Original Article

Evaluation of Foveal Avascular Zone and Capillary Plexus in Smokers Using Optical Coherence Tomography Angiography

Emine Çiloğlu[1], Fikret Unal[1], Emine Alyamac Sukgen[1], Yusuf Kocluk[1], Nese Cetin Dogan[1]

[1]Department of Ophthalmology, Adana City Training and Research Hospital, Adana, Turkey

Abstract

Purpose: To evaluate the macular microvasculature in smokers in comparison to healthy subjects using optical coherence tomography angiography (OCTA).

Methods: Fifty chronic, regular smokers and 50 healthy non-smokers, as a control group, were recruited for the study. Foveal avascular zone (FAZ) area (mm^2) and vessel density (VD) (%) in the superficial (SCP) and deep capillary plexus (DCP) were evaluated.

Results: FAZ area was 0.424 ± 0.100 mm^2 in the smoker group and 0.333 ± 0.093 mm^2 in the non-smoking control group (P = 0.002). The deep foveal VD was 31.76 ± 6.33% in the smoker group and 53.09 ± 5.88% in the non-smoking control group (P = 0.006). Superficial foveal and parafoveal, deep parafoveal VD were not statistically different between the groups (P = 0.120), (P = 0.337), (P = 0.287), respectively.

Conclusion: In our study, there was an enlargement of FAZ and reduction of foveal VD at DCP in the eyes of smokers compared with non-smoking adults.

Keywords: Capillary plexus, Foveal avascular zone, Optical coherence tomography angiography, Smoking, Vessel density

Address for correspondence: Emine Çiloğlu, Adana City Training and Research Hospital, Department of Ophthalmology, Adana 01160, Turkey.
E-mail: drciloglu@gmail.com
Submitted: 28-Jul-2019; **Revised:** 18-Sep-2019; **Accepted:** 27-Sep-2019; **Published:** 23-Mar-2020

Introduction

Smoking is a highly prevalent modifiable risk factor for many pulmonary, cardiovascular, and additional systemic diseases. Smoking is also known to be a risk factor for the development of ocular vascular disorders, such as hypertensive retinopathy, age-related macular degeneration, and anterior ischemic optic neuropathy.[1,2] In particular, smoking is associated with anatomic alterations in both the microvasculature and macrovasculature.[1,3]

Smoking impacts vascular endothelium by increasing oxidative stress, decreasing antioxidant vitamin C, and inducing an abnormal nitric oxide activity.[4] Previous studies have shown that smokers have decreased blood flow in retinal and optic nerve head veins because of increased vascular resistance.[5-7]

Access this article online

Quick Response Code:

Website: www.jcurrophthalmol.org

DOI: 10.1016/j.joco.2019.09.002

Optical coherence tomography angiography (OCTA) is a new non-invasive imaging technique that uses motion-controlled contrast imaging to provide high-resolution volumetric blood flow information. It is helpful for analyzing the retinal microvasculature without dye injection. OCTA is able to separately visualize superficial (SCP) and deep capillary plexus (DCP).[8]

Previous studies have reported that retinal blood flow alters in smokers.[1,9-11] However, these studies are limited by number, and they do not report alterations in long-term smokers. In this study, we aimed to investigate the effect of smoking on the foveal avascular zone (FAZ) and vessel density (VD) in the SCP and DCP using OCTA in long-term smokers.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Çiloğlu E, Unal F, Sukgen EA, Kocluk Y, Dogan NC. Evaluation of foveal avascular zone and capillary plexus in smokers using optical coherence tomography angiography. J Curr Ophthalmol 2020;32:53-7.

Methods

This cross-sectional study examined healthy age- and sexmatched participants. Fifty non-smokers and 50 chronic, regular smokers were included. This study was performed in adherence with tenets of the Declaration of Helsinki and was approved by our ethics committee. Informed consent was obtained from all study participants. The study group consisted of subjects coming to the ophthalmology clinic for routine ophthalmologic examination.

The following exclusion criteria were applied: history of ocular surgery, glaucoma, uveitis, age-related macular degeneration, retinal dystrophy, any systemic disease such as diabetes mellitus, hypertension, and current use of medication. The inclusion criteria were as follows: smokers who had been smoking for at least five years, aged 35-55 years, having <3 D of spherical and <1 D cylindrical refractive error, <25 mm axial length, no history of ocular disease, normal blood pressure (<140/90 mmHg), normal blood parameters (e.g. blood sugar, cholesterol levels). Non-smokers lived in smoke-free homes. Additionally, inclusion criteria were sufficiently clear ocular media, and adequate pupillary dilation and fixation to permit quality OCTA imaging.

A detailed ophthalmic examination was performed. Spectral domain optical coherence tomography systems (SD-OCT) (Retina Scan RS 3000 Advance, Nidek Inc, Gamagori, Japan) was used to measure the central retinal thickness (CRT). We captured the OCT scans using the macula line 12-mm horizontal scan. The scans consisted of 1024 A-scans with high definition. Each image consisted of 120 averaged B-scans, with a 4-µm resolution. Before imaging, each subject's pupils were dilated with tropicamide and phenylephrine. OCTA (Optovue RTVue XR Avanti; Optovue Inc., Fremont, California; Software version is 2017.1.0.151) was used for macular retinal vascularization assessment. AngioVue uses the split-spectrum amplitude-decorrelation angiography (SS-ADA) algorithm to detect erythrocyte movement. When using this software, it makes it possible to non-invasively visualize the retinal and choroidal vasculature via motion contrast. Each OCTA volume was acquired in 3 s, and two orthogonal OCTA volumes were acquired to perform motion correction to minimize motion artifacts due to microsaccades and fixation changes. FAZ area (mm^2), superficial foveal and parafoveal VD (%), and deep foveal and parafoveal VD (%) were evaluated. This instrument has an A-scan rate of 70,000 scans per second, uses a light source centered on 840 nm, a bandwidth of 45 nm, and axial resolution of 5 mm.

After setting the image scale to 3 mm x 3 mm in the software parameters, automated FAZ boundary detection is provided by the AngioVue software, applied on retina slab [inner limiting membrane (ILM) to outer plexiform layer (OPL) +11 µm], and can be reviewed on the en face screen, under "FAZ" measurements.

The 'en face' image was then automatically segmented to define the SCP and DCP using the built-in software segmentation algorithm. The en face images of the SCP were segmented with an inner boundary of the ILM and an outer boundary at 11 µm beneath the inner plexiform layer (IPL). The en face images of the DCP were segmented with an inner boundary 11 µm beneath the IPL and an outer boundary at 11 µm beneath the OPL.

Parafoveal VD was calculated for the ring-shaped area between a 1 mm and 3 mm from the center of the fovea. Parafoveal VD was defined as the percentage of total area occupied by vessels and microvasculature, and was quantified in the SCP and DCP. To calculate the VD, the AngioVue Analytics software was used to extract a binary image of the blood vessels from the grey-scale OCTA image, and then the percentage of pixels with flow signal greater than the threshold in the defined region was calculated.

Image quality was assessed for all OCTA scans. Patients who were not co-operative with OCTA were not included in the study. Poor quality images (defined as scan quality <6/10 or presence of significant artifact) were excluded. Projection artifact removal algorithm is available in this version of AngioVue software. In patients with multiple available OCTA images, the one with the highest scan quality was used for analysis. Segmentation errors, if present, were corrected manually in each patient.

All OCTA scans were performed at the same time of the day (in the morning) to avoid diurnal fluctuations. All scans were performed by the same technician.

The smokers were divided into two groups according to smoking in pack-years [pack-years = packs (20 cigarettes) smoked per day x years of smoking], (smokers less than 10 pack-years and more than 10 pack-years) and then compared with each other.

Statistical analysis

Statistical analyzes were performed using the Statistical Package for the Social Sciences software version 21.0 (IBM Inc. Chicago, IL, USA). The Shapiro-Wilk test was used to assess the appropriateness of calculations to normal distribution. The Mann-Whitney U test was used for variables that did not show normal distribution. A 5% level of significance was adopted; therefore, results with a *P* value <0.05 were considered statistically significant.

Results

Fifty smokers and 50 healthy non-smokers, as a control group, were recruited for the study. The smoker group consisted of 32 males (64%) and 18 females (36%), and the control group was comprised of 35 males (70%) and 15 females (30%). The mean age of the smokers group and control group was 48.47 ± 4.6 (range, 35–55) years and 44.07 ± 7.3 (range, 35–55) years, respectively. There were no significant differences

between the smokers and non-smokers in the measurements of age, sex, spherical equivalent, axial length, and CRT [Table 1].

The mean duration of smoking in smokers was 12 ± 2.5 (range, 5-15) years. The mean packs-per day of smoking was 1.3 (range, 0.5-2). Evaluation of OCTA findings: the FAZ area was 0.424 ± 0.100 mm^2 in the smokers group and 0.333 ± 0.093 mm^2 in the non-smoking control group (P = 0.002). Superficial foveal VD was 32.22 ± 4.70% in the smokers group and 34.43 ± 6.05% in the non-smoking control group (P = 0.120). Deep foveal VD was 31.76 ± 6.33% in the smokers group and 53.09 ± 5.88% in the non-smoking control group (P = 0.006) [Table 2].

When the parameters were evaluated according to the amount of smoked pack years (<10 pack-years, >10 pack-years), the FAZ area, superficial foveal VD, and deep foveal VD were statistically different between the groups (P = 0.005) (P = 0.021) (P = 0.012), respectively [Table 3].

Table 1: The demographics features in the smoker and non-smoker group

	Smoker (*n*=50)	Non-smoker (*n*=50)	*P*
Age (years)	48.47±4.6	44.07±7.3	0.085
Gender (male/female)	32/18	35/15	0.445
Spherical equivalent (D)	0.4±1.8	0.4±1.6	0.795
Axial length (mm)	23.2±0.6	23.3±0.4	0.625
CRT (mm)	195.5±14.3	186.8±12.8	0.596

CRT: Central retinal thickness

Table 2: The measurements in the smoker and non-smoker groups

	Smoker (*n*=50)	Non-smoker (*n*=50)	*P*
Age	48.47±4.6	44.07±7.3	0.085
FAZ area (mm^2)	0.424±0.100	0.333±0.93	0.002*
Superficial foveal VD (%)	32.22±4.70	34.43±6.050	0.120
Superficial parafoveal VD (%)	54.12±4.25	54.15±3.44	0.337
Deep foveal VD (%)	31.76±6.33	53.09±5.88	0.006*
Deep parafoveal VD (%)	62.97±3.90	63.09±5.88	0.287

*Statistically significant. FAZ: Foveal avascular zone, VD: Vessel density

Table 3: The measurements in the smoker group

	Smoker		*P*
	<10 pack-years	>10 pack-years	
Age	44.30±4.5	47.65±3.8	0.072
FAZ area (mm^2)	0.368±0.77	0.479±0.09	0.005*
Superficial foveal VD (%)	34.24±4.74	30.19±3.81	0.021*
Superficial parafoveal VD (%)	54.10±4.72	54.13±3.89	0.935
Deep foveal VD (%)	34.73±6.38	28.80±4.83	0.012*
Deep parafoveal VD (%)	62.53±4.54	63.41±3.24	1.000

*Statistically significant. FAZ: Foveal avascular zone, VD: Vessel density

Discussion

In this study, we investigated the effects of smoking on the macular microvasculature in at least 5 years in chronic, regular smokers.

Cigarette smoking has been linked with many vascular alterations, including experimental evidence of altered retinal and choroidal blood flow and endothelial reactivity.[12,13]

Rose *et al*. observed that smokers exhibited reduced retinal vascular reactivity to normoxic hypercapnia compared with healthy controls.[10] Cigarette smoking has been associated with low blood velocity of the ophthalmic artery.[14] Sızmaz *et al*. found a significant decrease in choroidal thickness due to smoking. They considered that this decrease could be associated with decreased blood flow to the choroid following smoking.[2]

Nicotine and vasoactive components present in cigarettes may cause an increase in choroidal vascular resistance by inducing vasospasm in the circulatory system and may cause anterior ischemic neuropathy as a result of construction of posterior ciliary arteries.[15,16]

Cigarette smoke contains a myriad of potential toxic and systemic vasoconstrictive compounds including nicotine during exposure.[17] Smoking appears to impair endothelial cell function in many vascular regions, and evidence supports long-term vasoconstriction and altered endothelial response.[18-20] Substances in cigarette smoke have additionally been demonstrated to induce direct oxidative damage to the endothelium.[21,22]

One of the metabolites that cigarettes contain is carbon monoxide (CO). CO causes a decrease in the transport capacity of hemoglobin for oxygen and organ oxygenation because hemoglobin has a greater affinity for CO than oxygen. A decrease in the perfusion and oxygenation of the microvascular system leads to the formation of an abnormal hemodynamic environment, which is a pathogenetic factor in the development of retinopathy.

In this study, we assessed FAZ, foveal and parafoveal vessel densities in the SCP and DCP in individuals who were regular smokers for at least 5 years and compared the results with non-smokers. In the smokers group, we found significant enlargement of the FAZ area and a significant decrease in deep foveal VD. There was no significant difference between the groups according to the superficial foveal VD and parafoveal VD.

Multiple properties, including the distance from the larger arterioles, and the proximity to the high metabolic demand of the outer retina and the complex vascular anatomical architecture may make the DCP more susceptible to damage.[23]

When we made an assessment based on the amount of cigarettes smoked, we found a significant decrease in the FAZ area and both the superficial and deep foveal VD in individuals

who smoked more than 1 pack per day. As the amount of smoking increases, there is a decrease of superficial foveal VD, in addition to deep foveal VD.

OCTA has the potential to provide objective automated evaluation of the vascularity of the superficial and DCP. There are numerous studies in the literature showing changes in vascular density using OCTA in patients with diabetes which mostly show a reduction of vascular density and enlargement of the FAZ.[24-29]

FAZ enlargement can be detected using fundus fluorescein angiography (FFA). However, smoking is not an indication for FFA imaging, so it was not possible to evaluate the FAZ in the smokers using this method. However, it is possible with OCTA, which is a reliable, rapid technique and does not require dye injection. OCTA offers the opportunity to quantitatively assess microangiopathies caused by cigarette smoking.

There is a study in which the effect of smoking on the eye was assessed using OCTA. Ayhan *et al*. showed that smoking caused a significant decrease in the blood flow index of choriocapillary area by the acute effects of nicotine, as evaluated using OCTA.[11]

FAZ dimension has a strong positive correlation with the severity of capillary non-perfusion in several retinal vascular diseases.[30] Studies using FFA to analyze FAZ dimension demonstrated large variability in healthy subjects.[31,32] Mastropasqua *et al*. reported excellent reproducibility and repeatability of FAZ area measurements in normal eyes using OCTA.[33]

Ciesielski *et al*. investigated in their study the acute effect of smoking on FAZ, parafoveal VD, and peripapillary VD with OCTA. They reported that no immediate influence of smoking on vessel density parameters measured by OCTA in healthy habitual smokers.[34]

The current study had some limitations. It remains unclear whether there is a linear dose effect of smoking on the retinal blood flow. Because of variations in the amount of nicotine per cigarette, the number of cigarettes consumed daily, and the amount of smoke actually inhaled, it may be difficult to examine in detail the dose-dependent effect of smoking on the retinal circulatory parameters in a clinical investigation. We could not evaluate the acute effect of smoking, which may have had an impact on outcomes. Caffeine and alcohol consumption before the measurements were not questioned. We used only one OCTA device in our study. The results were interpreted according to one OCTA device.

In conclusion; in this study, we used OCTA to demonstrate automated quantification of the FAZ and VD of the SCP and DCP in chronic, regular smokers and non-smokers. Our data suggest that smoker's eyes exhibit impairment of retinal microcirculation in the macula, especially in the fovea. It has shown that there is an enlargement of the FAZ and reduction of foveal VD of the SCP and DCP in the eyes of smokers compared with those of non-smoking healthy adults. The underlying pathophysiology of FAZ enlargement may be related to capillary non-perfusion and microinfarcts. We think that this situation develops as a result of the deterioration and reduction of blood flow through the effects of smoking. When we compared the amount of cigarettes consumed per day, we found that as well as the DCP, the SCP was beginning to be affected. As the amount of smoking increases, there is a decrease of foveal VD of both the SCP and DCP. It is possible to say that DCP is more susceptible to oxidative damage and poor perfusion caused by cigarette smoking as it is closer to the outer retina due to its high metabolic activity and complex vascular structure. Therefore, we think that the DCP is initially reduced, and as the amount of smoking increases, the SCP is also decreased due the severity of the damage. Furthermore, larger studies that investigate the long-term effects of smoking on retinal microcirculation in the macula may help explain the role of smoking as a risk factor on systemic vascular diseases such as diabetic retinopathy progression.

Acknowledgements

Professional language editing was performed by David Chapmann.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Registration number of the Ethics Committee: Adana City Training and Research Hospital Ethical Committee, number: 269-2018.

References

1. Garhöfer G, Resch H, Sacu S, Weigert G, Schmidl D, Lasta M, *et al*. Effect of regular smoking on flicker induced retinal vasodilatation in healthy subjects. Microvasc Res 2011;82:351-5.
2. Sizmaz S, Küçükerdönmez C, Pinarci EY, Karalezli A, Canan H, Yilmaz G. The effect of smoking on choroidal thickness measured by optical coherence tomography. Br J Ophthalmol 2013;97:601-4.
3. van den Berkmortel FW, Smilde TJ, Wollersheim H, van Langen H, de Boo T, Thien T. Intima-media thickness of peripheral arteries in asymptomatic cigarette smokers. Atherosclerosis 2000;150:397-401.
4. Wimpissinger B, Resch H, Berisha F, Weigert G, Polak K, Schmetterer L. Effects of isometric exercise on subfoveal choroidal blood flow in smokers and nonsmokers. Invest Ophthalmol Vis Sci 2003;44:4859-63.
5. Steigerwalt RD Jr., Laurora G, Incandela L, Cesarone MR, Belcaro GV, De Sanctis MT. Ocular and orbital blood flow in cigarette smokers. Retina 2000;20:394-7.
6. Tamaki Y, Araie M, Nagahara M, Tomita K. Acute effects of cigarette smoking on tissue circulation in human optic nerve head and choroid-retina. Ophthalmology 1999;106:564-9.
7. Havelius U, Hansen F. Ocular vasodynamic changes in light and darkness in smokers. Invest Ophthalmol Vis Sci 2005;46:1698-705.
8. Spaide RF, Klancnik JM Jr., Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. JAMA Ophthalmol 2015;133:45-50.
9. Omae T, Nagaoka T, Yoshida A. Effects of habitual cigarette smoking on retinal circulation in patients with type 2 diabetes. Invest Ophthalmol Vis Sci 2016;57:1345-51.

10. Rose K, Flanagan JG, Patel SR, Cheng R, Hudson C. Retinal blood flow and vascular reactivity in chronic smokers. Invest Ophthalmol Vis Sci 2014;55:4266-76.
11. Ayhan Z, Kaya M, Ozturk T, Karti O, Hakan Oner F. Evaluation of macular perfusion in healthy smokers by using optical coherence tomography angiography. Ophthalmic Surg Lasers Imaging Retina 2017;48:617-22.
12. Langhans M, Michelson G, Groh MJ. Effect of breathing 100% oxygen on retinal and optic nerve head capillary blood flow in smokers and non-smokers. Br J Ophthalmol 1997;81:365-9.
13. Wimpissinger B, Resch H, Berisha F, Weigert G, Schmetterer L, Polak K. Response of choroidal blood flow to carbogen breathing in smokers and non-smokers. Br J Ophthalmol 2004;88:776-81.
14. Williamson TH, Lowe GD, Baxter GM. Influence of age, systemic blood pressure, smoking, and blood viscosity on orbital blood velocities. Br J Ophthalmol 1995;79:17-22.
15. Branchini L, Regatieri CV, Flores-Moreno I, Baumann B, Fujimoto JG, Duker JS. Reproducibility of choroidal thickness measurements across three spectral domain optical coherence tomography systems. Ophthalmology 2012;119:119-23.
16. Tamaki Y, Araie M, Nagahara M, Tomita K, Matsubara M. The acute effects of cigarette smoking on human optic nerve head and posterior fundus circulation in light smokers. Eye (Lond) 2000;14(Pt 1):67-72.
17. Iida M, Iida H, Dohi S, Takenaka M, Fujiwara H. Mechanisms underlying cerebrovascular effects of cigarette smoking in rats *in vivo*. Stroke 1998;29:1656-65.
18. Fushimi H, Inoue T, Yamada Y, Matsuyama Y, Kameyama M. Profound vasoconstrictive effect of cigarette smoking in diabetics with autonomic neuropathy. Diabetes Res Clin Pract 1992;16:191-5.
19. Cao L, Xu CB, Zhang Y, Cao YX, Edvinsson L. Secondhand smoke exposure induces Raf/ERK/MAPK-mediated upregulation of cerebrovascular endothelin ETA receptors. BMC Neurosci 2011;12:109.
20. Cao L, Zhang Y, Cao YX, Edvinsson L, Xu CB. Cigarette smoke upregulates rat coronary artery endothelin receptors *in vivo*. PLoS One 2012;7:e33008.
21. Schweitzer KS, Hatoum H, Brown MB, Gupta M, Justice MJ, Beteck B, *et al*. Mechanisms of lung endothelial barrier disruption induced by cigarette smoke: Role of oxidative stress and ceramides. Am J Physiol Lung Cell Mol Physiol 2011;301:L836-46.
22. Edirisinghe I, Rahman I. Cigarette smoke-mediated oxidative stress, shear stress, and endothelial dysfunction: Role of VEGFR2. Ann N Y Acad Sci 2010;1203:66-72.
23. Nakahara T, Hoshino M, Hoshino S, Mori A, Sakamoto K, Ishii K. Structural and functional changes in retinal vasculature induced by retinal ischemia-reperfusion in rats. Exp Eye Res 2015;135:134-45.
24. De Carlo TE, Chin AT, Bonini Filho MA, Adli M, Branchini L, Salz DA, *et al*. Detection of microvascular changes in eyes of patients with diabetes but not clinical diabetic retinopathy using optical coherence tomography angiography. Retina 2015;35:2364-70.
25. Takase N, Nozaki M, Kato A, Ozeki H, Yoshida M, Ogura Y. Enlargement of foveal avascular zone in diabetic eyes evaluated by *en face* optical coherence tomography angiography. Retina 2015;35:2377-83.
26. Freiberg FJ, Pfau M, Wons J, Wirth MA, Becker MD, Michels S. Optical coherence tomography angiography of the foveal avascular zone in diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol 2016;254:1051-8.
27. Kim AY, Chu Z, Shahidzadeh A, Wang RK, Puliafito CA, Kashani AH. Quantifying microvascular density and morphology in diabetic retinopathy using spectral-domain optical coherence tomography angiography. Invest Ophthalmol Vis Sci 2016;57:OCT362-70.
28. Agemy SA, Scripsema NK, Shah CM, Chui T, Garcia PM, Lee JG, *et al*. Retinal vascular perfusion density mapping using optical coherence tomography angiography in normals and diabetic retinopathy patients. Retina 2015;35:2353-63.
29. Al-Sheikh M, Akil H, Pfau M, Sadda SR. Swept-source OCT angiography imaging of the foveal avascular zone and macular capillary network density in diabetic retinopathy. Invest Ophthalmol Vis Sci 2016;57:3907-13.
30. Bresnick GH, Condit R, Syrjala S, Palta M, Groo A, Korth K. Abnormalities of the foveal avascular zone in diabetic retinopathy. Arch Ophthalmol 1984;102:1286-93.
31. Zheng Y, Gandhi JS, Stangos AN, Campa C, Broadbent DM, Harding SP. Automated segmentation of foveal avascular zone in fundus fluorescein angiography. Invest Ophthalmol Vis Sci 2010;51:3653-9.
32. Parodi MB, Visintin F, Della Rupe P, Ravalico G. Foveal avascular zone in macular branch retinal vein occlusion. Int Ophthalmol 1995;19:25-8.
33. Mastropasqua R, Toto L, Mattei PA, Di Nicola M, Zecca IAL, Carpineto P, *et al*. Reproducibility and repeatability of foveal avascular zone area measurements using swept-source optical coherence tomography angiography in healthy subjects. Eur J Ophthalmol 2017;27:336-41.
34. Ciesielski M, Rakowicz P, Stopa M. Immediate effects of smoking on optic nerve and macular perfusion measured by optical coherence tomography angiography. Sci Rep 2019;9:10161.