool for monitoring of eyes where reactivation is suspected but not visible on CFP or FAF.

Our study aims to refine the consensus-based imaging criteria to create standardized definitions for diagnosing and monitoring MFCPU and PIC. These criteria are designed to ensure uniform application and interpretation of multimodal imaging across diverse clinical settings. The integration of these recommendations into routine practice could foster consistency in diagnosing, assessing disease activity, and determining the treatment response, ultimately enhancing patient outcomes.

The guidelines outlined herein provide a framework that supports evidence-based decision-making in clinical management. They emphasize the importance of OCT as the primary imaging modality for evaluating active inflammation, with complementary roles for FAF, OCTA, and ICGA in specific scenarios. By aligning imaging practices with standardized criteria, clinicians can achieve more accurate assessments, improve disease monitoring, and reduce variability in the interpretation of imaging findings, thus optimizing clinical practice and providing a better understanding of disease progression and enhancing the impact of therapeutic interventions.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Sapna Gangaputra: Writing – original draft, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Aniruddha Agarwal:** Writing – review & editing, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Jeannette Ossewaarde-van Norel:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Edmund Tsui:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Jennifer E. Thorne:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Alejandra de-la-Torre:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Michael Altaweel:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Jyotirmay Biswas:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Srinivas Sadda:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Alessandro Invernizzi:** Writing – review & editing, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Rupesh Agrawal:** Writing – review & editing, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Jessica G. Shantha:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Massimo Accorinti:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Amani Fawzi:** Writing – review & editing, Validation, Resources, Investigation, Data curation. **Douglas A. Jabs:** Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization. **David Sarraf:** Writing – review & editing, Validation, Supervision, Methodology, Formal analysis, Conceptualization. **Vishali Gupta:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Formal analysis, Data curation, Conceptualization.

Funding/Support: Unrestricted department support by Research to Prevent Blindness (Gangaputra).

Financial disclosures: *Tsui*: Cylite (grant support), Oculis (grant support), Kowa (grant support, consultant), Pfizer (grant support), EyePoint (grant support), Ani Pharmaceuticals (consultant), Kodiak Sciences (consultant). *Thorne*: Canfield (Consultant); Clearside (Consultant); Gilead (Consultant); Guidepoint (Consultant); Merck (consultant); Roche (Consultant); Sanofi (consultant); Tarsier Pharma (Scientific Advisory Board; Equity Owner); UptoDate (Consultant). Dr Jennifer E Thorne is the guest editor for this special issue (JET). *Jabs*: AbbVie (Other Research Support). *Agrawal*: Supported by National Medical Research Council Grant for Software Assisted medical Devices (SamD) in uveitis. CSIRG grant. *Sadda*: Consultant to 4DMT, Abbvie/Allregan Inc., Alexion, Alnylam, Amgen, Apellis, Astellas/IvericBio, Bayer, Biogen MA Inc., Boehringer Ingelheim, Carl Zeiss Meditec, ONL Therapeutics, Catalyst Pharmaceuticals, CharacterBio, iCare/Centervue Inc., Ocular Therapeutics, Eyepoint, Heidelberg Engineering, Genentech/Roche, Janssen Pharmaceuticals Inc., Nanoscope, NotalVision, Novartis, Optos Inc., Oxurion/Thrombogenics, Oyster Point Pharma, Regeneron, Samsung Bioepis, Topcon Medical Systems. Recipient of honoraria from Carl Zeiss Meditec, Heidelberg Engineering, Nidek Incorporated, Novartis Pharma AG, Topcon Medical Systems Inc.; Roche. Recipient of research instruments from Carl Zeiss Meditec, Heidelberg Engineering, Optos Inc., Nidek, Topcon, iCare/Centervue, Intalight. Rest of the authors have no potential conflict of interest to disclose.

EXPERT CONTRIBUTIONS

All members of the task force provided input and full list is included in Appendix below

Alejandra de-la-Torre, Neuroscience Research Group (NEUROS), Neurovitae Center for Neuroscience, Institute of Translational Medicine (IMT), School of Medicine and Health Sciences, Universidad del Rosario, Bogotá, Colombia

Alejandro Fonollosa, Department of Ophthalmology, Biocruces Bizkaia Health Research Institute, Cruces University Hospital, University of the Basque Country, Barakaldo, Spain

Alessandro Invernizzi, Eye Clinic, Department of Biomedical and Clinical Science, Luigi Sacco Hospital, University of Milan, Milan, Italy; Department of Ophthalmology, Save Sight Institute, University of Sydney, Sydney, Australia

Amani Fawzi, Northwestern University Feinberg School of Medicine, Chicago, USA

Andrew Dick, University of Bristol, UK; Bristol Eye Hospital, UK; Institute of Ophthalmology, University College London, London, UK; National Institute for Health Research Biomedical Research Centre, Moorfields Eye Hospital, London, UK.

Aniruddha Agarwal, Eye Institute, Cleveland Clinic, Abu Dhabi, United Arab Emirates; Cleveland Clinic Lerner College of Medicine, Cleveland, Ohio, USA

Anita Agarwal, California Pacific Medical Center (CPMC), San Francisco, CA, USA; West Coast Retina, San Francisco, CA, USA

Antoine Brezin , Department of Ophthalmology, Ophtalmopôle, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, AP-HP, Université Paris Cité, 75014 Paris, France

Ariel Schlaen, Hospital Universitario Austral, Derqui-Pilar, Argentina

Bahram Bodaghi, Department of Ophthalmology, IHU FOReSIGHT, Pitié-Salpêtrière Universtiy Hospital, Paris, France

Claudia Fabiani, Ophthalmology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena and Azienda Ospedaliero-Universitaria Senese [European Reference Network (ERN) for Rare Immunodeficiency, Autoinflammatory, and Autoimmune Diseases (RITA) Center], Sienna, Italy

David Sarraf, Stein Eye Institute, University of California, Los Angeles, California, USA

Debra A. Goldstein, Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois USA

Dilraj Grewal, Department of Ophthalmology, Duke University School of Medicine, Durham, NC, USA

Douglas A. Jabs, Center for Clinical Trials and Evidence Synthesis, Department of Epidemiology, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA.

Wilmer Eye Institute, Department of Ophthalmology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA

Edmund Tsui, Stein Eye Institute, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Elisabetta Miserocchi , School of Medicine, Vita-Salute San Raffaele University, Milan, Italy; Department of Ophthalmology, IRCCS San Raffaele Scientific Institute, Milan, Italy

Ester Carreño, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

Francesco Pichi, Eye Institute, Cleveland Clinic, Abu Dhabi, United Arab Emirates

Ilknur Tugal-Tutkun, Department of Ophthalmology, Istanbul University, Istanbul, Turkey

Inês Leal, Centro Hospitalar Universitário Lisboa Norte, Centro Académico de Medicina de Lisboa (CAML), Lisbon, Portugal.

Janet L. Davis, Department of Ophthalmology, University of Miami Miller School of Medicine, Bascom Palmer Eye Institute, Miami, FL, USA.

Jeanette Ossewaarde-van Norel, University Medical Center Utrecht, Utrecht, the Netherlands

Jennifer E. Thorne, Wilmer Eye Institute, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.

Jessica G. Shantha, Francis I. Proctor Foundation, Department of Ophthalmology, University of California, San Francisco, USA

Jose S. Pulido, Wills Eye Hospital, Thomas Jefferson University Philadelphia, PA

Justine Smith, College of Medicine and Public Health, Flinders University, Adelaide, South Australia, Australia.

Jyotirmay Biswas, Uveitis and Ocular Pathology Department, Sankara Nethralaya, Chennai, India

K. Bailey Freund, Vitreous Retina Macula Consultants of New York, New York, USA; Department of Ophthalmology, NYU Grossman School of Medicine, New York, NY, USA

Kathryn Pepple, Department of Ophthalmology, University of Washington, Seattle, USA

Lee M. Jampol, Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois USA

Luca Cimino, Ocular Immunology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; Department of Surgery, Medicine, Dentistry and Morphological Sciences, with Interest in Transplants, Oncology and Regenerative Medicine, University of Modena and Reggio Emilia, Modena, Italy

Marc De Smet, Micro Invasive Ocular Surgery Clinic, Lausanne, Switzerland

Maria Vittoria Cicinelli, Department of Ophthalmology, IRCCS San Raffaele Scientific Institute, Milan, Italy

Marion R. Munk, Augenarzt Praxisgemeinschaft Gutblick, Pfäffikon, Switzerland

Massimo Accorinti, IRCSS Fondazione G. B. Bietti, Rome, Italy

Maura Di Nicola, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL, USA

Meghan Berkenstock, Wilmer Eye Institute, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.

Michael Altaweel, Department of Ophthalmology and Visual Sciences, University of Wisconsin, Madison, WI, USA; McPherson Eye Research Institute, University of Wisconsin, Madison, WI, USA

Phoebe Lin, Cleveland Clinic Foundation, Cole Eye Institute, Cleveland, USA

Quan Dong Nguyen, Spencer Center for Vision Research, Byers Eye Institute, Stanford University, Palo Alto, CA

Richard Spaide, Vitreous Retina Macula Consultants of New York, New York, USA

Rupesh Agrawal, National Healthcare Group Eye institute, Tan Tock Seng Hospital, Singapore; LKC School of Medicine, Nanyang Technological University, Singapore; Duke NUS Medical School, Singapore

Sapna S. Gangaputra, Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, TN, USA

Soon Phaik Chee, Department of Ocular Inflammation and Immunology, Singapore National Eye Centre, Singapore

Srinivas Sadda, Doheny Eye Institute, University of California, Los Angeles, Pasadena, California, USA

Sumit Sharma, Cleveland Clinic Foundation, Cole Eye Institute, Cleveland, USA

Timothy M. Janetos, Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois USA

Vishali Gupta, Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Zohar Habot-Wilner, Tel Aviv Medical Center, Tel Aviv University, Tel Aviv, Israel

REFERENCES

1. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol*. 2005;140(3):509–516.
2. Harvey J, Lee IJ, Lee CS, Hinkle D. Ocular syphilis on the rise: a 10-year analysis from 2010 to 2020. *Int Ophthalmol*. 2023;43(12):4419–4426.
3. Agrawal R, Gunasekeran DV, Agarwal A, et al. The Collaborative Ocular Tuberculosis Study (COTS)-1: a multinational description of the spectrum of choroidal involvement in 245 patients with tubercular uveitis. *Ocul Immunol Inflamm*. 2020;28(sup1):38–48.
4. Hatef E, Turkcuoglu P, Ibrahim M, et al. Importance of proper diagnosis for management: multifocal choroiditis mimicking ocular histoplasmosis syndrome. *J Ophthalmic Inflamm Infect*. 2011;1(2):55–63.
5. Mochizuki M, Smith JR, Takase H, Kaburaki T, Acharya NR, Rao NAInternational Workshop on Ocular Sarcoidosis Study Group. Revised criteria of International Workshop on Ocular Sarcoidosis (IWOS) for the diagnosis of ocular sarcoidosis. *Br J Ophthalmol*. 2019;103(10):1418–1422.
6. Essex RW, Wong J, Jampol LM, Dowler J, Bird AC. Idiopathic multifocal choroiditis: a comment on present and past nomenclature. *Retina*. 2013;33(1):1–4.
7. Grange LK, Kouchouk A, Dalal MD, et al. Neoplastic masquerade syndromes in patients with uveitis. *Am J Ophthalmol*. 2014;157(3):526–531.
8. Muradova E, Hine AM, Falcone M, Kels JMG, Weston G. Malignancies with a tendency to metastasize to the eyelid or ocular structures. *Clin Dermatol*. 2024;42(4):390–395.
9. Standardization of Uveitis Nomenclature (SUN) Working GroupClassification criteria for multifocal choroiditis with panuveitis. *Am J Ophthalmol*. 2021;228:152–158.
10. Park HS, Kang HG, Kim YJ, et al. Exploring the challenges of distinguishing punctate inner choroidopathy from multifocal choroiditis and panuveitis. *Retina*. 2024;44(11):1869–1875.
11. Standardization of Uveitis Nomenclature (SUN) Working GroupClassification criteria for punctate inner choroiditis. *Am J Ophthalmol*. 2021 Aug;228:275–280.
12. Palinkas LA, Horwitz SM, Green CA, Wisdom JP, Duan N, Hoagwood K. Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. *Adm Policy Ment Health*. 2015;42(5):533–544. doi:10.1007/s10488-013-0528-y.
13. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. *Acad Med*. 2014;89(9):1245–1251. doi:10.1097/ACM.0000000000000388.
14. Fink A, Kosecoff J, Chassin M, Brook RH. Consensus methods: characteristics and guidelines for use. *Am J Public Health*. 1984 Sep;74(9):979–983.
15. Allen J, Dyas J, Jones M. Building consensus in health care: a guide to using the nominal group technique. *Br J Community Nurs*. 2004 Mar;9(3):110–114. doi:10.12968/bjcn.2004.9.3.12432.
16. McMillan SS, King M, Tully MP. How to use the nominal group and Delphi techniques. *Int J Clin Pharm*. 2016;38(3):655–662. doi:10.1007/s11096-016-0257-x.
17. Qaseem A, Forland F, Macbeth F, et al. Guidelines international network: toward international standards for clinical practice guidelines. *Ann Intern Med*. 2012;156(7):525–531. doi:10.7326/0003-4819-156-7-201204030-00009.
18. EULAR Recommendations: Recommendations for management. Accessed December 4, 2024. https://www.eular.org/recommendations-management
19. Association of the Scientific Medical Societies in Germany (AWMF) – Standing Guidelines Commission. AWMF guidance manual and rules for guideline development. Version 2.1, 2023. Accessed December 4, 2024. https://www.awmf.org/fileadmin/user_upload/dateien/downloads_regelwerk/en_20230905_AWMF-Regelwerk_2023_V2.1.pdf
20. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) – a

metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–381.
21. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software partners. *J Biomed Inform*. 2019. doi:10.1016/j.jbi.2019.103208.
22. Moussa K, Alsberge JB, Munk MR, Vora RA, Emami–Naeini P, Yiu G, Cunningham Jr ET. Idiopathic multifocal choroiditis with serpiginous-like peripapillary chorioretinal atrophy. *Retina*. 2022;42(8):1574–1582.
23. Hady SK, Xie S, Freund KB, Cunningham Jr ET, et al. Prevalence and characteristics of multifocal choroiditis/punctate inner choroidopathy in pathologic myopia eyes with patchy atrophy. *Retina*. 2022;42(4):669–678.
24. Deutsch TA, Tessler HH. Inflammatory pseudohistoplasmosis. *Ann Ophthalmol*. 1985;17(8):461–465.
25. Ramtohul P, Cicinelli MV, Dolz-Marco R, et al. The chrysanthemum phenotype of idiopathic multifocal choroiditis. *Retina*. 2023;43(8):1377–1385.
26. Hoang QV, Cunningham ET, Sorenson JA, et al. The "pitchfork sign" a distinctive optical coherence tomography finding in inflammatory choroidal neo vascularization. *Retina*. 2013;33(5):1049–1055.
27. Cicinelli MV, Ramtohul P, Marchese A, et al. Latest advances in white spot syndromes: new findings and interpretations. *Prog Retin Eye Res*. 2023;97:101207.
28. Papasavvas I, Mantovani A, Herbort Jr CP. Diagnosis, mechanisms, and differentiation of inflammatory diseases of the outer retina: photoreceptoritis versus choriocapillaritis; A multimodal imaging perspective. *Diagnostics (Basel)*. 2022;12(9):2179.
29. Gilbert RM, Niederer RL, Kramer M, et al. Differentiating multifocal choroiditis and punctate inner choroidopathy: a cluster analysis approach. *Am J Ophthalmol*. 2020;213:244–251.
30. Zhang J, Zhang M, Ouyang W, Wang F, Li S. Characteristics of punctate inner choroidopathy complicated by choroidal neovascularisation on multispectral imaging in comparison with other imaging modalities. *Ocul Immunol Inflamm*. 2022;30(2):402–408.
31. Shi X, Cai Y, Luo X, Liang S, Rosenfeld PJ, Li X. Presence or absence of choroidal hyper-transmission by SD-OCT imaging distinguishes inflammatory from neovascular lesions in myopic eyes. *Graefes Arch Clin Exp Ophthalmol*. 2020;258(4):751–758.
32. Thompson IA, Caplash S, Akanda M, et al. Optical coherence tomography angiography changes in choroidal vasculature following treatment in punctate inner choroidopathy. *Ocul Immunol Inflamm*. 2021;29(5):944–950.
33. Gan Y, Zhang X, Su Y, Shen M, Peng Y, Wen F. OCTA versus dye angiography for the diagnosis and evaluation of neovascularisation in punctate inner choroidopathy. *Br J Ophthalmol*. 2022;106(4):547–552.
34. Gan Y, Su Y, Zhang Y, Zhang X, Liao N, Wen F. Patchy hyperautofluorescence as a predictive factor for the recurrence of punctate inner choroidopathy. *Photodiagnosis Photodyn Ther*. 2021;33:102146.
35. Kaden TR, Gattoussi S, Dolz-Marco R, Balaratnasingam C, Yannuzzi LA, Freund KB. The nature and frequency of outer retinal disruption in idiopathic multifocal choroiditis associated with persistent fundus hyperautofluorescence. *Ophthalmic Surg Lasers Imaging Retina*. 2019;50(11):675–683.
36. Li J, Li Y, Li H, Zhang L. Imageology features of different types of multifocal choroiditis. *BMC Ophthalmol*. 2019;19(1):39.
37. de Groot EL, Ten Dam-van Loon NH, Kouwenberg CV, de Boer JH, Ossewaarde-van Norel J. Exploring imaging characteristics associated with disease activity in idiopathic multifocal choroiditis: a multimodal imaging approach. *Am J Ophthalmol*. 2023;252:45–58.
38. Airaldi M, Zicarelli F, Forlani V, et al. Correlation between inflammatory foci reactivation and atrophy growth in eyes with idiopathic multifocal choroiditis. *Retina*. 2023;43(3):472–480.
39. Astroz P, Miere A, Mrejen S, et al. Optical coherence tomography angiography to distinguish choroidal neovascularization from macular inflammatory lesions in multifocal choroiditis. *Retina*. 2018;38(2):299–309.
40. Minkus CL, Lavine JA, Lee J, Skondra D, Goldstein DA. Use of short-wave blue fundus autofluorescence to detect and monitor acute regional outer retinopathy in punctate inner choroidopathy. *Ocul Immunol Inflamm*. 2022;30(4):887–893.