

Evidence and Consensus-Based Imaging Guidelines in Serpiginous Choroiditis—Multimodal Imaging in Uveitis (MUV) Task Force Report 4



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- **PURPOSE:** To develop imaging and consensus-based guidelines for the application of multimodal imaging in serpiginous choroiditis (SC).
- **DESIGN:** Consensus agreement guided by literature search, and an expert committee using a nominal group technique.
- **METHODS:** An expert committee gathered cases of noninfectious SC based on predefined informatics-driven inclusion criteria. These criteria focused primarily on

high-quality imaging, including color fundus photographs (CFP), optical coherence tomography (OCT), fundus fluorescein angiography (FFA), indocyanine green angiography, and OCT angiography (OCTA). A structured nominal group technique was applied to achieve consensus-based recommendations on imaging use for specific disease characteristics, biomarkers of activity, and complications. These recommendations were further voted upon by members of the full task force.

- **RESULTS:** CFP and fundus autofluorescence are key imaging modalities for the diagnosis of SC. SC is characterized by amoeboid/serpentine choroiditis lesions on CFP, with hypo-autofluorescence in older inactive lesions and hyper-autofluorescence along the broad active edges. Fundus autofluorescence is the most important tool for assessing disease activity. Indocyanine green angiography findings, particularly at the leading active edge, and OCT further aid in disease characterization. Early hypofluorescence of the active edge with uniform hyperfluorescent staining in the late phase of FFA are key features that help differentiate SC from other placoid chorioretinopathies. FFA, OCT, and OCTA are useful in identifying underlying choroidal neovascularization, with OCTA being an important modality.

- **CONCLUSIONS:** Multimodal Imaging in Uveitis imaging criteria for SC extend the Standardization of Uveitis Nomenclature classification, by providing guidelines for the use of multimodal imaging. These criteria also provide a framework for evaluation of disease activity and complications. (Am J Ophthalmol 2025;278: 81–92. © 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/>))

This invited article was submitted as part of the Virtual Special Issue on Multimodal Imaging of Non-Infectious Posterior Uveitis by the The International Uveitis Study Group MUV Working Group.

Accepted for publication May 30, 2025.

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INTRODUCTION

SERPIGINOUS CHOROIDITIS (SC) IS CHARACTERIZED BY the presence of gray/white or yellow choroiditis lesions that have a characteristic amoeboid or serpen-

tine pattern. Active lesions are captured at the advancing border of older lesions and typically involve the posterior pole, midperiphery, or the peripapillary retina. The absence of anterior chamber cells and vitreous haze is a key feature of SC.¹⁻⁵ The Standardization of Uveitis Nomenclature (SUN) Working Group provided classification criteria for diagnosing SC and differentiating it from tubercular choroiditis using machine learning techniques.⁶ Using the formal techniques, the SUN Working Group summarized that paucifocal or multifocal serpentine choroiditis lesions with a characteristic appearance on fundus fluorescein angiography (FFA) and/or fundus autofluorescence (FAF) without anterior chamber/vitreous inflammation are required to be classified as SC. Since phenotypic presentations of infectious etiologies such as syphilis and tuberculosis, and other conditions such as sarcoidosis can rarely mimic SC, these must be excluded by relevant investigations.⁶

SC is a rare condition that shares overlapping features with other posterior uveitic disorders affecting the outer retina/inner choroid, sometimes classified collectively under the misleading umbrella term “white dot syndromes.”^{7,8} Given that each entity within this group has distinct pathological and clinical manifestations, it is crucial to conduct an in-depth study of these conditions. Imaging modalities such as FFA, FAF, and optical coherence tomography (OCT) offer near-histological insights into the pathological involvement, facilitating a better understanding of SC.⁹⁻¹³

Although the SUN Working Group determined which imaging modalities are essential for the diagnosis of SC, given the development of more advanced imaging techniques (multimodal imaging), there is a need to identify consensus-driven imaging guidelines for their application and interpretation in the management of SC. The imaging features of SC have been studied in retrospective cohort studies, case series, and reports, but no comprehensive guidelines for their use and interpretation have been developed.

The Multimodal Imaging in Uveitis (MUV) task force, an international collaboration, has developed imaging-based guidelines to enhance the SUN classification for five of the most common multifocal choroidopathies. This manuscript specifically focuses on the imaging for SC.

METHODS

The MUV task force is an international research collaboration initiated by the International Uveitis Study Group. The MUV utilized the SUN criteria⁶ to diagnose and identify cases of SC to be included in imaging analysis. The study was conducted under the tenets of the Declaration of Helsinki. The study employed retrospectively collected, deidentified data and images from the practices of the study investigators. The study was granted Institute Review Board

(IRB) exemption by the Vanderbilt University Medical Center (IRB #240146).

- **SUBCOMMITTEE SELECTION:** The MUV task force used purposeful sampling strategy¹⁴ to establish a subcommittee of seven specialists with diverse expertise in uveitis and medical retina. Committee members from various regions worldwide were selected to ensure a diversity of perspectives, recognizing the variability in disease presentation across different populations. This team was tasked with selecting SC cases that included comprehensive imaging sets and developing imaging guidelines using formal consensus methods. Before conducting the study, the subcommittee members performed a thorough review of the published literature. The committee agreed to utilize at least 15 illustrative cases to support the development of imaging guidelines. We followed the principles of Standards for Reporting Qualitative Research: A Synthesis of Recommendations (SRQR)¹⁵ for reporting the results of our study.

- **CASE SELECTION:** The subcommittee selected both active and inactive cases of SC, ensuring a complete set of imaging assessments, including color fundus photographs (CFP) as a surrogate for clinical examination, OCT, FFA, FAF, and, when available, indocyanine green angiography (ICGA) and OCT angiography (OCTA). Cases with infectious diseases, such as syphilis and tuberculosis, were excluded. Deidentified images were shared by all members of the MUV task force, and a final set was prepared, which was agreed upon by >75% of the subcommittee members.

- **NOMINAL GROUP TECHNIQUE:** We chose the nominal group technique (NGT) to help the subcommittee achieve its goal of providing guidelines for SC. Among the members of the subcommittee, one acted as a neutral facilitator (AA). The subcommittee members conducted a series of virtual meetings to allow decision-making. As the first step, the members convened for an introduction and orientation to the goals of the study. In the next step, the subcommittee was provided with the main research question focused on imaging guidelines for SC, and each participant was allowed to present their ideas without interruption, discussion, or criticism in a round-robin format. The experts presented their opinions on the imaging findings of SC based on the selected cases of active and inactive disease (excluding mimickers such as tuberculosis and acute posterior multifocal placoid pigment epitheliopathy [APMPPE]), as well as their clinical experience and relevant literature review, rather than solely on the supplied images. After equal representation by all members, the facilitator ensured a discussion to clarify and elaborate on the key features of SC across each imaging modality. The facilitator allowed anonymous voting to achieve supermajority

consensus. The subcommittees also performed NGT discussions for identifying the most effective modalities for assessing disease activity and complications, including choroidal neovascularization (CNV).

- **ESTABLISHMENT OF CONSENSUS:** The subcommittee members drafted guidelines for using imaging to diagnose and monitor SC and its complications. These preliminary recommendations were developed following two online meetings held by the subcommittee members (attended by all the participants). Subsequently, the MUV task force (comprising 49 members; [Appendix I](#)) from diverse geographical regions and subspecialty training in uveitis reviewed the draft. Using an anonymous online survey system, the task force members assessed the recommendations, and any requested modifications were discussed collaboratively among the team members. Finally, a consensus was achieved by all the members of the MUV task force defined 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, including Guidelines International Network,¹⁶ European League Against Rheumatism,¹⁷ and Association of Scientific Medical Associations of Germany (AWMF).¹⁸ In case there was no consensus achieved (<50% vote), the guidelines were rejected. Study data were collected and managed using REDCap (Research Electronic Data Capture), a secure web-based platform hosted at Vanderbilt University Medical Center, designed to support research with validated data entry, audit trails, automated exports, and integration with external sources.^{19,20}

RESULTS

- **IMAGING FEATURES OF SC: CFP:** The subcommittee reviewed the imaging of SC and unanimously agreed that the clinical description provided by the SUN classification aligns well with the appearance of lesions on CFP. On CFP, SC lesions are typically uni-, pauci-, or multifocal, presenting as gray/white or yellow amoeboid/serpentine chorioiditis lesions, generally larger than 125 microns, coalescing, and primarily involving the posterior pole, peripapillary region, or midperipheral retina. Multifocal peripheral lesions should raise suspicion for the tuberculoid variant of SC.

Healed lesions exhibit atrophy with varying degrees of pigmentation ([Figure 1](#)). The subcommittee stressed that early lesions of SC may be indistinguishable from lesions of

APMPPE, and imaging may not help differentiate between the two entities. Evolution of the lesions over time, documented on CFP, may help differentiate between SC and APMPPE.

OCT: In active SC, the OCT shows outer retinal layer (photoreceptor ellipsoid and myoid zone) hyper-reflectivity, disruption of external limiting membrane and interdigitation zone, and retinal pigment epithelium (RPE) disruption. In addition, the active lesion area shows choriocapillaris thickening (typically not involving full-thickness choroid, unlike tubercular choroidal involvement). In healed areas, the OCT shows variable clumping or atrophy of the outer retina and RPE. The choriocapillaris may be thinned and atrophic in healed areas ([Figures 1 and 2](#)).

FAF: FAF reveals hypo-autofluorescence in older, inactive lesions with hyper-autofluorescence at the active edges ([Figure 1](#)). The subcommittee agreed that FAF was the most useful technique for the assessment of activity at the active edges ([Figures 1 and 3](#)). However, certain cases with subtle activity may be undetectable on FAF and require additional imaging modalities such as ICGA, OCT, and OCTA through the active edges.

FFA and ICGA: The subcommittee agreed that FFA is useful in diagnosing active SC. FFA in SC shows early variable hypofluorescence at the site of inactive lesions and early diffuse hypofluorescence in active areas, followed by late-phase uniform hyperfluorescence along the active borders ([Figure 3](#)). To some extent, FFA may help differentiate SC from APMPPE, because in the latter, the entire lesion is more uniformly hypofluorescent in the early phase with uniform late staining. The subcommittee noted that ICGA reveals extensive hypofluorescence throughout the lesion, often more widespread than what is seen clinically ([Figure 4](#)). Areas of atrophy typically show hypofluorescence, though underlying large choroidal vessels may be visible.

OCTA: OCTA in patients of active SC shows choriocapillaris flow void areas visible as diffuse areas of hyper-reflectivity, especially at the active edges of the lesions. The flow void areas indicate reduced flow in the choriocapillaris. In areas with healing, the OCTA shows variable recovery of flow void areas, with patchy large underlying choroidal vessels visible in areas of choriocapillaris atrophy.

Consensus statements for the various imaging modalities used in SC are provided in [Table 1](#).

- **DETERMINATION OF ACTIVITY AND COMPLICATIONS:** Based on the autofluorescence pattern of the lesions, the subcommittee determined that FAF was the most critical imaging tool for assessing disease activity ([Figures 1, 3, and 5](#)). However, in certain cases, the activity at the edge may be very subtle, and it may be challenging to detect using FAF. In such cases, performing an ICGA, OCT or an OCTA at the active edge may depict choriocapillaris flow deficit indicating an active border of ischemic inflammation. The subcommittee also agreed that FFA can provide valuable information in active lesions. CNV is rare

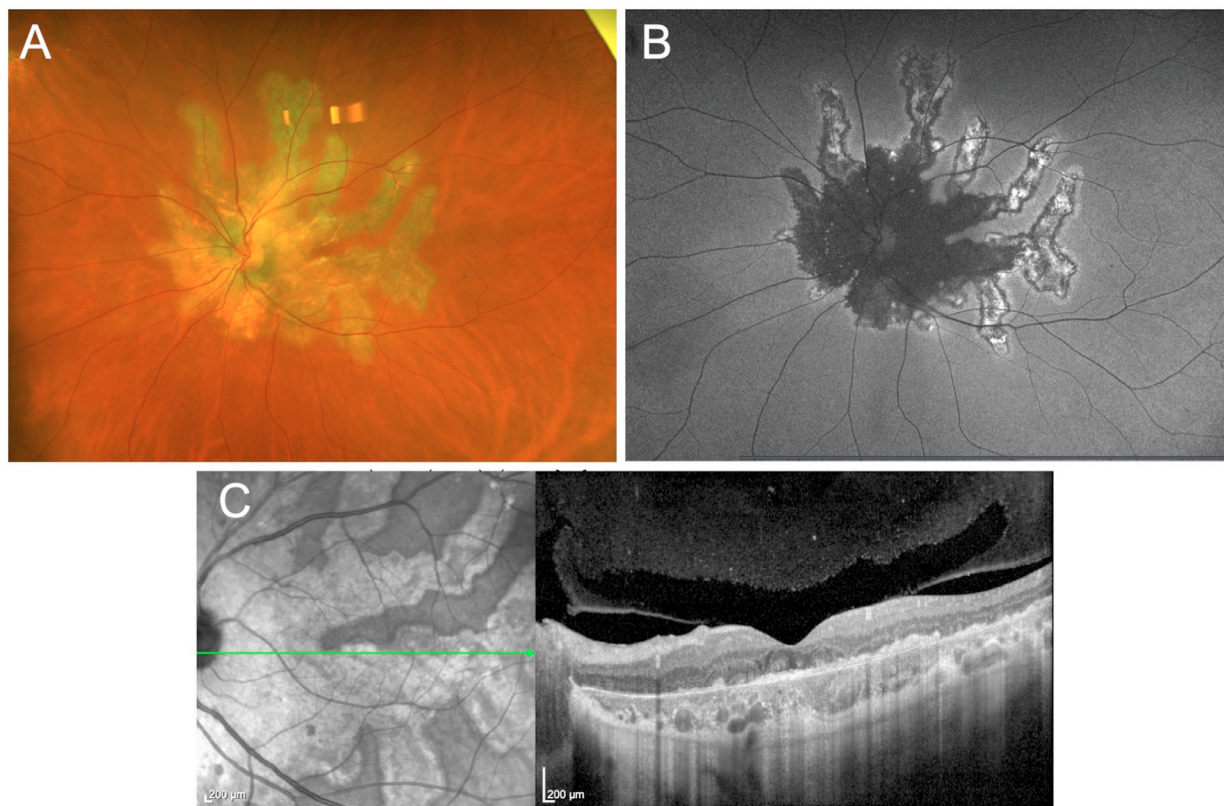


FIGURE 1. This figure shows a representative case of serpiginous choroiditis. The color fundus photograph (A) shows characteristic dull yellow serpentine lesions with active edges in the peripapillary retina. The fundus autofluorescence (B) shows hyperautofluorescence at the active edges of the lesions. The optical coherence tomography (OCT) passing through the lesion shows variable outer retinal and retinal pigment epithelial (RPE) atrophy, clumping, and choriocapillaris thickening suggestive of ischemia (C).

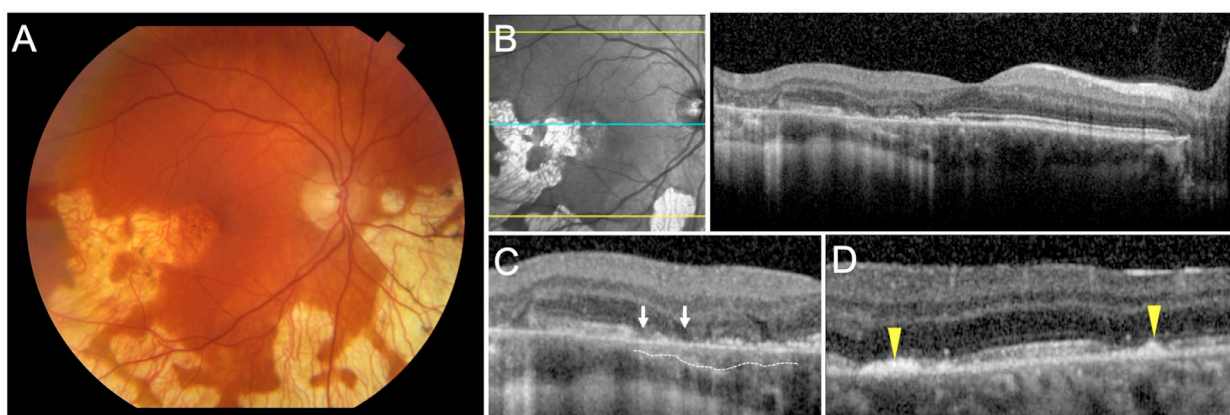


FIGURE 2. This figure shows a patient with serpiginous choroiditis in the right eye with a characteristic serpentine active edge close to the foveal center (A). The optical coherence tomography (OCT) line scan passing through the fovea (B) is shown. The magnified view (C) passing through the temporal macula (in the area of the active edge of the serpiginous choroiditis) shows disruption of the photoreceptor ellipsoid and myoid zone (white arrows). There is underlying thickening of the choriocapillaris (white dashed line) suggestive of choriocapillaris ischemia. Another magnified image passing through the lesion (D) shows clumping and hypertrophy of the retinal pigment epithelium (yellow arrowhead).

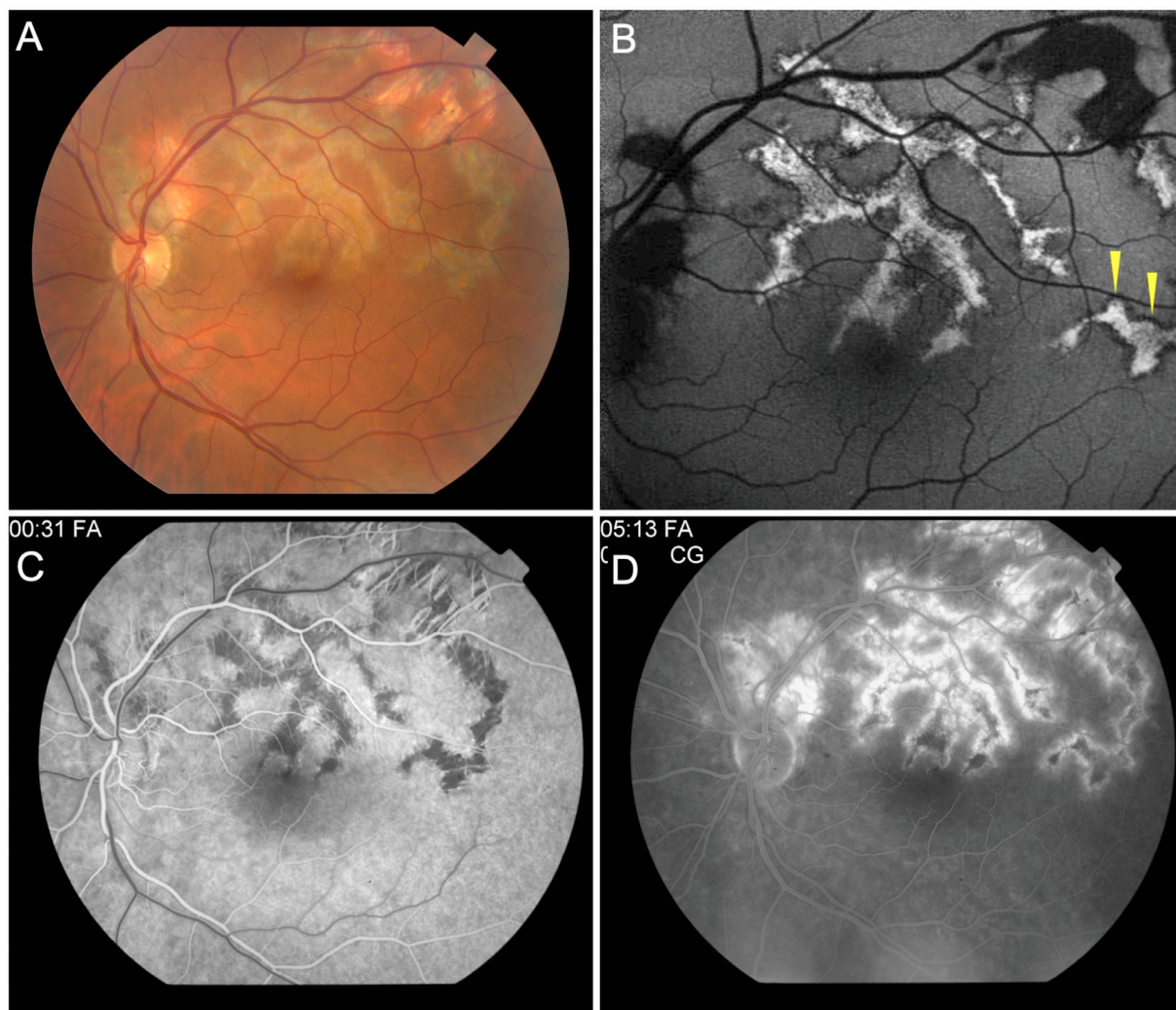


FIGURE 3. Imaging of a patient with serpiginous choroiditis is shown in this figure. The fundus of the left eye (A) shows characteristic dull yellow serpentine lesions with fuzzy borders in the area near the foveal center suggestive of activity. The fundus autofluorescence (FAF) image (B) shows hyper-FAF signal within the lesion, but the edges are hypo-FAF (yellow arrowheads). This contrasts with the FAF of the patient shown in [Figure 1](#), which has hyper-FAF at the active edge. The hypo-FAF edge suggests that the lesion is limited and is in early stages of healing. The fluorescein angiography in the early (C) and late phase (D) are shown. In the early phase (C), the lesions appear hypofluorescent. The active lesions closer to the fovea are diffusely hypofluorescent compared to the lesions near the superior arcade, which show underlying choroidal vasculature due to outer retinal and retinal pigment epithelial atrophy. The late phase FA (D) shows diffuse hyperfluorescence of the edges of the choroiditis.

in SC, and the subcommittee agreed that the CNV can be detected using FFA (focal leakage), OCT (appearing as outer retinal hyper-reflectivity with intra-/subretinal fluid), or OCTA (visible neovascular network in the outer retinal layer/choriocapillaris slab with flow signal on corresponding B-scan OCT) ([Figure 6](#)). The committee's consensus was that OCTA may be the most sensitive method for detecting CNV ([Table 2](#)).

- **CONSENSUS-BASED RECOMMENDATIONS:** The details of the recommendations drafted by the SC subcommittee and reviewed by the MUV task force is presented

in [Table 3](#). The table also provides the strength of the consensus.

DISCUSSION

The primary objectives of the MUV were to establish consensus statements, imaging guidelines, and methods for assessing lesion activity and complications. These goals are well-aligned with the SUN classification criteria, which incorporated machine learning. The integration of multi-modal imaging guidelines for diagnosis and disease evalua-

TABLE 1. Imaging-Based Consensus Criteria for Serpiginous Choroiditis

Imaging Modality	Consensus Criteria
Color fundus photography	Gray-white/yellow (true color) or dull yellow (pseudocolor) uni-, pauci-, or multifocal lesions > 125 μ m with amoeboid or serpentine shape (coalescing) Lesions in the posterior pole, peripapillary region, or midperipheral retina with no vitreous haze Healed lesions have atrophy with variable pigmentation
Fundus autofluorescence	Lesions have active hyper-autofluorescent edge Healed lesions (central) or areas of atrophy have hypo-autofluorescence
Fluorescein angiography	Early phase: Diffuse hypofluorescence at the active edge, and variable hypofluorescence at the older inactive lesion Late phase: Diffuse uniform hyperfluorescence at the active edge
Indocyanine green angiography	Lesions are hypofluorescent and more extensive than clinical examination
Optical coherence tomography	Hyper-reflectivity of ellipsoid and myoid zone (active disease) Disruption of external limiting membrane and retinal pigment epithelium Variable clumping/atrophy of the outer retina and the retinal pigment epithelium (healed disease) Thickening of choriocapillaris typically not involving the deep choroid (active lesions)
Optical coherence tomography angiography	Confluent flow deficit areas in the sites of active lesions Detection of choroidal neovascularization as an abnormal vascular network with flow signal

TABLE 2. Imaging Modalities for Monitoring the Activity and Detecting Complications in Serpiginous Choroiditis

Modality	Criteria/Utility
Fundus autofluorescence	Hyper-autofluorescence at the active edges Progressive hypo-autofluorescence of the lesion in healing stages
Indocyanine green angiography, optical coherence tomography angiography, or optical coherence tomography	Determination of activity in certain challenging cases where autofluorescence changes are subtle; detection of choriocapillaris hypoperfusion in active edges
Fundus fluorescein angiography, optical coherence tomography, and optical coherence tomography angiography	Detection of choroidal neovascularization

TABLE 3. Consensus-Based Guidelines for Imaging in Serpiginous Choroiditis^a

No.	Guidelines	Strength of Consensus
1.	CFP to document the active lesions SC and detect characteristic serpentine pattern (strong consensus)	97.3%
2.	FFA at baseline in active SC (consensus)	89.5%
3.	ICGA at baseline in active SC to detect disease extent (consensus)	92.1%
4.	FAF imaging to determine the activity of lesions of SC (unanimous consensus)	100%
5.	OCT images through the active lesions of SC to determine the outer retinal, RPE, and choriocapillaris involvement (consensus)	89.5%
6.	FAF imaging to monitor the healing of SC and demonstrate progressive hypo-autofluorescence of the lesions (unanimous consensus)	100%
7.	Serial OCT images to determine the healing pattern and development of outer retinal/RPE atrophy following treatment (unanimous consensus)	100%
8.	Use of FFA or OCTA to determine the presence of CNV lesions in SC (consensus)	92.1%

CFP = color fundus photography; CNV = choroidal neovascularization; FAF = fundus autofluorescence; FFA = fluorescein angiography; ICGA = indocyanine green angiography; OCT = optical coherence tomography; OCTA = optical coherence tomography angiography; RPE = retinal pigment epithelium; SC = serpiginous choroiditis.

^aThe seven members of the expert subcommittee did not cast their votes.

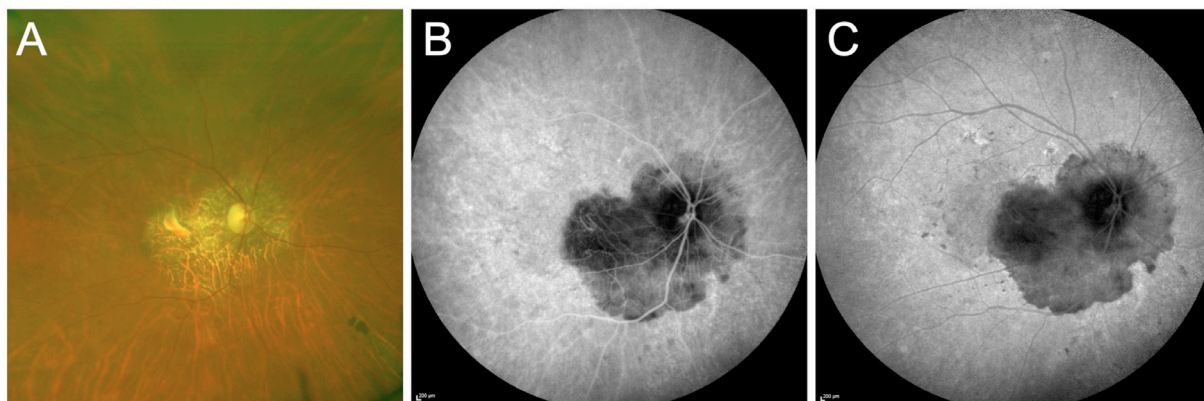


FIGURE 4. This figure shows indocyanine green angiography (ICGA) imaging of a patient with serpiginous choroiditis. The fundus shows peripapillary serpiginous choroiditis (A) in the right eye. The early phase ICGA (B) shows hypofluorescence of the lesion, larger than what is seen clinically. The late phase (C) shows persistent hypofluorescence of the lesion.

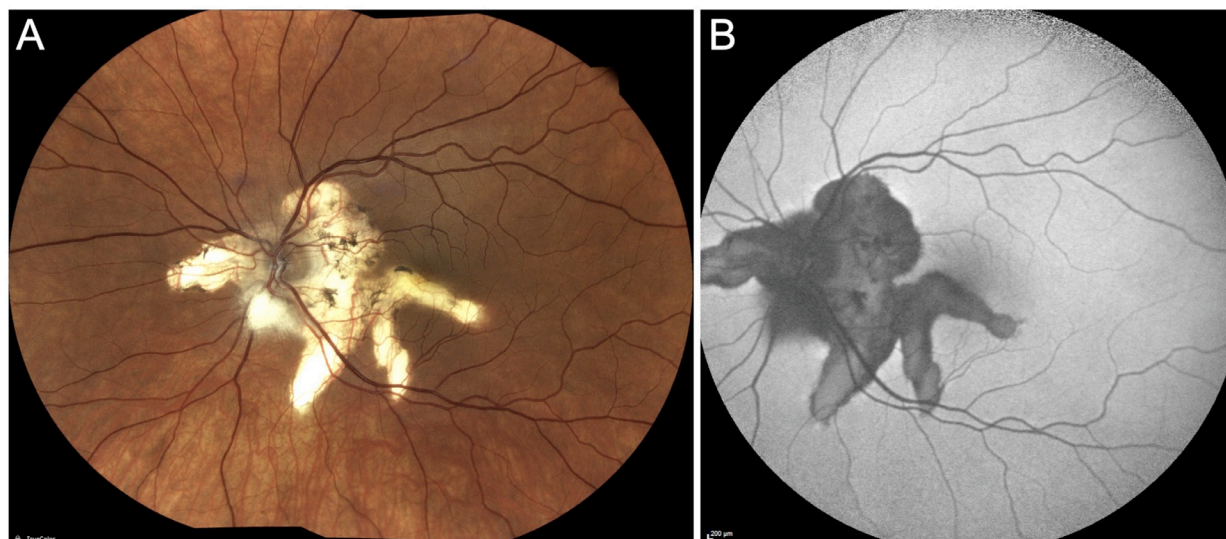


FIGURE 5. This figure shows a patient of healed serpiginous choroiditis. The fundus lesion is discrete, sharply demarcated yellowish, and located in the peripapillary retina (A). The fundus autofluorescence (FAF) (B) shows a hypo-FAF lesion without any active hyper-FAF edge, suggestive of a completely healed lesion of serpiginous choroiditis.

tion into the existing SUN framework⁶ is particularly important for SC and other uveitic conditions, as it provides objective evidence of pathological involvement across different tissue layers. Imaging criteria not only refine the definition of “multifocal choroidopathies,” sometimes grouped under the potentially misleading term “white dot syndromes,” but also highlight key distinguishing imaging features between conditions that may otherwise appear similar, such as SC and APMPE.

The MUV subcommittee emphasized the importance of lesion evolution in diagnosing SC, noting that early SC lesions may appear indistinguishable from APMPE on imaging. Consequently, serial CFP can be instrumental in tracking lesion progression over time, aiding in establishing the

diagnosis of SC. The subcommittee noted that SC lesions typically progress and coalesce over time. The characteristic evolution is important for differentiating SC from other placoid diseases such as relentless placoid chorioretinitis in addition to APMPE.

The MUV consensus criteria emphasize the critical role of FAF in assessing lesion activity in SC. FAF has been extensively utilized in the literature, including a grading system for serial assessment of patients undergoing immunosuppressive therapy, demonstrating its efficacy in monitoring treatment response in SC. Cardillo Piccolino et al²¹ provided one of the earliest descriptions of SC on FAF imaging, detailing the healing pattern characterized by the transition from hyper-autofluorescence to progressive

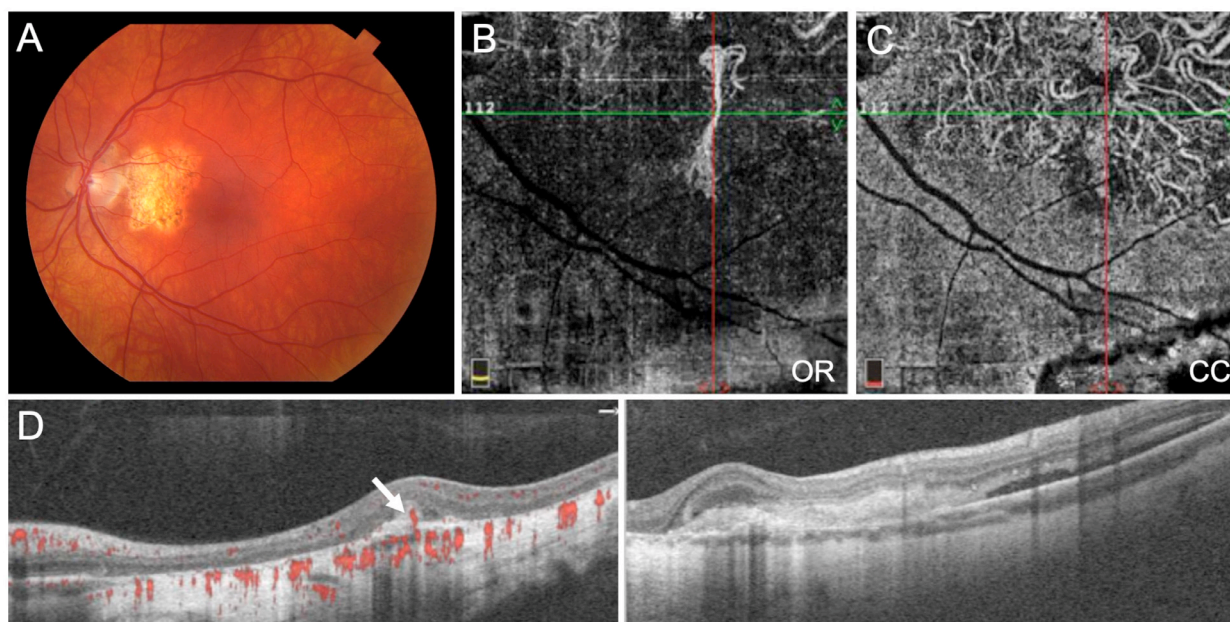


FIGURE 6. This figure shows a patient of serpinginous choroiditis complicated by the development of choroidal neovascularization (CNV) in the left eye. The lesion is located in the nasal macula of the left eye and has few spots of preretinal hemorrhage (A). The en-face optical coherence tomography angiography (OCTA) through the lesion (outer retinal slab; marked as OR) (B) shows the CNV network. The OCTA passing through the choriocapillaris slab (C) (marked as CC) shows choroidal vasculature, but it is difficult to delineate the CNV. The corresponding horizontal and vertical B-scan OCT (D) shows the subretinal hyper-reflective material (SHRM) and streak of subretinal fluid suggestive of an active CNV. The flow signal is noted within the SHRM (white arrow) suggestive of activity of the CNV.

hypo-autofluorescence following therapy. Subsequent studies with larger cohorts have consistently demonstrated this pattern of progressive hypo-autofluorescence on FAF after treatment initiation.^{11,22-25} Notably, this healing pattern has been shown to remain consistent in eyes treated with local intravitreal therapy in a study published by Miserocchi et al.²⁶ However, in certain cases of SC, FAF changes may be very subtle, and the active edge of the lesion may not be clearly visible on FAF. In such cases, the subcommittee recommended the use of additional imaging tools such as ICGA, OCTA, or OCT to determine choriocapillaris involvement which suggests lesion activity.

FFA, as emphasized in the SUN classification criteria, plays a vital role in diagnosing SC. In addition, the subcommittee noted that FFA plays a role in distinguishing SC from conditions such as APMPE and occasionally multifocal choroiditis, which can mimic SC.⁶ This distinction is based on the pattern of hyper- and hypoautofluorescence corresponding to the active edge and healing center, respectively, in SC, which differs from the typical lesion pattern in APMPE.

The consensus statements by MUV emphasize the value of additional imaging modalities, such as OCT, ICGA, and OCTA, in assessing pathological involvement in SC. OCT reveals key features of SC, including acute findings of outer retinal hyper-reflectivity involving the Henle fiber layer

(Angular Sign of HFL hyperreflectivity or ASHH), photoreceptor ellipsoid and myoid zones, and external limiting membrane as well as subacute alterations of the RPE including disruption, pigment clumping and atrophy.

Our description of OCT changes in SC are consistent with the reports in the literature.^{2,9,10,27,28} Wang et al²⁷ and Nazari Khanamiri et al² compared the OCT findings in SC with those in serpinginous-like choroiditis associated with tuberculosis, an overlapping condition. In serpinginous-like choroiditis due to tuberculosis, there may be deep choroidal involvement which is unlike classic SC. In SC, ICGA demonstrates diffuse hypofluorescence, particularly at the active lesion edges, which become isofluorescent or remains hypofluorescent in the late phase. In ICGA, the central healed areas show variable hypofluorescence, with prominent large choroidal vessels visible in regions of atrophy.^{2,9,10,12,29} These areas of acute hypofluorescence on ICGA correlate with flow voids detected on OCTA. There are several reports on the use of OCTA in SC in the literature.^{10,30-35} These authors report the presence of diffuse flow deficit areas on OCTA in SC, which represent true flow void in the choriocapillaris layer rather than signal loss and are an acute manifestation of disease activity. The subcommittee agreed that CNV, a complication of SC, is best detected using OCTA, as occult CNV may not be visible on ICGA.

The strength of the MUV guidelines on imaging-based recommendations for SC include its comprehensive and rigorous approach and structured NGT discussions. The expert subcommittee included participants from various geographic regions representing a diverse landscape of phenotypic disease, which supported the development of widely applicable imaging guidelines. Despite the strengths of such a collaborative effort, there are various limitations that must be acknowledged. It must be emphasized that imaging alone cannot differentiate other mimickers of SC, including tuberculosis and syphilis. Clinical characteristics and compatibility with SUN criteria are essential to arrive at the accurate diagnosis. Prospective validation studies are needed to establish the reliability and accuracy of imaging guidelines in the diagnosis and follow-up of SC. Certain atypical and uncommon manifestations of SC may not conform to the broad imaging guidelines and should be carefully considered while evaluating patients.

In conclusion, the MUV task force aims for the consensus imaging guidelines for SC to standardize uveitis diagnostics and assessment of activity by establishing uniform definitions for disease activity. Consistent use and interpretation of multimodal imaging in the classification and diagnosis of SC will enhance both clinical practice and research.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

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Financial Disclosures: The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Rupesh Agrawal reports a relationship with Council for Scientific and Industrial Research that includes: funding grants. Rupesh Agrawal reports a relationship with National Medical Research Council that includes: funding grants. Douglas A. Jabs reports a relationship with AbbVie Inc that includes: funding grants. Quan Dong Nguyen reports a relationship with ACELYRIN Inc that includes: funding grants. Quan Dong Nguyen reports a relationship with Boehringer Ingelheim Corp USA that includes: consulting or advisory and funding grants. Quan Dong Nguyen reports a relationship with Priovant Therapeutics, Inc that includes: funding grants. Quan Dong Nguyen reports a relationship with Regeneron Pharmaceuticals Inc that includes: consulting or advisory and funding grants. Quan Dong Nguyen reports a relationship with Genentech Inc that includes: consulting or advisory. Quan Dong Nguyen reports a relationship with Kriya Therapeutics Inc that includes: consulting or advisory. Quan Dong Nguyen reports a relationship with Rezolute, Inc that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

APPENDIX I

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