HHS Public Access

Author manuscript

JAMA Ophthalmol. Author manuscript; available in PMC 2017 November 24.

Published in final edited form as:

JAMA Ophthalmol. 2017 April 01; 135(4): 377–378. doi:10.1001/jamaophthalmol.2017.0149.

Consensus on Optical Coherence Tomographic Angiography Nomenclature:

Do We Need to Develop and Learn a New Language?

Amani A. Fawzi, MD

Department of Ophthalmology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois

In this issue of *JAMA Ophthalmology*, Durbin et al[1] evaluate the ability of optical coherence tomographic angiography (OCTA) to distinguish healthy eyes from those with diabetic retinopathy (DR). They compared a population of individuals with early to moderate DR with age-matched controls and examined several OCTA-derived measures, including vessel density and perfusion density, as well as the size of the foveal avascular zone (FAZ). Receiver operating characteristic curves and areas under the curve were generated to examine the sensitivity and specificity of these measures in distinguishing groups. The authors found that mean vessel density in the superficial capillary network had the best sensitivity and specificity for distinguishing healthy eyes from those with DR, and that this measure also correlated with severity of DR within the study group of patients with predominantly mild to moderate DR.

This study adds to the growing controversy regarding the ability of OCTA measures to distinguish healthy individuals from those with DR and, further within DR, to determine the correlation between OCTA-derived measures and DR severity. Recent studies, including that by Durbin et al,[1] explore similar questions using different OCT technologies. Although some studies have shown that early microvascular changes are evident on OCTA scans and strongly correlate with severity of DR, others have not found the same results. Also, the deep capillaries have emerged as a potentially important biomarker of DR severity in some studies but not in others. Similarly, measuring the size of the FAZ to distinguish healthy individuals from those with diabetes or to determine severity of DR remains a controversial issue.

There are several important unresolved issues. The first is a perceived need to reach consensus in the field in terms of nomenclature and definitions of the various OCTA-based capillary nonperfusion measures. *Perfusion density*, as defined by Durbin et al,[1] is the percentage area occupied by perfused binarized vessels. The same measurement is defined in other studies as *vessel density*, which can potentially create confusion. The other term presented in the study by Durbin et al[1] is *vessel density*, which is based on vascular length rather than area. This measure removes the effect of vessel diameter and any extra effect

Corresponding Author: Amani A. Fawzi, MD, Department of Ophthalmology, Feinberg School of Medicine, Northwestern University, 645 N Michigan Ave, Ste 440, Chicago, IL 60611 (afawzimd@gmail.com).

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

carried by larger vessels in the superficial network, which distinguishes this term from *perfusion density* in the study by Durbin et al.[1] Another term that has been introduced recently is *intercapillary area*, which uses several preprocessing steps to highlight continuous vessels and categorizes nonvessel, intercapillary areas by their size.

The second issue relates to how these 2 capillary networks (superficial and deep) are segmented. The article by Durbin et al[1] sets the inner retinal boundary based on a predefined distance from the retinal pigment epithelium, regardless of the overall retinal thickness, and then splits the inner retina into sections of 70% and 30% to isolate the 2 capillary networks. This approach could potentially introduce bias in the estimation of capillary networks based on these somewhat arbitrary boundaries, especially when the inner retina is focally thin, edematous, or distorted, as in eyes with edema or ischemia. Other approaches use segmentation boundaries based on anatomical location and/or the corresponding retinal sublayers. This latter approach might have greater clinical relevance, assuming these segmentation algorithms are sufficiently robust in the face of pathologic conditions that distort the retinal structures. However, most algorithms do not agree even on the boundaries between the superficial and deep capillaries. So while some algorithms use the middle of the inner nuclear layer as the boundary (OptoVue), others use the top of the inner nuclear layer (Topcon).

The third issue relates to projection artifacts, or *decorrelation tails*, as they are termed in the article by Durbin et al.[1] This is an artifact ubiquitous to all OCTA devices, where the superficial capillary structures are projected onto deeper networks (and any highly reflective retinal layer, including the retinal pigment epithelium). This artifact is particularly relevant when evaluating the importance of the deep capillary networks in DR. Although Durbin et al[1] used their proprietary algorithm to suppress these vascular artifacts, other studies did not incorporate such an algorithm to remove artifacts, thus potentially underestimating capillary loss in the deeper networks. In general, however, based on the measures and thresholds used by the different algorithms, they could be considered too aggressive at removing artifacts and, therefore, could potentially also remove aspects of the true deep capillary plexus (DCP), leading to an overestimation of capillary loss at the DCP. Or, alternatively, if the threshold were too permissive, residual superficial capillary network projections would lead to an underestimation of the capillary loss at the DCP. Algorithms leaning in either direction could affect the measurements in the DCP. Some researchers have sought to completely bypass this issue and instead use the full projection of the retinal vasculature when evaluating capillary density. This approach, while avoiding decorrelation tail artifacts, comes with the limitation that it does not permit any conclusions regarding the relevant depth or location of the plexus.

The fourth issue is a need for software algorithms that are specifically designed for measuring the FAZ. This issue remains highly debated as a result of the wide variability in the size of the FAZ in healthy individuals. The field might benefit from a normative database of the FAZ and normal capillary density, including large population studies exploring the effects of age, sex, race/ethnicity, and axial length.

Finally, most algorithms currently do not identify the intermediate capillary plexus, and most include it partially or completely within one of the other plexuses.[2] This could potentially confound comparisons and the ability to define the network that is most affected by the earliest changes in DR. Histopathologic 3-dimensional studies in human donor eyes have shown that microaneurysms, another important biomarker of DR, are more predominant in the inner nuclear layer.[3] Since microaneurysms generally surround areas of capillary loss,[4] this finding would suggest relatively more capillary loss occurring in the deeper retina, whether at the intermediate or deep capillary plexus. Now that we have the ability to examine the 3-dimensional capillary structure in great detail in vivo, it behooves us to use approaches that identify the individual networks.

This may be a good time for clinicians and researchers to come to an agreement about terminology in this field. A similar agreement on terms has been created for other retinal imaging tools, such as fluorescein angiography. Do we call the absence of capillary flow signal on an OCTA scan *no-flow*, *nonperfusion*, *avascular area*, *flow void*, or just *absent flow*? Then, if there is agreement on terminology, there also may be a need to identify the best approach for evaluating this OCTA nonperfusion metric; should we quantify vessel density, perfusion density, intercapillary area, or other measures that are a combination of all of these? Should all software strive to use similar segmentation boundaries for the different capillary networks so that clinicians are comparing the same capillary structures? Finally, what role, if any, do refractive error, sex, and race/ethnicity play in vascular density? Women and African American individuals have thinner maculae[5]; it is therefore plausible that sex and racial/ethnic background are potential confounders when evaluating capillary density. This possibility is relevant to the study by Durbin et al,[1] as well as many others, if study participants and controls are not balanced.

In summary, there seems to be a need to create consensus in OCTA terminology. With the new depth dimension offered by this technology comes a need to ensure that clinicians and researchers are evaluating the same capillary structures and using the same language to characterize them.

Acknowledgments

Funding/Support: This work was funded in part by grant 1DP3DK108248 from the National Institutes of Health.

Role of the Funder/Sponsor: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

References

1. Durbin MK, An L, Shemonski ND, et al. Quantification of retinal microvascular density in optical coherence tomographic angiography images in diabetic retinopathy. JAMA Ophthalmol. [published online March 16, 2017].
2. Park JJ, Soetikno BT, Fawzi AA. Characterization of the middle capillary plexus using optical coherence tomography angiography in healthy and diabetic eyes. Retina. 2016; 36(11):2039–2050. [PubMed: 27205895]
3. Moore J, Bagley S, Ireland G, McLeod D, Boulton ME. Three dimensional analysis of microaneurysms in the human diabetic retina. J Anat. 1999; 194(pt 1):89–100. [PubMed: 10227670]

4. Cogan DG, Toussaint D, Kuwabara T. Retinal vascular patterns, IV: diabetic retinopathy. Arch Ophthalmol. 1961; 66:366–378. [PubMed: 13694291]

5. Wagner-Schuman M, Dubis AM, Nordgren RN, et al. Race- and sex-related differences in retinal thickness and foveal pit morphology. Invest Ophthalmol Vis Sci. 2011; 52(1):625–634. [PubMed: 20861480]