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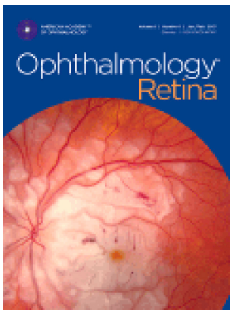

Recommendations for OCTA reporting in retinal vascular disease: A Delphi approach by International Experts

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Recommendations for OCTA reporting in retinal vascular disease: A Delphi approach by International Experts

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Running head: OCTA nomenclature in retinal vascular disease

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Abbreviations and Acronyms:

CME (cystoid macular edema), DCP (deep capillary plexus), DMI (diabetic macular ischemia), DR (diabetic retinopathy), EURETINA (European Society of Retina Specialists), FAZ (foveal avascular zone), FOV (field of view), IRMAs (intraretinal microvascular abnormalities), JRVS (Japanese Retina and Vitreous Society), NV (neovascularization), OCTA (optical coherence tomography angiography), ONH (optic nerve head), RVO (retinal vein occlusion), SCP (Superficial capillary plexus)

ABSTRACT:

Purpose: To develop a consensus nomenclature for reporting optical coherence tomography angiography (OCTA) findings in retinal vascular disease (e.g., diabetic retinopathy, retinal vein occlusion) by international experts.

Design: Delphi-based survey

Subjects, Participants and/or Controls: Twenty-five retinal vascular disease and OCTA imaging experts

Methods, Intervention, or Testing:: A Delphi method of consensus development was used, comprising two rounds of online questionnaires, followed by a face-to-face meeting conducted virtually. Twenty-five experts in retinal vascular disease and retinal OCTA imaging were selected to constitute the OCTA Nomenclature in Delphi Study Group for retinal vascular disease. The four main areas of consensus were: definition of parameters of "widefield (WF)" OCTA, measurement of decreased vascular flow on conventional and WF-OCTA, nomenclature of OCTA findings, and OCTA in retinal vascular disease management and staging. The study endpoint was defined by the degree of consensus for each question: "strong consensus" was defined as ≥ 85% agreement, "consensus" as 80-84% and "near consensus" as 70-79%.

Main Outcome Measures: Consensus and near-consensus on OCTA nomenclature in retinal vascular disease

Results:

A consensus was reached that a meaningful change in percentage of flow on WF-OCTA imaging should be an increase or decrease ≥30% of the absolute imaged area of flow signal and that a "large area" of WF-OCTA reduced flow signal should also be defined as ≥ 30% of absolute imaged area. The presence of new vessels (NV) and intra-retinal microvascular abnormalities (IRMAs), the foveal avascular zone (FAZ) parameters, the presence and amount of "no flow" area and the assessment of vessel density in various retinal layers should be added for the staging and classification of DR. Decreased flow ≥ 30% of the absolute imaged area should define an ischemic central retinal vein occlusion (CRVO). Several other items did not meet consensus requirements or

were rejected in the final discussion round.

Conclusions: This study provides international consensus recommendations for reporting OCTA findings in retinal vascular disease, which may help to improve the interpretability and description in clinic and clinical trials. Further validation in these settings is warranted and ongoing. Efforts are continuing to address unresolved questions.

INTRODUCTION

The advent of optical coherence tomography angiography (OCTA) has revolutionized our knowledge of retinal vascular disease (e.g., diabetic retinopathy, retinal vein occlusion) with its non-invasive and high-resolution capacity to image intraocular structures with near histologic resolution.[1-12] However, no consensus has been reached on the terminology of OCTA parameters and definition of abnormalities. Numerous and diverse terms have been used to report the findings of OCTA. These terms are in many cases even conflicting, which makes it impossible to describe findings from OCTA using consistent and reproducible nomenclature. Therefore, harmonization of OCTA terminology is necessary, which would be helpful to improve the quality of communication and the accuracy of measurement and quantification. This study is focused on retinal vascular disease, and the consensus on OCTA nomenclature for reporting neovascular age-related macular degeneration (nAMD), as well as other retinal diseases, is underway.[13-16]

Our previous survey highlighted that consensus terminology is warranted in retinal vascular disease.[16] Disagreements exist in many areas, such as the definition of wide-field OCTA, the terms used to describe a decrease in blood flow due to disease, and the guidelines to define and quantify ischemia due to diabetic retinopathy or retinal vein occlusion (RVO). The Delphi method has been shown to be very useful to reach consensus in many research areas.[17] In this study, we used the Delphi method to establish a standardized nomenclature for describing OCTA methodology and findings in retinal vascular disease.

METHODS

The Delphi technique has proven to be a reliable method in building consensus on terminology and usage.[18] This approach consults a group of experts in order to assess the level of agreement on an issue and to resolve differences.[19] For our purposes, voting participants from multiple countries and continents were invited based on their expertise in retinal vascular disease and OCTA. The final Delphi process included 25 participants, all of whom are listed as authors. It further included an Executive Committee made up of non-voting facilitators/mediators (MRM, RT, AHK, MT, JFK, SW), who drafted the questionnaire, assessed the answers and comments and compiled the comments and questionnaires for the next round and were primarily responsible for manuscript preparation and revisions. The questions and answer options were based on a previous comprehensive literature review to identify the areas and terms of highest discrepancies and significance.

The Delphi rounds were based on the initially conducted survey including 165 retina specialists.[16] Two rounds of multiple-choice electronic questionnaires were followed by a final virtual face-to-face meeting for the modified Delphi procedure. The degree of consensus for each question was defined as: “strong consensus” ≥85% agreement, “consensus” as 80-84% and “near consensus” as 70-79%. The definition of consensus was based on previous literature and is typical for the Delphi Technique in health sciences.[20] In the first round 27 questions from 4 categories were included. Questions, which reached consensus were closed and deleted for the next round. Questions that did not reach consensus in the first round, were rephrased to enhance the question's clarity and to guide respondents to possible agreement. Answer options with the fewest responses were deleted for the next round. Individual participants were given 2 weeks to respond to the questionnaires. After each round the anonymous results and comments were sent out to all the experts to evaluate

their answers with respect to the group's choices and to reconsider their vote. Questions that did not achieve agreement within the first or second round were submitted for the 3rd and final face-to-face round that was held virtually via Zoom videoconference (http://www.zoom.usa). The meeting was recorded. One of the non-voting executive members (MRM) moderated the session. Another non-voting moderator (AHK) read aloud each question and each individual answer option. In random order, the participants had one minute to choose an answer option and to comment. Other non-voting members (MRM, RT, MT and JFK) recorded the comments of the individual participants. After each of the experts responded, a final voting round was performed via the zoom platform voting function for each question. All questions lacking consensus (<70%) are reported as "non-consensus" in the manuscript.

RESULTS

28 experts were invited to participate in this study, and 25 agreed to participate. Response rates for round one and two were 100%, respectively, and 72% (18/25) attended the final virtual face-to-face round. Table 1 summarizes the results for each item in every round until it reached consensus. Supplemental Table 1 summarizes all questions and answer options of the Delphi rounds.

OCTA Wide-field Imaging

The majority of the Delphi experts (88%, 1st round) agreed that the definition of "wide-field" OCTA should be based on degrees of field-of-view (FOV). There was strong consensus in round three (88%, 3rd round) that FOV greater than 90 degrees should be considered as wide-field OCTA (Figure 1). Most of the experts (80%, 1st round) agreed that the term "ultra-wide field" OCTA is relevant

and that an exact definition should be adopted in the future. Two experts preferred wide-field OCTA to be defined by FOV of 70 degrees and "ultra-wide field" OCTA as greater than 90 degrees FOV. However, there was a lot of discussion after the vote that FOV may not be the best way to define wide-field imaging. Choudhry et al defined wide-field as images that captured the region between the posterior pole up to the anterior part of the vortex ampulla in all 4 quadrants. Although the OCTA wide-field definition proposed by Choudhry et al.[21] was rejected in the initial survey, after face-to-face discussion some experts felt that this would still be the appropriate definition. Others felt that the initial Choudhry et al. definition was not ideal, since most of the commercially available devices cannot produce an OCTA wide-field image meeting the previous definition. So, despite apparent consensus in the 3rd Delphi round, no final recommendation can be given in this matter.

Measurement of Decreased Vascular Flow on Conventional and Wide-field OCTA

In the previous survey a consensus was reached that automated measurement in square millimeters (mm^2) using OCTA manufacturer software should be used to assess area of decrease flow.[16] The Delphi group (80%, 2nd round) agreed that in cases where the OCTA manufacturer does not provide commercially available measurement software, the area of decreased flow should be assessed using third party software such as ImageJ (https://imagej.nih.gov/ij/). This consensus was reached although 88% of the experts (1st round) were of the opinion that importing OCTA images in ImageJ is not reasonable for day-to-day clinical practice because it is too time consuming. Seventy-six percent of the experts (2nd round) agreed that all direct measurements on OCTA images should be corrected for magnification error by incorporating axial length measurements. Where axial length measurements are not available, the refractive error should be used as a proxy for axial length.

As pertains to analysis of wide-field OCTA, most respondents (76%, 2nd round) preferred to use the percentage decrease of flow signal to quantify impaired flow. We reached a consensus that a meaningful change in percentage of flow on wide-field imaging should be change of ≥ 30% of the absolute imaged area of flow signal (80%, 3rd round) and that a "large area" of wide-field OCTA reduced flow signal should be defined as ≥ 30% of absolute imaged area (100%, 3rd round) (Figure 1). The initial wording of the question (see Table 1) included the term "clinically" meaningful. However, there was agreement in the open discussion of the 3rd face-to-face Delphi round, that this statement cannot be made based on our current knowledge. Since large prospective datasets will be needed to prove and assess any parameter for its clinical impact, the group agreed to remove the word "clinical" from these questions. The need to specify the location of decreased vascular flow (e.g. optic nerve head vs. macula vs. outside vascular arcades) was also emphasized in the discussion round, which will be subject of future ongoing efforts.

Terminology and Nomenclature of Decreased Vascular Flow on Conventional and Wide-field OCTA

In the initial survey there was consensus that the underlying cause of flow change on OCTA should be distinguished by using different terms. Apparent flow changes due to vessel displacement (e.g., cystoid macular edema), due to ischemia, due to blockage/shadowing/attenuation, due to projection artefact/removal and flow changes not associated with vascular structures should be differentiated. The initial survey included 13 different terms for flow change based on a large literature review. From round-to-round, answer options were removed based on the percentage of responses.

There was near consensus in the Delphi 2 round that flow change due to projection artefact and

projection artefact removal (76%) should be termed as Decorrelation abnormality due to projection artefact (DAPA). In the Delphi 2 round, experts also preferred (72%) the term Decorrelation abnormality due to flow displacement (DAFD) to describe flow change due to vessel displacement (i.e. CME). However, in the open Delphi 3 round discussion, a lot of experts were not comfortable with the wording of "decorrelation abnormality" and suggested the term "signal abnormality" instead. Although there was full consensus (100%) in the Delphi 3 round that the term flow deficit should be used to describe flow change due to ischemia (which is consistent with the consensus of the uveitis expert group on how to describe flow change in ischemia)[15], there was broad agreement in the following open discussion that none of these terms should be officially recommended for now. A future expert panel should be formed to address this terminology. Another important point raised by the panel was to consistently use either descriptive terms or established terms, which already include the potential underlying pathology and cause. This approach should be systematically applied for all suggested terms. Thus, for now no final recommendation for this terminology can be made.

OCTA in Retinal Vascular Disease Management and Staging

Diabetic Retinopathy

In our previous survey, a consensus was achieved that OCTA should be implemented for identification and staging of DR.[16] There was consensus that the parameters "the presence of NV", "the FAZ parameters", and "the presence and amount of no flow areas" should be added for the staging and classification of DR. In the present Delphi round, most experts (88%, 1st round) agreed that the assessment of IRMAs on OCTA and that the assessment of vessel density in various retinal

layers on OCTA should be additionally included in identification and staging of severity of DR (Figure 2). There was no consensus on which parameter should be used to define presence and severity diabetic macular ischemia.

Retinal Vein Occlusion

There was consensus in the initial survey that ischemic vs non-ischemic RVO can be diagnosed via OCTA. In Delphi 2 round there was consensus (84%) that percentage of decreased flow area on wide-field OCTA compared to absolute imaged area can be used for definition. In the final zoom poll 93% of Delphi experts agreed to use a cut off of ≥ 30% absolute decrease flow area to define ischemic vs. non ischemic RVO. The importance of limiting this definition to CRVO was made in the open discussion and that this is an inappropriate value for BRVO.

Discussion

In the present study, we aimed to establish a consensus for OCTA nomenclature in retinal vascular disease, which can be used in both clinical and research settings.

OCTA Wide-field Imaging

The term wide-field OCTA is inconsistently used in the literature. Single images covering 12x12mm, 15x9mm, and montage images consisting of either five 12x12mm images, four 9x9mm images, two 15x9mm images, sixteen 6x6mm images, twenty-five 3x3mm images, or extended field images covering approximately 60-70 degree FOV have been labelled as wide-field OCTA imaging.[22] A consistent definition is crucial for retinal vascular disease. Sensitivity and specificity of pathological features on wide-field OCTA for staging and prognosis of retinal vascular disease cannot be assessed without a standardized definition of this term (e.g. the percentage of flow deficit in a 15x9mm

"wide-field" OCTA will have different significance than the same percentage of flow deficit in a five 12x12mm montage "wide-field" OCTA). Findings of different studies lack comparability if different areas are captured and assessed. The initially proposed definition by Choudhry et al.[21] was not felt to be applicable, at least for now, because commercially available OCTA modules do not meet a consistent FOV requirement. It was agreed that the term wide-field OCTA should be defined by images covering ≥ 90°, however the group discussion showed clearly that it would be premature to make a final recommendation. A similar effort in the field of uveitis proposed ≥70 degrees FOV as "wide-field" OCTA. Some of the retinal vascular disease experts also considered 70 degrees of FOV as appropriate and suggested that ≥ 90 degrees FOV should be defined as "ultrawide-field OCTA". Based on this inconsistency, no final recommendation can be made, and future efforts are warranted to resolve this issue.

Measurement of Decreased Vascular Flow on Conventional and Wide-field OCTA

The experts reached a consensus that a meaningful change in percentage of flow on wide-field imaging should be a change ≥ 30% of the absolute imaged flow area and that a "large area" of reduced flow signal should be defined as ≥ 30% of absolute imaged area. This suggests that experts recognize that detection of flow changes on OCTA at this time is still only a gross measurement of change and there is much room for improvement. Given the resolution of OCTA devices it is very likely that smaller increments of flow change can be reliably detected and used for diagnosis or prognosis in the future. However, for now, the initially proposed term "clinically" meaningful was rejected, with the rationale that large and longitudinal datasets will be necessary to prove any clinical utility. The clinical impact cannot be assessed based on our current knowledge. Prospective longitudinal data will be needed to evaluate whether these values correspond to disease progression and the development of complications. Another point raised was the impact of location of the decreased vascular flow, which had not been considered in the

current questionnaire. This open aspect is already topic of the currently ongoing efforts.

Terminology and Nomenclature of Decreased Vascular Flow on Conventional and Wide-field OCTA

Terms used to describe signal abnormalities vary in the literature and even within a single publication. In this instance agreement could not be reached even among the experts, regarding which terms are most appropriate and should be systematically used in the future. Although there was a near consensus in the Delphi 2 round to employ the term decorrelation abnormality due to projection artefact (DAPA) in case of signal abnormalities due to projection artefact or removal and a strong tendency (72%) to use the term "decorrelation abnormality due to flow displacement (DAFD) to describe signal alterations due to vessel displacement, the final discussion revealed that (at least for now) no explicit terms can be recommended. An additional expert group is now being formed to solve these discrepancies.

OCTA in Retinal Vascular Disease Management and Staging

Diabetic Retinopathy

In our previous survey, a consensus was achieved that OCTA should be implemented in identification and staging of severity of DR.[16] There was consensus that "the presence of NV", "the FAZ parameters", and "the presence and amount of no flow areas" are parameters that should be added for the staging and classification of DR. In the present Delphi round, the majority of experts (88%, 1st round) agreed that the assessment of IRMAs and vessel density in the inner retinal layers should be included along with the previously identified parameters for the identification and staging of severity of DR. The implementation of OCTA in current and future

severity assessment warrants further evaluation and efforts. It is notable that both the currently accepted staging systems, the ETDRS and the simpler international DR grading scale, have significant limitations. They do not consider vascular changes in the retinal periphery and do not grade capillary nonperfusion in general and lack the incorporation of the neurodegenerative character of the disease. Furthermore they are suboptimal in their sensitivity to identify regression and progression of neovascularization in PDR.[23] Efforts are therefore ongoing to update the DR severity scale and it is an opportune time to incorporate OCTA in the new, evolving multidimensional diabetic retinal disease severity grading system which will improve the representation and prognosis of DR in the future.[23]

For diabetic macular ischemia, the experts were unable to agree on an OCTA parameter that would define presence and severity. This is not surprising, given the heterogenous definitions of diabetic macular ischemia in the literature.

Retinal Vein Occlusion

There was consensus in the initial survey that ischemic vs non-ischemic RVO can be diagnosed via OCTA. In Delphi 2 round the experts agreed (84%) that percentage of decreased flow area on wide-field OCTA compared to absolute imaged area can be used for respective definition. In the zoom poll 93% consented that a cut off of ≥ 30% of decreased flow area of absolute imaged area is suitable to define ischemic RVO. In the open discussion however, it was emphasized that this definition should only be applied to CRVO not BRVO. In BRVO the impact of the area of ischemia is still unclear to this point. Despite this recommendation it must be emphasized that only future longitudinal follow-ups of large cohorts of CRVO patients will determine whether this definition is

valid and useful from a clinical standpoint. They should assess whether this cut off is associated with secondary complications such as the NVE/NVD, rubeosis and secondary glaucoma. The exact and optimal timing of the OCTA would be another important point to consider, given that the high number of hemorrhages in acute CRVO can impede OCTA interpretation.

In summary, based on our final consensus we recommend:

- To define a large flow decrease by ≥ 30% of the absolute imaged area
- To define a meaningful change in percentage of flow on wide field OCTA as increase or decrease of 30%
- To include OCTA in the assessment of DRP severity and progression. The assessment of IRMAs and the vessel density should be added beyond the already recommended parameters “presence of NV”, “FAZ parameters”, and “the presence and amount of no flow areas”
- To use % of decreased flow areas in the wide-field OCTA images compared to total imaged area to define ischemic CRVO
- To define ischemic CRVO by ≥ 30% decreased flow area compared to absolute imaged area.

To measure the area of decreased flow directly with third party software (i.e. ImageJ) in cases where the OCTA manufacturer does not provide commercially available software. These Delphi results are the first step towards a standardized nomenclature in retinal vascular disease. Improved understanding and insight into the new technology and the acquisition of large longitudinal datasets will help in the future to address the unresolved open questions and validate the current recommendations.

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Figure legend:

Figure 1: Representative example of a “large area” of reduced flow signal defined by **≥ 30% decreased flow area of absolute imaged area. Left:** Original Image **Right:** Areas of reduced flow assessed and quantified using Image J, Area of decreased flow is 49%.

Figure 2: Consensus OCTA parameters which should be considered for the staging of diabetic retinopathy: Top left: Vessel density. Top Middle: Foveal avascular zone parameters. Top right: Presence and amount of flow deficit/no flow areas. Middle: Presence of Intraretinal microvascular abnormalities (IRMA): Left: En face OCTA scan (red arrow). Right: B-scan with flow overlay (right arrow). Bottom: Presence of neovascularization: Left: En face OCTA scan (red arrow). Right: B-scan with flow overlay (right arrow)

	Answer	Round 1	Round 2	Round 3	Consensus
Wide field OCTA definition					
How do you feel about **using degrees of FOV to define wide-field OCTA**?	Agree	88%			**Strong consensus***
How many degrees of FOV would you consider as wide-field OCTA? Of note: conventional wide field imaging is defined by visibility of vortex vein ampulla in all 4 quadrants which translates to ~130 degree FOV.	⩾ **90 degrees**	32%	56%	88% (6% abstention from vote)	**Strong consensus***
In how many retinal vascular disease cases do you perform more than one OCTA scan to obtain a wider field-of-view than is available from a single scan acquisition?	Less than 20%	56%			N.A.
What's your opinion about the relevance and utility of the term ultrawide field OCTA being adopted in the future?	Agree	80%			Consensus
Size of decreased flow					
The experts in the survey agreed that automated measurement in square millimeters (mm^2) using OCTA manufacturer software should be used to assess area of decrease flow. (74%) However, not all OCTA manufacturers provide commercially available software measurements for automated assessment of flow. In cases where the OCTA manufacturer does not provide commercially available software would you prefer to manually measure the area of decreased flow using a direct method with third party software (i.e. ImageJ) or estimate the area of decreased flow using an indirect method (such as FAZ equivalents)?	**Direct**	68%	80%		Consensus
All direct measurements on OCTA images should be corrected for magnification error by incorporating axial length measurements. Where axial length measurements are not available, a less ideal option is to use refractive error as a proxy for axial length.	Agree	60%	76%		Near Consensus

Importing OCTA images in ImageJ is time consuming and primarily a research tool. It is not reasonable for day-to-day clinic applications:	**Agree**	88%			**Strong consensus**
If you were to use the FAZ size to indirectly assess decreased OCTA flow, what would you define as the smallest measurable area of decreased flow on conventional (3x3, 6x6 and 9x9mm) OCTA?°	> ½ FAZ area	36%	52%	deleted	NA
If you were to use the FAZ size to indirectly assess decreased OCTA flow, what would you define as a "large area of decreased flow" on conventional (3x3, 6x6 and 9x9mm) OCTA? °	> 1 FAZ area	52%	56%	deleted	NA
In wide-field OCTA images, would you rather measure decreased flow as a percentage of the absolute retinal area imaged or as optic nerve head area equivalents.	% of absolute retinal area	60%	76%		Near consensus
Assessment of quantitative measurements in wide-field imaging: If you would rather measure decreased flow as a percentage of the absolute retinal area imaged, how would you define a clinically meaningful change in percentage of flow on wide-field imaging?[X]	Increase or decrease of 30%		20%	80% (17% abstention from vote)	Consensus
Assessment of quantitative measurements in wide-field imaging: If you would rather measure decreased flow as a percentage of the absolute retinal area imaged, how would you define a large flow decrease?	**≥ 30% of absolute area**	56%	40%	100% (6% abstention from vote)	**Strong consensus**
Terminology					
In case of apparent flow changes in any retinal layer of unknown origin, which general term would you suggest?	Decorrelation abnormality of unknown origin (DAUO)	24%	60%	57% (22% abstention from vote)	No consensus
In the case of apparent flow changes in any retinal layer due to vessels displacement (by for example CME), which specific term would you suggest?	Decorrelation abnormality due to flow displacement (DAFD)	36%	72%	56% (11% abstention from vote	No consensus

In the case of apparent **flow changes in any retinal layer due to ischemia**, which specific term would you suggest?	**Flow deficit**	36%	44%	100%	**Strong consensus***
In the case of apparent **flow changes in any retinal layer due to signal blockage/shadowing/attenuation**, which specific term would you suggest?	**Non detectable flow signal**	52%	32%	85% (28% abstention from vote)	Strong consensus*
In the case of apparent flow changes in any retinal layer due to projection artifact, which specific term would you suggest?	Decorrelation abnormality due to projection artifact (DAPA) 76%	56%	76%		Near consensus*
In the case of apparent flow changes in any retinal layer not associated with vascular structures, which specific term would you suggest?	Flow artifact	48%	44%	76% (6% abstention from vote	Near consensus*
Severity assessment of Diabetic Retinopathy, Retinal Vein Occlusion and Diabetic Macular Ischemia					
Do you believe that the assessment of IRMAs on OCTA should be included?	**Agree**	88%			**Strong consensus**
Do you believe that the assessment of vessel density in various retinal layers on OCTA should be included?	**Agree**	88%			**Strong consensus**
There was consensus in the survey that Diabetic macular ischemia (DMI) can be diagnosed/assessed via OCTA. However, there was no consensus on the parameter to use. How would you define and quantify DMI?	Perifoveal vessel density (excluding FAZ area)	44%	36%	28%	No consensus
There was consensus in the survey that ischemic vs non-ischemic RVO can be diagnosed/assessed via OCTA. However, there was no consensus on the parameter to use. How would you define ischemic retinal vein occlusion?	% of decreased flow areas in the wide-field OCTA images compared to total area	64%	84%		Consensus
If you use ONH area equivalents as a parameter to define ischemic vs. non-	I prefer not to use this method	35%	52%	deleted	NA

ischemic flow decrease in wide-field OCTA images, how would you define ischemic?					
If you use the number of subfields occupied by flow decrease as parameter to define ischemic vs. non-ischemic retinal vascular disease in wide-field OCTA images, how would you define ischemic?	I prefer not to use this method	64%	deleted		NA
If you use % of decrease flow area as a parameter to define ischemic vs. non-ischemic retinal vascular disease in wide-field OCTA images, how would you define ischemic?	**⩾ 30% of absolute area**	24%	44%	93% (22% abstention from vote)	**Strong consensus**

Table 1.- Delphi items with the final answer and the percentage of agreement each round.

* After discussion it was agreed that no final recommendation can be given at this point, despite consensus

° Direct measurement was chosen, so these questions were deleted in the following rounds

[X] After discussion it was agreed to delete "*clinically"* in clinically meaningful.

N.A. Not applicable