

Asymmetrical behaviour of disappearance of reticular pseudodrusen in both eyes during long-term follow-up with spectral domain optical coherence tomography

Abstract

Objective: To describe asymmetrical disappearance of reticular pseudodrusen (RPD) in patients with age-related macular degeneration (AMD).

Methods: SDOCTs and infrared images of four patients with RPD were retrospectively collected and evaluated during long-term follow-up of up to 47 months (range 35–47 months).

Results: Unilateral fading of RPD was detected on SDOCTs and infrared images in eyes with and without choroidal neovascularisation (CNV) and intravitreal injections. Presence of RPD in the fellow eyes remained stable in three cases, in one case very few RPD newly developed. Three of the four cases demonstrated unilateral outer retinal atrophy following regression of RPD.

Conclusions: This report highlights that RPD may almost completely disappear after occurrence and treatment of CNV in neovascular AMD, but also in dry AMD without any treatment and that this phenomenon may be unilateral.

Keywords: reticular pseudodrusen, disappearance, age-related macular degeneration, spectral domain optical coherence tomography

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Introduction

Reticular pseudodrusen (RPD) have been identified as a risk factor for late age-related macular degeneration (AMD) [1], [2], [3]. RPD can be visualized on blue-channel fundus photography and near infrared, red-free or autofluorescence images obtained with a scanning laser ophthalmoscope (SLO) [4]. On spectral domain optical coherence tomography (SDOCT), subretinal hyperreflective material is seen in those eyes. Histologically, RPD are corresponding to subretinal drusenoid deposits [5].

Choroidal thinning in eyes with RPD and early AMD as well as the localization of RPD related to choroidal watershed zones suggest involvement of the choroid and a possible influence of choroidal hypoxia for pathogenesis [6], [7].

Querques et al. recently analysed progression and fading of single RPD on SDOCT in eyes with dry AMD, suggesting that RPD are dynamic structures [8].

In our case series, we describe nearly complete disappearance of RPD on SDOCT and infrared images during long-term follow-up in AMD patients with and without choroidal neovascularisation (CNV), and demonstrate asymmetrical behaviour in both eyes.

Case reports

SDOCT and infrared images of 4 patients with RPD, who were examined during retina clinic at the Department of

Ophthalmology at the University of Cologne, were collected. The presence of RPD on infrared images as well as the presence of subretinal drusenoid deposits on SDOCT volume scans was evaluated on all available follow-up images. Ophthalmic history including history of intravitreal injections was reviewed. This study adhered to the tenets set forth in the Declaration of Helsinki.

Case 1

A 79-year-old male presented with decrease in vision in his left eye due to neovascular AMD. His right eye showed dry AMD with RPD (Figure 1A), his left eye predominantly classic CNV and RPD (Figure 1B). Visual acuity was 20/25 in the right and 20/100 in the left eye. The left eye was treated with 13 intravitreal ranibizumab injections over 35 months. His right eye did not develop CNV during follow-up and did not receive any therapy. Twenty-five months after baseline, the subretinal deposits on SDOCT started to disappear in the right eye. After 35 months, nearly all RPD in the macular area had disappeared on the infrared image and the photoreceptor layer in this area appeared disturbed on SDOCT (Figure 1C). In the left eye, RPD appeared stable during follow-up (Figure 1D).

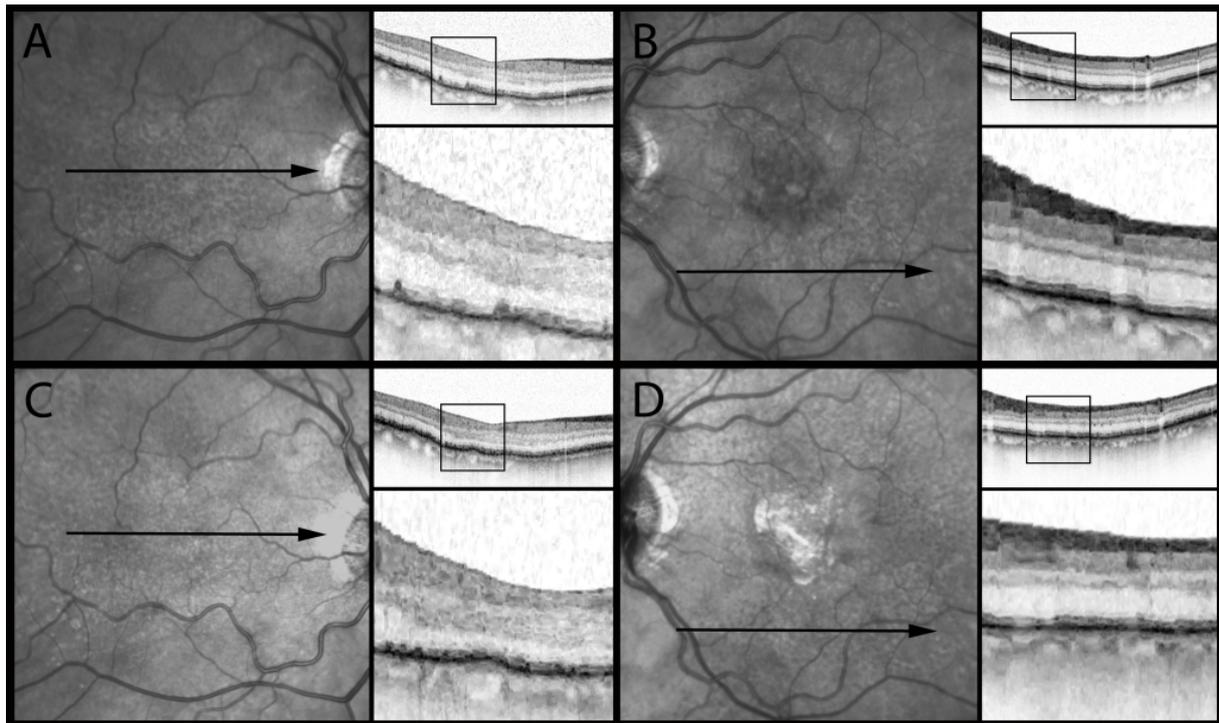


Figure 1: Spectral domain optical coherence tomography (SDOCT) and infrared images of Case 1. **A:** Large number of reticular pseudodrusen (RPD) is visible within the macular area on infrared imaging in the right eye. SDOCT shows subretinal deposits with a maximum of stage 3 according to Zweifel et al. **B:** Large number of RPD is visible within the macular area on infrared imaging in the left eye. SDOCT shows subretinal deposits with a maximum of stage 3. **C:** After 35 months, number and severity of RPD significantly decreased within the macula on infrared and SDOCT in the right eye. Photoreceptor layer disturbance and alterations of the ellipsoid band are visible. **D:** RPD in the left eye appeared stable.

Case 2

A 68-year-old female presented with neovascular AMD in her left eye. Her right eye showed dry AMD and few RPD (Figure 2A), her left eye occult CNV without RPD (Figure 2B). Visual acuity was 20/32 in the right and 20/400 in the left eye. After 23 months, the number of RPD had increased in the right eye (Figure 2C). One month later, the right eye developed occult CNV and was treated with intravitreal ranibizumab. At 29 months follow-up, the number of RPD had decreased. After 9 injections of ranibizumab, 43 months after baseline, no subretinal deposits were visible on SDOCT scans, only few RPD were present near the superior vascular arcade on infrared images (Figure 2E). The left eye was treated with a total of 10 injections and SDOCT scans did not show RPD during follow-up (Figure 2D, 2F).

Case 3

A 80-year-old male presented with neovascular AMD with predominantly classic CNV and few RPD on his right eye (Figure 3A) and dry AMD and RPD in his left eye (Figure 3B). Visual acuity was 20/32 in the right and 20/50 in the left eye. The right eye received 22 intravitreal ranibizumab injections during 47 months follow-up, RPD remained stable (Figure 3C). Thirty-two months after baseline, the left eye developed predominantly classic CNV. At 43 months follow-up, after 5 injections of ranibi-

zumab, RPD started to disappear. No further injections were required. After 47 months, RPD had nearly completely disappeared on infrared imaging and only few remaining subretinal deposits were visible on SDOCT (Figure 3D).

Case 4

A 81-year-old female presented with dry AMD and RPD in her right eye (Figure 4A) and predominantly classic CNV and RPD in her left eye (Figure 4B). Visual acuity was 20/20 in the right and 20/40 in the left eye. RPD in the right eye remained approximately stable during follow-up (Figure 4C). The left eye showed a decrease of RPD at 22 months follow-up after 12 ranibizumab injections. After 47 months, following 25 intravitreal injections, progressive decrease of RPD and subretinal deposits was detected on infrared and SDOCT images (Figure 4D).

Discussion

RPD were first described on color fundus photography in 1990 [9]. SDOCT imaging allows a more detailed analysis of pathological changes in eyes with RPD [10], leading to a new definition and staging system of the disease [5]. Pumariega et al. described fading of RPD on color fundus photographs in eyes with and without CNV over a three-year period [11]. Smith et al. detected fading of RPD in cases with CNV on infrared images using a SLO [2].

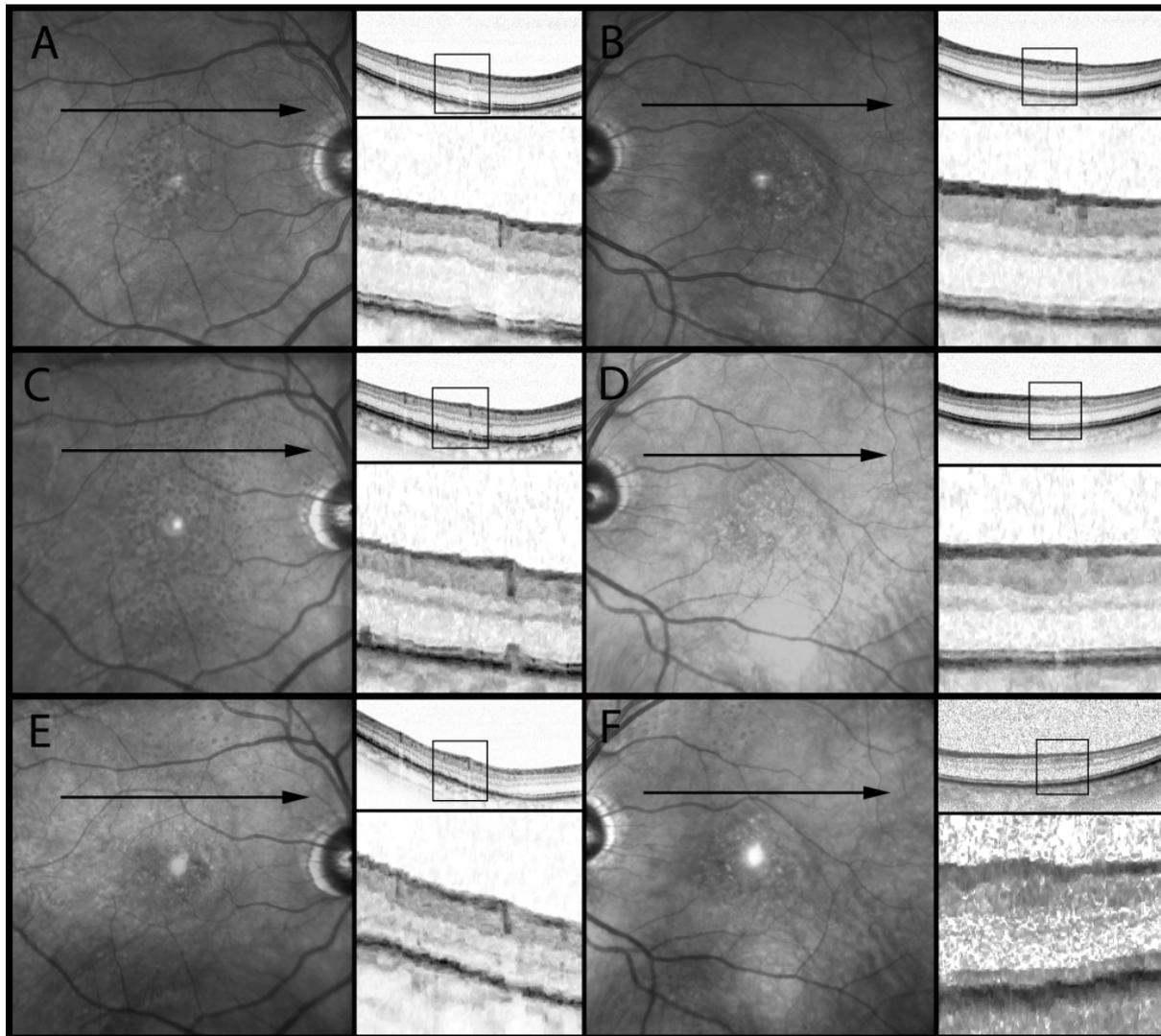


Figure 2: Spectral domain optical coherence tomography (SDOCT) and infrared images of Case 2. **A:** Few reticular pseudodrusen (RPD) were visible in the right eye with a maximum of stage 3 of subretinal deposits according to Zweifel et al. on SDOCT. **B:** Left eye showed no RPD. **C:** After 23 months, the number of RPD increased in the right eye. **D:** Left eye showed no RPD on SDOCT scans. **E:** After 43 months, RPD nearly completely disappeared within the macula on infrared and SDOCT in the right eye. Outer retinal thinning is visible at this time point. **F:** On SDOCT scans, no RPD could be detected. On the infrared image, there is evidence for few new RPD at the superior vascular arcades.

Querques et al. reported progression followed by fading of singular subretinal deposits on SDOCT images [8]. The reported changes suggest that RPD are dynamic structures. Progression and fading of single subretinal deposits may result in changes of the RPD-pattern on infrared images, however, complete disappearance of RPD may rather be explained by external influencing factors such as inflammatory stimuli following intravitreal injections or ophthalmic surgery as described for soft drusen [12].

In three of our 4 reported patients, RPD disappeared after CNV occurrence and treatment. One patient showed disappearance of RPD without CNV development or treatment for other ophthalmic diseases, indicating that CNV development, intravitreal injections or surgery may not fully explain this finding. In addition, all 4 cases show only unilateral disappearance of RPD.

Outer retinal atrophy with thinning of the photoreceptors and loss of the ellipsoid band has been described previously following regression of RPD [13]. In accordance with this, outer retinal alterations and thinning are visible in three of our cases after RPD regression.

A limitation of the detection of progression and regression of RPD on SDOCT is a possible misalignment of SDOCT scans during follow-up [14]. Fading of individual RPD may be misinterpreted, if e.g. RPD are located between two B-scans in the following SDOCT examination. However, it seems unlikely that all RPD visible on one visit are not captured on another visit. Further, a gradual decrease of subretinal deposits was detected over a long follow-up time corresponding to a decrease of RPD on infrared images. Therefore, fading of RPD in our cases is more likely than missing detection caused by misalignment of OCT scans.

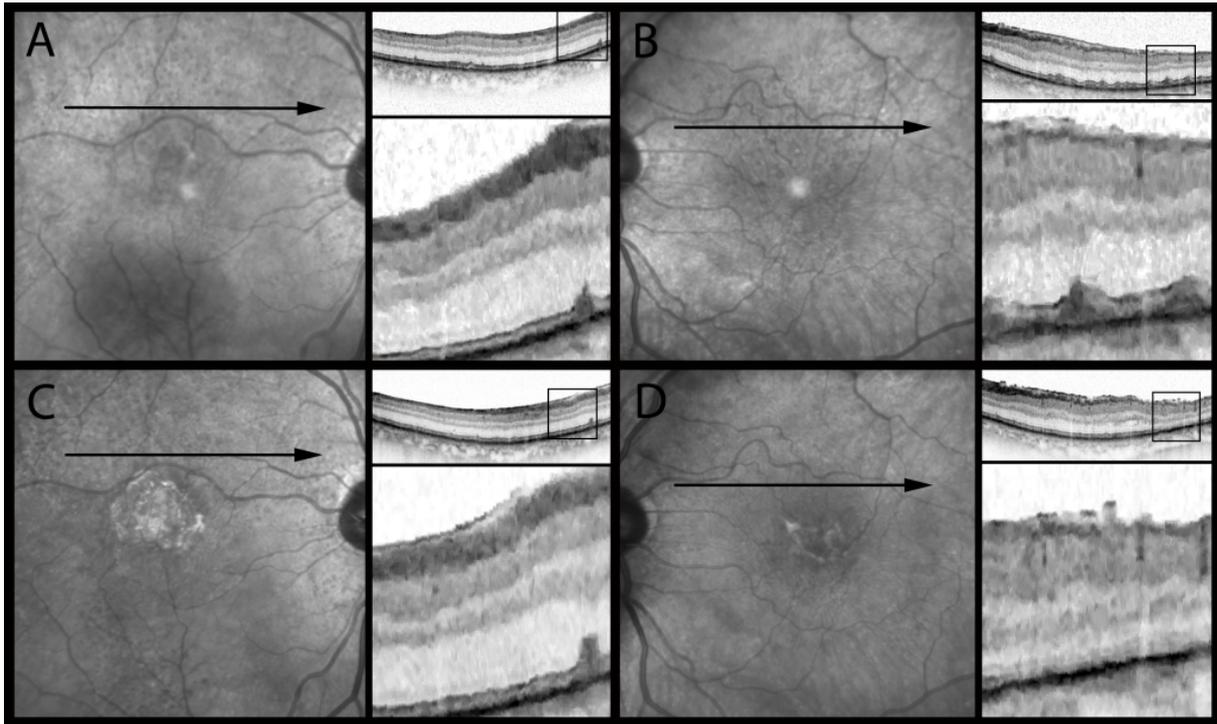


Figure 3: Spectral domain optical coherence tomography (SDOCT) and infrared images of Case 3. **A:** Reticular pseudodrusen (RPD) are visible within the macular area on infrared imaging in the right eye. SDOCT shows subretinal deposits with a maximum of stage 3 according to Zweifel et al. **B:** RPD are visible within the macular area on infrared imaging in the left eye. SDOCT shows subretinal deposits with a maximum of stage 3 of subretinal deposits. **C:** 47 months after baseline, the right eye appeared stable. **D:** RPD nearly completely disappeared within the macula on infrared and SDOCT images in the left eye. Thinning of the outer retina is visible at this time point.

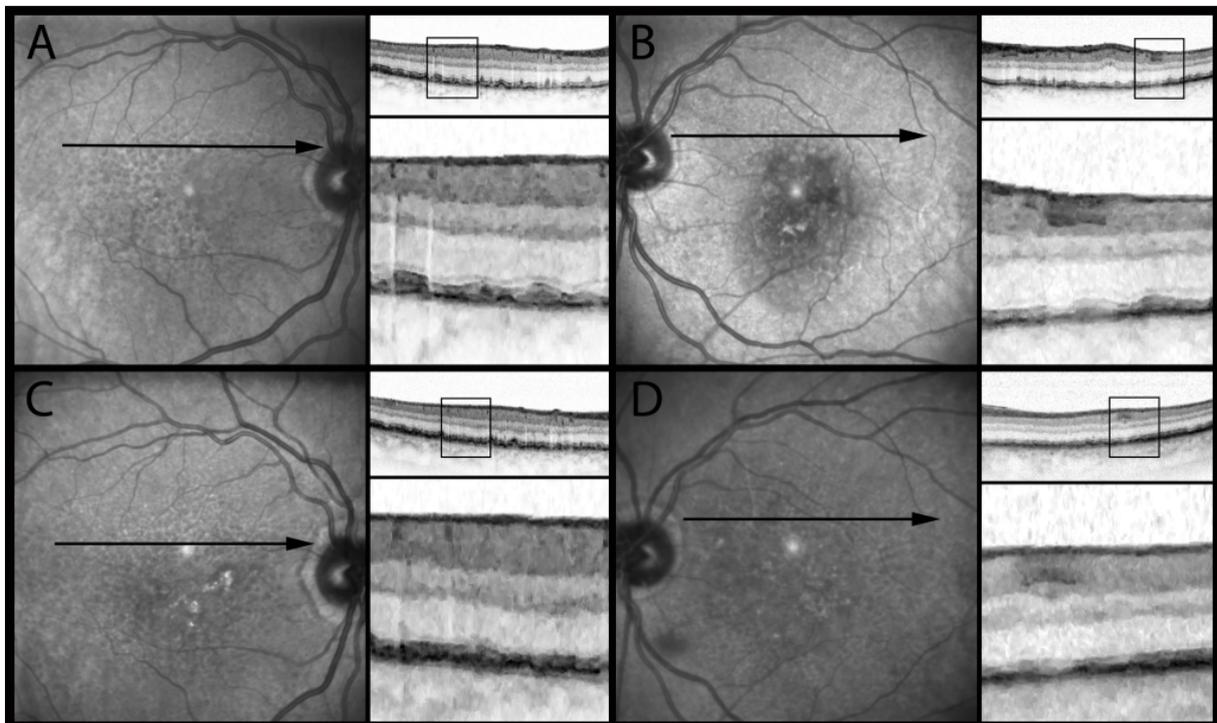


Figure 4: Spectral domain optical coherence tomography and infrared images of case 4. **A:** Reticular pseudodrusen (RPD) are visible within the macular area on infrared imaging in the right eye. SDOCT shows subretinal deposits with a maximum of stage 3 according to Zweifel et al. **B:** RPD are visible within the macular area on infrared imaging in the left eye. SDOCT shows subretinal deposits with a maximum of stage 3 of subretinal deposits. **C:** 47 months after baseline, RPD decreased within the macula on infrared and SDOCT images in the right eye **D:** Left eye appeared approximately stable.

In summary, high resolution SDOCT and infrared imaging allow to identify various stages of RPD and to follow their course over time. The reason for progression or fading of RPD as well as for the asymmetrical behaviour of these changes remains unclear. Careful attention to RPD in clinical practice and studies with a larger cohort of patients and long-term follow-up may help to understand reasons for progression and regression of RPD and to analyse their role in AMD.

Notes

Competing interests

Tina Schick received honoraria for presentations by Novartis Pharma, Germany. Lebriz Ersoy: none. Bernd Kirchhof: none. Sandra Liakopoulos served as a consultant for Novartis Pharma and received honoraria for presentations by Novartis Pharma and Heidelberg Engineering, Germany.

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References

- Zweifel SA, Imamura Y, Spaide TC, Fujiwara T, Spaide RF. Prevalence and significance of subretinal drusenoid deposits (reticular pseudodrusen) in age-related macular degeneration. *Ophthalmology*. 2010 Sep;117(9):1775-81. DOI: 10.1016/j.ophtha.2010.01.027
- Smith RT, Sohrab MA, Busuioc M, Barile G. Reticular macular disease. *Am J Ophthalmol*. 2009 Nov;148(5):733-743.e2. DOI: 10.1016/j.ajo.2009.06.028
- Marsiglia M, Boddu S, Bearely S, Xu L, Breaux BE Jr, Freund KB, Yannuzzi LA, Smith RT. Association between geographic atrophy progression and reticular pseudodrusen in eyes with dry age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2013 Nov;54(12):7362-9. DOI: 10.1167/iovs.12-11073
- Ueda-Arakawa N, Ooto S, Tsujikawa A, Yamashiro K, Oishi A, Yoshimura N. Sensitivity and specificity of detecting reticular pseudodrusen in multimodal imaging in Japanese patients. *Retina (Philadelphia, Pa)*. 2013 Mar;33(3):490-7. DOI: 10.1097/IAE.0b013e318276e0ae
- Zweifel SA, Spaide RF, Curcio CA, Malek G, Imamura Y. Reticular pseudodrusen are subretinal drusenoid deposits. *Ophthalmology*. 2010 Feb;117(2):303-12.e1. DOI: 10.1016/j.ophtha.2009.07.014
- Garg A, Oll M, Yzer S, Chang S, Barile GR, Merriam JC, Tsang SH, Bearely S. Reticular pseudodrusen in early age-related macular degeneration are associated with choroidal thinning. *Invest Ophthalmol Vis Sci*. 2013;54(10):7075-81. DOI: 10.1167/iovs.13-12474
- Alten F, Clemens CR, Heiduschka P, Eter N. Localized reticular pseudodrusen and their topographic relation to choroidal watershed zones and changes in choroidal volumes. *Invest Ophthalmol Vis Sci*. 2013 May;54(5):3250-7. DOI: 10.1167/iovs.13-11923
- Querques G, Canoui-Poitrine F, Coscas F, Massamba N, Querques L, Mimoun G, Bandello F, Souied EH. Analysis of progression of reticular pseudodrusen by spectral domain-optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2012 Mar;53(3):1264-70. DOI: 10.1167/iovs.11-9063
- Mimoun G, Soubrane G, Coscas G. Les drusen maculaires [Macular drusen]. *J Fr Ophtalmol*. 1990;13(10):511-30.
- Sohrab MA, Smith RT, Salehi-Had H, Sadda SR, Fawzi AA. Image registration and multimodal imaging of reticular pseudodrusen. *Invest Ophthalmol Vis Sci*. 2011 Jul;52(8):5743-8. DOI: 10.1167/iovs.10-6942
- Pumariega NM, Smith RT, Sohrab MA, Letien V, Souied EH. A prospective study of reticular macular disease. *Ophthalmology*. 2011 Aug;118(8):1619-25. DOI: 10.1016/j.ophtha.2011.01.029
- Holz FG, Staudt S. Disappearance of soft drusen following macular hole surgery. *Retina (Philadelphia, Pa)*. 2001;21(2):184-6.
- Spaide RF. Outer retinal atrophy after regression of subretinal drusenoid deposits as a newly recognized form of late age-related macular degeneration. *Retina (Philadelphia, Pa)*. 2013 Oct;33(9):1800-8. DOI: 10.1097/IAE.0b013e31829c3765
- Auge J, Steinberg JS, Fleckenstein M, Holz FG, Schmitz-Valckenberg S. Retikuläre Drusen über die Zeit mittels SD-OCT [Reticular drusen over time with SD-OCT]. *Ophthalmologie*. 2014 Aug;111(8):765-71. DOI: 10.1007/s00347-013-2965-0

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