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Evaluation of Superficial and Deep Capillary Plexa in Retinal Vein Occlusion Using Optical Coherence Tomography Angiography

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسببائك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الكبير

صدق الله العظيم

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Candidate

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List of Abbreviations

Abb.	Full term
AO-CSLO	Adaptive Optics Confocal Scanning Laser Ophthalmoscopy
BCVA.....	Best Corrected Visual Acuity
BRVO	Branch Retinal Vein Occlusion
CRVO	Central Retinal Vein Occlusion
DCP	Deep Capillary Plexuses
DVC	Deep Vascular Complexes
EFI	Extended Field Imaging
ERG	Electro Retinography
EZ	Ellipsoid Zone
FA	Fluorescein Angiography
FAZ	Foveal Avascular Zone
FVD	Foveal Vascular Density
GCL	Ganglion Cell Layer
ICP.....	Intermediate Capillary Plexuses
INL	Inner Nuclear Layer
IPL	Inner Plexiform Layer
MCT.....	Motion Correlation Technology
NFL	Nerve Fiber Layer
NPA.....	Non-Perfusion Areas
NVD	Neo Vascularization of The Disc
NVE	Neo Vascularization Elsewhere
OCT	Optical Coherence Tomography
OCTA	Optical Coherence Tomography Angiography
OMAG	Optical Micro Angiography
ONL	Outer Nuclear Layer

List of Abbreviations Cont...

Abb.	Full term
OPL	Outer Plexiform Layer
OVCs	Optic disc Venous Collaterals
PR	Photoreceptor Layer
RPCP	Radial Peripapillary Capillary Plexuses
RPE	Retinal Pigment Epithelium
RVO	Retinal Vein Occlusion
SCP	Superficial Capillary Plexus
SD	Spectral Domain
SS	Swept Source
SSADA	Split Spectrum Amplitude De-correlation Angiography
SVC	Superficial Vascular Complexes
SVP	Superficial Vascular plexus
VD.....	Vessel Density
VD %.....	Vessel Density Percentage
VEGF	Vascular Endothelial Growth Factor

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INTRODUCTION

Retinal vein occlusion (RVO) is the second most common cause of retinal vascular disease worldwide after diabetic retinopathy, and its prevalence increases with age. macular edema is the main complication of well-perfused forms of RVO, limiting visual recovery in about half the cases (*Rogers et al., 2010; Coscas et al., 2016*).

Fluorescein Angiography (FA) is the gold standard in detecting and evaluating retinal perfusion in clinical practice. Dye leakage in the late phases of FA, usually associated with the presence of macular cystoid spaces, is used to identify macular edema (*Coscas et al., 2010; Spaide et al., 2018*).

A noninvasive technique, spectral-domain optical coherence tomography (SD OCT), has provided high-resolution images of both retinal and choroidal structures. SD OCT scans of the retina show bands of different reflectivity that appear to correspond to the histologic layers of the human retina, although strict correlation with histology has not yet been demonstrated (*Murakami et al., 2012; Muraoka et al., 2014*).

A more recent development in OCT imaging, called “en face” OCT, combines OCT with transverse confocal scans.

EN face OCT allows the selection of a frontal OCT image (c-scan) of a single retinal layer. This tomographic image has high pixel-to-pixel correspondence with fundus and

angiographic images. Large retinal vessels may be visible on en face OCT because of their reflectivity; however, no information is available about blood flow (*Coscas et al., 2012*).

An amplitude decorrelation algorithm provides information about blood flow by comparing 2 consecutive b-scans. The “ANGIOVUE” optical coherence tomography angiography (RTVUE XR; OPTOVUE, INC, FREMONT, CALIFORNIA, USA) is the first commercially available OCT device able to provide OCT angiography images (*Coscas et al., 2016*).

As already reported, the split-spectrum amplitude decorrelation algorithm (SSADA) analyzes OCT scans and enables distinction between static and nonstatic tissue with a scale of flow signals of variable intensity (*Jia et al., 2012; Tokayer et al., 2013*). The SSADA algorithm also improves the signal-to-noise ratio in order to minimize bulk axial motions and artifacts within angiography scans. Thus, by calculating the amplitude of decorrelation signal coming from consecutive b-scans, blood flow can be clearly visualized (*Jia et al., 2012; Tokayer et al., 2013; Choi et al., 2013*).

It has already been demonstrated that a combination of C-scan OCT angiographies and corresponding conventional B-scan provides clear images of both superficial and deep macular capillary plexa (*Spaide et al., 2015*).

Kuehlewein and associates reported a patient with BRVO evaluated with FA and swept-source OCT microangiography (*Kuehlewein et al., 2015*).

Areas of nonperfusion following BRVO could be precisely delineated at several retinal levels using swept-source OCT microangiography. Moreover, *De Carlo and associates* described an area of diffuse capillary nonperfusion, continuous with the FAZ and telangiectatic vessels, in a case of CRVO (*De Carlo et al., 2015*).

Jia and associates then reported for the first time the clinical applications of optical coherence tomographic angiography in age-related macular degeneration (*Jia et al., 2014*). while *Savastano and associates* reported its clinical applications in healthy subjects (*Savastano et al., 2015*).

The aim of our study was to evaluate the retinal microvasculature in human subjects with central and branch retinal vein occlusion using OCT angiography.

Chapter 1

ANATOMY OF THE RETINA

The retina is the innermost, light-sensitive layer of tissue of the eye of most vertebrates and some molluscs. The optics of the eye create a focused two-dimensional image of the visual world on the retina, which translates that image into electrical neural impulses to the brain to create visual perception, the retina serving a function analogous to that of the film or image sensor in a camera (*Kolb and Helga, 2018*).

Anatomic layers of the retina

Each of the microscopic layers of the retina has a name and contains various structures. Beginning with the innermost layer (closest to the vitreous) and proceeding outwards towards the choroid and sclera, **these layers are as follows:**

1. The inner limiting membrane
2. The nerve fiber layer
3. The ganglion cells layer
4. The inner plexiform layer
5. The inner nuclear layer
6. The outer plexiform layer
7. The outer nuclear layer
8. The outer limiting membrane
9. The rod and cone layer
10. The pigment epithelium

The inner limiting membrane is the boundary between the retina and the vitreous body. It is formed by astrocytes and the footplates of Muller cells together with a basal lamina. The nerve fiber layer is the layer of optic nerve fibers consisting of ganglion cell axon fibers. There are also some displaced amacrine cells within this layer (*Sterling, 1999*).

The inner plexiform layer contains the synapses between dendrites of ganglion cells and amacrine cells and the axons of bipolar cells. The inner nuclear layer contains the nuclei of horizontal, bipolar and amacrine cells. The inner nuclear layer is thicker in the central area of the retina compared with peripheral retina because of a greater density of cone-connecting second-order neurons (cone bipolar cells) and smaller and more closely spaced horizontal cells and amacrine cells concerned with the cone pathways. There are also nuclei of the supporting Muller cells (*Kolb et al., 1995*).

The outer plexiform layer contains the rod and cone axons, horizontal cell dendrites, and bipolar cells dendrites. Synapses among these structures occur within this layer. In the macular region, this layer is termed the fiber layer of Henle. The outer plexiform layer is also known as the outer synaptic layer. The outer nuclear layer consists of the cell bodies of the retinal rods and cones. In the peripheral retina, the rod cell bodies outnumber the cone cell bodies, whereas the reverse is

true for the central retina. The outer limiting membrane (external limiting membrane) is the layer that separates the inner segment portions of the photoreceptors from their cell nuclei. The rod and cone layer (bacillary layer) contains the inner and outer segments of the rod and cone photoreceptors cells. The pigment epithelium is the most external layer of the retina. It abuts on the choroidal layer of the eye. It contains a single layer of cuboidal-supporting cells for the neural portion of the retina. These cells contain melanin, which absorbs light and decreases light scatter within the eye (*Dahl, 2017*).

Blood supply of the retina (Figure 1,2)

There are two circulations to the retina, both supplied by the ophthalmic artery, the first branch of the internal carotid artery on each side. The outer and middle retinal layers, including the outer plexiform and outer nuclear layers, the photoreceptors, and the retinal pigment epithelium, are nourished by choriocapilaris. The inner retina is supplied by the central retinal artery, the branch of the ophthalmic artery that enters the optic nerve 4 mm posterior to the eye. The central retinal artery has 4 main branches within the retina. These vessels emerge from the optic nerve head and run radially away from the optic nerve (*Dahl, 2017*).