Intravital Imaging of Retinal Capillary Blood Flow Velocity in Diabetic Retinopathy Mouse Model

Jehwi Jeon[1], Jingu Lee[2], Pilhan Kim[1, 2]
[1]Graduate School of Medical Science and Engineering, KAIST
[2]Graduate School of Nanoscience and Technology, KAIST
E-mail: *pilhan.kim@kaist.ac.kr*

KEY WORDS: Intravital imaging, Retinal capillary, Blood flow velocity, Diabetic retinopathy

Abstract

Recent development of ultra-wide field fluorescence angiography and optical coherence tomography (OCT) angiography enabled high-resolution imaging of retina vasculature in human eye, identifying large vessels and capillaries. However, evaluation of blood flow speed in retinal vessels is seldom performed despite its importance in many retinal diseases such as diabetic retinopathy and age-related macular degeneration. It is mainly due to low accuracy and limited reproducibility in currently available technology for retinal blood flow measurement such as Doppler OCT or Doppler ultrasonography. Furthermore, there are no reliable technology to measure blood flow velocity in small retinal capillary. In this work, we used a custom-design video-rate laser-scanning confocal microscope modified for noninvasive direct *in vivo* visualization of retina of live mouse model [1]. To directly image flowing red blood cell (RBC) in retinal capillary, fluorescent RBCs labelled by far-red fluorophore, DiD, was intravenously injected via tail vein. By tracking individual RBCs in retinal vessels with high spatiotemporal resolution, we successfully quantified blood flow speed in retinal artery, vein and capillary. Retinal blood flow velocity in growing mice of two different strains, C57B6 and BALB/c, from 3 to 16 weeks old was measured in longitudinal manner to analyze changes in aging. Additionally, we further analyzed blood flow velocity changes in two diabetic retinopathy (DR) mouse models, APB5 induced pericyte-depletion model [2] and Streptozotocin induced type1 like diabetic retinopathy model [3]. DR is common microvascular complication in the retina of patients with diabetes mellitus with high risk of vision impairment. It has been suggested that blood flow of retinal capillary might be important factor in the progression of DR as a continued dysfunction of retinal blood circulation induce more ischemic condition in retina causing retinal cell death. We observed decreased capillary blood flow velocity in early phase of DR mouse model. In conclusion, intravital imaging of retinal capillary blood flow can be a valuable tool to analyze unknown pathophysiology of retinal diseases involving retinal ischemia including diabetic retinopathy.

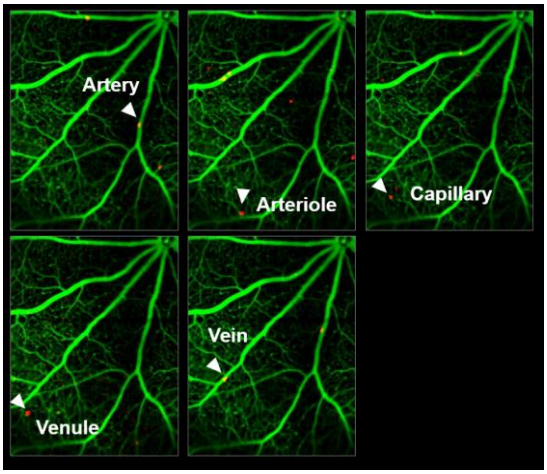

Figure 1. Intravital RBC flow imaging in retina. (Green: CD31 (endothelial cell), Red: DiD (RBC))

[1] Lee JY, Hwang Y, Kim JH, Kim YS, Jung BK, Kim P, et al. In Vivo Fluorescence Retinal Imaging Following AAV2-Mediated Gene Delivery in the Rat Retina. Invest Ophthalmol Vis Sci. 2016;57(7):3390-6.

[2] Ogura S, et al. Sustained inflammation after pericyte depletion induces irreversible blood-retina barrier breakdown. JCI Insight. 2017;2(3):e90905.

[3] Gong C el atl. Streptozotocin induced diabetic retinopathy in rat and the expression of vascular endothelial growth factor and its receptor. Int J Ophthalmol. 2013;6(5):573-7.