Progress in Retinal and Eye Research 52 (2016) 130–155

Contents lists available at ScienceDirect

Progress in Retinal and Eye Research

journal homepage: www.elsevier.com/locate/prer

Investigating the choriocapillaris and choroidal vasculature with new optical coherence tomography technologies

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ARTICLE INFO

Article history:
Received 2 July 2015
Received in revised form
9 October 2015
Accepted 12 October 2015
Available online 23 October 2015

Keywords:
Optical coherence tomography
En face
Optical coherence tomography angiography
Choriocapillaris
Choroid

ABSTRACT

The body of knowledge of in vivo investigation of the choroid has been markedly enhanced by recent technological advances in optical coherence tomography (OCT). New insights elucidating the morphological features of the choriocapillaris and choroidal vasculature, in both physiological and pathological conditions, indicate that the choroid plays a pivotal role in many posterior segment diseases. In this article, a review of the histological characteristics of the choroid, which must be considered for the proper interpretation of in vivo imaging, is followed by a comprehensive discussion of fundamental principles of the current state-of-the-art in OCT, including cross-sectional OCT, en face OCT, and OCT angiography using both spectral domain OCT and swept source OCT technologies. A detailed review of the tomographic features of the choroid in the normal eye is followed by relevant findings in prevalent chorioretinal diseases, focusing on major causes of vision loss such as typical early and advanced age-related macular degeneration, polypoidal choroidal vasculopathy, central serous chorioretinopathy, pachychoroid spectrum disorders, diabetic choroidopathy, and myopia.

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Abbreviations: AMD, age-related macular degeneration; CNV, choroidal neovascularization; CSCR, central serous chorioretinopathy; EDI-OCT, enhanced-depth imaging optical coherence tomography; FA, fluorescein angiography; ICGA, indocyanine-green angiography; logMAR, logarithm of the minimum angle of resolution; OCT, optical coherence tomography; PCV, polypoidal choroidal vasculopathy; RPED, retinal pigment epithelium detachment; RPD, reticular pseudodrusen; RPE, retinal pigment epithelium; SD-OCT, spectral-domain optical coherence tomography; SS-OCT, swept source optical coherence tomography; VEGF, vascular endothelial growth factor.

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http://dx.doi.org/10.1016/j.preteyeres.2015.10.002
1350-9462/

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Recent advances in optical coherence tomography (OCT) have revolutionized the field of retina, both in the research setting and in the clinical practice. New findings from investigating choroidal vessels *in vivo* suggest that the choroid is directly implicated in retinal pathologies, as a primary cause or a secondary consequence. In variable circumstances, choroidal changes play a role in triggering disease mechanisms, natural history of disease progression, and response to treatment interventions. Therefore, a better understanding of the morphological and functional features of the choroid can impact our ability to diagnose and manage chorioretinal conditions, lead to new insights related to underlying physiopathogenesis, and potentially indicate new therapeutic targets. In this review, we characterize the choroid on state-of-the-art OCT imaging. Detailed choroidal features in healthy eyes are presented, followed by a systematic description of choroidal changes in prevalent diseases that cause visual loss. Providing fundamental knowledge to interpret novel choroidal imaging, this work starts with the two pillars for proper multimodal imaging analysis: relevant histologic features of the choroid, and basic principles of OCT.

1. Basic histology of the choroid in normal eyes

The morphological features of the Bruch membrane/choriocapillaris complex and choroidal vasculature on ex-vivo histology, described herein, are relevant for the proper interpretation of the optical reconstruction of the tissue through *in vivo* fundus imaging.

1.1. Bruch membrane

The Bruch membrane lies anteriorly to the choriocapillaris, which is the capillary component of the choroidal vasculature. It is a thin connective tissue of collagen-rich and elastin-rich extracellular matrix that separates the choriocapillaris and the retinal pigment epithelium (RPE). It supports RPE cell adhesion and RPE migration and differentiation, while acting as a barrier to cellular migration between the choroid and the retina (Del Priori et al., 2002; Gong et al., 2008). The Bruch membrane is 2 μm–4 μm in thickness and is composed of five acellular layers: the basement membrane of the RPE, the inner collagenous layer, the porous elastic layer, the outer collagenous layer, and the basement membrane of the endothelium of the choriocapillaris (Hogan, 1961). It regulates the reciprocal passive diffusion of molecules, serum constituents and other elements between choriocapillaris and the RPE. This transport mechanism varies according to the location in the retina (Bhutto and Lutty, 2012) and is directly dependent on Bruch membrane structure and molecular composition, which is influenced by several factors including genetics and environment. Thus, functional properties of Bruch membrane depend on physiological changes such as aging, as well as variable pathological mechanisms. Since choriocapillaris and Bruch membrane, along with RPE and photoreceptors, form a structural and metabolic complex, their interdependence is of fundamental importance for the integrity of each of these components (Bhutto and Lutty, 2012). Anatomical or functional abnormalities at the level of each of these layers may lead to dysfunction and cell death of all components of the complex.

1.2. Choriocapillaris and choroidal vasculature

The choriocapillaris has small vessels with a lumen slightly larger than a typical capillary, and is arranged in a distinct layer limited to the inner portion of the choroid. The vascular network at the level of the choriocapillaris is so tightly arranged in the posterior pole that distinct capillary tubes are difficult to identify. Fenestrated endothelial cells are a fundamental characteristic of tissues involved in secretion or filtration such as the choriocapillaris, which is fenestrated mostly on the retinal aspect of the vessels. Specific functions of the retinal side of the choriocapillaris have been identified. For example, vascular endothelial grown factor (VEGF) receptors-1 and -2 are expressed specifically on the retinal side of the endothelial cellular membrane (Blaauwgeers et al., 1999). Soluble VEGF isoforms maintain the vitality of the choriocapillaris and the integrity of the choriocapillaris fenestrations, which disappear with VEGF depletion (Mrejen and Spaide, 2013; Saint-Geniez et al., 2009). Moreover, the choriocapillaris expresses intracellular adhesion molecule-1, which promotes firm adherence of leukocytes such as macrophages and neutrophils to endothelial cells (McLeod et al., 1995).

A major biological function of the choriocapillaris is to supply oxygen and metabolites to the RPE and the outer neurosensory retina, which has the highest metabolic demand of all biological tissues (Wangsa-Wirawan and Linsenmeier, 2003). Of note, the choriocapillaris is the only route for metabolic exchange in the retina within the foveal avascular zone, and may also contribute in the circulatory demand of the prelaminar portion of the optic nerve (Hayreh, 2001; Mrejen and Spaide, 2013).

The architecture of the choroidal microvasculature remains controversial. Anatomically, the lobular appearance of the choriocapillaris was demonstrated in only part of the posterior pole. Also,