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OCT angiography and visible-light OCT in diabetic retinopathy

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ABSTRACT

In recent years, advances in optical coherence tomography (OCT) techniques have increased our understanding of diabetic retinopathy, an important microvascular complication of diabetes. OCT angiography is a non-invasive method that visualizes the retinal vasculature by detecting motion contrast from flowing blood. Visible-light OCT shows promise as a novel technique for quantifying retinal hypoxia by measuring the retinal oxygen delivery and metabolic rates. In this article, we discuss recent insights provided by these techniques into the vascular pathophysiology of diabetic retinopathy. The next milestones for these modalities are large multicenter studies to establish consensus on the most reliable and consistent outcome parameters to study diabetic retinopathy.

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1. Basics of optical coherence tomography angiography

Optical coherence tomography angiography (OCTA) is a relatively recent technique that provides three-dimensional (3D)

imaging of the retinal and choroidal vasculature. While conventional OCT excels at capturing static 3D structural information within the retina, the image contrast from blood vessel walls alone is not sufficient to provide meaningful angiograms. On the other hand, OCTA exploits the movement of blood cells to generate angiograms with exquisite image contrast.

In order to extract information about blood cell movement, OCTA systems acquire two or more consecutive B-scans at the same location in the retina (Fig. 1). Recent improvements in OCT data acquisition speeds have allowed complex scanning protocols to be implemented within a few seconds, leading to the feasibility of clinical OCTA (Gao et al., 2016). Algorithms were then developed to extract motion contrast from the variable scattering of moving blood cells. For example, red blood cells scatter differently depending on their motion, orientation, or shape (Srinivasan, Chan, & Lam, 2012). OCTA algorithms remove OCT signals with unchanged scattering from static tissue and preserve the OCT signals associated with motion in order to produce the 3D OCTA volume and *en face* projection (Fig. 1(F)).

Raw data from OCT A-scans is complex-valued, therefore OCTA algorithms can compare the amplitude, the phase, or both between B-scans (Zhang, Zhang, Chen et al., 2015). The optical microangiography (OMAG) algorithm compares both amplitude and phase differences between consecutive B-scans (An, Shen, & Wang, 2011; Wang, An, Francis, & Wilson, 2010, while split-spectrum amplitude-decorrelation (SSADA) uses only amplitude. The SSADA

Abbreviations: DCP, deep capillary plexus; DM, diabetes mellitus; DME, diabetic macular edema; DMI, diabetic macular ischemia; DO₂, retinal oxygen delivery rate; DR, diabetic retinopathy; EAA, extrafoveal avascular area; FA, fluorescein angiography; FAZ, foveal avascular zone; FD, fractal dimension; HC, healthy controls; HR, horizontal radius of the foveal avascular zone; IRMA, intraretinal microvascular abnormalities; MA, microaneurysms; MCP, middle capillary plexus; MCT, motion correction technology; MFD, maximum foveal avascular zone diameter; MRO₂, retinal oxygen metabolic rate; NoDR, diabetes mellitus without diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; NV, neovascularization; OCTA, optical coherence tomography angiography; OIR, oxygen-induced retinopathy; OMAG, optical microangiography; PDR, proliferative diabetic retinopathy; PI, perfusion index (vessel density); PIA, perifoveal intercapillary area; PR-OCTA, projection-resolved optical coherence tomography angiography; RPE, retinal pigment epithelium; SCP, superficial capillary plexus; SD, skeletonized vessel density; SD-OCT, spectral domain optical coherence tomography; sO₂, hemoglobin oxygen saturation; SSADA, split-spectrum amplitude-decorrelation angiography; SS-OCTA, swept-source optical coherence tomography angiography; TAA, total avascular area; VA, visual acuity; VAD, vessel area density; VEGF, vascular endothelial growth factor; VD, vessel density; VDI, vessel diameter index; Vis-OCT, visible-light OCT; VISTA, variable interscan time analysis; VLD, vessel length density; VR, vertical radius of the foveal avascular zone.

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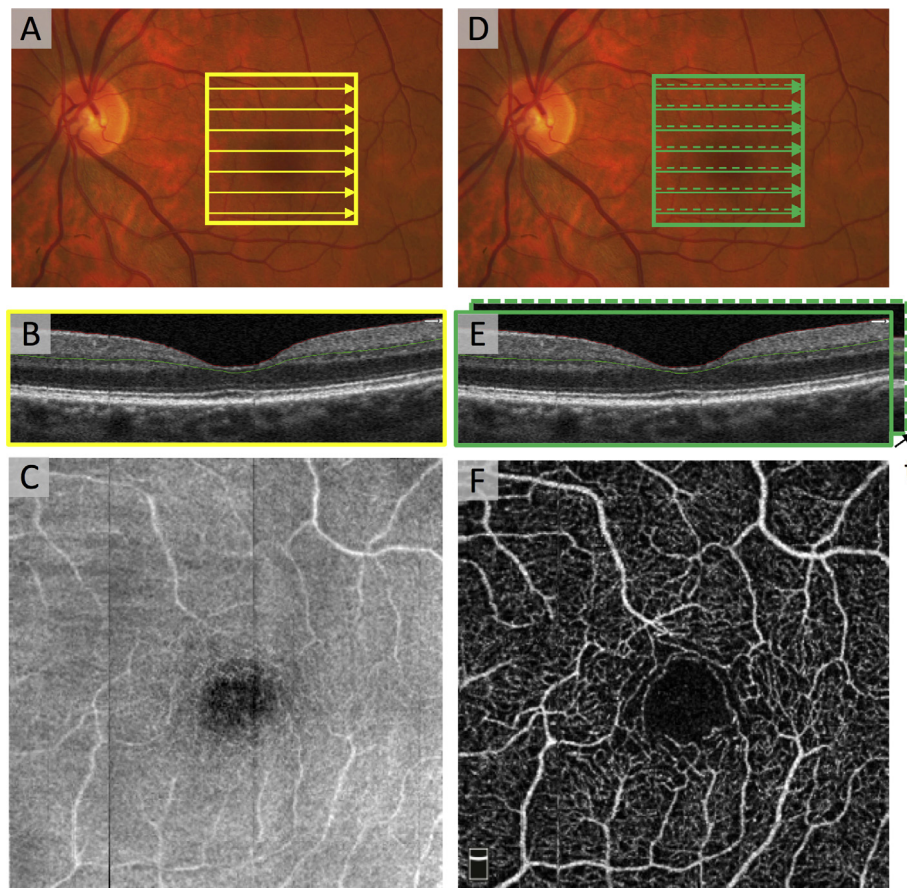


Fig. 1. Scanning Patterns Used in OCT and OCTA. (A) Fundus photograph of the macula and optic nerve head in a healthy eye. The solid yellow box denotes $3 \times 3 \text{ mm}^2$, which was imaged by OCT. The yellow arrows depict the path that the illumination beam takes as it raster scans. The scanning density along the y direction is sparse for illustration purposes. (B) The OCT B-scan corresponding to arrow across the fovea in (A). (C) The *en face* OCT acquired from the region in (A). (D) The solid green box indicates a region on the macula imaged with OCTA. The green solid arrow and green dashed arrow indicate the first and second B-scan locations for OCTA. (E) The two co-localized B-scans are separated in time. (F) Co-localized B-scans are fed into an OCTA algorithm to produce *en face* OCTA image of the region.

algorithm also splits the OCT spectrum into 11 sub-bands, thereby improving the signal to noise ratio but decreasing axial resolution of the final image (Gao, Liu, Huang, & Jia, 2015).

Patients were recruited for this study in the Department of Ophthalmology at Northwestern University in Chicago, Illinois between June 15, 2015 and December 9, 2016. This study was approved by the Institutional Review Board of Northwestern University, followed the tenets of the Declaration of Helsinki and was performed in accordance with the Health Insurance Portability and Accountability Act regulations. Written informed consent was obtained from all participants.

2. Comparison of Fluorescein and OCT angiography

Fluorescein angiography (FA) is the current “gold standard” for evaluating the vasculature in diabetic retinopathy (DR). This procedure requires intravenous dye injection which can lead to adverse reactions (Kwiterovich et al., 1991). OCTA is a non-invasive, label-free technique that has expanded our understanding of the microvascular changes in DR and could potentially reduce the need for FA. Many of the common vascular features of DR are clearly visualized in OCTA (Choi et al., 2016; Ishibazawa et al., 2015) (Fig. 2). Yet, most OCTA studies utilize a $3 \times 3 \text{ mm}^2$ ($\sim 7^\circ$) scanning area centered on the macula, compared the much wider field (50° , 120° , and 200°) possible with more conventional imaging modalities (Fig. 3).

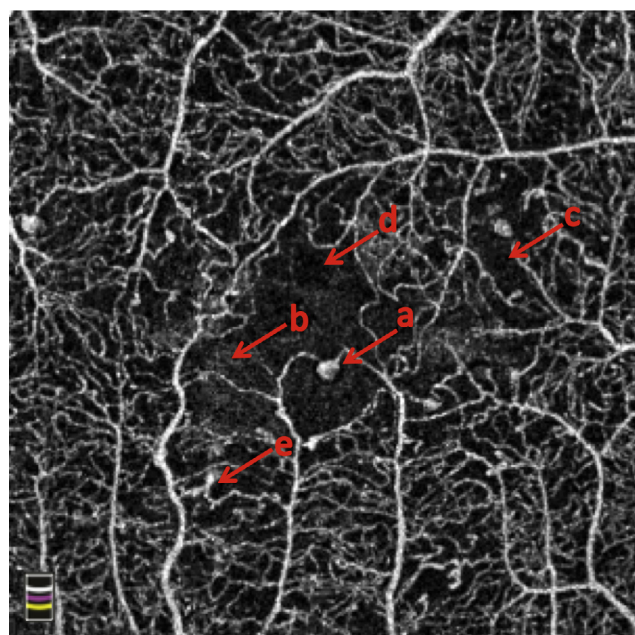


Fig. 2. Common Features of Diabetic Retinopathy on OCTA. (a) microaneurysms, (b) enlarged foveal avascular zone, (c) non-perfusion, (d) edema, (e) abnormal vascular loops.

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