American Journal of Ophthalmology Case Reports 25 (2022) 101249

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

In-vivo visualization of the photoreceptors using Spectralis High Magnification Module imaging in central serous chorioretinopathy

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ARTICLE INFO

Keywords:
High-magnification module
Central serous chorioretinopathy
Photoreceptors
Optical coherence tomography angiography
OCT

ABSTRACT

Purpose: To visualize photoreceptors using the Spectralis High Magnification Module (HMM) in a case of central serous chorioretinopathy (CSCR) and to correlate the findings with those of optical coherence tomography (OCT) and optical coherence tomography angiography (OCT-A).

Observations: A 35-year-old Caucasian male presenting with chronic CSCR in the left eye was examined using HMM, OCT and OCT-A. The photoreceptors mosaic was assessed both in diseased and apparently uninvolved areas. A partial topographic correlation between the loss of photoreceptors on HMM images and an altered reflectivity of the photoreceptor layer on en-face OCT was noted. Interestingly, a correlation between the photoreceptor damage on HMM and choriocapillaris flow-void areas on OCT-A was seen.

Conclusions and Importance: HMM is a non-invasive imaging modality, allowing the in-vivo visualization of photoreceptor damage in a diseased retina. A focal abnormal perfusion of the choriocapillaris might influence the integrity of the overlying photoreceptors in CSCR.

1. Introduction

Central serous chorioretinopathy (CSCR) is a condition in which fluid accumulates under the retina, causing a serous detachment of the neurosensory retina, sometimes associated with retinal pigment epithelium (RPE) detachment.[1] The chronic stages of the disease are characterized by the presence of widespread RPE decompensation with or without SRD, associated or not with active leakage sites.[2]

The introduction of indocyanine green angiography allowed to detect choroidal hyperpermeability as part of the pathophysiological mechanism of CSCR.[3,4] Fundus autofluorescence imaging provides the evidence of structural changes in the photoreceptor and RPE layers.[5] Commonly used techniques to examine the retinal structure and vascular perfusion in CSCR include Optical Coherence Tomography (OCT) and Optical Coherence Tomography Angiography (OCT-A). Nevertheless, due to the limited transverse resolution, these imaging techniques, do not allow to distinguish the photoreceptors as single entities.[6] Adaptive optics (AO) is an innovative technology that allows the acquisition of quasi-histologic photoreceptor images of a resolution up to 2 μm making cells visible as single elements.[7,8] A decrease in cone density has already been reported using AO imaging in CSCR patients.[9–11] Till date, it is considered the best in-vivo imaging technique for human photoreceptors, nevertheless, there are some limitations of AO which restrict the use in clinical settings such as limited scanning field, separate set-up for clinical imaging, higher cost and long acquisition time.[12]

A novel imaging modality, the Spectralis High Magnification Module (HMM, Spectralis ®, Heidelberg Engineering, Germany), has recently been introduced, as a lens-attachment for the company's Spectralis confocal scanning laser ophthalmoscope, providing an optimized visualization of the retinal photoreceptors mosaic pattern (Fig. 1).[13] It is designed to visualize in detail ocular fundus structures with a higher resolution (1.47 μm/pixel) without the need for pupillary dilation.[13] To acquire an optimized image, it is mandatory to minimize the pupil size to about 1.5 mm and maintain the room light. It magnifies the fundus image with a field of view of about 8° × 8° (2500 μm × 2500 μm

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https://doi.org/10.1016/j.ajoc.2021.101249
Received 8 June 2021; Received in revised form 19 October 2021; Accepted 30 December 2021
Available online 31 December 2021
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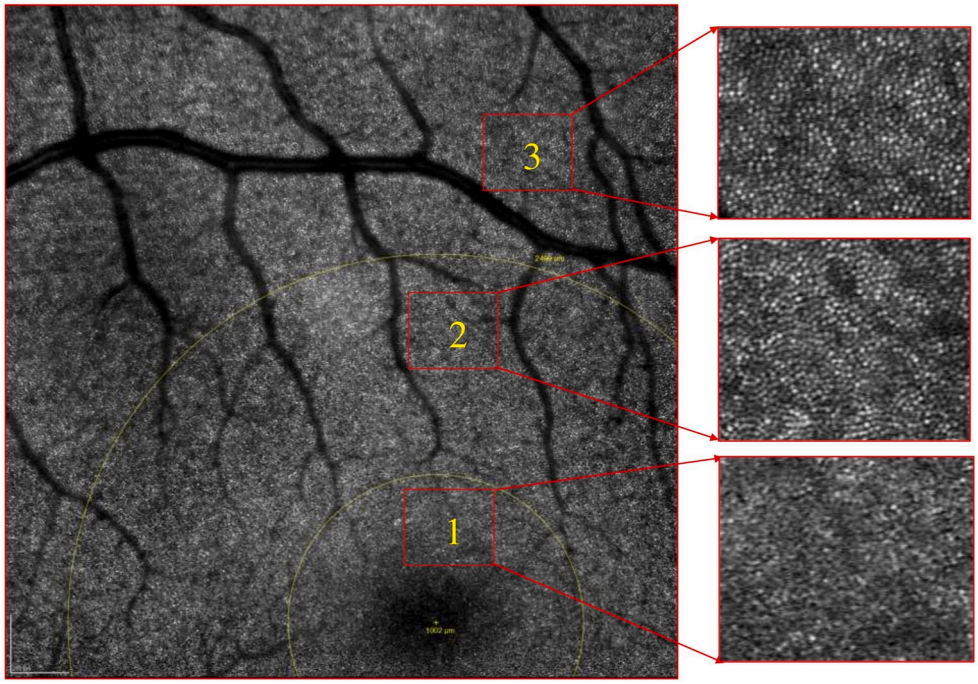

Fig. 1. A normal mosaic pattern of the photoreceptors in foveal area (zone 1), parafoveal area (zone 2) and perifoveal area (zone 3) in a healthy eye imaged on Spectralis High Magnification Module.

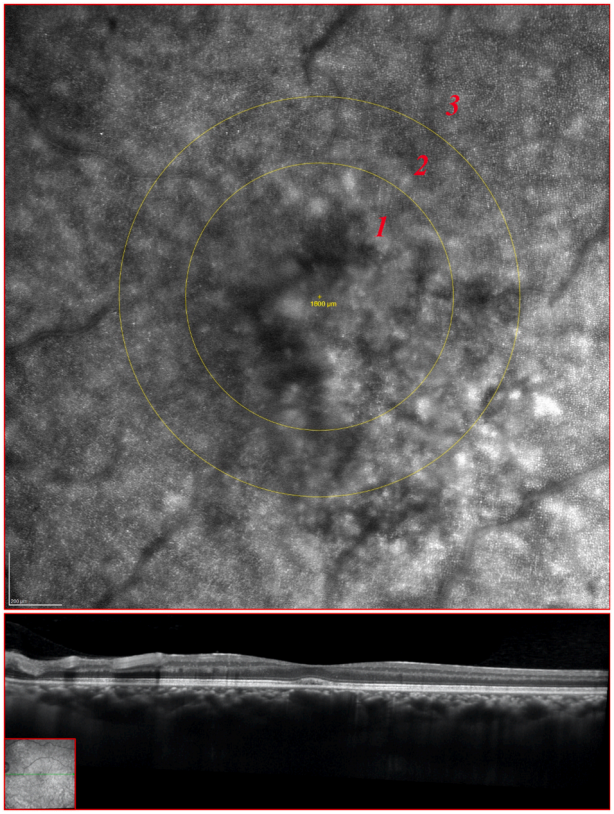

Fig. 2. The HMM image of the macula of the reported chronic-CSCR patient showing photoreceptors representation and its morphology in different areas distinguished as zone 1 (foveal area), zone 2 (parafoveal area), and zone 3 (perifoveal area) and corresponding to structural OCT B-scan (bottom image) passing through the foveal center.

approximately).[13] Once identified a region of interest on 30° lens, the HMM module it's applied to acquire magnified images of a certain area in order to investigate its microstructure of the cone mosaic. Advantages of HMM include easy applicability in clinical settings, faster acquisition time and reproducibility.

So far, there are no reports which correlate high-resolution images of photoreceptors with more commonly used imaging techniques such as OCT/OCT-A in CSCR. Correlation of photoreceptor mosaic with changes on structural OCT and angiographic alterations on OCT-A could contribute further in the pathogenesis of CSCR. Aim of the case report is to integrate the HMM findings with OCT and OCT-A imaging modalities in a case of chronic-CSCR.

2. Case report

A 35-year-old Caucasian male with no past medical history or family history and with a recent diagnosis of CSCR in his left eye, was referred to our ophthalmological department since complaining of persistent blurred vision and metamorphopsias from six months. Best-corrected visual acuity was 20/20 in the right eye and 20/32 in the left eye. Intraocular pressure was normal on both eyes. Anterior segment slit lamp examination was unremarkable. The fundus examination of the right eye was within normal limits while the left eye fundus showed some focal pigmentary changes in macular area. The patient underwent spectral-domain OCT (Spectralis ®, Heidelberg Engineering) imaging that revealed a minimal sub-foveal neurosensory detachment. Moreover, OCT-A and HMM imaging modalities were acquired. The Spectralis OCT2 (Heidelberg Engineering, Heidelberg, Germany), based on a probabilistic amplitude decorrelation algorithm, was used to acquire OCT-A images.[14] The diagnosis of chronic-CSCR was confirmed and, due to the limited amount of subretinal fluid accumulation, a watchful waiting strategy was adopted.

On HMM imaging, the photoreceptor damage appeared as extensively involving the foveal area (zone 1) and the parafoveal area (zone 2). The perifoveal area (zone 3) was having only a minimal involvement, mostly in the inferior sectors (Fig. 2). To define the different areas on HMM images, according to the published literature, two concentric

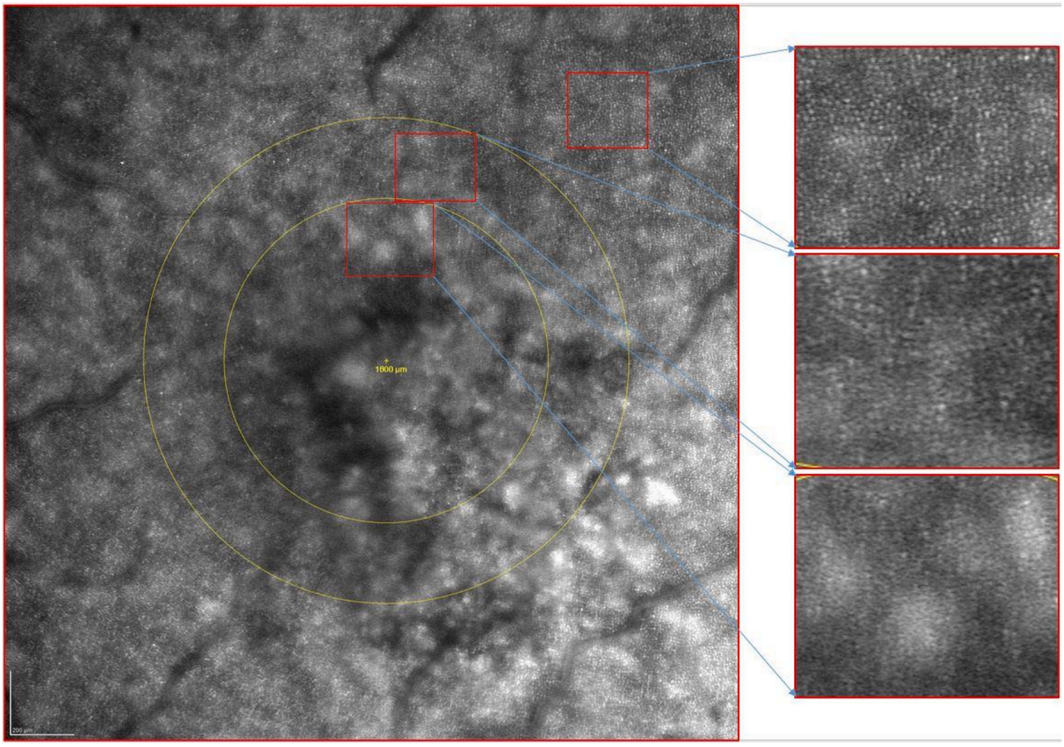

Fig. 3. The HMM imaging showing a mosaic pattern of photoreceptors with bright (hyperreflective) spots in zone 3; some blurred hyporeflective areas with few hyperreflective dots in lesion areas (Zone 1 & 2).

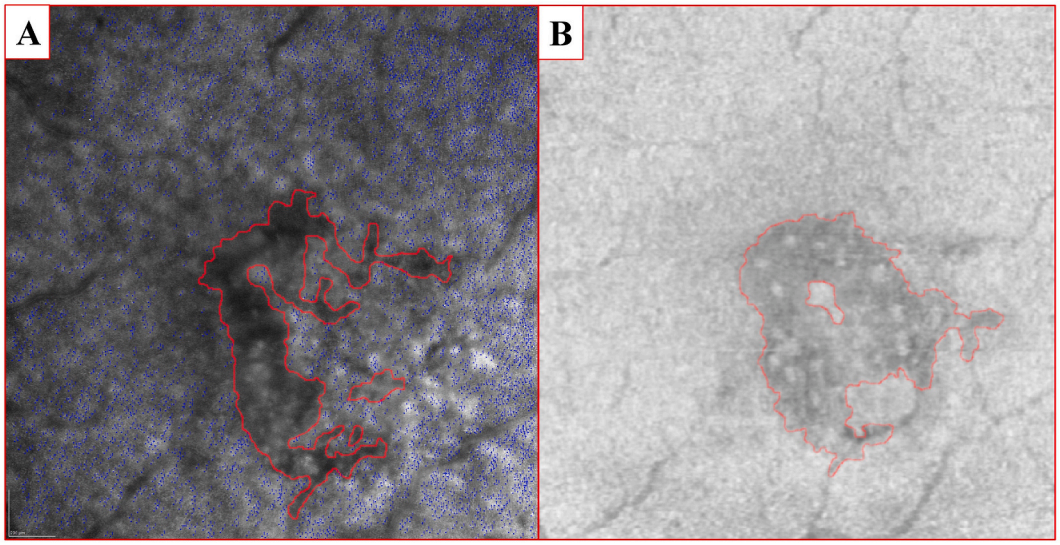

Fig. 4. Topographical correlation between the HMM imaging modality (A) and the photoreceptors layer (PR1-PR2) of the structural en-face OCT scan (B). On HMM image the photoreceptors are highlighted with blue marks from the manual cone quantification plugin of the ImageJ software. The red line outlines in both images (A–B) the area of photoreceptors loss. A partial correlation between these two imaging modalities is shown since the photoreceptor damage visualized on en-face OCT scan seems more extensive than the corresponding one on HMM. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

circles with diameters of 1000 and 2500 μm were positioned centered on the foveal depression using the in-built software of the Spectralis ® OCT device (Heidelberg Eye Explorer, Heyex, Heidelberg Engineering, Heidelberg, Germany). The inner circle with 1000 μm diameter outlines the foveal area, the area between 1000 μm and 2500 μm is the parafoveal area and the area between 2500 μm and 5000 μm is the perifoveal area.[15] This distinction of the macular area into three different zones is made necessary since the photoreceptors packing density and distribution vary across the retina, especially within and around the fovea.[16,17] Therefore, the absence of a definite mosaic pattern in foveal area (Fig. 1), where cones are strongly close together might be due to a resolution limit, that makes the device unable to distinguish the photoreceptors as single entities when so close one to the other. The photoreceptor density at 1 mm from the foveal center in the current CSCR case was 6049.1 cells/mm.[2]

The HMM imaging showed the photoreceptor pattern as a mosaic of

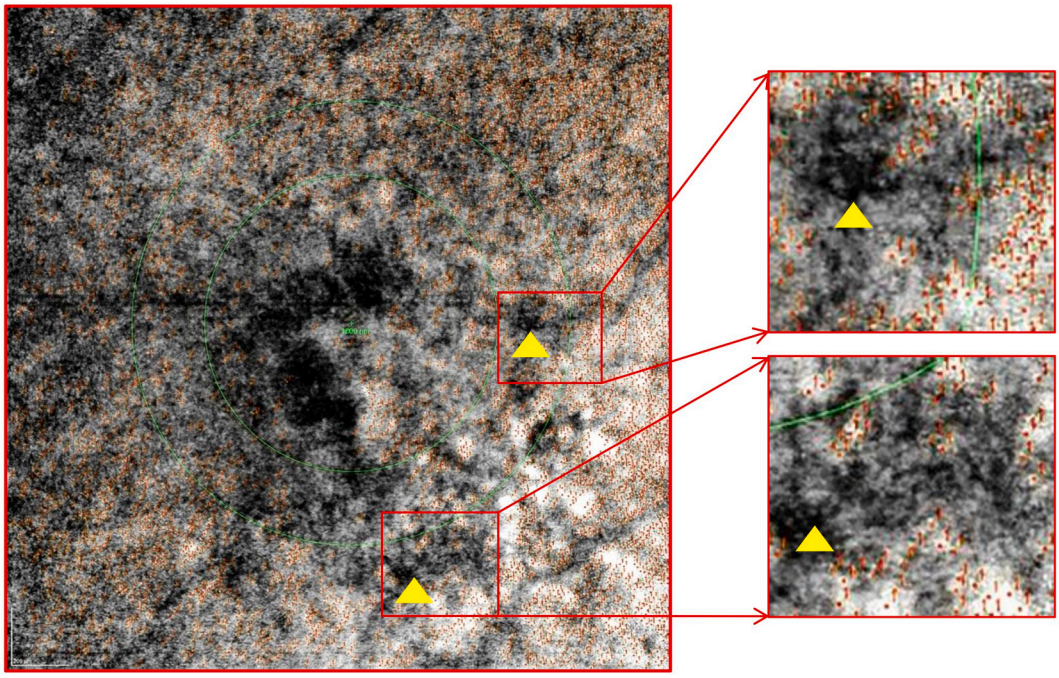

Fig. 5. The photoreceptor mosaic (orange dots) is superimposed on the OCT-angiogram of the choriocapillaris (CC). A clear correlation between abnormally perfused areas (flow-voids) in the CC and focal loss of photoreceptors is shown (yellow arrowheads). . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

hyperreflective spots in zone 3; some blurred hyporeflective areas with few hyperreflective dots were shown in lesion areas (Zone 1& 2) (Fig. 3). A partial topographical correlation was seen between the photoreceptor loss on HMM and the photoreceptor layer (PR1-PR2 on Spectralis automated segmentation algorithm) of the structural en-face OCT (Fig. 4). The OCT-A revealed focal flow void areas in the choriocapillaris (CC) layer. Interestingly, a topographical correlation between the photoreceptor damage on HMM and CC flow-void areas on OCT-A was seen on superimposed images (automated overlay tool, Adobe Photoshop software CS6,13.0.1, https://www.adobe.com/products/photoshop.html) (Fig. 5).

3. Discussion

CSCR is characterized by an idiopathic serous neurosensory detachment in the macula which often induces a disruption of the ellipsoid zone where outer segments of the photoreceptors are located.[11] CSCR might cause a significant decrease in photoreceptor density, even in patients with a very good visual acuity.[18] A new imaging challenge might be visualizing in vivo the morphology of photoreceptors and their changes in a diseased eye. Therefore, we used the novel Spectralis HMM in addiction to conventional tomographic imaging modalities to evaluate a patient with chronic-CSCR.

The HMM seem able to visualize the cones as single cell entities. Indeed, our acquisitions performed in healthy retinal zones, clearly showed the classical mosaic pattern of hexagonal hyperreflective elements and their density distribution that progressively decreases from the central fovea to the perifoveal quadrants. Areas of damaged or not-aligned cones appear as darker patches, similar to those described by Ooto et al. using AO in CSCR.[10] Moreover, although coming from a single patient, our quantitative results (6049.1 cells/mm^2) show a certain degree of similarity with those of Ooto at al that reported a cone density at 1 mm from the center of the fovea of 6860 cells/mm.[2,10] Further studies are needed to evaluate the role of HMM modality as a potential alternative to AOSLO imaging.

Unexpectedly we found only a partial topographical correlation between the extension of the area of cells loss visualized on HMM modality and the area of photoreceptor layer damage detected on en-face OCT modality. The damaged area was more extensive in structural en-face OCT compared to HMM modality, suggesting that the latter has a higher sensitivity to detect spared photoreceptors within the lesion.[19]

Another interesting finding was the topographic correlation between areas of photoreceptor loss visualized on HMM modality and areas of impaired perfusion at the CC (flow-void areas) detected on OCT-A.[20] This correlation might support the hypothesis that a relevant rate of photoreceptors damage could arise from the depletion of nutrient and oxygen support supplied from the underlying CC, instead of a mechanical stress due to the subretinal fluid accumulation. Nevertheless, further studies on larger cohorts would be needed to confirm these findings. Follow up studies using such high-resolution multimodal imagining will explore further in pathogenesis by correlating progressive CC loss on OCTA with structural loss on HMM, with further quantification.

To our knowledge, this is the first patient with chronic CSCR imaged on HMM imaging modality as well as with conventional tomographic imaging. This technology provided a reliable non-invasive visualization of the photoreceptor mosaic both in diseased and healthy areas.

In conclusion, the HMM is a non-invasive imaging modality, which may lead to a better understanding of the relationship between photoreceptor alteration and the functional performance in CSCR.

Patient consent

Consent to publish this case report has been obtained from the patient in writing.

Funding

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: RG, AM, CC, CM, FCP, JC, ML. The authors report no financial disclosures, grants, or any other supports relevant to this study.

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