AMERICAN ACADEMY OF OPHTHALMOLOGY®

In Vivo Mapping of the Choriocapillaris in Healthy Eyes

A Widefield Swept-Source OCT Angiography Study

Enrico Borrelli, MD, FEBO,[1] Akihito Uji, MD, PhD,[2] Lisa Toto, MD, PhD,[1] Pasquale Viggiano, MD,[1] Federica Evangelista, MD,[1] Rodolfo Mastropasqua, MD, FEBO[3]

Purpose: To report variation of choriocapillaris flow in peripapillary, macular, and near- and mid-periphery regions in healthy participants using widefield swept-source (SS) OCT angiography (OCTA).

Design: Prospective, cross-sectional study.

Participants: Fifty healthy participants.

Methods: Healthy young participants were imaged with the SS OCTA system (PLEX Elite 9000; Carl Zeiss Meditec, Inc, Dublin, CA). OCT angiography scans were obtained in primary and extreme gazes and a montage was created automatically. The en face choriocapillaris images then were exported to ImageJ software version 1.50 (National Institutes of Health, Bethesda, MD), and a semiautomated algorithm was used for subsequent quantitative analysis.

Main Outcome Measures: Quantitative analysis of the choriocapillaris performed in 3 different regions: (1) peripapillary, (2) macular, and (3) periphery. In addition, choriocapillaris variables were investigated further in distinct fields within these 3 different regions.

Results: Fifty eyes (50 participants) were included in the analysis. Mean age ± standard deviation was 25.2±5.1 years (median, 24.5 years; range, 20.0−40.0 years). The peripapillary region exhibited the greatest total signal void area ($P < 0.0001$ vs. the macular region; $P < 0.0001$ vs. the peripheral region). Within the macular region, the foveal area exhibited a greater total signal void area in comparison with both the parafoveal area ($P = 0.009$) and the perifoveal area ($P = 0.015$). In the analysis investigating the near- and mid-periphery region, the temporal sector was characterized by a lower total signal void area compared with both the superior and inferior areas ($P = 0.016$ and $P = 0.003$, respectively).

Conclusions: We report quantitative mapping of the choriocapillaris in healthy individuals. Choriocapillaris perfusion seems to have a wide topographic variation. *Ophthalmology Retina 2019;3:979-984 © 2019 by the American Academy of Ophthalmology*

The choriocapillaris is a highly anastomosed network of capillaries limited to the innermost part of the choroid, located between Bruch's membrane and the medium choroidal vessels.[1] Histologic evidence suggests that this thin vascular layer is organized into a series of hexagonal lobules that are smaller at the posterior pole and become progressively larger toward the periphery.[1,2] Furthermore, these tiny capillaries characteristically are separated by many small intercapillary spaces that are wider and progressively more elongated toward the retinal periphery.[2]

The introduction of OCT angiography (OCTA) has improved our capability to visualize and investigate the choriocapillaris. In OCTA en face images of the choriocapillaris, small dark regions (called *signal voids*) alternate with granular bright areas, which are likely to be secondary to choriocapillaris flow and vascular dropout, respectively.[3,4] Importantly, morphologic and histologic images of the choriocapillaris are strikingly similar to the OCTA versions, and the signal voids seem to represent the intercapillary spaces. Using OCTA, several studies have demonstrated that these signal voids expand regionally with age and disease (hypertension, high myopia, age-related macular degeneration).[1,5–9] Although these studies shed further light on choriocapillaris function and characteristics, an important limitation is that this assessment was limited to the macular region.

The recent introduction of high-speed swept-source (SS) OCTA devices has expanded significantly the assessment of the choriocapillaris. These devices use a longer wavelength (~1050 nm) with better retinal pigment epithelium penetration, and thus provide a more accurate evaluation of the choriocapillaris.[1,10] Importantly, a higher-speed system allows for acquiring a larger field of view.[11,12] A wider investigation of the choriocapillaris may become essential to understand better several chorioretinal disorders that are not limited to the macula.

https://doi.org/10.1016/j.oret.2019.05.026
ISSN 2468-6530/19

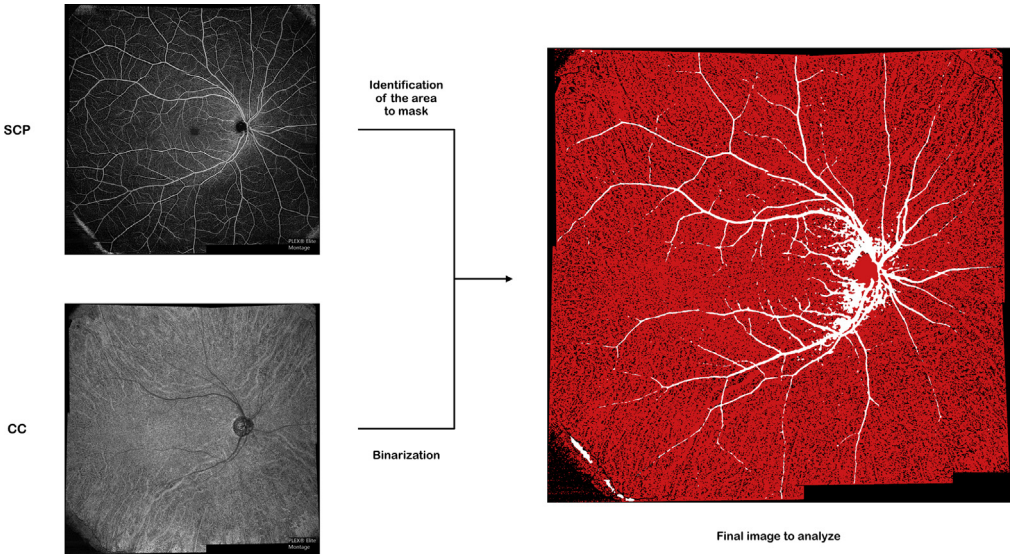

Figure 1. Representation of the algorithm used to study the choriocapillaris (CC) with widefield swept source OCT angiography (OCTA). The CC en face image was imported into ImageJ, and a Phansalkar threshold was applied to binarize the CC image. Pixels with an intensity over the applied threshold are marked in red in the final image, and those pixels below the threshold are marked in black. To identify and mask precisely the major superficial vessels (white in the final image), we used the superficial capillary plexus (SCP) en face OCTA image, which was thresholded and binarized. The 2 obtained thresholded images then were merged to obtain the final image.

The aim of this study was to report normal measurements of the choriocapillaris in healthy young individuals using widefield SS OCTA analysis. Notably, these measurements were determined in different retinal regions to provide a topographic analysis of choriocapillaris perfusion. Establishing healthy OCTA reference parameters of choriocapillaris vascularization is essential for proper interpretation of pathologic values.

Methods

Study Participants

In this prospective, observational cross-sectional study, healthy volunteers between 18 and 40 years of age were enrolled at the Ophthalmology Clinic of University G. d'Annunzio, Chieti-Pescara, Italy. The study was approved by the institutional review board and adhered to the tenets of the Declaration of Helsinki. Institutional review board–approved informed consent was obtained from all patients.

All enrolled participants were imaged with the PLEX Elite 9000 device (Carl Zeiss Meditec Inc, Dublin, CA) between April 2018 and July 2018. Moreover, all patients underwent a complete ophthalmologic examination, which included measurement of best-corrected visual acuity, intraocular pressure, and dilated ophthalmoscopy. Exclusion criteria were (1) evidence or history of ocular disease; (2) evidence or history of systemic disorders, including diabetes and systemic hypertension; (3) history of previous ocular surgery; (4) ocular axial length of more than 26 mm; (5) refractive error of more than 6 diopters; and (6) presence of peripapillary atrophy.

Imaging

Participants underwent OCTA imaging using the PLEX Elite 9000 device, which uses a swept laser source with a central wavelength of 1050 nm (1000–1100 nm full bandwidth) and operates at 100 000 A-scans per second. For each eye, 5 12 × 12-mm OCTA volume scans were acquired. FastTrac motion correction software (PLEX Elite 9000, Carl Zeiss Meditec Inc, Dublin, CA) was used while the images were acquired. These scans were acquired in 5 different patient gazes (central, nasal inferior, nasal superior, temporal inferior, and temporal superior) by moving the internal fixation light. For each eye, we thus obtained 5 OCTA scans from 5 distinct and partially overlapping retinal regions. Poor-quality images (signal strength index, <8) with either significant motion artifact or incorrect segmentation, were excluded and repeated. Finally, the software included in the device automatically combined these 5 scans in a final montage image.

Image Processing

The main outcome measure was the total signal void area, which represents a measure of the total area of choriocapillaris vascular dropout (absence of flow or flow less than the slowest detectable threshold). To quantify this variable, a slight modification of a previously reported algorithm was used (Fig 1).[5,8,9,13–15] In brief, for each eye, we first exported the superficial capillary plexus and choriocapillaris en face OCTA images (resolution, 500 × 500 pixels), which were segmented automatically by the PLEX Elite 9000 device. These images then were imported in ImageJ software version 1.50 (National Institutes of Health, Bethesda, MD; available at http://rsb.info.nih.gov/ij/index.html), and consequently, the Phansalkar method was used to binarize the choriocapillaris images. Obtained images were processed with the Analyze Particles command to assess the total signal void area. The choriocapillaris directly beneath major superficial retinal vessels was excluded from analysis to eliminate potentially confounding shadow or projection artifacts.

The quantitative analysis was performed in 3 different regions: (1) the macular region, which was defined as a circle centered on the fovea with diameter of 6.0 mm; (2) the peripapillary region, which consists of a 500-μm wide ring around the optic disc; and (3) the near- and mid-periphery region, which was assessed in 3 circles tangential to the macula and with diameters of 4.5 mm (Fig 2).[16]

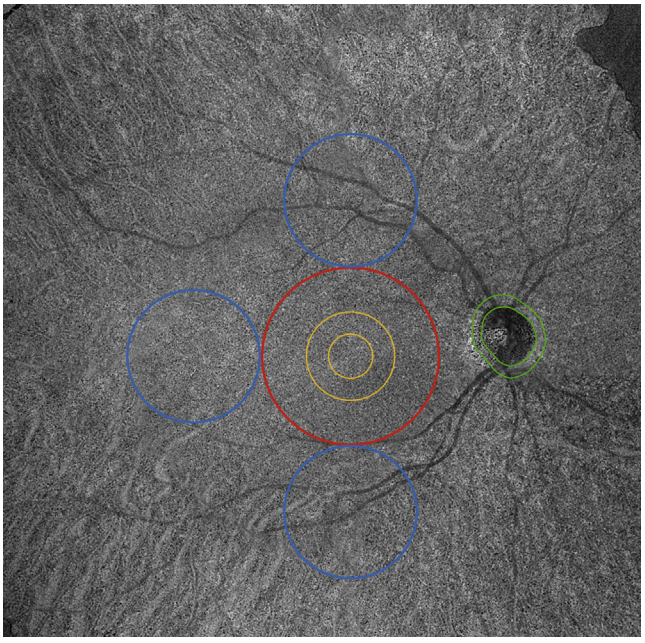

Figure 2. Representation of the regions used to investigate OCT angiography variables. OCT angiography variables were investigated in 3 different regions of the choriocapillaris: (1) the macular region (red circle) with a diameter of 6 mm; (2) the peripapillary region, which consists of a 500-μm wide annulus around the optic disc (green annulus); and (3) the periphery region, which was assessed in 3 circles tangential to the macula (blue circles) and with diameters of 4.5 mm. The macular region was divided further into the foveal area (within the inner yellow circle; diameter of 1.5 mm), the parafoveal area (annulus between the inner and outer yellow circles; diameter of 3 mm), and the perifoveal area (annulus between the outer yellow circle and the red circle; diameter of 6 mm). The periphery region was investigated separately in the superior, temporal, and inferior areas (blue circles).

The latter choice was made to investigate the choriocapillaris in the near and mid periphery (1.5-mm wide annulus around the macula and 3.0-mm wide annulus around the near periphery, respectively) and consequently to exclude the far periphery from the analysis (see "Discussion"). Furthermore, the analysis of the macular and near- and mid-periphery regions was performed further in different subfields: the macular region was divided further into the foveal, parafoveal, and perifoveal areas (with diameters of 1.5 mm, 3.0 mm, and 6.0 mm, respectively),[16] whereas the near and mid periphery was split into the superior, temporal, and inferior areas (Fig 2). To assess reproducibility of our measurements, 15 healthy patients underwent second OCTA measurements on a different day.

Statistical Analysis

All quantitative variables were reported as mean and standard deviation (SD) or median and interquartile range (IQR) in "Results" and in the tables. To detect departures from normality distribution, Shapiro-Wilk's test was performed for all variables. Because choriocapillaris variables did not show a normal distribution, the nonparametric Friedman test was conducted to investigate regional differences in quantitative choriocapillaris variables. The analysis of variance was used to assess the reproducibility between the 2 measurements. Spearman's correlation coefficient was used to assess correlations. Statistical calculations were performed using Statistical Package for Social Sciences version 20.0 (SPSS, Inc., Chicago, IL). The chosen level of statistical significance was $P < 0.05$.

Results

Characteristics of Participants Included in the Analysis

Fifty eyes of 50 participants (20 men, 30 women) were included in the analysis. Mean age ± SD was 25.2±5.1 years (median, 24.5 years; range, 20.0−40.0 years). Mean axial length ± SD was 23.9±1.1 mm (median, 23.9 mm; range, 21.8−25.9 mm).

Widefield OCT Angiography Analysis of the Choriocapillaris

The difference between the 2 measurements was not statistically significant in all the analyzed regions ($P = 0.21$ for the macular region [95% limits of agreement, 1.0%−2.6%], $P = 0.11$ for the peripapillary region [95% limits of agreement, 0.8%−2.2%], and 0.62 for the near- and mid-peripheral region [95% limits of agreement, 0.1%−0.9%], respectively), indicating an overall good reproducibility. The total signal void area was significantly greater in the peripapillary region as compared with both the macular ($P < 0.0001$) and near- and mid-periphery ($P < 0.0001$) regions (peripapillary region: median, 16.6% [IQR, 13.6%−19.2%]; macular region: median, 13.3% [IQR, 11.4%−16.1%]; and near- and mid-periphery region: median, 12.8% [IQR, 11.4%−14.8%]; Table 1). Within the macular region, the foveal area exhibited a greater total signal void area in comparison with both the parafoveal area ($P = 0.009$) and the perifoveal area ($P = 0.015$; Table 2). In the analysis investigating the near- and mid-periphery region, the temporal sector was characterized by a lower total signal void area as compared with both the superior and inferior areas ($P = 0.016$ and $P = 0.003$, respectively; Table 3). The total signal void area was not associated with age in any of the analyzed regions ($P > 0.05$ for all the analyses).

Table 1. Choriocapillaris OCT Angiography-Tested Variables in the Analyzed Regions

	Macula	Periphery	Peripapillary Region
Total signal void area (%)	13.3 (11.4−16.1)	12.8 (11.4−14.8)	16.6 (13.6−19.2)
P value (vs. macular region)*		0.801	<0.0001
P value (vs. periphery)*	0.801		<0.0001

Data are median (interquartile range).
*Friedman test.

Table 2. Choriocapillaris OCT Angiography-Tested Variables in the Macular Region

	Fovea	Parafovea	Perifovea
Total signal void area (%)	14.8 (12.1–16.6)	13.3 (11.0–16.1)	13.6 (11.7–15.5)
P value (vs. foveal area)*		0.009	0.015
P value (vs. parafoveal area)*	0.009		1.0

Data are median (interquartile range).
*Friedman test.

Discussion

In this cross-sectional study, we reported quantitative mapping of the choriocapillaris in healthy eyes using widefield SS OCTA. We found regional differences in the perfusion of the choriocapillaris, which should be taken into account because OCTA-based parameters are used increasingly for the diagnosis of choroidal vascular disorders in adult eyes. Our results illustrated that the peripapillary region displays the lower perfusion of the choriocapillaris, whereas the perfusion was similar in the macula and near and mid periphery. Furthermore, a topographic subanalysis within these distinct regions revealed that the choriocapillaris does not exhibit a uniform perfusion. Importantly, in the assessment of the choriocapillaris in the retinal periphery, we excluded the far periphery from the evaluation. This assessment is indeed still limited by significant shadowing artifacts, given that the very large depth of field commonly results in the patient's eyelashes appearing in the image (Fig 3).[17] Thus, we believed that the safer strategy was to look at just the near and mid periphery.

Although the introduction of OCTA has expanded the evaluation of the choriocapillaris significantly, previous notable studies investigating this vascular plexus were limited to assessing the macular region.[1] The choriocapillaris perfusion in this field was demonstrated to be correlated inversely with age and axial length, as assessed in both pediatric and adult cohorts.[5,6,18] Notably, using OCTA, choriocapillaris perfusion was demonstrated to be reduced in the foveal area as compared with the parafoveal and perifoveal regions.[6] Our results similarly showed topographic differences within the macular region, because the choriocapillaris directly beneath the fovea was characterized by a lower perfusion. These results are in agreement with previous studies showing that the region below the fovea is characterized by the lowest choriocapillaris perfusion in comparison with both the parafoveal and perifoveal regions.[19–21] Al-Sheikh et al[19] suggest that this finding may be related to an increased difficulty in detecting the flow inside the subfoveal choriocapillaris. This may be the result of the masking effect of the densely packed and taller foveolar retinal pigment epithelium cells or of the higher concentration of macular pigment in the central fovea.[22]

Previous histopathologic studies have revealed that the choriocapillaris originates from larger-diameter vessels that are supplied by the short and long posterior ciliary arteries.[1] Although the short posterior ciliary arteries intrude on the eye in a circle around the optic disc, the long posterior ciliary arteries supply the region extending from the macula to the periphery in a triangular pattern with the apex directed toward the posterior pole.[23–25] In addition to this concept, it has been postulated that the choroid may be divided in specialized and distinct zones, which include the peripapillary zone, the region underlying the macula, and the periphery. As a result of widefield imaging application to choroidal description, in a recent study by Singh et al,[26] widefield structural OCT imaging was obtained in 20 healthy eyes to report variation of choroidal vascularity index in macular and peripheral areas in healthy participants. This study provided evidence that choroidal vascularity index has a wide topographic variation.

Using widefield SS OCTA imaging, we add to the literature by reporting quantitative data of the choriocapillaris in these distinct choroidal zones. We demonstrated that, although the macular and near- and mid-peripheral regions have comparable choriocapillaris perfusion, the peripapillary area displays the highest signal void area. The latter finding is in agreement with previous histopathologic studies illustrating that the total area occupied by

Table 3. Choriocapillaris OCT Angiography-Tested Variables in the Periphery

	Temporal	Superior	Inferior
Total Signal Void Area (%)	12.2 (11.0–14.4)	13.0 (11.7–15.1)	13.2 (11.0–16.4)
P value (vs. temporal field)*		0.016	0.003
P value (vs. superior field)*	0.016		1.0

Data are median (interquartile range).
*Friedman test.

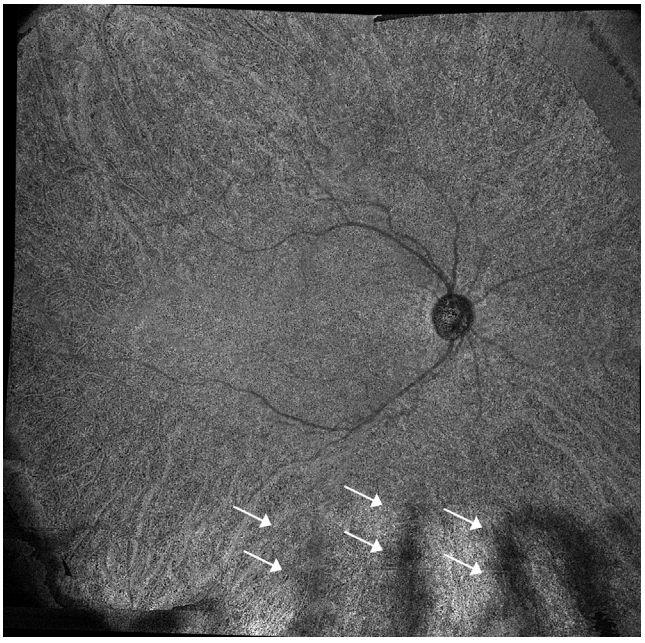

Figure 3. Representation of the eyelashes artifact. The obtained en face image of the choriocapillaris showed the presence of some linear regions of reduced brightness in the inferior far retinal periphery (white arrows). These regions of false-positive hypoperfusion are secondary to shadowing artifacts resulting from the superior eyelashes.

intercapillary spaces, identified as signal or flow voids with OCTA, is increased in this region.[27,28]

In our adult healthy cohort, we also assessed topographic differences in choriocapillaris perfusion within the near- and mid-peripheral region and we noted a lower perfusion in the temporal field. Future studies investigating the retinal periphery may provide additional substantive information regarding zonal differences in choriocapillaris perfusion within this region and may identify whether these differences predispose patients to different chorioretinal disorders. As an example, these regional differences may explain, at least in part, the peculiar reticular pseudodrusen development, which is known to be driven from choriocapillaris ischemia[29,30] and to colocalize preferentially within the superior and inferior regions of the near- and mid-retinal periphery.[31,32]

Our study has some limitations that should be considered when interpreting our results. First, the 12 × 12-mm scan has limited sampling density with a larger sampling space (24 μm) that is larger than the system lateral resolution (14 μm). Therefore, the choriocapillaris assessment may be severely downsampled. However, widefield OCTA imaging is still a technology in evolution, and the optimal technological approach has yet to be reached. Second, although we excluded the far peripheral regions from the analysis to avoid eyelash artifacts from confounding the quantitative assessment, we are not able to exclude that these artifacts also may have impacted, at least in part, the investigation of the inferior and superior near- and mid-periphery regions. Future studies using improved technologies will clarify this aspect. In addition, we used information from only 1 OCTA device, and thus our findings are almost certainly not applicable to other instruments. Furthermore, shadowing and projection artifacts from superficial retinal vessels still can confound the analysis of the choriocapillaris. However, we did use a longer wavelength to image the choriocapillaris and we used image processing to mask the region beneath major superficial vessels to limit shadowing or projection artifacts from confounding the analysis, respectively. Finally, our study was aimed at describing choriocapillaris perfusion in healthy young participants (mean age ± SD, 25.2±5.1 years), and thus we included healthy eyes with a narrow range of axial length (mean ± SD, 23.9±1.1 mm); therefore, we are unable to comment on the effect of these 2 variables (age and axial length) on widefield choriocapillaris perfusion. Finally, we are not able to comment on the magnification effect (distortion) secondary to the shape of eye globe that might have occurred in our images.

In summary, in this widefield SS OCTA study of the choriocapillaris, we observed that healthy eyes show topographic variability in choriocapillaris flow. Future studies with extended longitudinal follow-up and further analysis of age and axial length on choriocapillaris vasculature may provide additional substantive information.

References

1. Borrelli E, Sarraf D, Freund KB, Sadda SR. OCT angiography and evaluation of the choroid and choroidal vascular disorders. *Prog Retin Eye Res*. 2018;67:30–55.
2. Olver JM. Functional anatomy of the choroidal circulation: methyl methacrylate casting of human choroid. *Eye*. 1990;4:262–272.
3. Choi W, Moult EM, Waheed NK, et al. Ultrahigh-speed, swept-source optical coherence tomography angiography in nonexudative age-related macular degeneration with geographic atrophy. *Ophthalmology*. 2015;122:2532–2544.
4. Spaide RF. Choriocapillaris signal voids in maternally inherited diabetes and deafness and in pseudoxanthoma elasticum. *Retina*. 2017;37:2008–2014.
5. Borrelli E, Lonngi M, Balasubramanian S, et al. Macular microvascular networks in healthy pediatric subjects. *Retina*. 2018;39:1216–1224.
6. Al-Sheikh M, Phasukkijwatana N, Dolz-Marco R, et al. Quantitative OCT angiography of the retinal microvasculature and the choriocapillaris in myopic eyes. *Invest Ophthalmol Vis Sci*. 2017;58:2063–2069.
7. Borrelli E, Uji A, Sarraf D, Sadda SR. Alterations in the choriocapillaris in intermediate age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2017;58:4792–4798.
8. Borrelli E, Souied EH, Freund KB, et al. Reduced choriocapillaris flow in eyes with type 3 neovascularization due to age-related macular degeneration. *Retina*. 2018;38:1968–1976.
9. Borrelli E, Shi Y, Uji A, et al. Topographical analysis of the choriocapillaris in intermediate age-related macular degeneration. *Am J Ophthalmol*. 2018;196:34–43.
10. Spaide R, Fujimoto JG, Waheed NK, et al. Optical coherence tomography angiography. *Prog Retin Eye Res*. 2017;64:1–55.
11. 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;256:1275–1280.

12. Liu G, Yang J, Wang J, et al. Extended axial imaging range, widefield swept source optical coherence tomography angiography. *J Biophotonics*. 2017;10:1464−1472.
13. Borrelli E, Uji A, Sarraf D, Sadda SR. Alterations in the choriocapillaris in intermediate age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2017;58:4792−4798.
14. Borrelli E, Mastropasqua R, Senatore A, et al. Impact of choriocapillaris flow on multifocal electroretinography in intermediate age-related macular degeneration eyes. *Invest Ophthalmol Vis Sci*. 2018;59:AMD25−AMD30.
15. Borrelli E, Balasubramanian S, Triolo G, et al. Topographic macular microvascular changes and correlation with visual loss in chronic Leber hereditary optic neuropathy. *Am J Ophthalmol*. 2018;192:217−228.
16. Forrester JV, Dick AD, McMenamin PG, et al. *The Eye: Basic Sciences in Practice*. 3rd ed. Edinburgh: Elsevier; 2008:568.
17. Borrelli E, Viggiano P, Evangelista F, et al. Eyelashes artifact in ultra-widefield optical coherence tomography angiography. *Ophthalmic Surg Lasers Imaging Retin*. 2019. In press.
18. Spaide RF. Choriocapillaris flow features follow a power law distribution: implications for characterization and mechanisms of disease progression. *Am J Ophthalmol*. 2016;170:58−67.
19. Al-Sheikh M, Falavarjani KG, Pfau M, et al. Quantitative features of the choriocapillaris in healthy individuals using swept-source optical coherence tomography angiography. *Ophthalmic Surg Lasers Imaging Retina*. 2017;48:623−631.
20. Sacconi R, Borrelli E, Corbelli E, et al. Quantitative changes in the ageing choriocapillaris as measured by swept source optical coherence tomography angiography. *Br J Ophthalmol*. 2019;103:1320−1326.
21. Nassisi M, Baghdasaryan E, Tepelus T, et al. Topographic distribution of choriocapillaris flow deficits in healthy eyes. *PLoS One*. 2018;13:e0207638.
22. Smith RT, Koniarek JP, Chan J, et al. Autofluorescence characteristics of normal foveas and reconstruction of foveal autofluorescence from limited data subsets. *Invest Ophthalmol Vis Sci*. 2005;46:2940−2946.
23. Nemiroff J, Phasukkijwatana N, Vaclavik V, et al. The spectrum of amalric triangular choroidal infarction. *Retin Cases Br Reports*. 2017;11:S113−S120.
24. Garrity ST, Holz EJ, Sarraf D. Amalric triangular syndrome associated with outer nuclear layer infarction. *Ophthalmic Surg Lasers Imaging Retin*. 2017;48.
25. Reddy S, Goldman DR, Hubschman JP, et al. Cocaine and choroidal infarction, revisiting the triangular sign of amalric. *Retin Cases Br Reports*. 2011;5:91−93.
26. Singh SR, Invernizzi A, Rasheed MA, et al. Wide-field choroidal vascularity in healthy eyes. *Am J Ophthalmol*. 2018;193:100−105.
27. Flower RW, Fryczkowski AW, McLeod DS. Variability in choriocapillaris blood flow distribution. *Invest Ophthalmol Vis Sci*. 1995;36:1247−1258.
28. Hayreh SS. Segmental nature of the choroidal vasculature. *Br J Ophthalmol*. 1975;59:631−648.
29. Nesper PL, Soetikno BT, Fawzi AA. Choriocapillaris nonperfusion is associated with poor visual acuity in eyes with reticular pseudodrusen. *Am J Ophthalmol*. 2017;174:42−55.
30. Cicinelli MV, Rabiolo A, Marchese A, et al. Choroid morphometric analysis in non-neovascular age-related macular degeneration by means of optical coherence tomography angiography. *Br J Ophthalmol*. 2017;101:1193−1200.
31. Querques G, Querques L, Forte R, et al. Choroidal changes associated with reticular pseudodrusen. *Invest Ophthalmol Vis Sci*. 2012;53:1258−1263.
32. Rabiolo A, Sacconi R, Cicinelli MV, et al. Spotlight on reticular pseudodrusen. *Clin Ophthalmol*. 2017;11:1707−1718.

Footnotes and Financial Disclosures

Originally received: December 8, 2018.
Final revision: May 1, 2019.
Accepted: May 24, 2019.
Available online: May 31, 2019. Manuscript no. ORET_2018-479.

[1] Ophthalmology Clinic, Department of Medicine and Science of Ageing, University G. D'Annunzio Chieti-Pescara, Chieti, Italy.

[2] Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan.

[3] Bristol Eye Hospital, University Hospitals NHS Foundation Trust, Bristol, United Kingdom.

Financial Disclosure(s):
The author(s) have no proprietary or commercial interest in any materials discussed in this article.

HUMAN SUBJECTS: Human subjects were included in this study. The human ethics committees at University G. d'Annunzio approved the study. All research adhered to the tenets of the Declaration of Helsinki. All participants provided informed consent.

No animal subjects were included in this study.

Author Contributions:

Conception and design: Borrelli, Toto, Viggiano, Evangelista, Mastropasqua

Analysis and interpretation: Borrelli, Toto, Viggiano, Evangelista, Mastropasqua

Data collection: Borrelli, Viggiano, Evangelista

Obtained funding: N/A

Overall responsibility: Borrelli, Uji, Toto, Mastropasqua

Abbreviations and Acronyms:
IQR = interquartile range; **OCTA** = OCT angiography; **SD** = standard deviation; **SS** = swept-source.

Correspondence:
Enrico Borrelli, MD, FEBO, Ophthalmology Clinic, Department of Medicine and Science of Ageing, University G. D'Annunzio Chieti-Pescara, Va dei Vestini 31, 66100 Chieti, Italy. E-mail: borrelli.enrico@yahoo.com.