Editorial Commentary

Comment: bleaching of photoreceptors in eyes with reticular pseudodrusen

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Reticular pseudodrusen (RPD) represents a distinct phenotype of age-related macular degeneration (AMD) that is characterized by worse macular function and an overall greater occurrence of development of both forms of late AMD (1-5).

Based on both *in vivo* and *ex vivo* observations, RPD are known to be associated with a fibrotic replacement of the choroidal vessels (6), this resulting in a choroidal thinning (7-11) and choriocapillaris hypoperfusion (12,13). The latter features were speculated to cause a dysfunction of the retinal pigment epithelium (RPE) and resulting disturbance in turnover of the photoreceptor outer segment (OS) (14), this ultimately causing the accumulation of photoreceptor OS over the RPE (15,16). Alternatively, RPE cells may fail to bind or uptake cycled lipids, this eventually leading to the accumulation of lipids above the RPE (16).

As specified above, the presence of RPD is associated with worse visual function. As an example, dark adaptation, which is an indicator of macular function, is known to be impaired in eyes with AMD, especially in presence of RPD. Dark adaptation can be described as the deferred recuperation of light responsiveness in darkness after photobleaching (light exposure). Using structural optical coherence tomography (OCT), important studies on healthy subjects have demonstrated that exposure to light (photobleaching), and the following recuperation in the dark, is characterized by distinguishing modifications in the measures of photoreceptor OS (17-20).

In a recent study (21), our group employed structural OCT to investigate photoreceptors' structural modifications following photobleaching and throughout the successive recuperation in darkness, in intermediate AMD eyes, with and without RPD. In details, we prospectively enrolled 20 eyes of 20 intermediate AMD patients and 15 matched controls without disease. In normal subjects, our data demonstrated that photobleaching is followed by an increase in OS volume in the foveal region. This expansion was succeeded by a rapid recuperation of baseline values. Similarly, in the perifoveal region, healthy subjects had a late expansion of the photoreceptors' OS (approximately 10 minutes after photobleaching). Importantly, the OS thickening was speculated to be secondary to an osmotic swelling reaction following a phototransduction-related raise in OS osmolarity (18,19). On contrary, in intermediate AMD eyes with RPD, this physiologic response was significantly affected as these eyes were characterized by an early and longstanding photoreceptor OS broadening after photobleaching, without a significant recuperation.

Assuming that OCT structural modifications following photobleaching could be contemplated as an imaging surrogate for functional dark adaptation, this study further corroborated the theory that eyes with RPD are characterized by a significant damage in dark adaptation. This reflects a larger impairment of the unit comprised of photoreceptors and RPE in RPD eyes (1). These results are helpful to further understand the disease pathophysiology.

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References

1. Flamendorf J, Agrón E, Wong WT, et al. Impairments in dark adaptation are associated with age-related macular degeneration severity and reticular pseudodrusen. Ophthalmology 2015;122:2053-62.
2. Thorell MR, Goldhardt R, Nunes RP, et al. Association Between Subfoveal Choroidal Thickness, Reticular Pseudodrusen, and Geographic Atrophy in Age-Related Macular Degeneration. Ophthalmic Surg Lasers Imaging Retina 2015;46:513-21.
3. Sohrab MA, Smith RT, Salehi-Had H, et al. Image Registration and Multimodal Imaging of Reticular Pseudodrusen. Invest Ophthalmol Vis Sci 2011;52:5743-8.
4. Querques G, Massamba N, Srour M, et al. Impact of reticular pseudodrusen on macular function. Retina 2014;34:321-9.
5. Zhou Q, Daniel E, Maguire MG, et al. Pseudodrusen and Incidence of Late Age-Related Macular Degeneration in Fellow Eyes in the Comparison of Age-Related Macular Degeneration Treatments Trials. Ophthalmology 2016;123:1530-40.
6. Arnold JJ, Sarks SH, Killingsworth MC, et al. Reticular pseudodrusen: A risk factor in age-related maculopathy. Retina 1995;15:183-91.
7. Corvi F, Souied EH, Capuano V, et al. Choroidal structure in eyes with drusen and reticular pseudodrusen determined by binarisation of optical coherence tomographic images. Br J Ophthalmol 2017;101:348-52.
8. Switzer DW, Mendonça LS, Saito M, et al. Segregation of ophthalmoscopic characteristics according to choroidal thickness in patients with early age-related macular degeneration. Retina 2012;32:1265-71.
9. Garg A, Oll M, Yzer S, et al. Reticular pseudodrusen in early age-related macular degeneration are associated with choroidal thinning. Invest Ophthalmol Vis Sci 2013;54:7075-81.
10. Querques G, Querques L, Forte R, et al. Choroidal changes associated with reticular pseudodrusen. Invest Ophthalmol Vis Sci 2012;53:1258-63.
11. Capuano V, Souied EH, Miere A, et al. Choroidal maps in non-exudative age-related macular degeneration. Br J Ophthalmol 2016;100:677-82.
12. Nesper PL, Soetikno BT, Fawzi AA. Choriocapillaris Nonperfusion is Associated With Poor Visual Acuity in Eyes With Reticular Pseudodrusen. Am J Ophthalmol 2017;174:42-55.
13. Cicinelli MV, Rabiolo A, Marchese A, et al. Choroid morphometric analysis in non-neovascular age-related macular degeneration by means of optical coherence tomography angiography. Br J Ophthalmol 2017;101:1193-200.
14. Curcio CA, Messinger JD, Sloan KR, et al. Subretinal drusenoid deposits in non-neovascular age-related macular degeneration: morphology, prevalence, topography, and biogenesis model. Retina 2013;33:265-76.
15. Rabiolo A, Sacconi R, Cicinelli MV, et al. Spotlight on reticular pseudodrusen. Clin. Ophthalmol 2017;11:1707-18.
16. Rudolf M, Malek G, Messinger JD, et al. Sub-retinal drusenoid deposits in human retina: Organization and composition. Exp Eye Res 2008;87:402-8.
17. Li Y, Fariss RN, Qian JW, et al. Light-Induced Thickening of Photoreceptor Outer Segment Layer Detected by Ultra-High Resolution OCT Imaging. Invest Ophthalmol Vis Sci 2016;57:OCT105-11.
18. Zhang P, Zawadzki RJ, Goswami M, et al. In vivo optophysiology reveals that G-protein activation

triggers osmotic swelling and increased light scattering of rod photoreceptors. Proc Natl Acad Sci U S A 2017;114:E2937-46.
19. Lu CD, Lee B, Schottenhamml J, et al. Photoreceptor layer thickness changes during dark adaptation observed with ultrahigh-resolution optical coherence tomography. Invest Ophthalmol Vis Sci 2017;58:4632-43.
20. Abràmoff MD, Mullins RF, Lee K, et al. Human photoreceptor outer segments shorten during light adaptation. Invest Ophthalmol Vis Sci 2013;54:3721-8.
21. Borrelli E, Costanzo E, Parravano M, et al. Impact of Bleaching on Photoreceptors in Different Intermediate AMD Phenotypes. Transl Vis Sci Technol 2019;8:5.

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