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Optical coherence tomography angiography in comparison with fluorescein angiography in diabetic retinopathy

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Abstract

Background
Diabetic retinopathy (DR) is a microvascular complication of diabetes, and it is a leading cause of blindness. Fluorescein angiography (FA) is a vitally crucial diagnostic tool for evaluating fundus features of diabetic retinopathy.

Purpose
The purpose of the study was to evaluate optical coherence tomography angiography (OCTA) in eyes with diabetic maculopathy (DM) compared with the findings in fundus fluorescein angiography.

Design
It is a cross-sectional study.

Patients and methods
The study involved 40 eyes of 40 patients suffering from DM. The patients' ages ranged from 30 to 66 years with a mean value of 51.4 ± 8.55 years, of which –28 (70%) were females and 12 (30%) were males. We compared OCTA with FA in terms of the ability to visualize the DM changes detected, such as microaneurysms, capillary nonperfusion, foveal avascular zone interruption, perifoveal changes, hemorrhages, and edema in both superficial and deep capillary plexuses.

Results
Microaneurysms were detected in all eyes in OCTA and FA. Retinal hemorrhages were detected using OCTA in deep capillary plexuses (42.5% (17/40) of eyes compared with 7.5% (3) in superficial capillary plexuses with a significant difference that may better evaluate the level of retinal hemorrhage among diabetic eyes. Areas of capillary loss obscured by fluorescein leakage on fluorescein angiography were more clearly defined on OCTA. Capillary nonperfusion showed no statistically significant difference between FA and OCTA. FA could detect intraretinal microvascular abnormalities/collaterals in eight (20%) eyes, while OCTA could detect four (10%) with *P* value = 0.210, which is insignificant.

Conclusion
Both FA and OCTA could detect microaneurysms in all eyes. OCTA could precisely locate their depth and origin, which is not possible in FA. OCTA showed higher accuracy in assessing capillary nonperfusion areas than FA, but with a statistically insignificant difference.

Keywords: Diabetic retinopathy, fluorescein angiography, optical coherence tomography angiography

Introduction

The most common cause of blindness in industrial countries is diabetic retinopathy (DR) [1]. As the number of patients who have diabetes and therefore DR is expected to increase, improving investigation methods of diagnosis, follow-up, and deciding the proper treatment of DR is a must [2].

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One of the essential diagnostic tools of DR is fluorescein angiography (FA). FA is vital in the diagnosis and, therefore, in deciding treatment protocols of DR. FA evaluates the clinical features of the fundus of nonproliferative DR changes such as microaneurysms (MA), intraretinal microvascular abnormalities (IRMA), and retinal capillary nonperfusion. Neovascularization can be identified by remarkable leakage of the dye toward the vitreous cavity [3].

However, fluorescein dye injection can cause serious side effects even to healthy individuals. It can cause mild symptoms such as nausea, vomiting, fatigue, and significant accidents such as anaphylactic shock. Patients with diabetic maculopathy (DM) often suffer from comorbidities such as chronic renal impairment or cardiovascular disease. Therefore, dye injection must be preceded by systemic investigations [4–6].

In addition, FA images are two dimensions restricted, making it harder to distinguish intraretinal structures such as superficial capillaries and deep capillaries [7].

The optical coherence tomography angiography (OCTA) is a noninvasive and safer investigation tool compared with FA [8]. Recently, many theoretically based OCTA methods were developed and applied to fundus imaging. The newly developed OCT angiography uses a split-spectrum amplitude-decorrelation angiography algorithm that can visualize structural changes of the retina and provide 3-dimensional vascular mapping at the level of microcirculation, improving the signal-to-noise ratio of flow detection [9–16].

The study aims to evaluate optical coherence tomography angiography in eyes with DM compared with findings in fundus fluorescein angiography in terms of the ability to visualize the DM changes. We focused on MA, IRMA, macular edema, neovascularization, and perifoveal changes.

Patients and methods

This is a cross-sectional, observational study. Participants carefully read and signed informed consents before participation. The study involved 40 eyes of 40 patients suffering from DM.

The study followed the ethical values in collecting data, data analysis, and keeping honesty. All patients signed a written informed consent to participate in the study and for publication of data before enrollment in the study. All information about patients' health status, medical condition, diagnosis, prognosis, treatment, and all other information of a personal kind was kept confidential. The study gained the approval of the Institutional Review Board.

We performed the following ophthalmic examinations on all participants: best-corrected visual acuity, slit-lamp biomicroscopy, and color-fundus photography. FA was done using the device Spectralis Heidelberg Retina Angiograph + OCT (Heidelberg Engineering, Heidelberg, Germany). Both fundus-colored photography and FA were done after pupillary dilatation and intravenous injection of 5 ml of 10% fluorescein sodium injection (fluorescein 500 mg i.v. amp, Chemical Industries Development, Giza, Egypt). OCTA was based on RTVue XR Avanti (Optovue, Inc., Freemont, California, USA).

We excluded patients with severe media opacities such as dense cataracts or vitreous hemorrhage, patients with macular edema due to conditions other than DR, and patients who underwent previous ocular surgeries.

FA images

Early, intermediate, and late phases of FA images were examined. They included central and peripheral images.

The following findings were evaluated on FA images:

(1) Perifoveal capillary arcade of the capillary plexus, whether visible or not, disrupted or not.
(2) Central and peripheral nonperfused areas (areas of capillary dropouts) in early phases.
(3) Dilated capillaries (telangiectatic vessels) with staining of their walls in late phases, and areas of intraretinal hemorrhages.
(4) Areas of hyperfluorescence in the macula denoting diffuse or cystoid (petaloid) macular edema, in late phases, MA.
(5) Disk hyperfluorescence (disk leakage) in late phases.
(6) Photocoagulation scars.
(7) Neovascularization elsewhere and disk neovascularization.

The parameters used in the OCTA machine

The AngioVue OCTA device (Optovue, Inc., Freemont, California, USA) was used to get amplitude-decorrelation angiography image with an A-scan rate of 70 000 scans/second, and a light source centered on 840 nm and a bandwidth of 50 nm. Every OCTA volume contained 304 × 304 A scans, with two consecutive B scans captured at fixed positions before subsequent sampling locations. The split-spectrum amplitude-decorrelation angiography algorithm was used to extract OCTA information.

Each OCTA volume was acquired in three seconds, and two orthogonal OCTA volumes were obtained to perform motion correction to reduce motion artifacts that happen due to microsaccades and fixation changes. The displayed angiography information was the mean of decorrelation values when viewed perpendicularly through the assessed thickness.

Acquisition workflow of angioretina scan

Scan size for retina was 3 × 3 mm. All were acquired with 304 × 304 A-scan per volume.

Image analysis of fundus examination for diffuse macular edema (DME), cystoid macular edema, clinically significant macular edema, nonproliferative DR (mild, moderate, or severe), and proliferative DR.

OCTA images

Angiographic analysis was done, focusing on the retina's two vascular layers: superficial capillary plexuses (SCP) and deep

capillary plexuses (DCP). The average capillary density, central capillary density, and foveal avascular zone (FAZ).

The following findings were evaluated at the level of both plexuses: FAZ interruption. Capillary nonperfusion areas. The presence of perifoveal changes (telangiectasia, dilatation, or rarefaction), and hemorrhages. Macular edema, with further evaluation on the coregistered OCT *en face* intensity images and OCT B-scan images, MA, and IRMA.

The AngioVue system (Avanti OCT, Optovue, Fremont, California, USA) using the split-spectrum amplitude-decorrelation angiography algorithm can divide the retina–choroid layer into four layers: the SCP, DCP, outer retina, and choroidal vessels.

Quantitative analysis

Vessel-density measurement was performed on the selected images; the instrument automatically measured the average and foveal capillary density. The device calculated vascular density as the percentage of the area occupied by blood vessels with flow above a threshold-detection level in a selected area and depth of vessels. The investigator manually outlined the FAZ in the SCP, and the FAZ area was calculated using the software.

Qualitative analysis

Diabetic changes were also detected as MA, capillary nonperfusion, FAZ interruption, perifoveal changes, hemorrhages, and edema in both superficial and deep capillary plexuses.

Statistical analysis

Data were collected, revised, coded, and entered into the Statistical Package for the Social Sciences IBM SPSS (SPSS Statistics for Windows, Version 23.0, 2015, Armonk, New York: IBM Corp.). The quantitative data were presented as mean, standard deviations, and ranges. Qualitative variables were presented as numbers and percentages. The comparison between groups regarding qualitative data was made using the χ^2 test and/or Fisher exact test when the expected count in any cell was found less than 5. The confidence interval was set to 95%, and the margin of error accepted was set to 5%. *P* value less than 0.05 was significant.

Results

Our study involved a total of 40 eyes of 40 patients. The patients' ages ranged from 30 to 66 years with a mean value of 51.4 ± 8.55 years, of which 28 (70%) were females, and 12 (30%) were males. Diabetes duration ranged between 5 and 23 years with a mean of 15.20 ± 5.28 years.

Twenty-six patients (65%) were on insulin, 8 patients (20%) were on oral treatment, and 6 patients (15%) were on combined oral and insulin treatment.

Among the patients with diabetes, eight (20%) had concomitant hypertension.

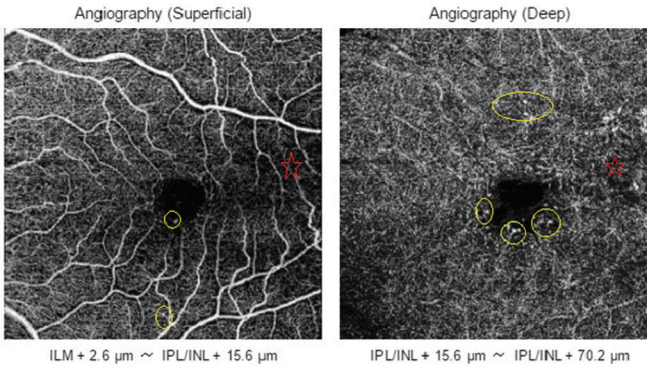

Figure 1: OCTA SCP (Left picture) and DCP (Rightpicture) of OD eye of a 52 years old female diabetic patient for 8 years showed microaneurysms (surrounded by yellow circles) more numerous in DCP, enlaged and interrupted FAZ in DCP.

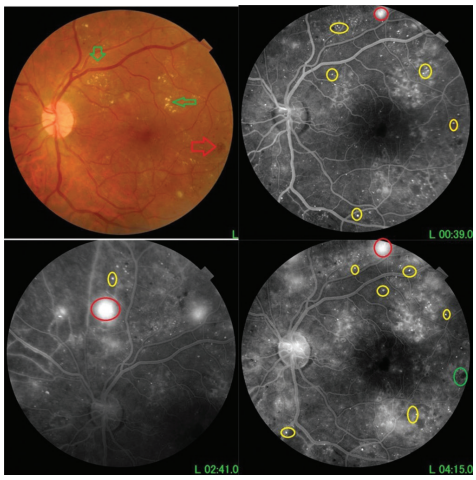

Figure 2: Colored fundus photo and fluorescein angiography of left eye eye of 42 years old male patient with 8 years duration of diabetes, Colored fundus photo shows hard exudates (pointed by green arrows), Haemorrhage (pointed by red arrow), FFA shows leaking and non leaking microaneurysms causing macular edema (examples surrounded by yellow circle), More numerous than OCTA, Evidence of blocked fluorescence corresponding to hemorrhage seen in colored photo (examples surrounded by green circle), Evidence of nves (examples surrounded by red circle) (not appear in OCTA due to narrower field), NVD and perifovea capillary drop out.

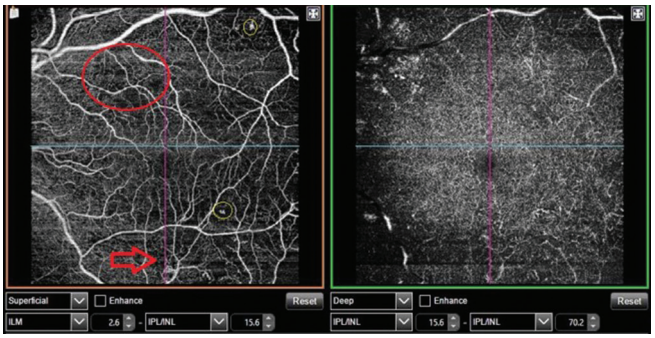

Figure 3: OCTA of left eye eye of 42 years old male patient with 8 years duration of diabetes, OCTA of LT eye of the same patient, SCP and DCP showing: Microaneurysms (examples surrounded by yellow circle) Less numerous than FFA due to narrower field and low blood flow in them, Capillary non perfusion areas (examples surrounded by red circle) that appear more clearly than FFA, IRMA pointed by red arrow not appear in FFA.

Table 1: Comparison of diabetic pathological changes detected in FA and OCTA

	Fundus fluorescein angiography, *n* (%)	Optical coherence tomography angiography superficial capillary plexus *n* (%)	Test value*	*P*	Sig.
Microaneurysms					
No	0	0	NA	NA	NA
Yes	40 (100.0)	40 (100.0)			
IRMA/collaterals					
No	32 (80.0)	36 (90.0)	1.569	0.210	NS
Yes	8 (20.0)	4 (10.0)			
Nonperfusion					
No	12 (30.0)	17 (42.5)	1.352	0.244	NS
Yes	28 (70.0)	23 (57.5)			

FA, fluorescein angiography; IRMA, intraretinal microvascular abnormalities; NS, nonsignificant; OCTA, optical coherence tomography angiography;. *χ^2 test. NA, Not applicable

Table 2: Overall prevalence of macular edema among all cases by clinical examination, FA, and OCTA examination of SCP and DCP

Edema	*n* (%)
Clinical	
Negative	0
Positive	40 (100.0)
Fluorescein angiography	
Negative	0
Positive	40 (100.0)
SCP	
Negative	28 (70.0)
Positive	12 (30.0)
DCP	
Negative	19 (47.5)
Positive	21 (52.5)

DCP, deep capillary plexus; FA, fundus fluorescein angiography; OCTA, optical coherence tomography angiography; SCP, superficial capillary plexus.

Table 3: Descriptive data found by OCTA in the studied cases

Optical coherence tomography angiography overview	Value
Av CD	
Mean±SD	45.16±4.14%
Range	37.51-52.2%
Central CD	
Mean±SD	27.74±7.14%
Range	15.24-47.53%
FAZ area	
Mean±SD	0.46±0.21 mm^2
Range	0.12-1.07 mm^2

Av CD, average capillary density; CD, capillary density; FAZ, foveal avascular zone; OCTA, optical coherence tomography angiography; SD, standard deviation.

Comparison between the results by FA and OCTA SCP of the studied cases

Showed that both FA and OCTA could detect the presence of MA in all eyes of the study [Figures 1-3].

FA could detect IRMA/collaterals in 8 (20%) eyes, while OCTA could detect 4 (10%) with *P* value = 0.210, which is not significant.

Similarly, capillary nonperfusion showed no statistically significant difference between FA and OCTA as FA could detect 28 (70%) eyes and OCTA detected 23 (57.5%) of the cases with *P* value = 0.244 [Table 1].

Macular edema was detected clinically in 40 eyes (100%), and in 40 eyes (100%) by fluorescein angiography. OCTA could detect macular edema in SCP in 12 eyes (30%), and in 21 eyes in DCP (52.5%) [Table 2].

Descriptive data found by OCTA in the studied eyes

The average capillary density (AvCD) ranged between 37.51 and52.2 mm with a mean of 45.16 ± 4.14, while the central capillary density (central CD) ranged between 15.24 and 47.53 mm with a mean of 27.74 ± 7.14 and the FAZ area ranged between 0.12 and 1.07 mm^2 with a mean of 0.46 ± 0.21 (Tables 3 and 4).

(1) FAZ interruption was detected in SCP in 17 (42.5%) of the eyes compared with 20 (50%) in DCP with *P* value = 0.057, which is not statistically significant.
(2) In total, 8 eyes (20%) were distorted in the SCP imaging compared with 14 (35%) in DCP imaging.
(3) Capillary nonperfusion could be detected in SCP imaging in 23 (57.5%) compared with 22 (55%) in DCP imaging with *P* value = 0.821, which is nonsignificant.
(4) Perifoveal changes: in SCP imaging, rarefaction was seen in 16 (40%), dilatation in 4 (10%), rarefaction + dilatation in 11 (27.5%), and rarefaction + telangiectasia were detected in 2 (5%) of the eyes. While in DCP imaging, the results were 16 (40%), 3 (7.5%), 7 (17.5%), and 1 (2.5%) of the eyes, respectively, which are all of no statistically significant difference.
(5) Hemorrhages: only 3 (7.5%) eyes showed hemorrhages in SCP, while 17 (42.5%) of the eyes showed hemorrhages in DCP imaging with *P* value = 0.000, which is a statistically high significant difference.
(6) Edema: there was a statistically significant difference with *P* value = 0.041 as SCP showed 12 (30%) eyes with edema and DCP showed 21 (52.5%).
(7) MA were easily shown by SCP 40 (100%) eyes and

Table 4: Comparison between results by OCTA, SCP, and DCP of the studied cases

	Superficial capillary plexus *n* (%)	Deep capillary plexus *n* (%)	Test value*	*P*	Sig.
FAZ interruption					
No	15 (37.5)	6 (15.0)			NS
Yes	17 (42.5)	20 (50.0)	5.737	0.057	
Distorted	8 (20.0)	14 (35.0)			
Cap nonperf					
No	17 (42.5)	18 (45.0)	0.051	0.821	NS
Yes	23 (57.5)	22 (55.0)			
Perifoveal changes					
No	4 (10.0)	3 (7.5)	0.157	0.692	NS
Rarefaction	16 (40.0)	16 (40.0)	0	1.000	NS
Dilatation	4 (10.0)	3 (7.5)	0.157	0.692	NS
Rarefaction + dilatation	11 (27.5)	7 (17.5)	1.147	0.284	NS
Rarefaction + telangiectasia	2 (5.0)	1 (2.5)	0.346	0.556	NS
Rarefaction + dilatation + telangiectasia	3 (7.5)	10 (25.0)	4.501	0.034	S
Hemorrhages					
No	37 (92.5)	23 (57.5)	13.067	0	HS
Yes	3 (7.5)	17 (42.5)			
Edema					
No	28 (70.0)	19 (47.5)	4.178	0.041	S
Yes	12 (30.0)	21 (52.5)			
Microaneurysms					
No	0	1 (2.5)	1.013	0.315	NS
Yes	40 (100.0)	39 (97.5)			
IRMA					
No	36 (90.0)	37 (92.5)	0.157	0.692	NS
Yes	4 (10.0)	3 (7.5)			

FAZ, foveal avascular zone; HS, highly significant; IRMA, intraretinal microvascular abnormality; NS, nonsignificant; OCTA, optical coherence tomography angiography; S, significant. *χ^2 test.

39 (97.5%) eyes by DCP with *P* value = 0.315, which is not statistically significant.

(8) IRMA was detected by SCP in 4 (10%) eyes and by DCP in 3 (7.5%) eyes with *P* value = 0.692, which is not significant statistically.

Discussion

FA is an essential investigation tool in diagnosing and following DR pathological changes, and because it needs a dye injection before imaging, it is considered as an invasive tool [17].

OCTA is a noninvasive investigation that does not need dye injection [18]. It could visualize the various clinical findings associated with different stages of DM on both SCP and DCP [19].

In our study, OCTA allowed visualization of MA that were seen as focally dilated and abnormally shaped capillaries similarly with no distinction between both layers and also no distinction detected in the ability of FA and OCTA in MA detection (100% in both). OCTA might precisely locate their depth and origin as well. Salz *et al.* conjointly found that OCTA did have the additional benefit of localizing the precise intraretinal depth of MA [20].

These results were comparable with the study conferred by Ishibazawa, whose study enclosed 42 eyes of 25 patients with DR. But he observed the presence of a difference between MA shown in FA and OCTA. They referred this to the histopathological configuration of MA lumen that consists of different structures such as thickened, hyalinized, fibrous, laminated, and lipid-containing basement membrane, and hypercellular or multilayered endothelial cells that cause turbulence in the blood flow within them. Therefore, they advised that the blood flow within some types of MA may not have been perfectly displayed using OCTA; additionally, he stated that around eighty percent of MA were located within the inner deep plexus [21]. Salz *et al.* stated that OCTA could detect MA with a higher capillary flow better than MA with a slow flow [20].

OCTA could visualize IRMAs as dilated vessels near the areas of capillary loss and could detect neovascularization by the flow signal at the interior-limiting membrane [20,22].

However, IRMA could be detected in our study by OCTA less than FA with a statistically insignificant difference. The result was consistent with the result conferred by Couturier *et al.*, who additionally showed the ability of OCTA to detect them in all cases and referred this to the character of IRMA that might have a more rapid blood flow than do MA, therefore enhancing their detection by OCTA [23].

Salz *et al.* also found that OCTA could visualize vascular abnormalities that were not seen clinically or on FA.

This could be explained by: Unlike FA, hyperfluorescence does not occur in OCTA, which does not cause any confusion due to any leaking of dye, Alsom OCTA has a higher resolution than FA that has a lower resolution, which could not visualize the small MA [20].

In our study, OCTA visualized IRMA in SCP (10%) slightly more than in DCP (7%) with a nonstatistically significant difference.

On the other hand, Ishibazawa *et al.* declared better visualization of IRMA in deeper capillaries by OCTA than superficial due to the thinner thickness of the inner retina in the nonperfused areas [21].

The assessment of capillary nonperfusion areas in our study by OCTA showed slightly lower accuracy than FA but with a difference that was not statistically significant. Capillary nonperfusion was visualized as capillary nonvisible areas between retinal vessels. Couturier *et al.* stated that edges of capillary nonperfusion areas are highly delimited on OCTA than on FA, and some capillary nonperfusion areas detected on OCTA were visualized as perfused on FA. Moreover, he referred this to the superposition of the two-capillary complex body part and a few early outpouring on FA [24].

In our study, we evaluated the enlargement and disruption of the FAZ and capillary dropout. According to recent studies, FAZ and parafoveal vessel density have been reported nearly as good indicators of vascular dropout in DM patients [23]. OCTA could also clearly identify capillary nonperfusion in DR eyes because it could distinguish the level of capillary dropout that may indicate ischemia between superficial and deep capillary plexus [25].

We conjointly could identify the perifoveal tube changes as well as rarefaction, dilatation, and telangiectasia by OCTA with delineation and distinguishment of the level in superficial and deep capillary plexus, notably OCTA allowed higher identification of combined vascular changes in the deep layer instead of the superficial layer compared with FA that had a wider field. Nevertheless, FA's low resolution could not focus on small microvascular pathologies [20]. Couturier *et al.* suggested that OCT angiography was better in detecting capillary rarefaction [23].

Couturier conjointly stated that the DCP nonperfused areas were observed in 35% of the subjects studied, whereas in our study, it may be observed in 55% of the subjects. Although OCTA could detect in our study FAZ interruption in SCP in 40 tries in DCP in five-hundredth, however, we had carefully interpreted these analyses because distorted images of FAZ were found in four-hundredth and five-hundredth in SCP and DCP, respectively, and the reason could be due to the use of one method only to observe the FAZ areas of the SCP or the DCP, which is one of the limitations of our study.

FAZ area measured by OCTA ranged between 0.12 and 1.07-mm square with a mean of 0.46 ± 0.21. The FAZ area was well visualized on OCTA in our study with better delineation than FA, and FAZ enlargement was detected altogether in the cases.

Moreover, that was similar to the result conferred by Kim *et al.*, who revealed that OCTA could display the FAZ zone more clearly than FA, and this was conjointly reported by Al-sheikh *et al.* [26,27].

In our study, we evaluated edema by observing any retinal capillary displacement or disappearance. OCTA did allow not only evaluation of macular edema but also visualization of its level. In our study, we also found that OCTA images of the deep-plexus 500th (21/40) eyes showed the most apparent edema compared with the superficial-plexus 30-min (12/40) eyes, which is consistent with Coscas *et al.*, who declared that edema might affect the DCP [28].

Notably, FA could detect DME in all cases 100 pc (40/40) compared with overall edema detection in both DCP and SCP 82% (33/40), which may be referred to as an artifact within the OCTA technique.

Conclusion

We were conjointly able to compare OCTA and FA images and assess the relative sensitivity of OCTA compared with FA that used to be the gold standard for evaluation of DME, but with many limitations associated with the need for dye injection. Our study showed the ability of FA and OCTA in MA detection in all eyes, but less numerous in OCTA than FA, and OCTA could precisely locate their depth and origin, which is not possible in FA. The assessment of capillary nonperfusion areas in our study by OCTA showed higher accuracy compared with FA, but with a difference that was not statistically significant.

We are hoping in the future that OCT angiography machines will provide us with imaging faster scanning speed, thus yielding images with larger scanning areas and better resolution in a trial to overcome the limited field of view.

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Conflicts of interest

There are no conflicts of interest.

References

1. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. Arch Ophthalmol 1984; 102:527–532.
2. Saaddine JB, Honeycutt AA, Narayan KV, Zhang X, Klein R, Boyle JP. Projection of diabetic retinopathy and other major eye diseases among people with diabetes mellitus: United States, 2005-2050. Arch Ophthalmol 2008; 126:1740–1747.
3. Gass JD. A fluorescein angiographic study of macular dysfunction secondary to retinal vascular disease: IV. Diabetic retinal angiopathy. Arch Ophthalmol 1968; 80:583–591.
4. Cheung N, Wang JJ, Klein R, Couper DJ, Sharrett AR, Wong TY. Diabetic retinopathy and the risk of coronary heart disease: the Atherosclerosis Risk in Communities Study. Diabetes Care 2007; 30:1742–1746.
5. Kawasaki R, Cheung N, Islam FA, Klein R, Klein BE, Cotch MF, *et al*. Multi-ethnic study of atherosclerosis. Is diabetic retinopathy related to subclinical cardiovascular disease?. Ophthalmology 2011; 118:860–865.
6. Fioretto P, Mauer M, Brocco E, Velussi M, Frigato F, Muollo B, *et al*. Patterns of renal injury in NIDDM patients with microalbuminuria. Diabetologia 1996; 39:1569–1576.
7. Kwiterovich KA, Maguire MG, Murphy RP, Schachat AP, Bressler NM, Bressler SB, Fine SL. Frequency of adverse systemic reactions after fluorescein angiography: results of a prospective study. Ophthalmology 1996; 98:1139–1142.
8. Yeung L, Lima VC, Garcia P, Landa G, Rosen RB. Correlation between spectral-domain optical coherence tomography findings and fluorescein angiography patterns in diabetic macular edema. Ophthalmology 2009; 116:1158–1167.
9. Mariampillai A, Standish BA, Moriyama EH, Khurana M, Munce NR, Leung MK, *et al*. Speckle variance detection of microvasculature using swept-source optical coherence tomography. Opt Lett 2008; 33:1530–1532.
10. Miura M, Makita S, Iwasaki T, Yasuno Y. Three-dimensional visualization of ocular vascular pathology by optical coherence angiography in vivo. Ophthalmol Vis Sci 2011; 52:2689–2695.
11. Jia Y, Tan O, Tokayer J, Potsaid B, Wang Y, Liu JJ, *et al*. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. Opt Express 2012; 20:4710–4725.
12. Schwartz DM, Fingler J, Kim DY, Zawadzki RJ, Morse LS, Park SS, *et al*. Phase-variance optical coherence tomography: a technique for non-invasive angiography. Ophthalmology 2014; 121:180–187.
13. Jia Y, Bailey ST, Wilson DJ, Tan O, Klein ML, Flaxel CJ, *et al*. Quantitative optical coherence tomography angiography of choroidal neovascularization in age-related macular degeneration. Ophthalmology 2014; 121:1435–1444.
14. Jia Y, Wei E, Wang X, Zhang X, Morrison JC, Parikh M, *et al*. Optical coherence tomography angiography of optic disc perfusion in glaucoma. Ophthalmology 2014; 121:1322–1332.
15. Spaide RF, Klancnik JM, Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. JAMA Ophthalmol 2015; 133:45–50.
16. Spaide RF, Klancnik JM, Cooney MJ. Retinal vascular layers in macular telangiectasia type 2 imaged by optical coherence tomographic angiography. JAMA Ophthalmol 2015; 133:66–73.
17. Witmer MT, Parlitsis G, Patel S, Kiss S. Comparison of ultra-widefield fluorescein angiography with the Heidelberg Spectralis® noncontact ultra-widefield module versus the Optos® Optomap®. Clin Ophthalmol 2013; 7:389.
18. Varman A, Muralidharan R, Balakumar D Optical coherence tomography angiography: A general view. TNOA J Ophthalmic Sci Res 2017; 55:107.
19. Johnson RN, Fu AD, McDonald HR, Jumper JM, Ai E, Cunningham ET, *et al*. Fluorescein angiography: basic principles and interpretation. Retina Fifth Edition. Elsevier Inc., Amsterdam, Netherlands, 2012. 2-25.
20. Salz DA, Talisa E, Adhi M, Moult E, Choi W, Baumal CR, *et al*. Select features of diabetic retinopathy on swept-source optical coherence tomographic angiography compared with fluorescein angiography and normal eyes. JAMA Ophthalmol 2016; 134:644–650.
21. Ishibazawa A, Nagaoka T, Takahashi A, Omae T, Tani T, Sogawa K, *et al*. Optical coherence tomography angiography in diabetic retinopathy: a prospective pilot study. Am J Ophthalmol 2015; 160:35–44.
22. de Carlo TE, Bonini Filho MA, Baumal CR, Reichel E, Rogers A, Witkin AJ, *et al*. Evaluation of preretinal Neovascularization in proliferative diabetic retinopathy using optical coherence tomography angiography. Ophthalmic Surg Lasers Imaging Retina 2016; 47:115–119.
23. Couturier A, Mané V, Bonnin S, Erginay A, Massin P, Gaudric A, *et al*. Capillary plexus anomalies in diabetic retinopathy on optical coherence tomography angiography. Retina 2015; 35:2384–2391.
24. Bresnick GH, Condit R, Syrjala S, Palta M, Groo A, Korth K. Abnormalities of the foveal avascular zone in diabetic retinopathy. Arch Ophthalmol 1984; 102:1286–1293.
25. Birol G, Wang S, Budzynski E, Wangsa-Wirawan ND, Linsenmeier RA. Oxygen distribution and consumption in the macaque retina. Am J Physiol Heart Circ Physiol 2007; 293:H1696–H1704.
26. 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. Investig Ophthalmol Vis Sci 2016; 57:OCT362–OCT370.
27. 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. Investig Ophthalmol Vis Sci 2016; 57:3907–3913.
28. Coscas F, Sellam A, Glacet-Bernard A, Jung C, Goudot M, Miere A, *et al*. Normative data for vascular density in superficial and deep capillary plexuses of healthy adults assessed by optical coherence tomography angiography. Investig Ophthalmol Vis Sci 2016; 57:OCT211–OCT223.