A consensus definition for lamellar macular hole

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Synopsis:

Optical coherence tomography based definitions for the diagnosis of lamellar macular hole, macular pseudohole and epiretinal membrane foveoschisis are suggested. Consistent terminology is seminal to the study of such macular conditions and may significantly improve their clinical management.

ABSTRACT

Background: A consensus on an optical coherence tomography (OCT) definition of lamellar macular hole (LMH) and similar conditions is needed.

Methods: The panel reviewed relevant peer-reviewed literature to reach a consensus on LMH definition and to differentiate LMH from other similar conditions.

Results: The panel reached a consensus on the definition of 3 clinical entities: LMH, epiretinal membrane (ERM) foveoschisis and macular pseudohole (MPH). LMH definition is based on 3 mandatory criteria and 3 optional anatomical features. The 3 mandatory criteria are the presence of irregular foveal contour, the presence of a foveal cavity with undermined edges, and the apparent loss of foveal tissue. Optional anatomical features include the presence of epiretinal proliferation, the presence of a foveal bump and the disruption of the ellipsoid line. ERM foveoschisis definition is based on 2 mandatory criteria: the presence of ERM and the presence of schisis at the level of Henle's fiber layer. Three optional anatomical features can also be present: the presence of microcystoid spaces in the inner nuclear layer (INL), an increase of retinal thickness, and the presence of retinal wrinkling. MPH definition is based on 3 mandatory criteria and 2 optional anatomical features. Mandatory criteria include the presence of a foveal sparing ERM, the presence of a steepened foveal profile and an increased central retinal thickness. Optional anatomical features are the presence of microcystoid spaces in the INL and a normal retinal thickness.

Conclusions: The use of the proposed definitions may provide uniform language for clinicians and future research.

Introduction:

The transformative shift from slit-lamp biomicroscopy to high resolution spectral-domain optical coherence tomography (OCT) has dramatically improved the ability to study foveal microanatomy.[1] However, with this change in diagnostic methods, the original slit lamp-based definition of lamellar macular hole (LMH) has become outdated, and there is no new definition that has achieved consensus amongst clinicians.[2-3] Currently, in the literature the term ‘‘*lamellar macular hole*’’ (LMH) refers to a wide spectrum of retinal conditions characterized by a break in the inner fovea and an irregular foveal contour.[1] This broad and inclusive terminology includes several distinct clinical entities, with different morphology and pathophysiology.[1-4] This overbroad and imprecise definition could negatively influence clinical practice, complicate inter-study comparisons, and hinder the decision between observation and intervention in the management of these conditions.

Recent histopathology and clinical reports have provided novel insights into the morphologic features of LMH which could help distinguish different pathological forms from each other.[1-10] Therefore, acknowledging that it was the appropriate time for a clear definition of LMH based on new retinal imaging, a panel of vitreo-retinal experts collected and evaluated published evidence on the subject and merged this information to reach a consensus on an OCT-based diagnosis and definition of what constitutes LMH. Furthermore, by updating the definition of LMH, the group sought to differentiate it from other overtly similar, but distinguishable entities.

Methods:

An international panel of vitreo-retinal experts was selected by the 2 panel organizers (JPH and RT), with the aim of providing a clear, up-to-date OCT-based definition of LMH. All experts have a history of relevant publications and/or research contribution on the subject, participation in other consensus efforts, and availability to participate. The assigned goal for this first work was to propose definitions meant to facilitate clinical practice and patient management by guiding differential diagnosis between LMH and other similar macular lesions, and to removing ambiguity from communication among clinicians, thus improving the

relevance of future studies and inter-study comparisons. This work was approved by the Institutional Review Board of the University of California Los Angeles, and the research project adhered to the tenets of the Declaration of Helsinki.

At the beginning of the review process, to identify the retinal imaging features and definitions used in the key publications to date, an initial selection of the relevant articles dealing with diagnosis or definition of LMH was performed on Pubmed (https://www.ncbi.nlm.nih.gov/pubmed/) using the following search strategy, with no language restriction: *lamellar AND macular AND (hole OR holes)*, last accessed April 15, 2018. Then the panel organizers selected from the initial list major peer-reviewed articles all published in journals in the first-quartile score (Q1, top 25% of the impact factor distribution) addressing the issue of lamellar macular hole definition and classification.[1-28] Articles in which the main outcome was the analysis of surgical results were excluded in the selection process. The selection was then reviewed by the panel organizers. The panel approved 28 papers (details bellow) to be used as basis for the following steps.

As a second step, to assess the agreement of the panelists to detect a range of image based features of various foveal defects, and gauge their ability to subdivide lesions based on the available definitions, the panel organizers developed two questionnaires named work package 1 and 2 (WP1 and 2). WP 1 and 2, of 12 and 8 cases respectively, included all OCT images (B-scans, en-face and/or 3D reconstruction) and some cases also included color fundus images, of LMH, ERM, foveoschisis and lesions currently defined as macular pseudoholes, as well as a series of open-ended questions directed to the panel members. WP1 and 2 were distributed among all the panel members, and their answers, based on the selected literature and their opinion, collected and collated by the panel organizers.

As a third step, all collected information from the responses was provided to the panel members and used to guide discussion among them during two group meetings. To reach a consensus on terminology and definitions, the Delphi method, also known as Estimate-Talk-Estimate, was applied. At the end of the process, a consensus among the panel members was reached on new terminology and definitions. This led to a proposal to differentiate 3 previously confused maculopathies: LMH, epiretinal membrane foveoschisis and macular pseudohole.

Results:

The literature search strategy retrieved 242 peer-reviewed articles. The panel organizers reviewed all articles titles and abstracts and initially selected 22 major articles focusing on LMH and macular pseudohole diagnosis and/or definitions. After review of the initial selection, 6 other articles were added by panel members and accepted by the entire group. A total of 28 articles were eventually selected to be used as base for discussions.

Panel members agreed that the proposed definitions of LMH, epiretinal membrane foveoschisis, and macular pseudohole should be

primarily based on OCT, with scans centered in the foveal region. The decision to use OCT (B-scans and en-face images) as the primary examination modality was based on its ability to image foveal microstructure, its availability and its non-invasive nature. For each definition, mandatory and optional diagnostic criteria were identified. Each OCT feature, or criteria used in disease definitions, was also defined by the group to help proper interpretation and diagnosis.

Terminology of OCT features

The panel agreed to the use of the following terminology to describe OCT features.

Epiretinal membrane (ERM): The definition of ERM was specified to differentiate from epiretinal proliferation described below. On OCT scans, an ERM was considered as the presence of an irregular and hyperreflective line over the inner limiting membrane (ILM), often associated with signs of wrinkling of the underlying retina, with the frequent presence of hyporeflective spaces between the epiretinal membrane and the ILM (supplementary file 1). The term "*premacular membrane*" was proposed by some panel members as more relevant since membranes in question are always anterior to the macula, when "epi", meaning adjacent, does not specify which side of the retina is affected. Nonetheless, use of "ERM" for further descriptions won the consensus for the sake of familiarity. It is important to note that the use of the term "ERM" as an OCT finding does not always imply the presence of a discernable macular pucker in the fundus.

Epiretinal proliferation: The OCT appearance of thick, homogeneous and iso-reflective epiretinal material over the ILM (figure 1) has to be distinguished from the hyperreflective ERM described earlier. Epiretinal proliferation is fully in contact with the ILM, with no hyporeflective spaces between the two anatomical structures, in distinction to ERM. It should be noted that the iso-reflective epiretinal proliferation as seen by OCT is often covered by a thin hyperreflective line. A quick inexpert look at the OCT scan can then misperceive the thick iso-reflective epiretinal material as part of the retina and the anterior reflection as the ERM. However, the identification of the retinal layers and the reflective ILM may help in reconsidering the diagnosis.

Beyond differences in OCT appearance between ERM and epiretinal proliferation, increasing evidences in the literature justify differentiating them. Actually, epiretinal proliferation was first described as "thick" or "thicker" ERM, and later renamed "lamellar-macular hole associated epiretinal proliferation" (LHEP) by Pang et al, as it was believed to be present only in association with LMH.[6] However, subsequent reports showed that the presence of this epiretinal material is not exclusive to LMH, as it can be found as well in full-thickness macular holes, in the presence of posterior uveitis, and even associated with macular pucker.[11] Histopathology studies demonstrated that, in contrast to the epiretinal membranes that cause macular pucker, such epiretinal proliferation has little or no contractile properties, suggesting that epiretinal proliferation

and ERM are two different entities.[5] Therefore, to describe the epiretinal proliferation as “thick” ERM may be misleading as it does not highlight the relevant pathophysiologic differences among these two distinct conditions. Finally, to name it “proliferation” appears appropriate, as there is significant evidence that the amount of this material increases over time, suggesting cellular proliferation.[13-15] Epiretinal membranes are also cellular proliferation on the surface of the retina, but the usual term ERM does not include the term “proliferation” allowing to use it for these proliferations. The location of the visible proliferation on the anterior surface of the retina would justify the use of the term “*premacular*”. However, here also to conform to the published nomenclature, in particular LHEP, it was accepted just to drop the “lamellar-macular hole associated” from LHEP as it is not precise anymore (described in other macular conditions) and keep the remaining “epiretinal proliferation” part for the subsequent descriptions.

Foveal “bump”: a bulge of retinal tissue in the foveal center, usually surrounded by foveal cavities with undermined edges (defined below), is common in LMH. It may represent “spared” retinal tissue not involved in the pathophysiological process which caused retinal tissue loss or some proliferation.

Foveal cavity with undermined edges: Intraretinal hyporeflective spaces which could affect all retinal layers and may be confluent. They may probably correspond to areas of tissue loss as they do not cause an increase in retinal thickness. Further, as seen with structural SD-OCT the retinal layers appear to be eroded rather than displaced. In case of LMH, they are often connected with the vitreous cavity through a break in the inner fovea (figure 2).[2] On en-face OCT segmented at the level of the INL they appear often as a single large central, homogeneous hyporeflective area with petaloid outer border (supplementary file 2,A). The term “*undermined edge*” is used in dermatology to describe skin ulcers which appear similar in morphology to LMH as seen with OCT.[29]

Cystoid spaces: the presence of round/elliptical intraretinal hyporeflective cystoid spaces, occasionally confluent and mainly located in the inner nuclear layer (INL) and outer plexiform layer (OPL). The distinction between foveal cavity with undermined edges and cystoid spaces is important, as, beside the opening to the vitreous, it also implies probable differences in the pathophysiology of these two conditions. While foveal cavity with undermined edges refers to the formation of a hyporeflective space within the retina, presumably caused by tissue loss, the presence of retinal cystoid spaces suggests the creation of spaces primary due to displacement of cells rather that loss of retinal tissue. The en-face OCT segmented at the level of the INL and ONL illustrates multiple hyporeflective roundish spaces disposed in a classic petaloid area. Small cystoid spaces almost exclusively located in the INL (supplementary file 2,B and 3) are often referred to as microcystoid spaces. Müller cell dysfunction has been suggested to play a role in microcystoid spaces development.[30]

Foveoschisis: The use of the term was proposed by the panel for an OCT feature analogous to what is found in myopic foveoschisis. When present in a non-myopic eye, on structural OCT, foveoschisis appears as a separation ("*schisis*") between foveal retinal layers, typically the outer nuclear layer (ONL) and OPL, at the level of the Henle's fiber layer (HFL). It is likely caused by the action of mechanical forces (i.e. vitreomacular traction or epiretinal membrane) over the central fovea.[31] As in myopic foveoschisis, inner and outer retina are typically connected through intraretinal, mainly beveled, hyperreflective bridges of tissue, which may correspond to stretched and verticalized Müller cells bodies and which are intermingled by hyporeflective intraretinal spaces (figure 3). The en-face imaging segmented at the level of the HFL can show stretched hyporeflective spaces disposed in radial pattern over the macular region, mimicking the disposition of z-shaped Müller cells in the central macula [32] The appearance on OCT is then different from round shape cystoid spaces and foveal cavity with undermined edges as described above.

Lamellar macular hole

In the original description by Gass in 1976, LMH was identified with slit lamp biomicroscopy as a partial-thickness macular lesion resulting from cystoid macular edema.[16] Later, it was proposed that such a definition of LMH should be revised, as the terminology derived from slit lamp biomicroscopy may be outdated and imprecise in the era of OCT imaging.[3] The first OCT-based description using the term LMH was published in 1998 and included an irregular foveal contour, an intraretinal split of the foveal edges, and a near normal perifoveal retinal thickness.[17] With the advent of SD-OCT imaging, other authors refined the definition of this lesion as the presence of irregular foveal contour, break in the inner fovea, intraretinal split and intact foveal photoreceptors.[1, 10] Some authors proposed that only lesions with apparent tissue loss should be named LMH, while other similar-looking changes of the fovea related to ERM contraction with no suggestion of tissue loss on OCT imaging could be called "*macular pseudohole with stretched edges*".[3] The presence or absence of tissue loss was thought to be critical to the distinction between "true" LMH and other entities referred to as macular pseudohole with stretched or lamellar dissection of edges by authors.[3] Similarly, it was suggested that the lesions diagnosed as LMH may consist of two distinct clinical entities, named "*degenerative*" and "*tractional*" LMH.[2] The former, was considered a partial thickness defect in the inner fovea, with foveal cavity with undermined edges, the presence of epiretinal proliferation, frequent disruption of the outer retina and in some cases, the appearance of a central "bump" of presumably spared foveal tissue (supplementary file 4). The latter was characterized by the presence of foveoschisis at the level of Henle's fiber layer, the presence of a tractional ERM, intact photoreceptors, and microcystoid macular edema in the INL. The presence or absence of tissue loss was not considered in the distinction between degenerative and tractional LMH.[2,4]

After evaluation of the previously mentioned reports and the relevant literature, the group of retinal experts proposed a definition of

LMH based on 3 mandatory and 3 optional diagnostic criteria. The diagnosis of LMH should be limited to cases that fulfill all the mandatory diagnostic criteria when optional criteria can also help confirm the diagnosis.

The mandatory criteria for the diagnosis of LMH were the presence of: 1. irregular foveal contour (i.e. abnormal, non-linear shape of the foveal pit contour); 2. foveal cavity with undermined edges; 3. Presence of at least one other sign evoking a loss of foveal tissue, i.e. pseudo-operculum, thinning of the foveal at its center, or around. Associated pathologic changes can include: 1. epiretinal proliferation; 2. foveal bump; 3. ellipsoid line disruption.

As single scan of OCT may miss some features, sufficiently dense central volume acquisition (macular raster with at least inter-scan distances of 120µm) or radial scans is required to allow for adequate analysis of all components that may not be present all around the center of the fovea. En-face OCT reconstructions is also very useful to confirm changes in the foveolar area.

Such a definition is similar to what was previously considered as "*true*" LMH or a "*degenerative*" LMH.[2-3] The concept of foveal cavity with undermined edges was considered by the panel as the key features of LMH. This OCT finding was considered a presumed sign of retinal cell loss that can be present at onset or may worsen with time and is differentiated from other entities such as cystoid spaces and foveoschisis as defined above.

While OCT remains superior to any other imaging modalities in the diagnosis of LMH, this entity can be seen on fundus color photos as roundish usually central lesion, slightly darker than the surrounding retina, on Blue-Fundus Autofluorescence (B-FAF) as roundish usually central lesion slightly brighter than the surrounding retina, on SLO near-infrared imaging it also appears as a dark roundish central lesion, and on fluorescein angiography as hyperfluorescent at early phases (no masking of choriocapillary fluorescence) with no late hyperfluorescence (figure 4). There is increasing evidence that the central fovea has unique features with specialized Müller cells and Henle's fibers containing macular pigment.[15,33,34] The alteration (disappearance and/or displacement) of macular pigment may then explain change in fluorescence on fundus B-FAF imaging.[4,9]

The presence of epiretinal proliferation was considered as a optional criterion for the diagnosis of LMH as it is not always present in such lesions, in particular at early stages.[2,11] Nevertheless, according to the published literature, the presence of epiretinal proliferation was considered an important anatomical and functional landmark, as it has been associated with lower visual acuity and higher rates of photoreceptors disruption.[2,6-7,13]

Similarly, the presence of ellipsoid line disruption was considered as an optional criterion. Although this outer retinal alteration is often visible with OCT in LMH, in many lesions the ellipsoid line is intact. Moreover, outer retinal disruption is a common feature in many macular pathologies.

Mechanical tangential traction does not seem to be critical in the development of LMH as signs of retinal traction are rarely evident, in contradistinction to ERM Foveoschisis.[8] Moreover, the epiretinal proliferation has shown little or no contractile properties as confirmed by en-face OCT (supplementary file 5).[5]

The presence of a foveal “bump” has been considered by many as a distinctive feature of LMH.[2] It can be related and connected to epiretinal proliferation. However, in some lesions it may not be present.

The pathophysiology of LMH is still largely unknown. Its occurrence, possibly in some cases after posterior vitreous detachment and sometimes with the presence of a pseudo-operculum on posterior vitreous cortex, suggests partial avulsion of foveal tissue. Although the term “degenerative” may suggest an additional slow progressive mechanism leading to additional loss of retinal tissue, this concept is still largely speculative, and no related terminology was included by the panel.

Beside posterior vitreous detachment-related LMH we discuss in this paper, which may can be called primary LMH, there may be other causes leading to other types of lamellar lesions involving the foveolar area, with some variants in the appearances of inner and outer lamellar defects depending of the cause. Such lesions may originate from unroofed cystoid macular edema,[16] end-stage age-related macular degeneration,[21] MacTel type 2,[22] Solar retinopathy,[23] Tamoxifen retinopathy,[35] and partial closure of full-thickness macular hole.[36] These lesions filling mandatary signs may be named LMH but be referred to as “non-primary LMH” and should be considered as different at least by etiology as they may not respond similarly to possible treatments of primary LMH.

Epiretinal Membrane Foveoschisis

The presence of foveoschisis in association with an ERM is the most common cause of misdiagnosis of LMH. It is now proposed to be named as "*Epiretinal membrane foveoschisis*" and diagnosed according to 2 mandatory and 3 optional diagnostic criteria, as summarized below and illustrated in figure 5. Similar to LMH, the diagnosis of ERM foveoschisis requires fulfillment of all mandatory criteria.

The mandatory criteria for the diagnosis of ERM foveoschisis were the presence of: 1. contractile ERM; 2. foveoschisis at the level of Henle’s fiber layer.

The optional criteria were the presence of: 1. microcystoid spaces in the INL; 2. retinal thickening; 3. retinal wrinkling.

ERM foveoschisis is included in this classification system as it could lead in some cases to an irregular foveal contour that can be confused with LMH. In the literature these cases have been also previously distinguished but referred to as "*tractional*" LMH and "*macular pseudohole with stretched edges*".[2-3] The panel considered that the word "lamellar hole" for such lesions is confusing. These lesions are likely caused by mechanical displacement and separation of inner and outer retina as in foveoschisis, as supported by a recent biomechanical model.[31]

According to this hypothesis, tissue loss in epiretinal membrane foveoschisis may be negligible. Blue FAF often illustrates hyperreflective

patterns in epiretinal membrane foveoschisis, a finding which can also be correlated with tissue loss in the published literature.[37] However, the pathophysiologic correlation of hyper autofluorescence in these lesions is uncertain and is probably caused by the displacement of macular pigment in the central macula, rather than loss of tissue.

As the interpretation of Blue FAF is still controversial, the authors considered this imaging modality not reliable enough to be included in the diagnostic criteria.

The OCT finding of a contractile ERM, best appreciated on en-face OCT, appeared to be critical in the development of foveoschisis and, therefore, considered as mandatory diagnostic criteria.[8] Moreover, it represents a key distinction from LMH, in which signs of traction upon the retina are infrequently seen. Another distinction in the presence of vitreo-papillary adhesion, which is four times more prevalent than in LMH.[8]

The terminology "*epiretinal membrane foveoschisis*" differentiates this condition from myopic foveoschisis or stellate non-hereditary idiopathic foveomacular retinoschisis, in which a significant tractional ERM may not be found. Further, the term underscores a causative association between the presence of a tractional ERM and the development of foveoschisis.

Microcystoid spaces in the INL are a frequent finding in tractional disorders such as vitreo-macular traction syndrome, ERM and macular hole, and are often present in ERM foveoschisis.[30] Similarly, retinal thickening and wrinkling very often present may sometimes not be visualized in ERM foveoschisis and were then considered as minor diagnostic criteria.

Macular pseudohole

Similar to the original definition of LMH, the initial concept of macular pseudohole was developed by Allen and Gass using slit-lamp biomicroscopy, and referred to a macular lesion characterized by the presence of an ERM sparing the fovea, with the creation of invaginated or heaped foveal edges.[18] The term "*pseudohole*" was used clinically when fundus examination shows a discrete reddish, round or oval lesion that mimics a full-thickness macular hole. Slit-lamp examination of the macula can sometimes result in a false diagnosis of full-thickness macular hole, but OCT imaging can easily distinguish between the two entities in most cases. macular pseudohole is then only a peculiar appearance of an epiretinal membrane on fundus examination. However, as the terminology is commonly used, the group found it useful to formalize an OCT definition for it as a differential diagnosis to LMH.

The OCT diagnosis of macular pseudohole is based on 3 mandatory and 2 optional criteria, as summarized below and illustrated in supplementary file 6.

Mandatory criteria are: 1. foveal center sparing ERM; and 2. retinal thickening and 3. verticalized or steepened foveal profile.

Minor criteria are: 1. presence of microcystoid spaces in the INL; 2. near normal central foveal thickness.

Such a definition is similar to that previously proposed by the International Vitreomacular Traction Study Group.[24]

Perhaps the defining feature of macular pseudohole is the presence of a concomitant foveal center sparing ERM and verticalized foveal edges. This configuration causes the distortion of the foveal contour into a shape with a steep slope; The ERM is supposed to have a causative role in the development of a pseudohole, as it displaces the retina toward the foveal center via centripetal tangential traction. The result is invagination of the perifoveal retina into a shape that mimics a partial thickness hole.

Conclusions

Consensus has been reached for the definitions of 3 conditions that are often confused in the literature: *lamellar macular hole*, *macular pseudohole* and *epiretinal membrane foveoschisis*. These proposed definitions should help to better distinguish these 3 conditions with the aim of providing uniform language for clinicians and researchers to use when discussing the subject.

Of note, some patients may present with features common to the 3 different conditions. The existence of “mixed” lesions such as LMH with ERM, particularly as both seem to be due to anomalous posterior vitreous detachment, is intrinsic to almost any classification system, and does not negate the terminology presented herein.

We fully recognize that these definitions may evolve with improved imaging, observation, and further study. Thus, classification systems should be dynamic and evolve with advances in our knowledge of diseases and their underlying pathophysiologic mechanisms. However, a consensus nomenclature at this time will facilitate collaboration for future research to improve patient management.

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FIGURE CAPTIONS

Figure 1. Epiretinal proliferation. In this case of lamellar macular hole, the epiretinal proliferation is visible with spectral-domain optical coherence tomography as a thick, homogeneous and iso-reflective preretinal material over the internal limiting membrane (white arrows). The epiretinal proliferation is often covered by a thin hyperreflective line.

Figure 2. Foveal cavity with undermined edges. Lamellar macular holes are characterized by the presence of foveal cavity with undermined edges, seen with spectral-domain optical coherence tomography as large, often confluent intraretinal hyporeflective cystoid spaces, connected with the vitreous cavity through a break in the inner fovea. The foveal cavity with undermined edges can potentially affect all retinal layers.

Figure 3. Foveoschisis. Foveoschisis is visible with spectral-domain optical coherence tomography as a sharp separation between the outer nuclear and outer plexiform layers, at the level of the Henle fiber layer. Intraretinal hyperreflective bridges of tissue (white star), possibly stretched Müller cells bodies, connect inner and outer retina, and are separated by hyporeflective intraretinal spaces.

Figure 4. Lamellar macular hole: multimodal imaging. A. Optical coherence tomography imaging. Optical coherence tomography illustrates a typical lamellar macular hole, with irregular foveal contour, foveal cavity with undermined edges and the presence of epiretinal proliferation. The ellipsoid line and the external limiting membrane appear disrupted. **B. Color fundus photo.** Lamellar macular hole appears as a roundish central lesion in the fovea, which is slightly darker than the surrounding retina. **C. Infrared imaging.** Similarly to color fundus imaging, lamellar macular hole appears as a darker area in the central fovea. **D. Fluorescein angiography: early phase.** At early phases fluorescein angiography illustrates a slightly hyperfluorescent lesion slightly temporal to the central fovea. **E. Fluorescein angiography: late phase.** At late phases, the hyperfluorescence is still present but gradually it fades out. **F. Blue-Fundus Autofluorescence.** Lamellar macular hole is visible as a para-central area of increased autofluorescence. **G: En-face optical coherence tomography**. Segmentation at the level of the vitreoretinal interface. No signs of traction like folds and retinal wrinkling are visible in the macular area. The lamellar macular hole appears as a dark circular area just temporal to the fovea.

Figure 5: Epiretinal membrane foveoschisis: multimodal Imaging. A. Optical coherence tomography imaging. Optical coherence tomography illustrates a typical epiretinal membrane foveoschisis, with irregular foveal contour, a contractile preretinal membrane and the presence of foveoschisis at the level of the Henle fiber layer. **B. Color fundus photo.** Epiretinal membrane foveoschisis appears as a roundish central lesion in the fovea, which is slightly darker than the surrounding retina. A contractile epiretinal membrane is visible as a yellowish area over the macula, associated with wrinkling of the underlying retina **C. Infrared imaging.** With infrared imaging, retinal wrinkles are clearly visible. **D. Blue-Fundus Autofluorescence.** Epiretinal membrane foveoschisis is visible as a central area of increased signal. **E. En-face optical coherence tomography.** Segmentation at the level of the vitreoretinal interface. Prominent signs of traction, folds and retinal wrinkling are appreciable in the macular area. The epiretinal membrane foveoschisis appears as a dark area centered in the fovea.