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Measurement of microcirculation in optic nerve head and retina using laser speckle flowmetry

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ABSTRACT

The demand for more precise microcirculation is rising. In the retina, microcirculation control is crucial in optic nerve head (ONH) surgeries or diabetic retinopathy surgery. Hence, novel techniques for examination of the blood flow were developed, including laser speckle flowmetry (LSF), which is based on the light scattering principle. LSF has already found many applications. However, some challenges still require further research on this method.

KEY WORDS: LSF; laser speckle flowmetry; microcirculation; retina; ONH

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INTRODUCTION

Microcirculation in the retina plays a crucial role in homeostasis and nutrition. The retina, the most sensitive part of the human eye, has a developed capillary network supplying the optic nerve, responsible for transmitting visual information to the brain. The optic nerve is supplied from the central retinal artery, the pre-laminar region from the peripapillary choroid, lamina cribrosa from posterior ciliary arteries, and the retrolaminar region is supplied by the pial vascular plexus and axial centrifugal vascular supply [1]. In operations such as diabetic retinopathy surgery, leaking capillaries from the retina cause severe issues to the surroundings; hence, control of the blood flow plays a crucial role in the proper finalization of the surgical blood clotting process. Alterations in optic nerve head (OHD) may lead to the pathogenesis of glaucoma, leading to damage to axons and retinal ganglion cells, along with altered autoregulation [1, 2]. Further development of advanced techniques is required to streamline surgical procedures pertaining to the retina to improve the examinations of retinal hemodynamics, blood flow, and measuring aspects of autoregulation, which are currently studied with laser Doppler flowmetry (LDF) technique.

Recent advancements have aided in developing several non-invasive techniques for measuring blood flow. Among them, we can distinguish, for example, bidirectional laser Doppler velocimetry, LDF, angiographic procedures, and finally, laser speckle flowmetry (LSF). LSF is an innovative technique based on laser waves scattering from tissues. This method can be used to determine the velocity of the red blood cells (RBCs), for example, in the ONH, microcirculation in the retina, or choroid [3]. A speckle is formed when homogeneous light from a laser diode (with a wavelength greater than 800 nm) interacts with a scattering medium. The scattered light signal is detected by a photo-detection device (with a resolution of 100 x 100 pixels and a scanning rate of 500 frames per second), which analyses the distance traveled by different particles as they vary due to destructive and constructive interference (Fig. 1) [4, 5]. Moving particles, such as RBCs, will cause inconsistency in the randomly varying intensity pattern, interfering with the speckle pattern. Local spectre contrast is calculated by dividing the standard de-

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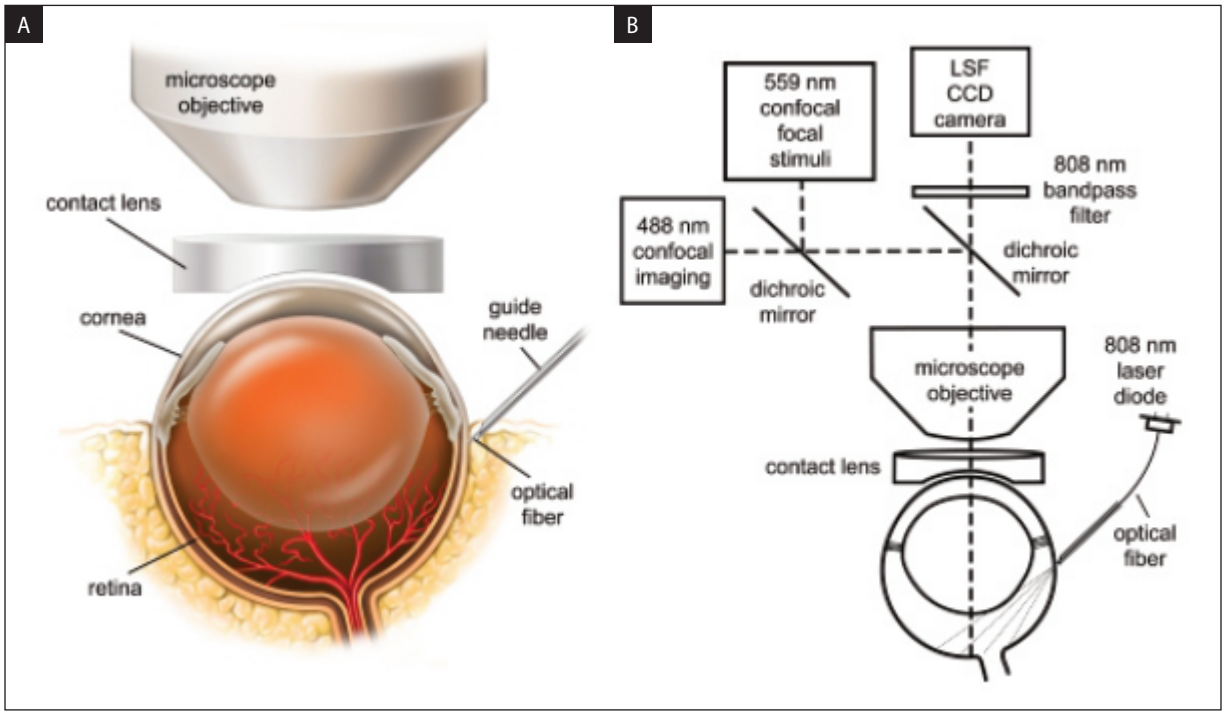

FIGURE 1. A schematic representation of the including laser speckle flowmetry (LSF) setup method — the retina is imaged simultaneously through a microscope for LSF and confocal microscopy. Dichronic mirror detects wavelengths for both instruments. 488 nm microscope scans blood vessels, while a 559 nm microscope generates stimulated light. Source: [4], reprinted based on license Creative Commons Attribution 4.0 International

viation of brightness by the mean brightness over a small area of pixels; this value allows us to calculate the velocity of RBCs, which can now be done almost instantly thanks to computing advances [6]. Generally speaking, the higher the blood velocity is, the more intense the signal from RBCs fluctuations is detected, resulting in a blur in the charge couple device (CCD) camera. The CCD device processes a 2D speckle map produced by blood movement (RBCs moving at different speeds cause spatial blurring, allowing us to obtain a speckle map — Fig. 2 [4, 5]). CCD camera allows for real-time visualisation at a framerate of 8 or 16 frames per second [7]. Analysis of the spatial scattering of the particles from the photodetector can provide us with detailed information about the velocity of RBCs, which can be gathered in 2 ways — either by analysing temporal or spatial variations [8]. The temporal contrast method offers greater spatial resolution when compared to the spatial method — however, spatial variation offers superlative temporal resolution of the two [5].

The laser speckle flowmetry method has been examined in choroidal vessels, showing satisfactory agreement and reproducibility with the currently widely-used laser Doppler flowmetry method based on the Doppler effect [9]. However, LSF currently

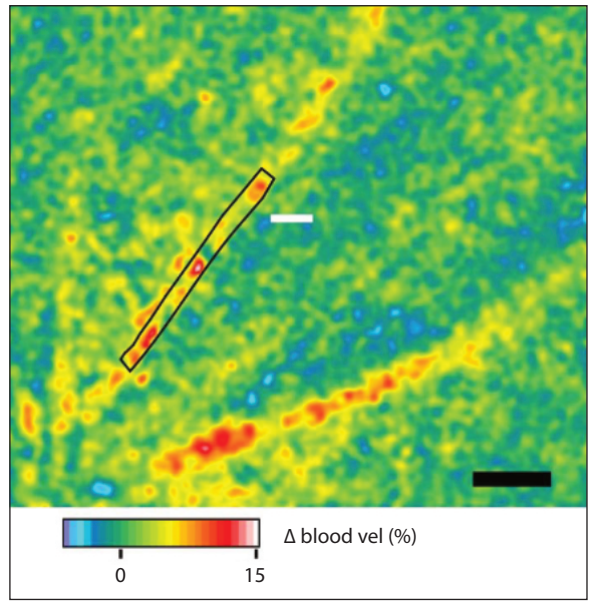

FIGURE 2. Example of laser speckle flowmetry (LSF) map, representing changes (scale bar shows a percentage change) in blood velocity of the retinal vessels, after 2–5 seconds offset of the light stimulation of eye photoreceptors with FluoView 1000 LSC microscope — a white on the map represents the location of the stimulus. Yellow, red, and white colours indicate increased blood velocity. The map shows a significant increase in blood velocity in the primary arterioles near the light stimulus and a minor increase in the velocity in adjacent venules. Source: [4]

offers a lower frame rate of real-time image than LDF (around 30 fps) — the current challenge for both methods is the development of a system that can project a map at a framerate of 100-200 fps for smooth imaging. Moreover, Doppler flowmetry is used for deeper examinations (1–1.5 mm), while LSF is used for superficial microcirculation (300 μm) [5]. Finally, LSF does not require constant scanning, making it easier to maintain [5].

LSF has been applied to the analysis of many pharmacological substances of blood flow during various exercises in the retina and iris [6], in conjunction with the mentioned earlier ONH analysis, with multiple methods, including the hydrogen gas clearance method [5, 6]. LSF may be used to study conditions such as diabetic retinopathy, retinal vascular occlusions, glaucoma, and age-related macular degeneration [10]. By evaluating retinal blood flow, LSF may help understand these diseases' pathophysiology and monitor their progression. LSF has been used to study ocular blood flow in conditions associated with ischemia, such as carotid artery disease and ocular ischemic syndrome. It can provide information about the severity and extent of ischemic damage. In diabetic retinopathy, LSF can help evaluate alterations in retinal microcirculation, contributing to early detection and monitoring of the disease. It can monitor changes in retinal blood flow following treatments such as anti-vascular endothelial growth factor (anti-VEGF) therapy, laser photocoagulation, or surgical procedures. Finally, it's worth mentioning that this technique is highly dependent on the optical properties of the tissue, which may vary between species. Further development of this method answers the high demand for high-resolution microcirculation imaging.

Conflict of interest

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