Original Research Article

EJO European Journal of Ophthalmology

Fluorescein angiography versus optical coherence tomography angiography: FA vs OCTA Italian Study

European Journal of Ophthalmology
1–7

DOI: 10.1177/1120672120909769
journals.sagepub.com/home/ejo
SAGE

Maria Cristina Savastano[1], Marco Rispoli[1], Bruno Lumbroso[1], Luca Di Antonio[2], Leonardo Mastropasqua[2], Gianni Virgili[3], Alfonso Savastano[3], Daniela Bacherini[3] and Stanislao Rizzo[3]

Abstract

Purpose: To assess the current role of fluorescein angiography after the introduction of optical coherence tomography angiography in real-life clinical practice.

Methods: This was a multicentric retrospective observational study to evaluate the number of fluorescein angiography and optical coherence tomography angiography procedures performed by different devices from January 2013 to December 2018. The centers involved were Centro Italiano Macula (Rome), and ophthalmology departments of University "G. D'Annunzio" Chieti–Pescara (Chieti) and "Azienda Ospedaliero Universitaria Careggi" (Florence).

Results: Out of 19,898 total fluorescein angiography procedures performed in the observation period, 3444 (17.3%) were in 2013, 3972 (19.9%) were in 2014, 3601 (18.1%) were in 2015, 3407 (17.2%) were in 2016, 3285 (16.5%) were in 2017, and 2189 (11%) were in 2018. Out of 7949 optical coherence tomography angiography procedures performed in the observation period, none were performed in 2013, 550 (6.9%) were in 2014, 908 (11.5%) were in 2015, 2098 (26.4%) were in 2016, 2090 (26.3%) were in 2017, and 2303 (28.9%) were in 2018.

Conclusion: Fluorescein angiography procedures were performed less often after the introduction of optical coherence tomography angiography technology. The ease, speed, and safety of the optical coherence tomography angiography procedure in everyday clinical practice have facilitated more optical coherence tomography angiography application compared to fluorescein angiography in recent years. In the future, we will probably evaluate the different pathologies that still need an evaluation by fluorescein angiography.

Keywords

Fluorescein angiography, optical coherence tomography angiography, retinal diseases

Date received: 3 July 2019; accepted: 23 January 2020

Introduction

Fluorescein angiography (FA) is currently regarded as the landmark in diagnosis and management of several systemic and ocular diseases involving the retinal vasculature. First introduced in 1961 by Novotny and Alvis,[1] two medical students, this imaging modality is based on the intravenous injection of a noniodinated contrast agent: fluorescein sodium ($C_{20}H_{12}Na_2O_5$).

Intravenous injection of the dye is followed by the acquisition of serial photographs to visualize the patency and the permeability of the retinal vessels. Although its introduction has represented a turning point in retinal imaging, FA suffers from several limitations. Indeed, several adverse effects—including staining of the sclera, skin, and urine—can be observed in all patients undergoing FA.[2] In addition, even though FA is considered a relatively safe diagnostic tool, possible adverse drug reactions

[1]Centro Italiano Macula, Rome, Italy
[2]Department of Ophthalmology, University "G. D'Annunzio" Chieti–Pescara, Chieti, Italy
[3]Department of Ophthalmology, Azienda Ospedaliero Universitaria Careggi, Florence, Italy

Corresponding author:
Maria Cristina Savastano, Centro Italiano Macula, Via Angelo Brofferio, 7, 00195 Rome, Italy.
Email: mariacristina.savastano@gmail.com

ranging from mild (i.e. nausea, vomiting) or moderate (i.e. urticarial and syncope) to serious episodes (i.e. respiratory difficulties, cardiac disturbances, and tonic–clonic seizures) and death can occur.[2–4]

Given the possibility that FA may result in one or more adverse reactions, the necessity of performing the angiographic examination on several categories of patients, including children and pregnant women should be carefully considered. Since there is a lack of data and information concerning the incidence of the adverse effects of FA in children, this imaging modality should be cautiously performed on young patients.[4] Although fluorescein can cross the placenta, FA has proved to be safe during pregnancy.[5] Nevertheless, there is general agreement that the angiographic examination should be avoided with pregnant women, unless necessary to prevent a threat to vision, and it should be preferably performed during the second or third trimester.[3,4] Caution should be used in considering the necessity of performing FA, possibly preceded by a prophylactic treatment, even in patients who have not previously exhibited any adverse reactions.[2,3] FA may also represent a risk for patients affected by sickle cell disease.[6] Similarly, subjects with a history of asthmatic bronchitis or severe cardiovascular disease should be warned about the danger of performing FA frequently.[3] Another disadvantage of FA is the inability to provide a complete anatomical and functional representation of all retinal capillary plexuses.[7]

Using animal models, Weinhaus et al.[8] pointed out that the visualization of retinal vessels provided by FA was limited to the superficial vasculature. This drawback may be imputed to the scattering of light from the inner tissues decreasing the contrast of the angiographic image[8] as well as to the choroidal fluorescence limiting the observer's ability to investigate the retinal circulation.[7] This major limitation of FA has been overcome since the introduction of optical coherence tomography angiography (OCTA).[9] OCTA is a new noninvasive imaging modality, based on high-frequency scanning for the detection of blood cell movement.[10]

This imaging modality takes advantage of the optical coherence tomography (OCT) capacity to generate images by measuring the amplitude and delay of reflected and backscattered light. Multiple repeated B-scans are carried out in the same retinal location, and the images obtained are compared to identify the signal differences between two consecutive scans. Because the retina is a static structure, it is reasonable to suppose that these changes are imputable to the blood flow.[11]

The purpose of this study was to investigate how the employment of FA in real-life clinical practice has changed since the introduction of OCTA: FA vs OCTA Italian Study (FOIS).

Methods

Three centers in Italy have been involved in this multicentric retrospective observational study: Centro Italiano Macula (Rome), and ophthalmology departments of University "G. D'Annunzio" Chieti–Pescara (Chieti) and "Azienda Ospedaliero Universitaria Careggi" (Florence).

This study was conducted in accordance with the tenets of the Declaration of Helsinki and received the Institutional Review Board ethical approval. Informed consent from all patients was obtained.

Different devices were used to perform FA and/or OCTA. In Centro Italiano Macula (Rome), OCTA images acquired with Avanti RTVue XR (Optovue, Fremont, CA, USA) and FA images detected by Spectralis (Heidelberg Engineering, Heidelberg, Germany) were retrospectively observed. In University "G. D'Annunzio" Chieti–Pescara (Chieti), OCTA imaging performed using Optovue Avanti RTVue XR, AngioPlex (Carl Zeiss Meditec, Dublin, CA, USA), and Spectralis OCTA (Heidelberg Engineering, Heidelberg, Germany) and FA images detected by Spectralis (Heidelberg Engineering, Heidelberg, Germany) were retrospectively observed. In "Azienda Ospedaliero Universitaria Careggi" (Florence), OCTA images acquired with Optovue Avanti RTVue XR, RS-3000 Advance (NIDEK Co., Ltd, Tokyo, Japan), and DRI-OCTA-Triton (Topcon Corporation, Tokyo, Japan) and FA images detected by FF 450 IR plus (Carl Zeiss Meditec) were retrospectively observed.

The time period from January 2013 to December 2018 was considered. The inclusion criteria included all FA and/or OCTA imaging performed on patients affected by any type of macular neovascularization (NV) (i.e. NV type 1, 2, and 3; polypoidal; central serous chorioretinopathy (CSC); and myopic eyes) and/or any ocular or systemic vascular disease, including retinal artery occlusion (AO) or retinal vein occlusions (RVO), diabetic retinopathy (RD), macular telangiectasia (MacTel), paracentral acute middle maculopathy (PAMM), acute macular neuroretinopathy (AMN), chorioretinal vasculitis, ocular tumors, and vitreoretinal diseases (epiretinal membrane, macular hole (MH), vitreomacular adhesion/traction).

Some patients received both FA and OCTA evaluations. The exclusion criteria were poor quality images in which it was not possible to make a diagnosis.

Results

A total of 19,898 FA imaging sessions were performed in all observed periods in the three involved centers. There were 3444 FA procedures in 2013, 3972 in 2014, 3601 in 2015, 3407 in 2016, 3285 in 2017, and 2189 in 2018. A total of 7949 OCTA procedures were performed in all observed periods. No OCTA was performed in 2013; 550 OCTA procedures were performed in 2014, 908 in 2015, 2098 in 2016, 2090 in 2017, and 2303 in 2018. Data of all FA and OCTA performed over the years are reported in Table 1.

Figure 1 shows the distribution of the three Italian centers involved in this retrospective observational study: "Centro

Table 1. Performance of FA and OCT from 2013 to 2018 in Centro Italiano Macula (Rome), and ophthalmology departments of University "G. D'Annunzio" Chieti–Pescara (Chieti) and "Azienda Ospedaliero Universitaria Careggi" (Florence).

	2013		2014		2015		2016		2017		2018	
	FA	OCTA	FA	OCTA	FA	OCTA	FA	OCTA	FA	OCTA	FA	OCTA
Rome	218	0	101	110	60	234	43	382	41	550	50	624
Chieti	1782	0	1290	440	920	631	715	920	732	847	520	1089
Florence	1444	0	2581	0	2621	43	2649	796	2512	693	1619	590
Total	3444	0	3972	550	3601	908	3407	2089	3285	2090	2189	2303

FA: fluorescein angiography; OCTA: optical coherence tomography angiography.

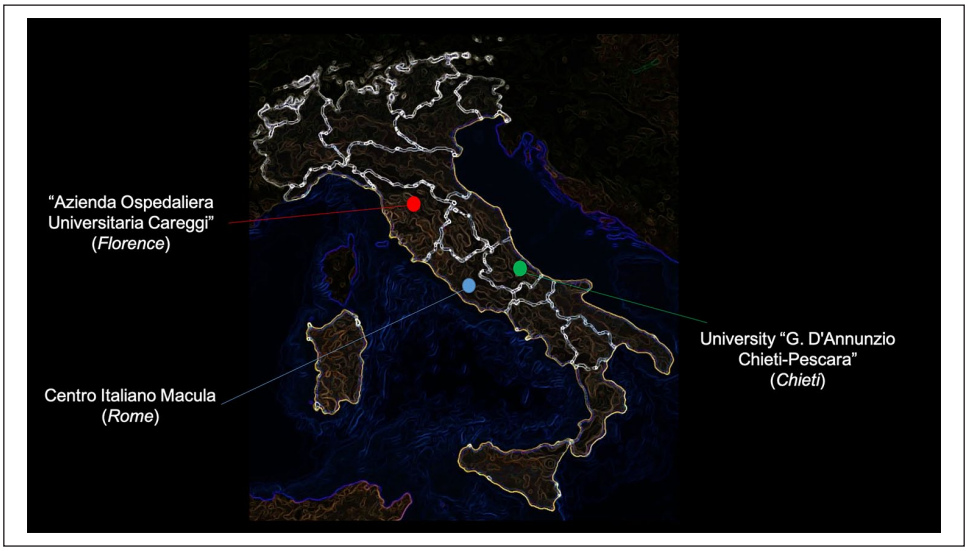

Figure 1. Italian distribution of three centers involved in this retrospective observational study: "Centro Italiano Macula" (Rome), and ophthalmology departments of University "G. D'Annunzio" Chieti–Pescara (Chieti) and "Azienda Ospedaliero Universitaria Careggi" (Florence).

Italiano Macula" (Rome), and ophthalmology departments of University "G. D'Annunzio" Chieti–Pescara (Chieti) and "Azienda Ospedaliero Universitaria Careggi" (Florence).

An overall increase in OCTA procedures between 2013 (n = 0) and 2018 (n = 624) was observed at "Centro Italiano Macula" in Rome (Figure 2). In contrast, a progressive decline in the use of FA was noticed during the study period (from 218 in 2013 to 50 in 2018). Analyzing the evolution in the use of OCTA, the curve of the trend from 2013 to 2017 was steep, as the number of examinations gradually improved, while the elevation was subsequently more gradual (from 2017 to 2018).

A similar trend to that in Rome has been reported for the ophthalmology department of the University "G. D'Annunzio" Chieti–Pescara in Chieti (Figure 3). There was an increase in the number of OCTA procedures performed in 2018 (n = 1089) in comparison to the number of examinations carried out in 2013 (n = 0). On the contrary, the number of FA procedures performed in 2018 (n = 520) was lower than that in 2013 (n = 1782). Analyzing the number of OCTA procedures performed during the study

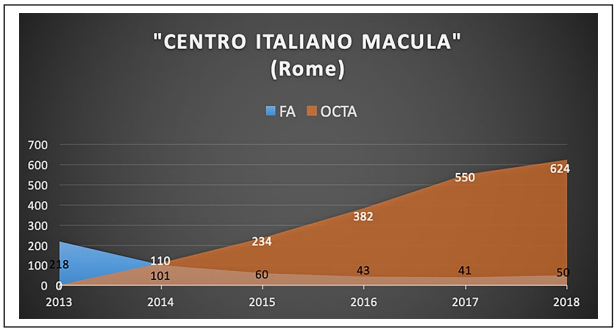

Figure 2. Data collected in "Centro Italiano Macula" in Rome show an increase in the number of OCTA procedures performed between 2013 (n = 0) and 2018 (n = 624). A progressive reduction in the use of FA has been observed during the study period (from 218 in 2013 to 50 in 2018).

period, a progressive increase was noticed in 2014 (n = 440) and in 2015 (n = 631) compared to the baseline in 2013 (n = 0). The augmentation reached a peak in 2016 (n = 920). This trend was opposite of the one observed for FA: while

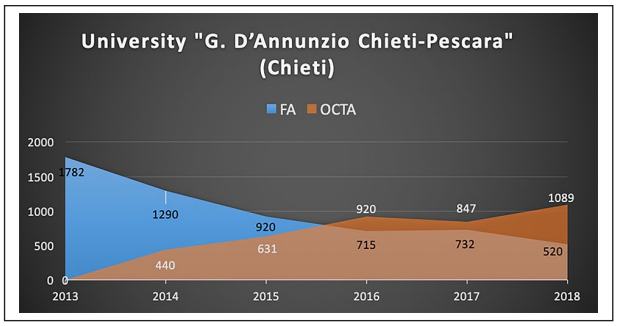

Figure 3. Data collected in the ophthalmology department of the University "G. D'Annunzio" Chieti–Pescara in Chieti show an increase in the number of OCTA examinations performed in 2018 (n = 1089) compared to the number of examinations carried out in 2013 (n = 0). On the contrary, the number of FA procedures performed in 2018 (n = 520) was lower than that in 2013 (n = 1782).

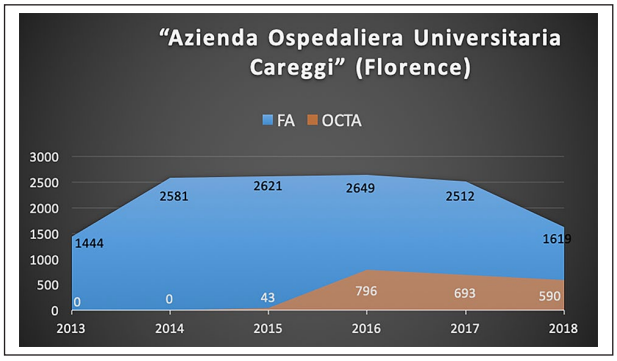

Figure 4. The introduction of OCTA in the ophthalmology department of the "Azienda Ospedaliero Universitaria Careggi" in Florence was delayed in comparison to the other centers. The number of OCTA examinations performed in 2013 and 2014 was zero. An increased number of OCTA procedures were observed in 2015, which was promptly augmented in 2016 and had little progressive decrease in 2017 and 2018. On the whole, the number of both FA and OCTA examinations performed in 2018 was higher than that observed in 2013.

the number of FA procedures performed in 2013 was 1782, a progressive reduction was found in 2014 (n = 1290) and 2015 (n = 920) and was even lower in 2016 (n = 715). A decrease in the number of OCTA procedures was observed in 2017 (n = 847). This reduction coincided with a slight elevation in the number of FA procedures (n = 732). Subsequently, the trends diverged, as an increase in the number of OCTA procedures (n = 1089) was accompanied by a decreased number of FA procedures (n = 520) in 2018.

The introduction of OCTA in the ophthalmology department of the "Azienda Ospedaliero Universitaria Careggi" in Florence was delayed in comparison to the other centers (Figure 4). Indeed, the number of OCTA examinations performed in 2013 and 2014 was zero. An increased number of OCTA procedures were observed in 2015 (n = 43), and it was promptly augmented in 2016 (n = 796). In contrast, a progressive decrease was seen in 2017 (n = 693) and in 2018 (n = 590). An initial increase in FA examinations was noticed in 2014 (n = 2581) in comparison to the number of examinations performed in 2013 (1444). This trend seemed to progress further during the following period in 2015 (n = 2621), reaching its highest point in 2016 (n = 2649). A subsequent decrease in the number of FA procedures carried out in 2017 (n = 2512) was found, and this reduction was even greater in 2018 (1619).

In Figure 5, data collected from all the three centers merged and analyzed on the whole have been reported. An overall increase in the use of OCTA was observed throughout the study period (from n = 0 in 2013 to n = 2303 in 2018), In contrast, in spite of an initial elevation observed in 2014 (n = 3972), the number of FA procedures was lower in 2018 (n = 2189) compared to the beginning of the study period in 2013 (n = 3444). Indeed, the number of both of these imaging modalities seemed to equally improve in 2014 (n = 3972 FAs and n = 550 OCTAs). This trend was followed by a reduction in the use of FA accompanied by a comparable augmentation in the amount of OCTA carried out in 2015 (n = 3601 FAs and n = 908 OCTAs). Furthermore, while the employment of FA slightly decreased in 2016 (n = 3407) and in 2017 (n = 3285), a dramatic increase in the number of OCTA procedures was seen in 2016 (n = 2089), remaining almost steady in 2017 (n = 2090). The curves showing the trend of the use of FA and OCTA crossed in 2018, as the amount of OCTA gradually increased (n = 2303), while the number of FA procedures promptly diminished (n = 2189).

In conclusion, out of 19,898 total FA procedures performed in the observation period, 3444 (17.3%) were in 2013, 3972 (19.9%) were in 2014, 3601 (18.1%) were in 2015, 3407 (17.2%) were in 2016, 3285 (16.5%) were in 2017, and 2189 (11%) were in 2018. Out of 7949 OCTA procedures performed in the observation period, none were performed in 2013, 550 (6.9%) were in 2014, 908 (11.5%) were in 2015, 2098 (26.4%) were in 2016, 2090 (26.3%) were in 2017, and 2303 (28.9%) were in 2018.

Discussion

Retinal vasculature is involved in many ocular diseases that cause visual loss. Until 5 years ago, in vivo retinal circulation was observable only by performing intravenous injection of fluorescein. Although FA is still considered the criterion standard for evaluation of the retinal vasculature, it has risks of adverse effects and known defects in imaging all capillary plexuses.

With the advent of OCTA, a new noninvasive technique capable of detecting the flow inside vessels without intravenous contrast agent injection, it is now possible to visualize retinal circulation directly in a multilayer, tridimensional way.[11–13] Mastropasqua et al.[14] first described the

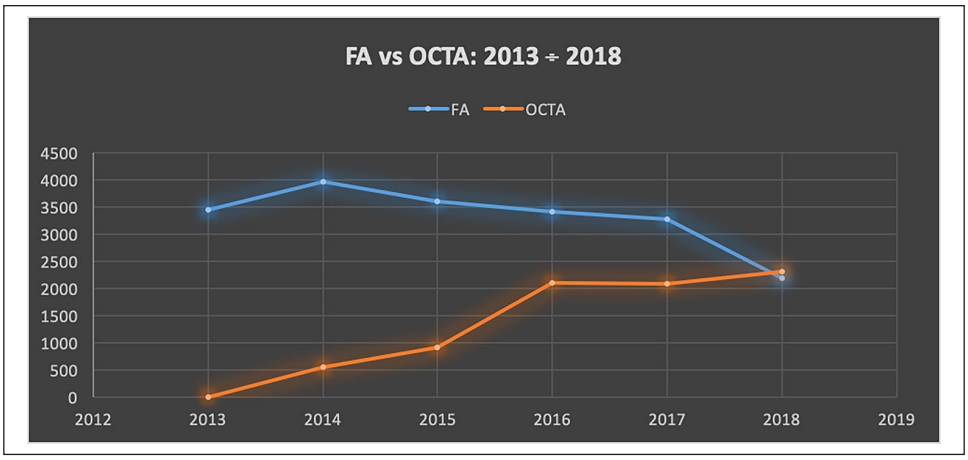

Figure 5. Data collected from the three centers were merged and analyzed on the whole. An overall increase in the use of OCTA was observed throughout the study period (from n = 0 in 2013 to n = 2303 in 2018). The curves showing the trend of the use of FA and OCTA crossed in 2018, as the amount of OCTA procedures gradually increased (n = 2303), while the number of FA procedures promptly diminished (n = 2189).

application of OCTA in different retinovascular diseases. In the FOIS study, we conducted a trend analysis on the use of OCTA in comparison to the application of FA between 2013 and 2018 in three different centers in middle Italy. As far as we know, this is the first study performed to assess the impact that the introduction of OCTA has had on the use of FA in daily clinical practice. Our results indicated that FA is still used, although its application has been decreasing over the years. In contrast, the use of OCTA is exponentially increasing with great applicability in daily clinical practice. The rate of change in the use of OCTA over the last few years has been phenomenal and may be explained by the evidence that OCTA is safer, easier, and faster than FA, relatively inexpensive and available to nearly everyone. Furthermore, this imaging modality enabled a very detailed visualization of the vascular networks. The first studies on OCTA were aimed at evaluation of the retinal circulation anatomy. Savastano et al.[12] first described different morphological features of the superficial capillary plexus (SCP) and the deep capillary plexus (DCP) by the use of OCTA. The narrow interconnections between the SCP and the DCP were described by Bonnin et al.,[15] suggesting differences in flow resistance and perfusion of the two plexuses. Even the peripapillary circulation has been evaluated by OCTA, showing that the radial peripapillary capillary network, inner retinal vascular plexus, and outer retinal capillary plexus were better observable with OCTA than FA.[9] OCTA provides volumetric data and shows both retinal structure and blood flow information in tandem. Furthermore, it also provides quantitative data about flow area, nonflow area, and vascular density.[16] The ability to provide an anatomically detailed visualization of all capillary plexuses has allowed a deeper investigation and comprehension of the diseases involving the retinal and choroidal vascularization. Even more, as a dyeless noninvasive imaging modality, OCTA is suitable to be performed more frequently than FA, and therefore it provides an essential tool in the follow-up of several ocular diseases. Previous studies showed the superiority of FA and indocyanine green (ICG) angiography in contrast to OCTA, concerning sensitivity and specificity in the diagnosis of treatment-naïve choroidal neovascularization (CNV).[17] Nevertheless, the isolation of CNV morphology and its repeatability in OCTA scans indicate its potential capacity for qualitative assessment and monitoring of response to antiangiogenic treatment in this chronic disease.[18–20] OCTA permits visualization of most clinically relevant vascular changes, not only CNV but also RVO,[21] MH,[22] MacTel,[23] and so on. According to the results of this study, FA is still used, although its application has been decreasing over the years. The use of FA is probably still indicated in the evaluation of the retinal periphery or in difficult cases in which the use of only OCTA could be limiting in making the correct diagnosis. The application of OCTA in daily clinical practice is likely to improve in the future as new algorithms to better visualize the periphery are coming, exciting researchers and retinal specialists. With respect to the inability of OCTA to image the retinal periphery, which is considered an important drawback to the application of this modality, recent advances have led to the introduction of wider scans. Indeed, the clinical usefulness of wide-angle OCT angiography in imaging nonperfused areas and neovascularization in eyes affected by retinal vascular disorders has already been described in the literature.[24,25] Although Pellegrini et al.[25] claimed a lack of details of the perfusion status of the retina when imaged by wide-field OCTA, both of these studies provided proof of the improvement in OCTA technology.[24,25]

To conclude, although the small number of centers considered can be regarded as a limitation to this study, the present analysis succeeded in demonstrating the

revolutionary role played by the introduction of OCTA in clinical practice. The increasing use of OCTA observed in this study may be explained by a growing familiarity with this imaging tool as well as the awareness of its potentialities and a spreading interest in exploring its possibilities. Perhaps in the future, OCTA will be helpful also in medicine with artificial intelligence. Surely, today it is a remarkable achievement for many ophthalmologists around the world to be able to perform angiography without dye injection.

Authors' Note

Maria Cristina Savastano, Stanislao Rizzo and Alfonso Savastano are now affiliated with UOC Oftalmologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italia; Università Cattolica del Sacro Cuore, Roma, Italia; and UOC Oftalmologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italia, respectively.

Acknowledgements

The authors thank Valeria Pagliei for her commitment and dedication in this article.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Précis

Speed and safety of the OCTA procedure in everyday clinical practice have facilitated the greater application of OCTA compared to FA in recent years. OCTA is suitable to be performed more frequently than FA.

ORCID iD

Maria Cristina Savastano https://orcid.org/0000-0003-1397-4333

References

1. Novotny HR and Alvis DL. A method of photographing fluorescence in circulating blood in the human retina. *Circulation* 1961; 24: 82–86.
2. Kwan AS, Barry C, McAllister IL, et al. Fluorescein angiography and adverse drug reactions revisited: the lions eye experience. *Clin Exp Ophthalmol* 2006; 34(1): 33–38.
3. Yannuzzi LA, Rohrer KT, Tindel LJ, et al. Fluorescein angiography complication survey. *Ophthalmology* 1986; 93(5): 611–617.
4. Kornblau IS and El-Annan JF. Adverse reactions to fluorescein angiography: a comprehensive review of the literature. *Surv Ophthalmol* 2019; 64(5): 679–693.
5. Halperin LS, Olk RJ, Soubrane G, et al. Safety of fluorescein angiography during pregnancy. *Am J Ophthalmol* 1990; 109: 563–566.
6. Acheson R and Serjeant G. Painful crises in sickle cell disease after fluorescein angiography. *Lancet* 1985; 1(8439): 1222.
7. Mendis KR, Balaratnasingam C, Yu P, et al. Correlation of histologic and clinical images to determine the diagnostic value of fluorescein angiography for studying retinal capillary detail. *Invest Ophthalmol Vis Sci* 2010; 51(11): 5864–5869.
8. Weinhaus RS, Burke JM, Delori FC, et al. Comparison of fluorescein angiography with microvascular anatomy of macaque retinas. *Exp Eye Res* 1995; 61(1): 1–16.
9. Spaide RF, Klancnik JM Jr and Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. *JAMA Ophthalmol* 2015; 133(1): 45–50.
10. Makita S, Hong Y, Yamanari M, et al. Optical coherence angiography. *Opt Express* 2006; 14: 7821–7840.
11. Spaide RF, Fujimoto JG, Waheed NK, et al. Optical coherence tomography angiography. *Progress in Retinal and Eye Research* 2017; 64: 1–55.
12. Savastano MC, Lumbroso B and Rispoli M. In vivo characterization of retinal vascularization morphology using optical coherence tomography angiography. *Retina* 2015; 35(11): 2196–2203.
13. Coscas G, Lupidi M and Coscas F. Optical coherence tomography angiography in healthy subjects. *Developments in Ophthalmology* 2016; 56: 37–44.
14. Mastropasqua R, Di Antonio L, Di Staso S, et al. Optical coherence tomography angiography in retinal vascular diseases and choroidal neovascularization. *J Ophthalmol* 2015; 2015: 343515.
15. Bonnin S, Mane V, Couturier A, et al. New insight into the macular deep vascular plexus imaged by optical coherence tomography angiography. *Retina* 2015; 35(11): 2347–2352.
16. Mané V, Dupas B, Gaudric A, et al. Correlation between cystoid spaces in chronic diabetic macular edema and capillary nonperfusion detected by optical coherence tomography angiography. *Retina* 2016; 36: S102–S110.
17. Gong J, Yu S, Gong Y, et al. The diagnostic accuracy of optical coherence tomography angiography for neovascular age-related macular degeneration: a comparison with fundus fluorescein angiography. *J Ophthalmol*. Epub ahead of print 23 March 2016. DOI: 10.1155/2016/7521478.
18. Muakkassa NW, Chin AT, de Carlo T, et al. Characterizing the effect of anti-vascular endothelial growth factor therapy on treatment-naive choroidal neovascularization using optical coherence tomography angiography. *Retina* 2015; 35(11): 2252–2259.
19. Lumbroso B, Rispoli M and Savastano MC. Longitudinal optical coherence tomography-angiography study of type 2 naive choroidal neovascularization early response after treatment. *Retina* 2015; 35(11): 2242–2251.
20. Phasukkijwatana N, Tan ACS, Chen X, et al. Optical coherence tomography angiography of type 3 neovascularisation in age-related macular degeneration after antiangiogenic therapy. *Br J Ophthalmol* 2017; 101(5): 597–602.

21. Rispoli M, Savastano MC and Lumbroso B. Capillary network anomalies in branch retinal vein occlusion on optical coherence tomography angiography. *Retina* 2015; 35(11): 2332–2338.
22. Rizzo S, Savastano A, Bacherini D, et al. Vascular features of full-thickness macular hole by OCT angiography. *Ophthalmic Surg Lasers Imaging Retina* 2017; 48(1): 62–68.
23. Toto L, Di Antonio L, Mastropasqua R, et al. Multimodal imaging of macular telangiectasia type 2: focus on vascular changes using optical coherence tomography angiography. *Invest Ophthalmol Vis Sci* 2016; 57(9): OCT268–OCT276.
24. Sawada O, Ichiyama Y, Obata S, et al. Comparison between wide-angle OCT angiography and ultra-wide field fluorescein angiography for detecting non-perfusion areas and retinal neovascularization in eyes with diabetic retinopathy. *Graefes Arch Clin Exp Ophthalmol* 2018; 256(7): 1275–1280.
25. Pellegrini M, Cozzi M, Staurenghi G, et al. Comparison of wide field optical coherence tomography angiography with extended field imaging and fluorescein angiography in retinal vascular disorders. *PLoS ONE* 2019; 14(4): e0214892.