OCT ANALYSIS OF RETINAL WHITENING IN CENTRAL RETINAL VEIN OCCLUSION

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CONTENTS

LIST OF ABBREVIATIONS

- **A-V** Arteriovenous.
- **CRA** Central retinal artery.
- **CRV** Central retinal vein.
- **CRVO** Central retinal vein occlusion.
- **CRVOS** Central retinal vein occlusion study.
- **CWS** Cotton wool spot.
- **DCP** Deep capillary plexus.
- **FA** Fluorescein angiography.
- **FAZ** Foveal avascular zone.
- **FFA** Fundus fluorescein angiography.
- **OCT** Optical coherence tomography.
- **OCTA** Optical coherence tomography angiography.
- **ONH** Optic nerve head.
- **PAMM** Paracentral acute middle maculopathy.
- **PIRW** Patchy ischemic retinal whitening.
- **RNFL** Retinal nerve fiber layer.
- **RVO** Retinal vein occlusion.
- **SD-OCT** Spectral domain optical coherence tomography.
- **SCP** Superficial capillary plexus.
- **VOCT** Volumetric optical coherence tomography.

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INTRODUCTION

Central retinal vein occlusion (CRVO) is a frequent primary vascular disorder of the retina with vein blockage in the optic nerve head. It is the second most common cause of vision loss due to retinal vascular disease after diabetes. Leibreich in 1855 first described the clinical appearance of CRVO as "retinal apoplexy". ***(Leibreich, 1855).*** Followed closely by leber in 1877 who preferred "hemorrhagic retinitis" ***(leber, 1877).*** We now use "central retinal vein occlusion" assuming the presence of a blockage of the vein in the optic nerve head. Hayreh in 1976, coined the phases "venous stasis retinopathy" for the milder types of CRVO and "hemorrhagic retinopathy" for the more severe disease Similarly, the terms "ischemic" and "non ischemic" CRVO have been employed ***(Hayreh, 1976)***.

Retinal vein occlusion typically affects people who are over 50 years of age and the incidence increase with age ***(Klein, et al., 2008).***

CRVO is further classified according to how much the occlusion inhibits blood flow**.** If the blood flow is restricted enough to result in tissue damage, the CRVO is classified as ischemic, which on fundus fluorescein angiography (FFA) there is marked delay in arteriovenous (A-V) transit time more than 20 seconds, and there is extensive areas of capillary non perfusion

and vessel wall staining greater than 10 disc areas of retinal capillary non perfusion which is associated with increased risk of neovascularization***. (CRVOS, 1995).***

The milder form of CRVO is called non ischemic. Most of CRVO cases (75%-80%) are classified as milder non ischemic form, which on FFA there is delayed A-V transit time and good retinal capillary perfusion. (***CRVOS, 1995***).

*** Two types of retinal white lesions can be seen in CRVO:**

a- Cotton wool spots.

b- Patchy ischemic retinal whitening.

Patchy ischemic retinal whitening (PIRW) occurs in younger patients with non-ischemic central retinal vein occlusion. It is located preferentially in a perivenular distribution near the macula, a pattern not respected by cotton wool spots, which are usually distributed around the optic disc ***(Hayreh, et al., 2008)***. It may also be associated with para central acute middle maculopathy (PAMM) which refers to characteristic hyper reflective spectral domain OCT lesion involving the middle layers of the retina at the level of the inner nuclear layer which may be the result of an ischemic insult at the level of intermediate and deep capillary plexus ***(Sarraf, et al., 2013).***

Toco, et al had described Cotton wool spots in the use of spectral domain optical coherence tomography (SD-OCT) to document the progression of an isolated cotton wool spot, from presentation to fundoscopic resolution.(***Toco, et al.,2009***).

Cotton wool spots are composed of accumulation of neuronal debris within the nerve fiber layer. They result from ischemic disruption of nerve axons. They appear as small fluffy whitish superficial lesions that obscure underlying blood vessels. ***(Loannides, et al., 2011).***

Firstly, in the acute phase, 3 days from the onset of symptoms, there was marked thickening of the retina confined to the retinal nerve fiber layer with no apparent thickness change in the other layers. Secondly, following ophthalmoscopic resolution at 9 weeks, there was over all retinal thinning at the area of the lesion compared with adjacent healthy retina ***(Loannides, et al., 2011).***

Identification of ischemic retinal white lesions with imaging is very important to understand disease pathophysiology, explain patient symptoms and to help to determine the prognosis.

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 the first 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 ***(Hayreh, 1962).***

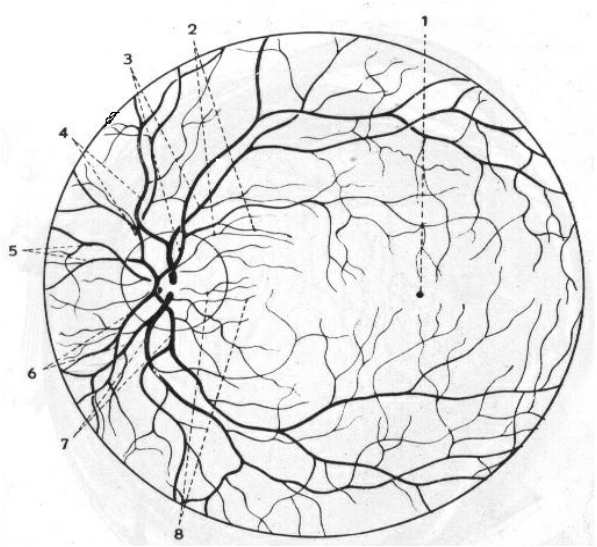

Figure 1. Retinal blood vessels ***(Hayreh,1962)***

1. Macula lutea.
2. Superior macular artery and vein.
3. Superior temporal retinal artery (vein).
4. Superior nasal retinal artery (vein).
5. Medial retinal artery (vein)
6. Inferior nasal retinal artery (vein)
7. Inferior temporal retinal artery (vein)
8. Inferior macular artery (vein)

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 170µm 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 quadrantic branches. The anatomic division of the retinal arteries into superior and inferior halves usually is maintained throughout the retina (figure1), because normal retinal vessels rarely cross the horizontal retinal raphe ***(Hayreh, 1962).***

The major arterial branches are about 100µm 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 ***(Hayreh, 1962).***

2-Retinal capillary layers:

Within the retinal circulation, the intra retinal arterial branches have been found to supply layers of capillaries (figure 4). Recently, four different retinal capillary networks were identified by confocal imaging and quantified by their layers:

1) Nerve fiber layer

2) Ganglion cell layer

3) Border of the inner plexiform layer and superficial boundary of the inner nuclear layer

4) Boundary of the deep inner nuclear layer and outer plexiform layer.

According to the plexus formation and their layers: inner layers 1 and 2 constitute the superficial capillary plexus (SCP), whereas outer layers 3 and 4 form the deep capillary plexus (DCP) (***Yu, et al., 2014).***

Auto segmented "full thickness" optical coherence tomography angiography (OCTA) scan was used to visualize the whole retina microvascularization (figure 2) (***Sophie, et al; 2015***)

In normal eyes, the OCT angiogram shows the foveal avascular zone (FAZ) demarcated with a foveal vascular ring. The fovea has a lower capillary density than parafoveal capillary regions in both superficial and deep inner layers. The deep retinal layers surrounding the fovea shows a spider-web pattern of vessels with many small discontinuous segments (figure 3) (***Marco, et al; 2015***)

Like capillary networks elsewhere in the body, the retinal capillaries assume a meshwork configuration to ensure adequate perfusion to all retinal cells. The deeper layers have a mesh diameter about 50 µm (15-130µm) and the more superficial layer has a slightly larger diameter 65µm (16-150µm) diameter ***(Duker and Weiter, 1991).***

A capillary-free zone is present around each of the larger retinal arteries and veins, but it is more prominent around arteries where it measures up to120µm in diameter. In the fovea and the far retinal periphery, retinal capillaries are absent. The foveal avascular zone (FAZ) is 350-750µm in diameter ***(Duker and Weiter, 1991).***

A radial peripapillary distinct layer of capillaries is found within the inner aspect of the nerve fiber layer, this is the most superficial of all retinal capillaries. They have relatively long, straight path with few anastomoses with adjacent or underlying capillary beds. Their distribution around the optic nerve, superior

and inferior temporal arcades reflects the thickest distribution. (***Alm, 2003***).

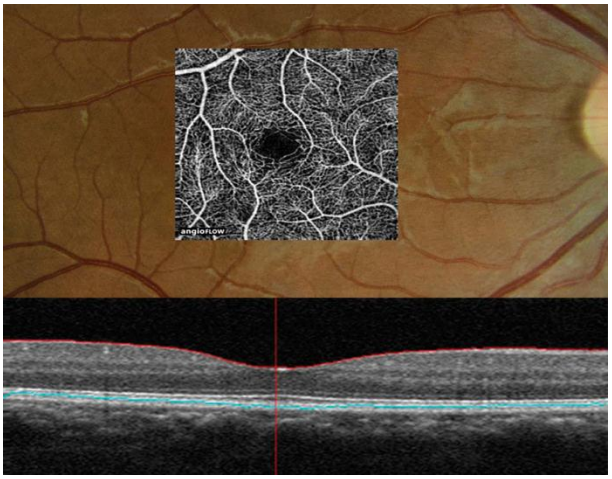

Figure 2. Full autosegmented capillary network on OCTA. Top image showing color fundus image with superimposition of 3 mm × 3 mm OCTA image comprising SCP and DCP. Bottom image showing the corresponding OCT (inner limiting membrane in red , retinal pigment epithelium in blue). ***(Sophie, et al 2015)***

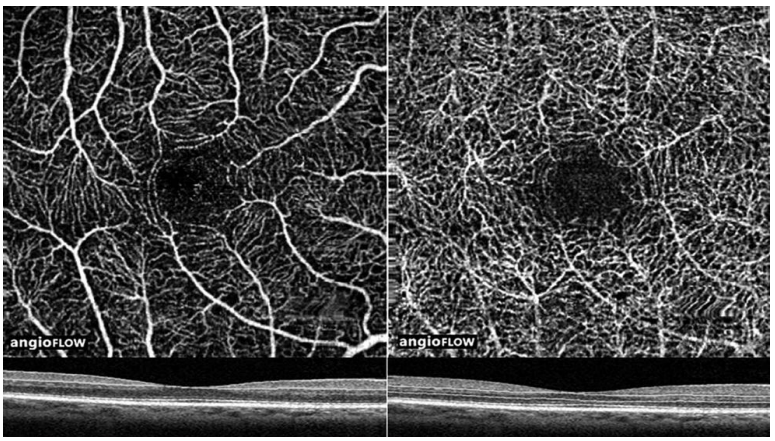

Figure 3. Normal SCP and DCP imaged by OCTA. 3 ×3 mm OCTA scans (top) and co-registered SD OCT scans (bottom) centered at the fovea showing normal superficial and deep capillary plexus. ***(Marco, et al. 2015)***