



Answer: vascular changes in age-related macular degeneration

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We were very pleased by the paper of Borrelli and colleagues (1) and we would thank for their consideration. Nowadays, macular diseases, such as age-related macular degeneration (AMD) underwent a strong improvement in terms of pathophysiology understanding and treatments efficacy monitoring, thank to multimodal imaging techniques. These methodologies are reliable, feasible, easily reproducible, and provide very detailed microstructural information regarding retinal status in a non invasively way. Their introduction in clinical practice opened new frontiers for the ophthalmologists to face macular diseases. One of the most recently introduced technique is optical coherence tomography angiography (OCTA), which offered for the first time the opportunity to study in detail the retinal vascular network without the adoption of dye. Although multimodal imaging is mainly analyzed from the qualitative point of view, in the last years even more advanced quantitative approaches were introduced to further improve the amount of information reached by images analyses. In the context of OCTA, vessel density still represents the most used measure; it provides useful information regarding vascular deficits occurring in macular diseases (2). However, vessel density reductions resulted not pathognomonic of given retinal diseases.

From this point of view, Borrelli and colleagues already showed how the adoption of even more sophisticated quantitative approaches can provide further details regarding structural changes occurring in macular diseases. In particular, they highlighted the differences between different AMD stages. For example, the deep study of choriocapillaris changes revealed an effect of drusen onset and progression in the peri-drusen region of the choriocapillaris, which showed remarkable decreases of

vascular perfusion (3,4). Furthermore, the choriocapillaris perfusion resulted highly deteriorated in patients affected by choroidal neovascularization (CNV) (5). The vascular impairment of this plexus resulted also linked with

functional alterations found by multifocal electroretinography, reflecting a phoreceptors damage (6).

In our previous paper, we proposed new quantitative parameters for the characterization of retinal vascular network features, namely vessel tortuosity, vessel dispersion and vessel rarefaction (7). Our attempt was to provide information regarding the amount of perfusion through the tortuosity quantification of retinal vacular plexa. Moreover, vessel dispersion would reflects the disorganization of the retinal vascular network, starting from the assumption that pathologic changes may lead to a disomogeneities of vessels distribution. Vessel rarefaction represents a measure of the distance between each retinal capillary, which was supposed to be increased after a reduction of the blood flow perfusion. Overall considered, these parameters allowed to characterized the different vascular features of eyes affected by early/intermediate AMD as well as of eyes affected by AMD-related choroidal neovascularization (CNV) (7).

Although the main criticism related with these new parameters is the lack of histological validation, these should be considered optimistically since they might be the basis for the extrapolation of new quantitative biomarkers for a better patients' categorization as well as for the prediction of the outcome reachable after treatments.

In conclusion, the quantitative analysis of retinal imaging techniques represents a promising way to increase our set of tools for the management of patients affected by macular diseases. Future prospective studies should be focused on the better interpretation of these quantitative biomarkers as

well as on their validation through histological analyses.

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