

SUPPLEMENTARY FILE S1

Morphology of the retinal and choroidal blood vessels

The neural retina is a nervous tissue comprised of nine layers described from the inner to the outer retina: inner limiting membrane (ILM), retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), external limiting membrane (ELM), and photoreceptor segments (PS). The interdigitations of the retinal pigment epithelium (RPE) surround the outer segment photoreceptors [1].

The high metabolic activity of the retina requires a large blood supply achieved through two different vascular systems. The inner two-thirds of the retina until the INL depends on blood supply from the central retinal artery. The blood supply for the outer retina depends on choroid vascularization [2]. The central retinal artery, a terminal branch of the ophthalmic artery, enters through the optic nerve and divides and forms different plexuses covering the entire retina, excluding the central foveal avascular zone (FAZ) and the most peripheral 1-1.5 mm [3–6]. The number of retinal plexuses varies from 1 to 4 depending on the eccentricity [7]. Close to the optic nerve head, the radial peripapillary capillary network (RPCN), the superficial vascular or capillary plexus (SVP/SCP), the intermediate capillary plexus (ICP), and the deep capillary plexus (DCP) exist [8]. The rest of the central retina is formed by the SCP, ICP, and DCP [8] (Figure 1).

The FAZ is the capillary-free region around the fovea [4]. The FAZ is delimited by a vascular ring at the ICP level resulting from the convergence of the three main vascular plexuses (SCP, ICP, and DCP). The blood supply to the fovea arrives from the underlying choroidal circulation [9].

The RPCN is a vascular plexus mainly located in the RNFL around the optic nerve and is composed of a simple layer of capillaries interconnected with each other and arranged parallel to the fibers [8,10]. The SCP comprises a three-dimensional vessel network at the GCL level formed by larger arteries, arterioles, veins, and venules [11]. This plexus presents a capillary-free zone in the central retina [10,12] and branches mainly into straight vessels. The ICP forms a simple vascular layer with tortuous vessels between the INL and IPL and disappears progressively towards the retinal periphery connecting the SCP and the DCP. Finally, the DCP is a single layer of vessels located in the outermost part of the INL formed by closed capillary loops and spider-like structures [8,12].

Vascular diseases, including DM, or other retinal diseases, could change the morphology and size of the FAZ in the different plexuses. Imaging techniques such as OCTA can detect and analyse vascular alterations such as MA, capillary dropout, slow blood flow areas, IRMA, or NV, among others [13–15].

Otherwise, this technique also eases the study of the choroid vessels responsible for nourishing the outer retina. The choroid is a complex structure mainly formed by vessels and connective tissue that extends from the limits of the optic nerve. Bruch's

membrane, the choriocapillaris (CC), Haller's and Sattler's layers, and the suprachoroidal space are included [16].

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