

**Assessment of Accuracy of Optical Coherence
Tomography Angiography in Evaluation of
Foveal Avascular Zone and Perifoveal
Intercapillary Area in Ischemic Diabetic
Maculopathy as Compared to Fluorescein
Angiography**

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدقة الله العظيم

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List of Abbreviations

Abb.	Full term
<i>A-V</i>	<i>Arteriovenous.</i>
<i>BRB</i>	<i>Blood-retinal barrier.</i>
<i>CNV</i>	<i>Choroidal neovascularization.</i>
<i>CRA</i>	<i>Central retinal artery.</i>
<i>CRV</i>	<i>Central retinal vein.</i>
<i>DCP</i>	<i>Deep capillary plexus.</i>
<i>DME</i>	<i>Diabetic macular edema.</i>
<i>DMI</i>	<i>Diabetic macular ischemia.</i>
<i>DR</i>	<i>Diabetic retinopathy.</i>
<i>ETDRS</i>	<i>Early Treatment Diabetic Retinopathy Study.</i>
<i>FA</i>	<i>Fluorescein angiography.</i>
<i>FAZ</i>	<i>Foveal avascular zone.</i>
<i>FFA</i>	<i>Fundus fluorescein angiography.</i>
<i>HE</i>	<i>Hard exudate</i>
<i>ILM</i>	<i>Internal limiting membrane.</i>
<i>IRMA</i>	<i>Intraretinal microvascular abnormality.</i>
<i>NPDR</i>	<i>Non proliferative diabetic retinopathy.</i>
<i>OCT</i>	<i>Optical coherence tomography.</i>
<i>OCTA</i>	<i>Optical coherence tomography angiography.</i>
<i>ONH</i>	<i>Optic nerve head.</i>
<i>PDR</i>	<i>Proliferative diabetic retinopathy.</i>
<i>RPE</i>	<i>Retinal pigment epithelium.</i>
<i>SCP</i>	<i>Superficial capillary plexus.</i>
<i>SD-OCT</i>	<i>Spectral domain optical coherence tomography</i>
<i>SSADA</i>	<i>Split-spectrum amplitude-decorrelation</i> <i>angiography</i>
<i>VEGF</i>	<i>Vascular endothelium growth factor.</i>

Abstract:

Purpose. To compare fluorescein angiography (FA) and optical coherence tomography angiography (OCTA) images of foveal avascular zone (FAZ) in patients with diabetic macular ischemia (DMI). Methods. Quantitative analyses of the FAZ were performed using ImageJ software. Results. 25 eyes from 25 diabetic patients were enrolled. The study showed that mean area on FA and OCTA of $1.1742 \pm .82621 \text{ mm}^2$ and $.9528 \pm .4627 \text{ mm}^2$, respectively. OCTA detected the majority but not all microaneurysms detected by FA. OCTA represents a novel technique for the diagnosis of DMI and it may become an alternative to FA for this purpose.

Keywords: **DR, DME, DMI,**

INTRODUCTION

Blindness is one of the most feared complications of diabetes but also one of the most preventable. Diabetes is the commonest cause of blindness in people aged 30 to 69 years. Twenty years after the onset of diabetes, almost all patients with type 1 diabetes and over 60% of patients with type 2 diabetes will have some degree of retinopathy, so it is essential to identify patients with retinopathy before their vision is affected⁽²⁰⁾.

Diabetic retinopathy occurs as a result of abnormal changes to the structure of blood vessels, which occur as a result of diabetes. In the early stages of the disease these changes affect the eye's retina (retinopathy). The changes which occur in proliferative and non-proliferative retinopathy may also affect the eye's macula. This causes diabetic maculopathy, in which changes to the retina lead to the loss of capillaries in the macula⁽²⁸⁾.

The severity of diabetic maculopathy can be partly established by examining the perifoveal circulation. The central macula has a foveal avascular zone (FAZ) surrounded by interconnected capillary beds. This vascular network terminates in the central macula and forms a ring at the peripheral edge of the FAZ. Depending on the vascular pattern, the physiological shape of the FAZ is oval or round and has an average diameter of 500 to 600 μm . Diabetes-related damage to the macular

circulation induces a number of changes in the vasculature. Enlargement of the FAZ observed on fundus angiography of the diabetic eye may indicate a poor prognostic visual outcome⁽³⁵⁾.

Fluorescein angiography (FA), the gold standard for evaluating the retinal vasculature, shows both morphologic and functional changes in the blood vessels in DR. Fluorescein dye in the plasma delineates vascular lesions including loss of the capillary beds, and the dye leakage suggests dysfunction of the tightly regulated blood-retinal barrier⁽³⁷⁾.

FA is invasive test that require intravenous administration of dye and imaging up to 10–30 minutes⁽⁶⁾. It provide two-dimensional image sets that allow for dynamic visualization of blood flow with a wide field of view. Therefore, patterns of dye leakage, pooling, and staining can be appreciated and are well-documented in the literature⁽⁴⁰⁾.

However, retinal pathology can be obscured by this leakage as well as hemorrhage or media opacities, and localization of the depth of the lesion and size delineation of neovascularization can be difficult due to dye leakage and poor stereopsis, and because the imaging modalities are not depth resolved. As a result, segmentation of different layers is not routinely possible with FA. Therefore, identification of the axial location of pathology requires an understanding of patterns of blockage and leakage⁽⁴⁰⁾.

FA has other drawbacks that can limit its widespread use. Since it is invasive, relatively expensive, and time-consuming, it is not ideal techniques to use on a regular basis in a busy clinical setting. Although considered safe, the dyes pose risks ranging from nausea to allergic reactions, including anaphylaxis in rare instances. Aside from allergic reactions of which the likelihood increases with frequency of use, the dye is contraindicated in pregnancy and kidney disease ⁽⁴⁹⁾.

Optical coherence tomography angiography (OCTA) is a new non-invasive imaging technique, without the use of dye, that employs motion contrast imaging to high-resolution volumetric blood flow information generating angiographic images in a matter of seconds ⁽¹¹⁾.

Each three-dimensional scan set takes approximately six seconds to obtain. The en-face images (OCT angiograms) can then be scrolled outward from the internal limiting membrane (ILM) to the choroid to visualize the individual vascular plexus and segment the inner retina, outer retina, choriocapillaris, or other area of interest. The 3×3 mm OCT angiograms appear to be higher resolution than the currently available FA images ⁽¹²⁾.

OCTA provides both structural and functional (i.e. blood flow) information in tandem. The “corresponding” OCT b-scans can be co-registered with the simultaneous OCT angiograms so the operator is able to scroll through the OCT angiogram like acube scan. As a result, the precise location of pathology can be viewed on the corresponding OCT b-scans ⁽¹²⁾.

ANATOMY OF THE RETINAL AND CHOROIDAL CIRCULATION

The retina receives its nutrition from two discrete circulatory systems, the retinal blood vessels and the uveal or choroidal blood vessels. Both are derived from the ophthalmic artery, which is a branch of the internal carotid artery. The major branches of the ophthalmic artery are the central retinal artery (CRA), the posterior ciliary arteries and the muscular branches. The retinal blood vessels provide nourishment for the inner retinal layers and carry off waste products from them. The outer retinal layers are avascular and supplied via diffusion from the choriocapillaris. Despite this dual circulation to the retina, functionally little overlap occurs ⁽¹⁾ (figure 1).

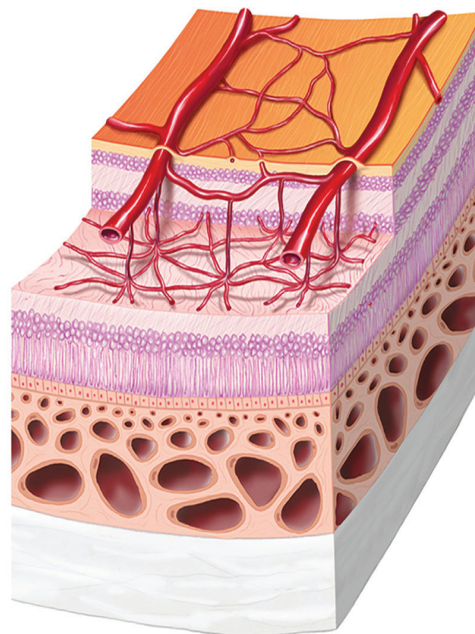


Figure (1): Anatomy of the normal retinal vasculature ⁽²⁾.

A- Retinal circulation:

1- Retinal arterial system:

Central retinal artery (CRA) is an end artery that has no significant anastomoses. In the area of the lamina cribrosa, its lumen measures about 170 μ m in diameter. Typically, just before its exit from the optic nerve it divides into the superior and inferior papillary arteries, which in turn divide into nasal and temporal quadrant branches. The anatomic division of the retinal arteries into superior and inferior halves usually is maintained throughout the retina, because normal retinal vessels rarely cross the horizontal retinal raphe ⁽¹⁾.

The major arterial branches are about 100 μ m in diameter as they cross the disc margin. They course within the nerve fiber layer and ganglion cell layer of the retina. Usually after the first branch, the retinal arteries lose the elastic fibers and the internal elastic membrane, thus the term arterioles is more appropriate. The ophthalmic artery contains sympathetic nerve fiber endings and so under the control of the autonomic nervous system. There is no central regulation of the blood flow in the retina due to absence of nerve fibers in the media or adventitia of human retinal vessels ⁽²⁾.