OCT ANGIOGRAPHY IN DISEASES OF THE VITREORETINAL INTERFACE

Dusová J.[1], Studnička J.[1,2], Stěpanov A.[1], Breznayová J.[1,2], Beran D.[1], Tarková A.[1], Jirásková N.[1]

[1]Department of Ophthalmology, University Hospital Hradec Králové, Czech Republic
[2]VISUS, Eye Centrum, Police nad Metují, Czech Republic

The authors of the study declare that no conflict of interests exists in the compilation, theme and subsequent publication of this professional communication, and that it is not supported by any pharmaceutical company. The authors further declare that the study has not been submitted to any other journal, nor has it been printed elsewhere, with the exception of congress abstracts and recommended procedures.

Received: 2 May 2021
Accepted: 19 July 2021
Available online: 15 October 2021

MUDr. Jaroslava Dusová, Ph.D.
Oční klinika Fakultní nemocnice
Hradec Králové
Sokolská 581
500 05 Hradec Králové
E-mail: jaroslava.dusova@fnhk.cz

SUMMARY

Aims: Present the use of Optical Coherence Tomography Angiography (OCTA) in vitreoretinal interface diseases and results of macular capillary network evaluation before and after idiopathic macular hole surgery (IMD).

Methodology: Prospective evaluation of functional results, anatomical and OCTA findings before and after IMD surgery. The group consists of 8 eyes of eight patients. Preoperatively and 1, 3 and 6 months after surgery, the best corrected visual acuity (BCVA) was examined, fundus photography was performed, examination of the macula by spectral-domain optical coherence tomography (SD OCT), determination of the stage of IMD according to Gases and also OCTA examination. The area of the foveal avascular zone (FAZ) and vascular density (VD) were evaluated by using of the OCTA. The operation was performed in all cases by transconjunctival suture 25G vitrectomy by one surgeon, always peeling the inner limiting membrane. An expansive gas, 7x 20% SF6, 1x 15% C3F8, was used for vitreous tamponade.

Results: In all 8 cases, the primary closure of the IMD occurred after the operation. The mean BCVA improved statistically significantly from 0.74 to 0.48 logMAR ($p = 0.0023$). The average FAZ area decreased from 0.345 mm^2 to 0.25 mm^2 after surgery ($p = 0.0458$). The mean VD increased from 7.93 mm^{-1} to 8.38 mm^{-1} ($p = 0.2959$).

Conclusions: Assessment of the macular capillary network in patients with diseases of the vitreoretinal interface offers new findings and important details that can lead to prognostic information and a better understanding of the pathogenesis of the disease. We demonstrated a statistically significant reduction in FAZ in the eyes after successful IMD surgery and an indirect relationship between the improvement of BCVA and the change in FAZ area in our cohort.

Key words: OCT angiography, vitreoretinal interface, idiopathic macular hole, epiretinal membrane, pars plana vitrectomy

Čes. a slov. Oftal., 77, 2021, No.5, p. 232–241

INTRODUCTION

The implementation of OCT in clinical practice at the end of the last century significantly improved diagnostics and monitoring of subclinical changes in vitreoretinal (V-R) interface diseases. Spectral-domain optical coherence tomography (SD OCT) is currently the gold standard in V-R interface pathology examinations [1].

Since 2015, OCT angiography (OCTA), another new non-invasive imaging technique, has been used in clinical practice. This technique facilitates the imaging of the retinal and choroidal vascular bed, without the necessity of administering a contrast agent [2]. OCTA is based on the detection of the motion of red blood cells; and the bloodstream image is generated by comparing the conventional OCT straight sections scanned repeatedly at the same retinal site [3]. This technique enables the imaging of retinal capillary plexuses in layers, which is of vital importance, because no other examination method can provide their imaging so separately. OCTA is widely applied, especially in cases of examining and diagnosing of vascular retinal diseases – diabetic retinopathy [4], aged-related macular degeneration [3,5,6] and retinal vein occlusions [7]. Because of the non-invasiveness of the examination, OCTA is currently also used in such cases in which traditional angiography was previously not indicated. Changes in the vitreomacular interface – epiretinal membrane (ERM) [8] and idiopathic macular hole (IMD) [9] – can be given as an example.

METHODOLOGY AND COHORT

We evaluated the functional and anatomical results and OCT angiographic findings in a group of patients before and after IMD surgery.

The group consists of 8 eyes of 8 consecutive patients who were indicated for IMD surgery. There were 6 females and 2 males in this group, their mean age was 70, the age range was 60-81. Six eyes were phakic, 2 eyes were artephakic. The stages of IMD according to Gass were as follows: one case of Stage II, one case of Stage III and six cases of IMD Stage IV.

Preoperatively and 1, 3 and 6 months after surgery, the best corrected visual acuity (BCVA) was examined on ETDRS (Early treatment diabetic retinopathy study). Optotypes, and intraocular pressure were measured, biomicroscopic examination of the fundus in artificial mydriasis was performed, fundus photography (Zeiss VISUCAM 500 fundus camera, the 3.0.1.0074 software version) examination was performed (Carl Zeiss Cirrus HD-OCT, the 6.5.0.772 software version, the 1280x1024 resolution) and OCT angio examination (Carl Zeiss Meditec AngioPlex, wavelength of 840 nm, scanning speed of 68,000 Ascan/sec, size of the scanned area: 3x3 mm) was performed. The foveal avascular zone (FAZ) area in the superficial capillary plexus and the central vascular density (VD) were measured with the device software. The values measured before surgery and then 6 months after surgery were compared and statistically processed by Student's paired t-test. The statistical significance was defined as $p < 0,05$. The strength of the linear relationship was determined by the Pearson correlation coefficient.

The operation was performed in all cases by one surgeon, applying a transconjunctival suture 25G vitrectomy (Alcon Constellation surgical unit). Peeling of the inner limiting membrane was performed in each case, five times with a flap. Expansive gas was used for vitreous tamponade in each case. Seven times 20 % SF_6 gas was used; in one case, 15 % C_3F_8 was used.

RESULTS

In the text we present the results obtained 6 months post-operatively. We achieved primary postoperative IMD closure in all operated eyes in the group. The visual acuity improved in 6 eyes, in 2 eyes BCVA did not change after surgery. OCTA showed a decrease in FAZ in 6 eyes after surgery; an increase in FAZ occurred in 1 eye (from 0.17 mm^2 to 0.27mm^2), and in 1 eye, the area of FAZ did not change. The VD after surgery decreased in half of the cases and increased in half of the cases. The results of the group of patients are presented in Table 1. The Tables in Figure 1 show the comparative measurement of the examination results processed by the device software. The measured values were statistically processed by the paired t-test (Table 2). The postoperative improvement of the visual acuity and the postoperative reduction of the area of the foveal avascular zone are statistically significant ($p < 0.05$). The mean central vascular density increased. Statistical significance was not demonstrated.

We also measured the strength of the statistical dependence between the improvement of the BCVA and the change in the FAZ area (Table 3).

DISCUSSION

Apart from the classic indications (age-related macular degeneration, diabetic macular oedema, venous retinal occlusion, glaucoma), OCTA is increasingly used in V-R interface diseases [8,9,10,11,12,13,14]. The SD-OCT examination has been and still remains the gold standard in diagnosing changes in the V-R interface; it allows a thorough evaluation of the surface, inner and outer layers of the retina. However, unlike OCTA, it cannot evaluate the microvasculature of the retina. Kim et al. demonstrated in the OCTA examination in their cohort that, in eyes after surgical

Table 1. Measured values for individual patients

patient	sex	age	stadium IMD after surgery	BCVA before	BCVA after	FAZ mm^2 before	FAZ mm^2 after	VD mm^1 before	VD mm^1 after
1	F	75	2/closed	20/100	20/40	0.17	0.27	8.4	10.8
2	F	69	4/closed	20/125	20/40	0.54	0.34	4	8
3	F	69	4/closed	20/100	20/50	0.38	0.24	7.6	6.7
4	F	81	3/closed	20/200	20/200	0.28	0.12	9.2	6.9
5	F	70	4/closed	20/50	20/32	0.39	0.37	7.1	8.4
6	F	68	4/closed	20/125	20/125	0.32	0.31	10.3	8.9
7	M	60	4/closed	20/100	20/40	0.24	0.24	10.7	12.3
8	M	66	4/closed	20/125	20/63	0.44	0.11	6.2	5

IMD – idiopathic macular hole, BCVA – best corrected visual acuity, FAZ – foveal avascular zone, VD – vascular density

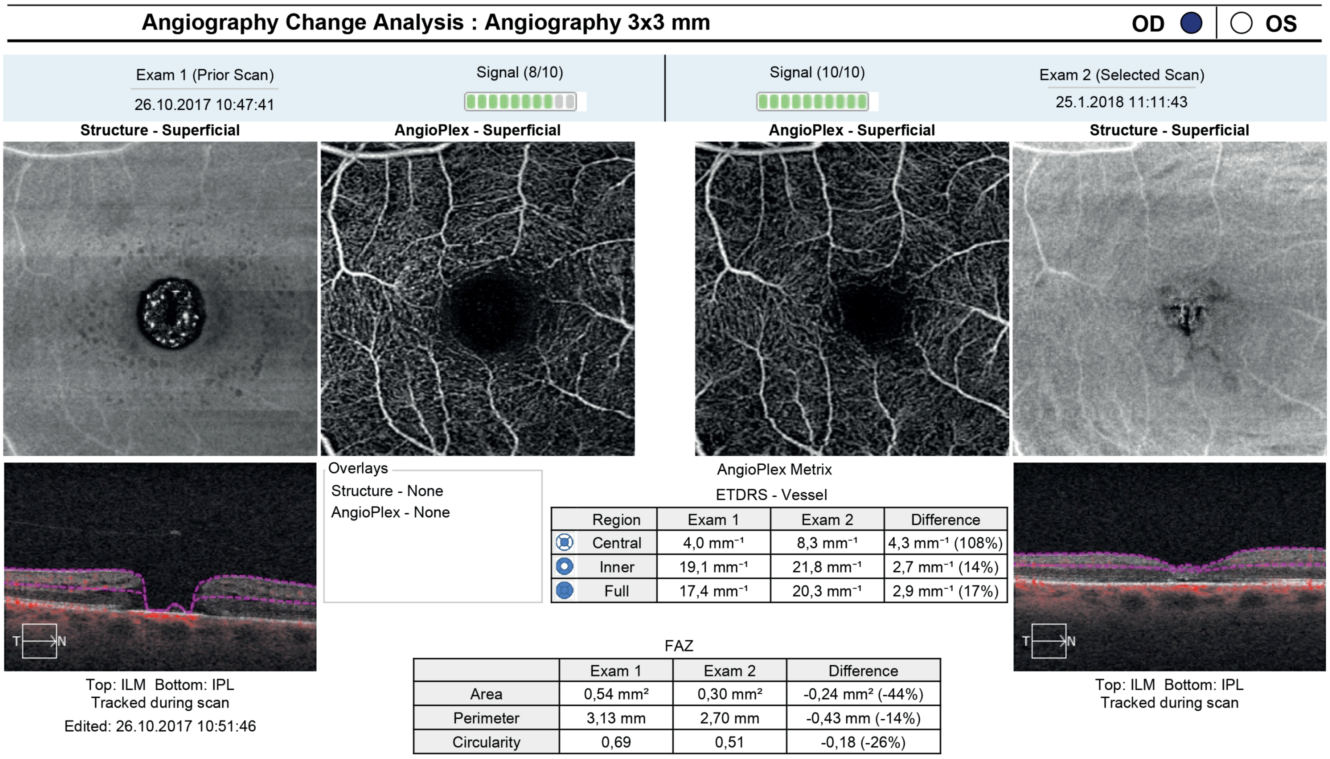

Figure 1. Comparison of OCTA findings before surgery (left part of the image) and 3 months after surgery (right part of the image) in Patient 2. The Tables show the values of the foveal avascular zone and vascular density in both measurements and their difference

Table 2. Average values of BCVA, FAZ and VD areas before and after surgery

	before surgery	6 months after surgery	*p*
BCVA (logMAR)	0.74 ±0.17	0.48 ±0.28	0.0023
FAZ mm^2	0.35 ±0.12	0.25 ±0.1	0.0458
VD mm^{1}	7.94 ±2.22	8.38 ±2.33	0.2959

BCVA – best corrected visual acuity, FAZ – foveal avascular zone, VD – vascular density

closure of the IMD, the FAZ area is smaller and the macular parafoveal VD is lower than in non-affected eyes [9]. When comparing pre- and post-surgery findings in eyes with IMD, consistently with our results, it was revealed that the FAZ area decreases after surgery and the decrease in FAZ correlates with better BCVA [9,10,15]. Rizzo at al. compared cystic changes in the IMD area in the OCT angiographic image with structural en face OCT images [14]. Our experience (Figures 2,3) also demonstrates that, in the OCTA examination, hyporeflective areas with the preserved microvasculature in their vicinity are clearly visible in the deep capillary plexus (DCP), and that they correlate well with the hyporeflective, elongated, radially oriented areas on en face images. These result from morphological changes caused by the distribution of supportive Müller cells in the macula [14,15].

Measurement and evaluation of vascular density still remain arguable. Vascular density is defined as the percentage of moving blood elements per unit area. It is measured by the device software; the measuring methods are varied and dependent on the manufacturer. The currently available OCTA devices

Table 3. Dependence between the change of BCVA and the change of FAZ area

Patient	The difference between BCVA before and after (LogMar)	Difference of FAZ area before and after (mm^2)
1	0.4	0.1
2	0.5	-0.2
3	0.3	-0.14
4	0	-0.16
5	0.2	-0.02
6	0	-0.01
7	0.4	0
8	0.3	-0.33
mean	0.26	-0.95

BCVA – best corrected visual acuity, FAZ – foveal avascular zone

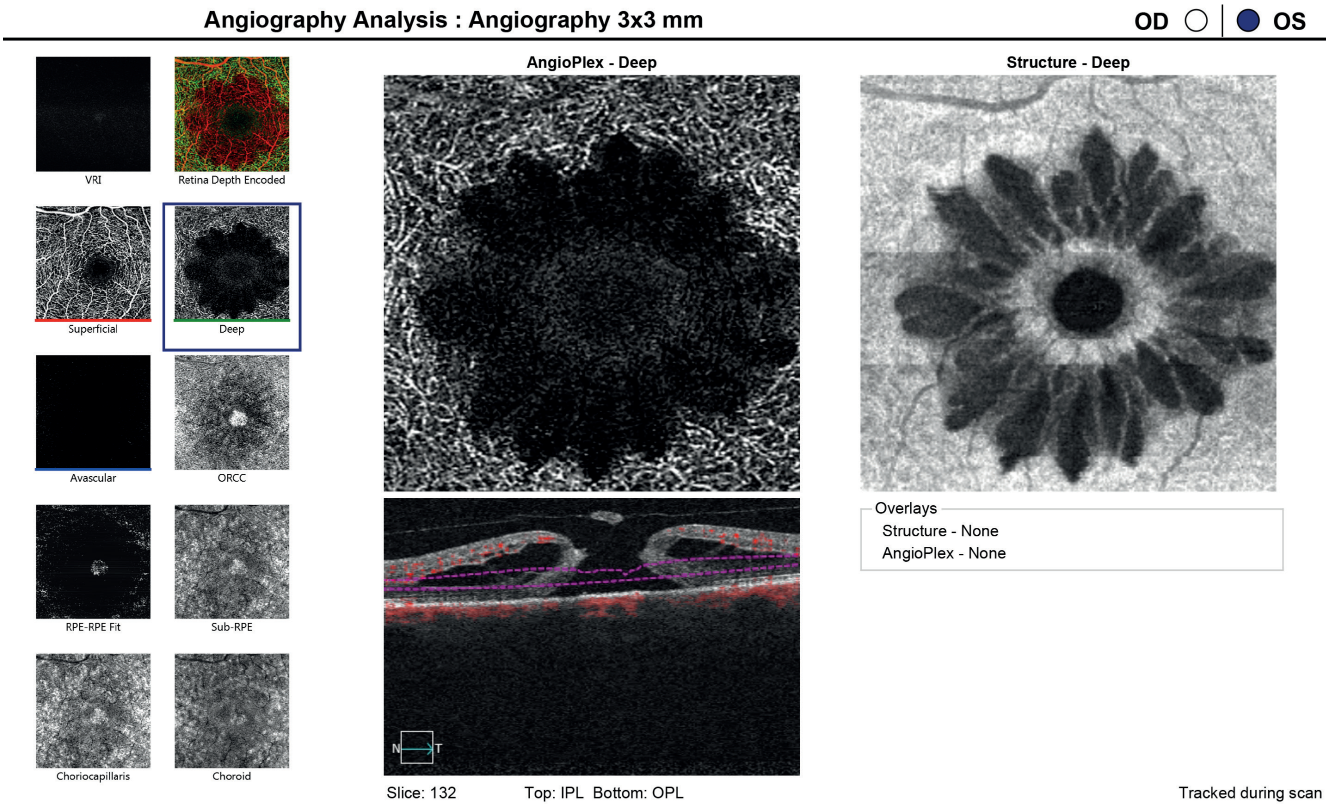

Figure 2. Deep capillary plexus in OCTA image, structural en face image and OCT B scan in Patient 5 before surgery.

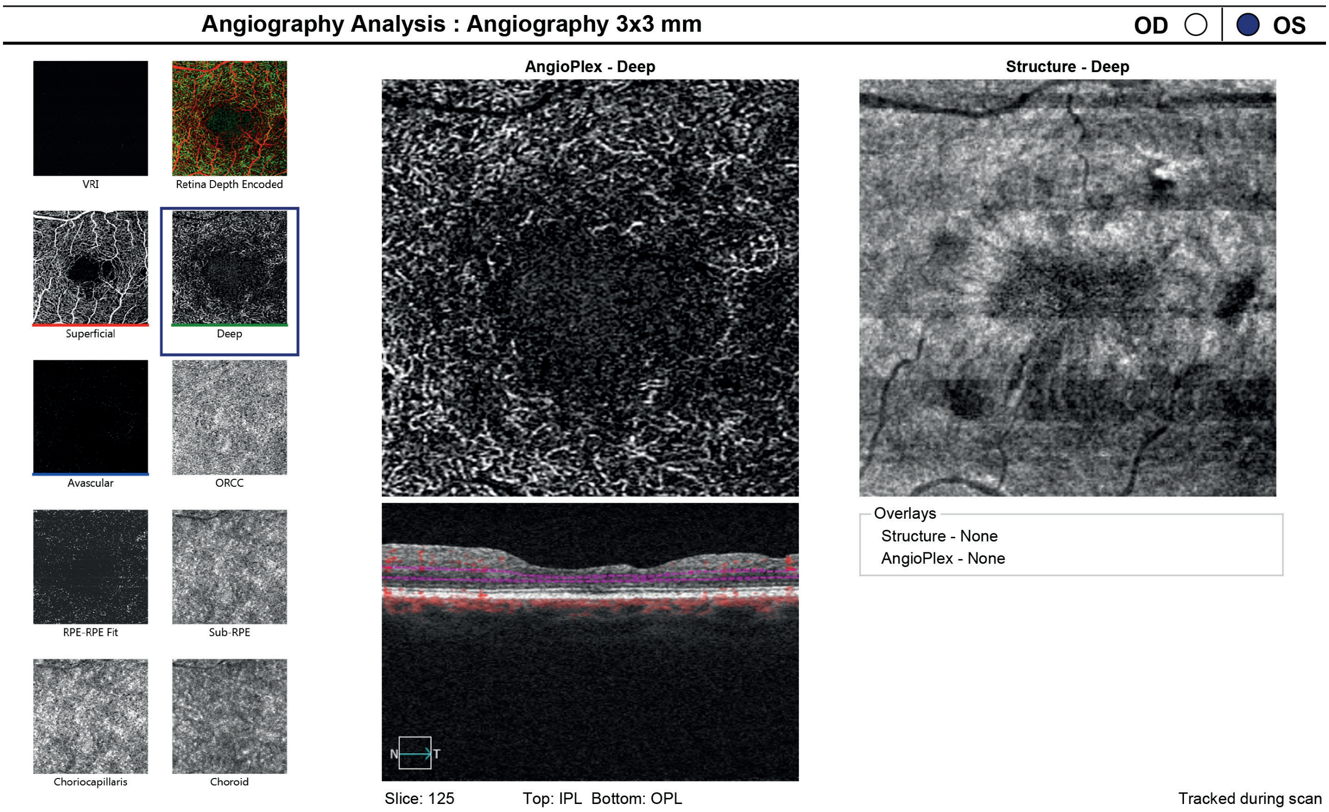

Figure 3. Deep capillary plexus in OCTA image, structural en face image and OCT B scan in the same patient after surgery

show significant variability in the assessment of parafoveal VD [13,16].

OCTA is also applied in examinations of patients with ERM. ERMs formed on the surface of the inner limiting membrane of the retina cause centripetal traction. The OCTA examination shows a smaller FAZ area in the superficial capillary plexus in eyes with ERM, compared to eyes without ERM [17]. Surgical release of the centripetal traction induces the enlargement of the originally narrowed FAZ. The ERM delamination not only effectively improves the morphology of the macular area, but it also normalises the blood

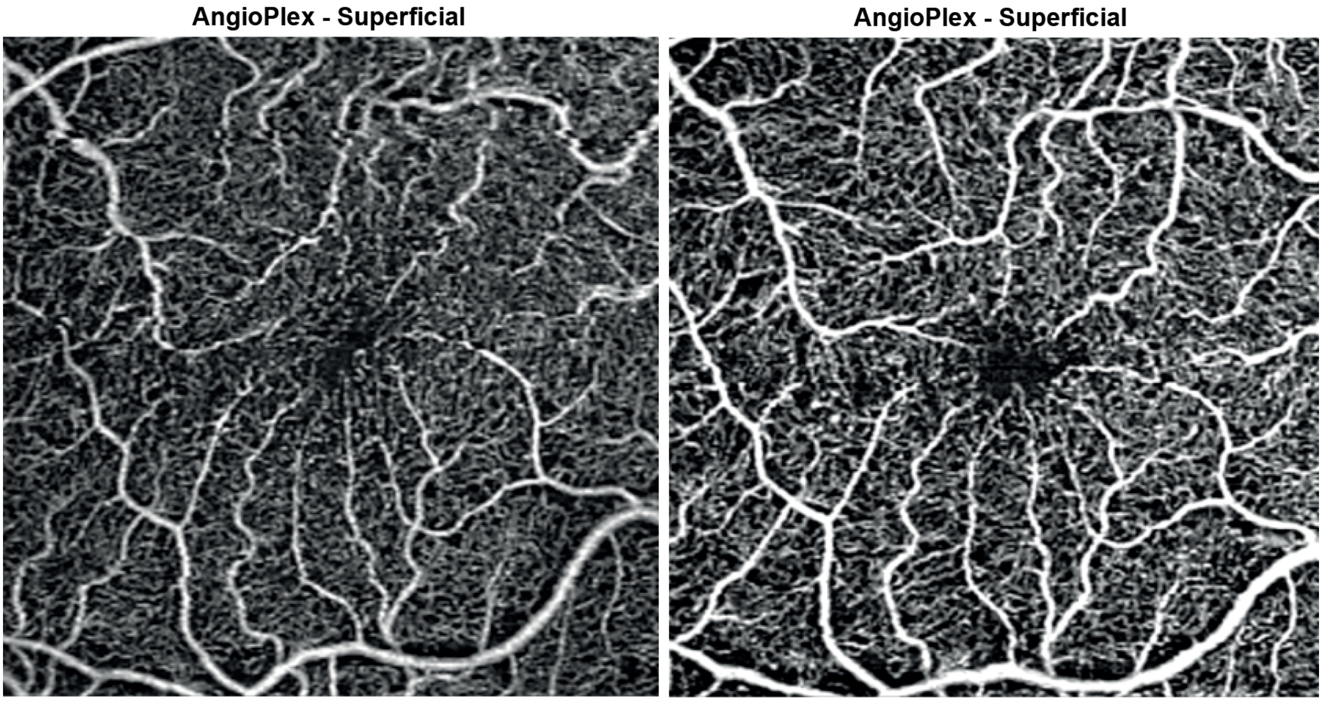

Figure 4. OCTA, superficial capillary plexus before and after surgery in a patient with an epiretinal membrane. The preoperative image on the left shows the tortuosity of the vessels due to traction forces of the membrane and the narrowed foveal avascular zone. The image on the right shows the adjustment of anatomical conditions after the operation

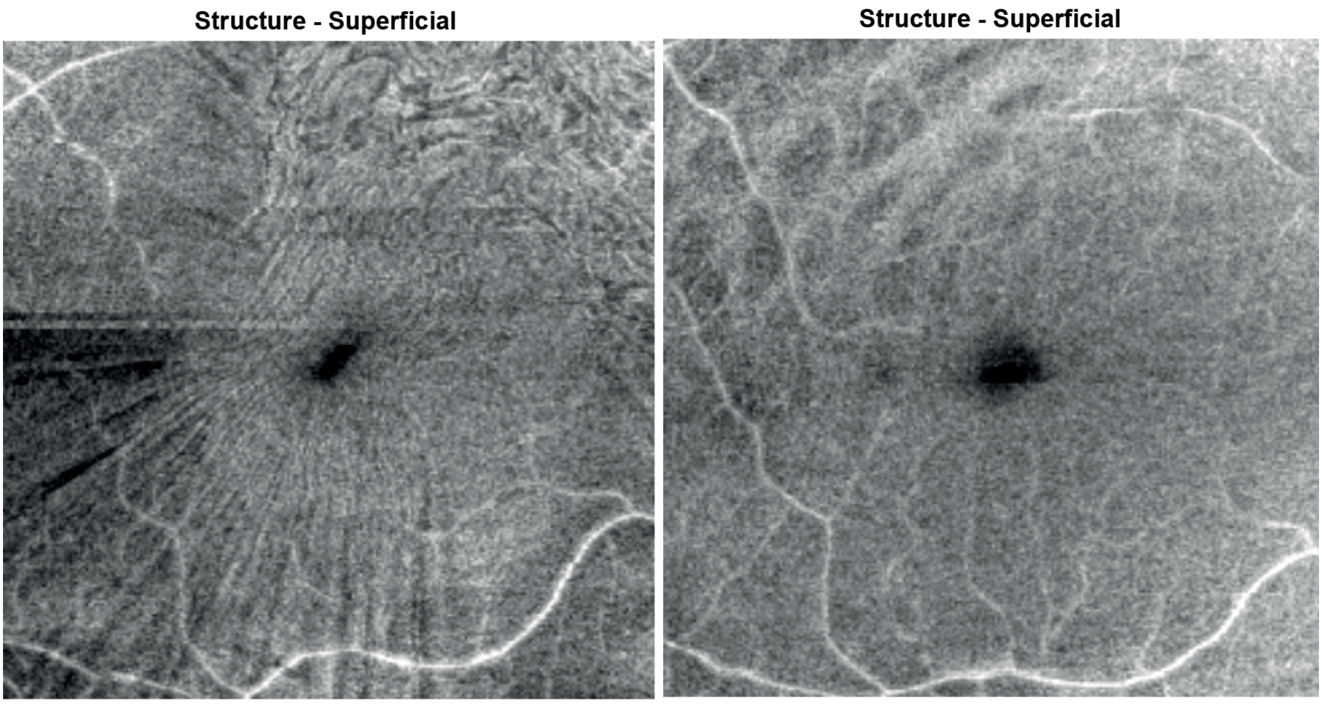

Figure 5. En face images of the macula of the same patient before surgery (on the left) and after surgery (on the right)

flow [13]. This is consistent with the findings made in the case of our patients operated for idiopathic ERM (Figures 4,5).

Apart from research focused on comparing the retinal microvasculature before and after ERM surgery [13,17,19], there is other research focused on examining the changes in individual layers of the retina. It is pointed out that ERMs affect vascular distortion, not only in the inner retinal layers, but also in the outer layers of the retina, and, to some extent, they even affect the choroid [12,18]. Nonperfusion zones and capillary congestion are often evident in DCP [12]. This is also confirmed by our experience (Figures 6,7,8) – a female patient with ERM and cysts in neuretina.

Changes in the foveal avascular zone in diabetic patients are generally well known [20,21].

Surgical removal of ERM in eyes with diabetic macular oedema (DME) significantly improves microcirculation and helps to reduce DME. Romano et al. evaluate OCT angiographic findings after delamination of ERM and peeling of the inner limiting membrane in patients with idiopathic ERM, versus diabetic ERM [22]. The authors explain the significant increase in the FAZ area in DCP in diabetic patients by a greater sensitivity which the diabetic perifoveolar capillary network has to peeling-induced iatrogenic damage of Müller cells.

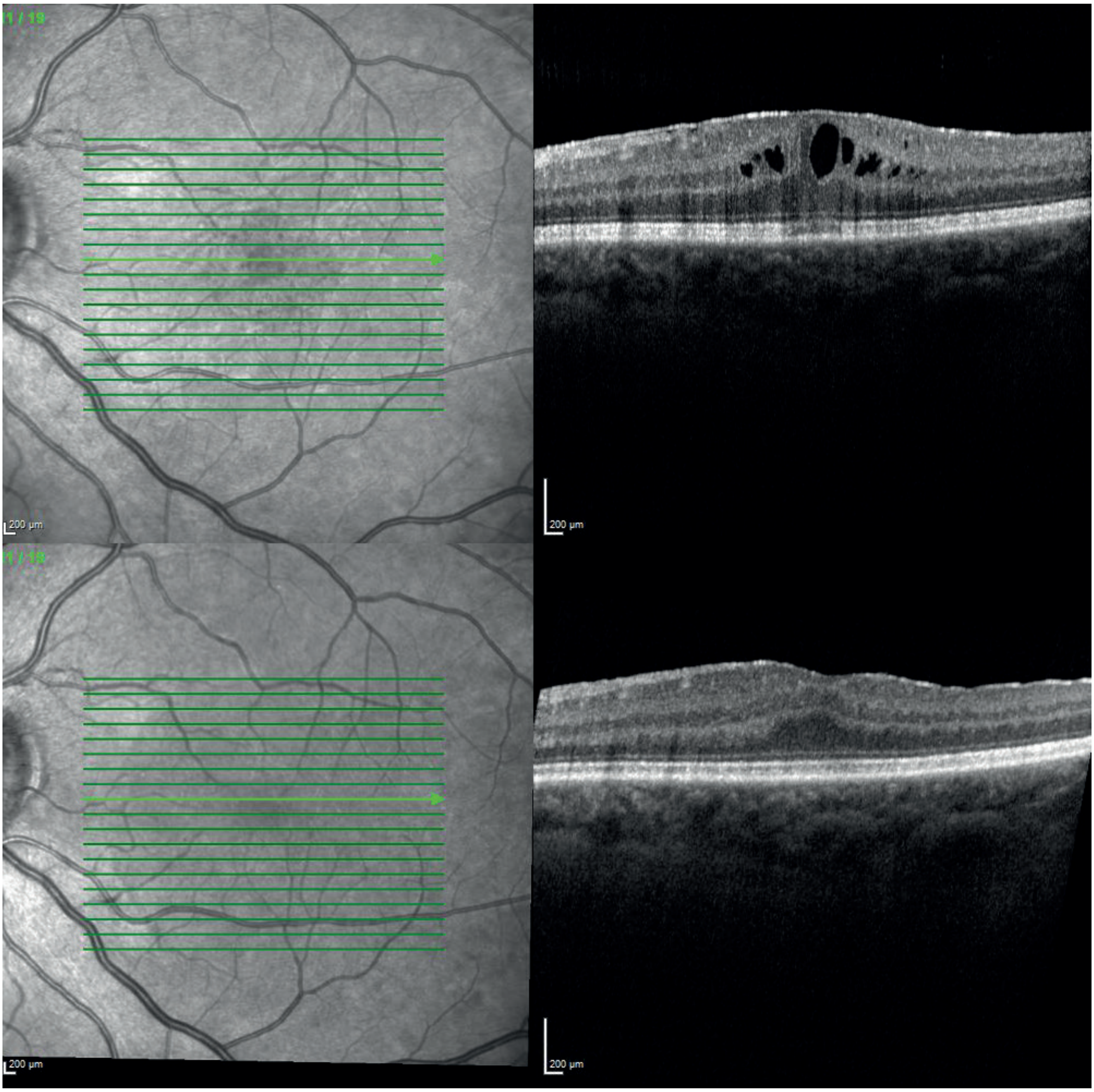

Figure 6. OCT B scan of the patient with an epiretinal membrane and cystic changes in the neuretina before surgery (upper part of the image) and after surgery (lower part of the image)

We present an example of our patient with DME and ERM indicated for pars plana vitrectomy with the ERM delamination and the inner limiting membrane peeling. The FAZ area measured in the deep capillary plexus was 0.55 mm^2 before surgery, and 0.75 mm^2 after surgery. The BCVA before surgery was 20/50; 20 months after

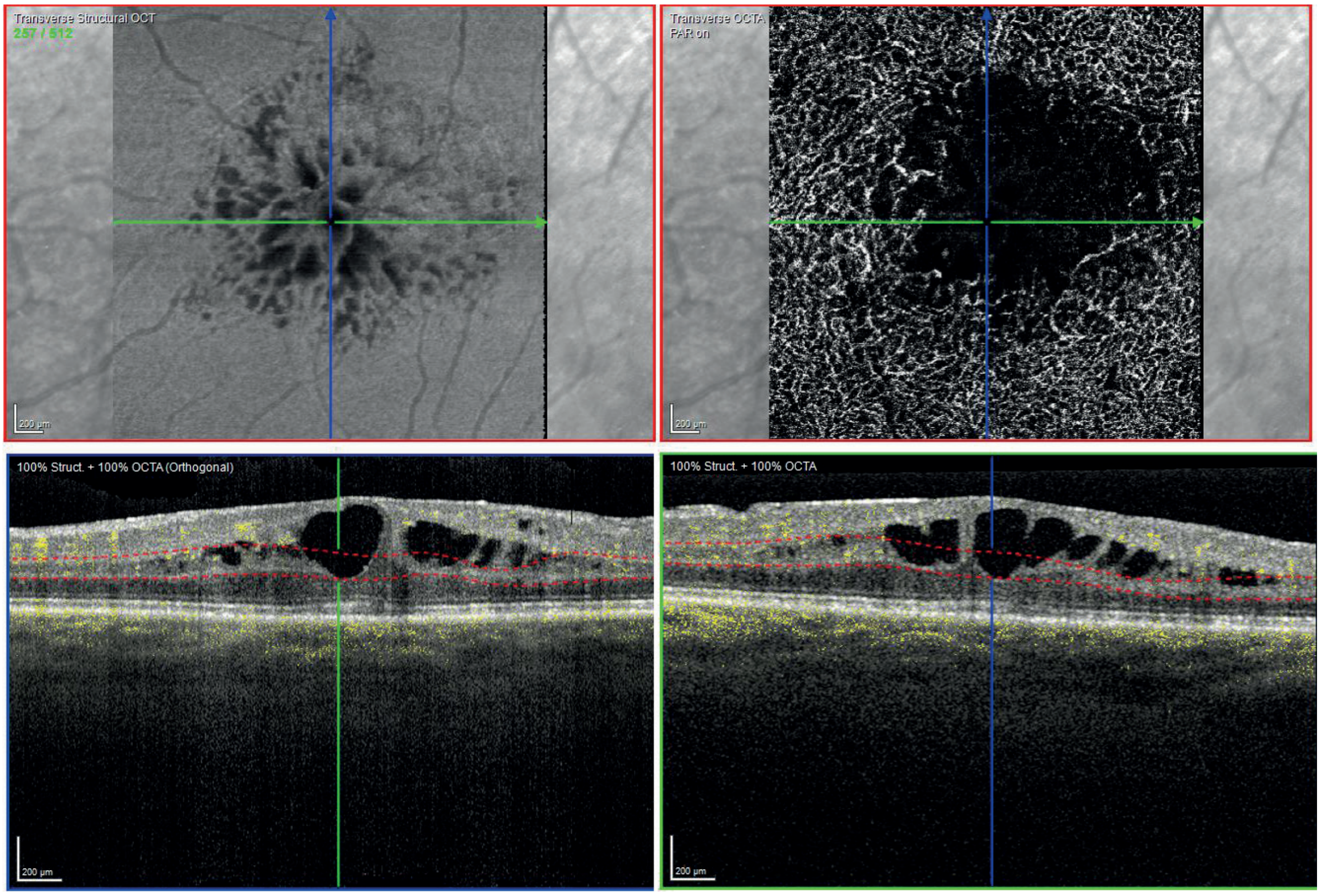

Figure 7. OCTA of the patient from Figure 6 before surgery; zones of nonperfusion and capillary congestion are visible in the deep capillary plexus

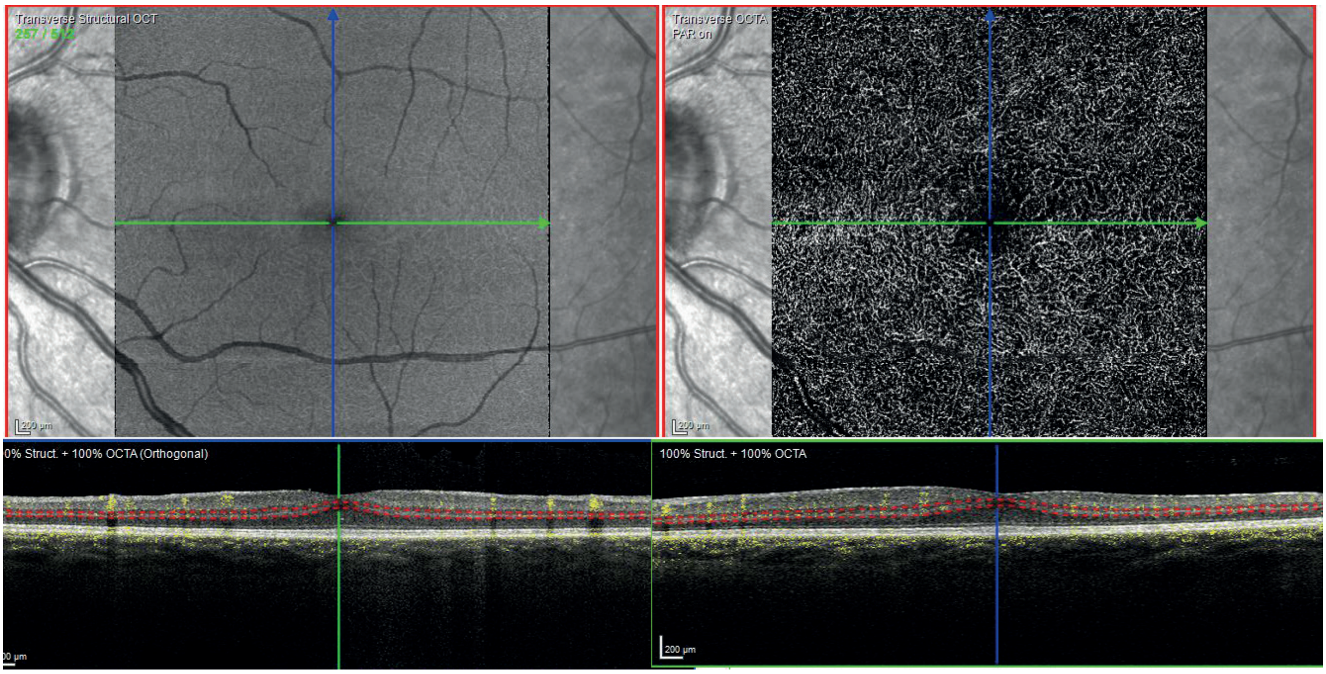

Figure 8. OCTA of the same patient after surgery – adjustment of the state in the deep capillary plexus

the surgery, the BCVA was 20/25. Throughout the whole monitoring period, it was not necessary to administer anti-VEGF (vascular endothelial growth factor) medications for DME (Figures 9,10,11,12,13,14).

CONCLUSIONS

OCTA is also implemented in the case of V-R interface changes. OCTA can detect a potential impact of retinal vasculature on primarily non-vascular retinal diseases, and it can provide new and important details, giving prognostic information and resulting in a better understanding of the disease pathogenesis. In the case of V-R interface diseases, OCTA is used to detect possible vascular damage, in the occurrence of which vitreoretinal interface diseases can play a role. OCTA is also beneficial for evaluating the effect brought on the retinal vasculature by macular surgery itself. Changes in FAZ

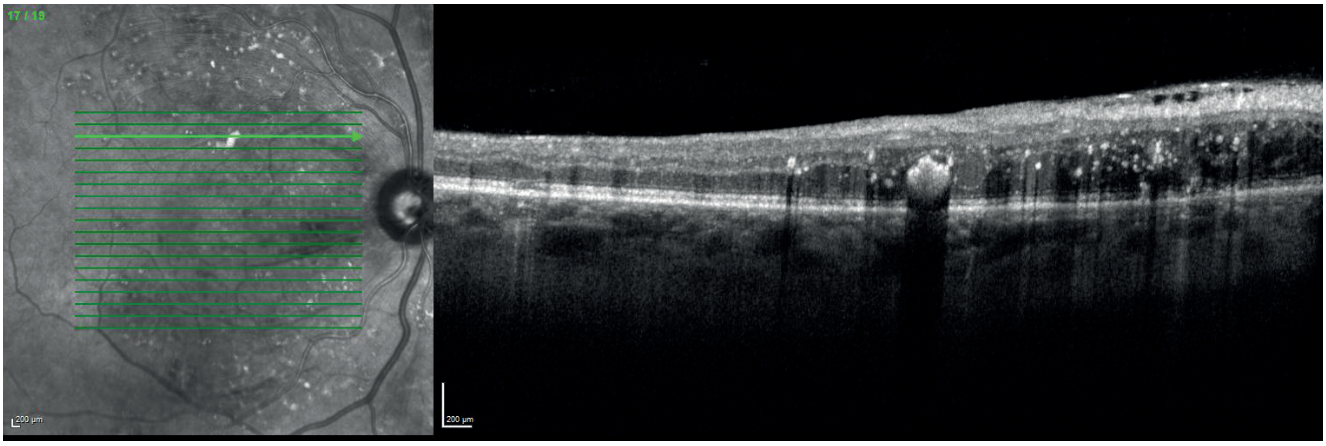

Figure 9. OCT horizontal straight section before surgery – diabetic macular oedema with epiretinal membrane present, highlighted in the upper nasal part of the macula

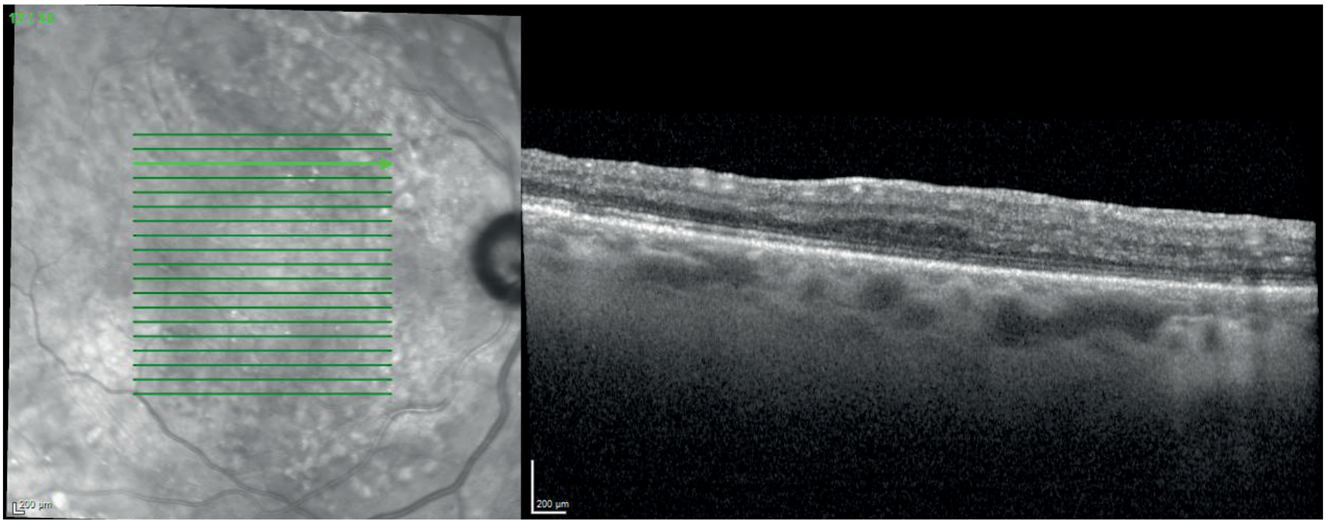

Figure 10. OCT horizontal straight section in the same retinal place 20 months after surgery

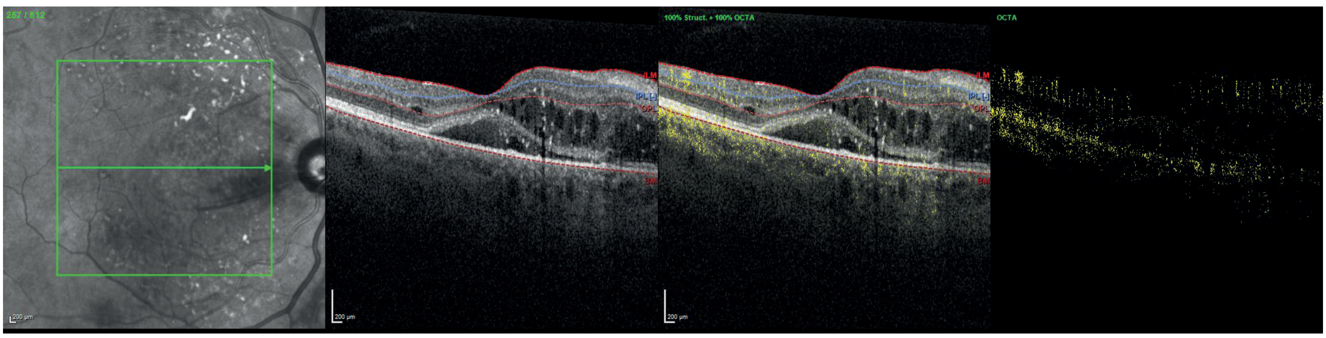

Figure 11. Structural OCTA in the same patient before surgery

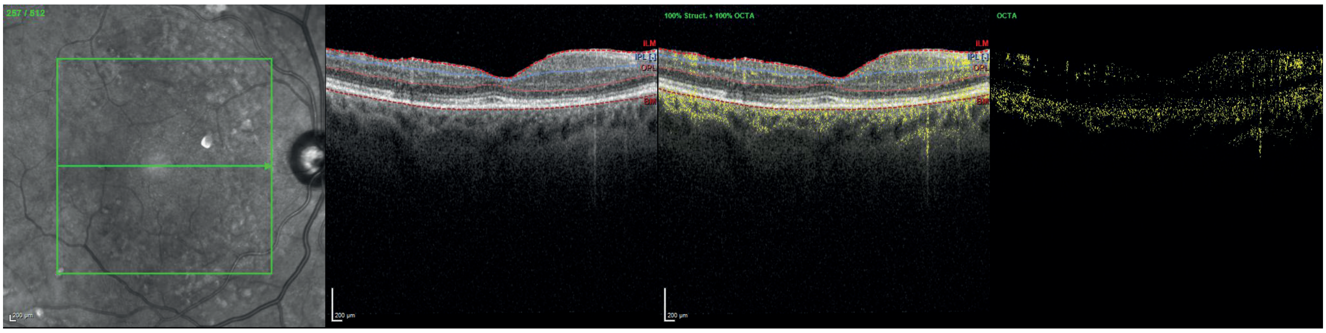

Figure 12. Structural OCTA 20 months after surgery

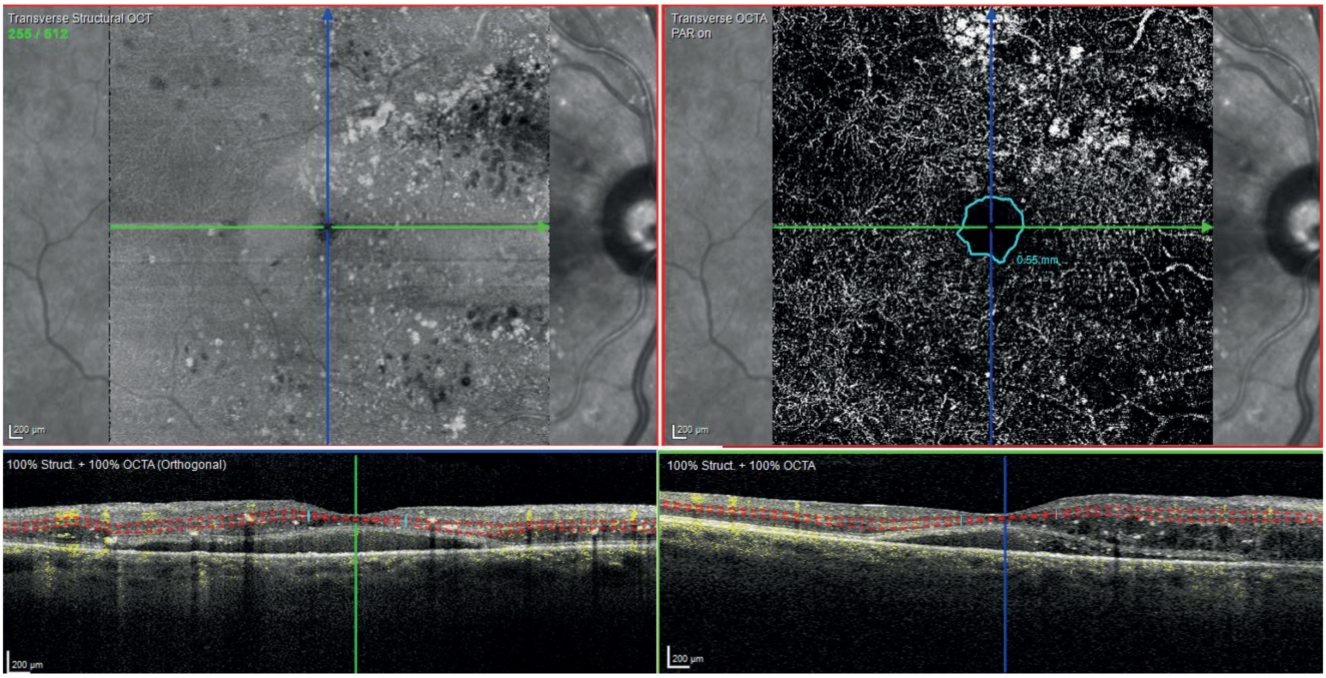

Figure 13. OCTA, deep capillary plexus before surgery, area of foveal avascular zone 0.55 mm^2

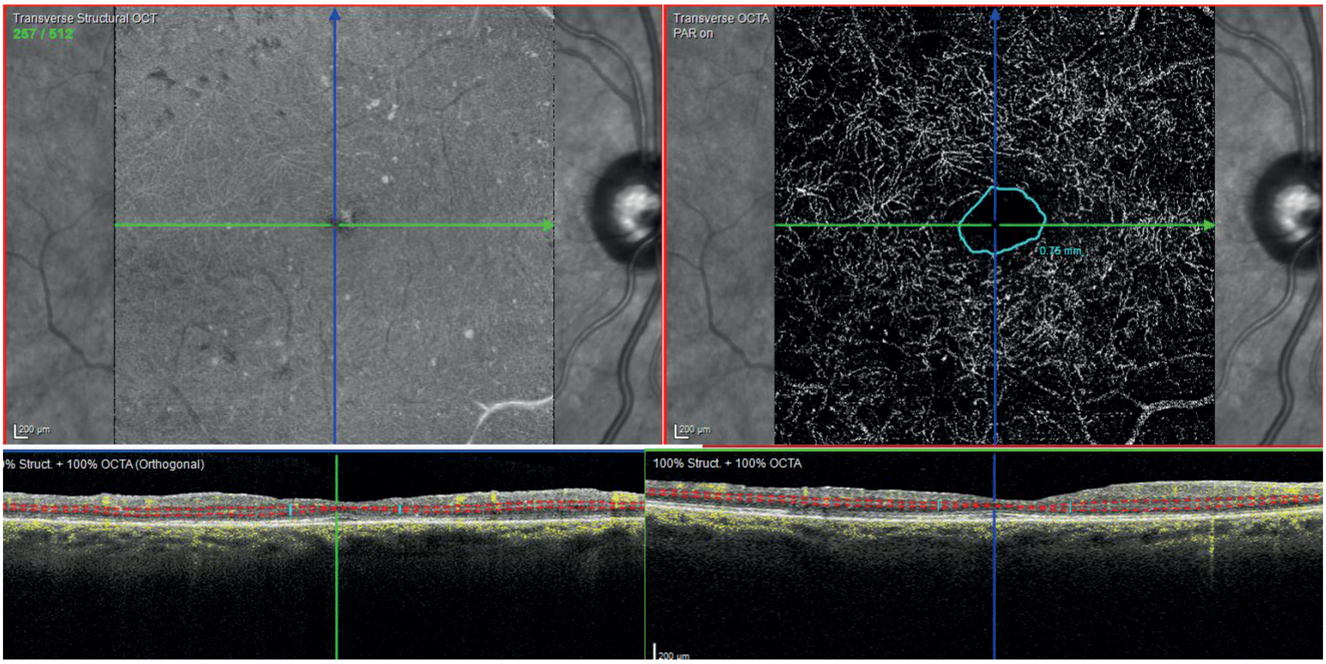

Figure 14. OCTA, deep capillary plexus 20 months after surgery, area of foveal avascular zone 0.75 mm^2

and in VD caused by V-R interface failures can become indicators of the timing of surgery. In our cohort, we demonstrated a statistically significant reduction in FAZ in the eyes after successful IMD surgery, and an indirect relationship between the improvement of BCVA and the change in the FAZ area.

LITERATURE

1. Hee MR, Puliafito CA, Wong C, et al. Optical coherence tomography of macular holes. Ophthalmology. 1995;102(5):748-756.
2. Spaide RF, Klancnik JM, Cooney MJ. Retinal Vascular Layers Imaged by Fluorescein Angiography and Optical Coherence Tomography Angiography. JAMA Ophthalmol, 2015; 133(1): 45-50.
3. De Carlo TE, Romano A, Waheed N, Duker JS. A review of optical coherence tomography angiography (OCTA). International Journal of Retina and Vitreous. 2015;1: doi 10.1186/s40942-015-005-8
4. Hwang TS, Jia Y, Gao SS, et al. Optical coherence tomography angiography features of diabetic retinopathy. Retina. 2015; 35(11):2371-2376.
5. Jia Y, Bailey ST, Wilson DJ, et al. Quantitative optical coherence tomography angiography of choroidal neovascularization in aged related macular degeneration. Ophthalmology. 2014;121(7):1435-1444.
6. Coscas GJ, Lupidi M, Coscas F, Cagini C, Souied EH. Optical coherence tomography angiography versus traditional multimodal imaging in assessing the activity of exudative age-related macular degeneration: A new diagnostic challenge. Retina. 2015;35(11):2219-2228.
7. Rispoli M, Savastano MC, Lumbroso B. Capillary network anomalies in branch retinal vein occlusion on optical coherence tomography. Retina. 2015;35(11):2332-2338.
8. Nelis P, Alten F, Clemens CR, Heiduschka P, Eter N. Quantification of changes in foveal capillary architecture caused by idiopathic epiretinal membrane using OCT angiography. Graefes Arch Clin Exp Ophthalmol, 2017;255(7):1319-1324.
9. Kim YJ, Jo J, Lee JY, Yoon YH, Kim JG. Macular capillary plexuses after macular hole surgery: an optical coherence tomography angiography study. Br J Ophthalmol. 2018;102(7):966-970.
10. Baba T, Kakisu M, Nizawa T, Oshitari T, Yamamoto S. Superficial foveal avascular zone determined by optical coherence tomography angiography before and after macular hole surgery. Retina. 2017;37(3):444-450.
11. Onishi AC, Fawzi AA. An overview of optical coherence tomography angiography and the posterior pole. Ther Adv Ophthalmol. 2019;00(0):1-16.
12. Bacherini D, De Luca M, Rizzo S. Optical coherence tomography angiography in vitreoretinal interface disorders. Minerva Ophthalmologica. 2018;60(3):137-143.
13. Chen H, Chi W, Cai X, et al. Macular microvasculature features before and after vitrectomy in idiopathic macular epiretinal membrane: an OCT angiography analysis. Eye. 2019; 33(4):619-628.
14. Rizzo S, Sevastano A, Bacherini D, Sevastano AC. Vascular features of full-thickness macular hole by OCT angiography. Ophthalmic Surg Lasers Imaging Retina. 2017;48(1):62-68.
15. Shahlaee A, Rahimy E, Hsu J, Gupta OP, Ho AC. Preoperative and postoperative features of macular holes on en face imaging and optical coherence tomography angiography. American Journal of Ophthalmology Case Reports. 2017;5:20-25.
16. Arya M, Rebhun CB, Alibhai AY, et al. Parafoveal retinal vessel density assessment by OCT A in healthy eyes. Ophthalmology Times. 2018;49(10):5-17.
17. Kim YJ, Kim S, Lee JY, Kim JG, Yoon YH. Macular capillary plexuses after epiretinal membrane surgery: an optical coherence tomography angiography study. Br J Ophthalmol. 2018;102(8):1086-1091.
18. Yu Y, Teng Y, Gao M, Liu X, Chen J, Liu W. Quantitative choriocapillaris perfusion before and after vitrectomy in idiopathic epiretinal membrane by optical coherence tomography angiography. Ophthalmic Surg Lasers Imaging Retina. 2017;48(11):906-915.
19. Kitagawa Y, Shimada H, Shinojima A, Nakashizuka H. Foveal avascular zone area analysis using optical coherence tomography angiography before and after idiopathic epiretinal membrane surgery. Retina. 2019;39(2):339-346.
20. Magera L, Krásný J, Pluhovský P, Holubová L. Foveal avascular zone and macular microvasculature changes by OCT angiography in young pacients with type 1 diabetes (pilot study). Cesk Slov Oftalmol. 2020;76(3):111-117.
21. Molnárová M, Zelníková M. Angio OCT – nová neinvazívna zobrazovacia vyšetrovacia metóda diagnostiky a monitoringu diabetickej retinopatie. Forum Diab 2017;6(1):11-18.
22. Romano MR, Cennamo G, Schiemer S, Rossi C, Sparnelli F, Cennamo G. Deep and superficial OCT angiography changes after macular peeling: idiopathic vs diabetic epiretinal membranes. Graefes Arch Clin Exp Ophthalmol. 2017;255(4):681-689.