Warsaw Summer School on Advanced Optical Imaging 3-5 September 2024

Quantitative estimation of total retinal arterial blood flow using real-time Doppler holography at 24,000 frames per second

Yann Fischer[a], Zacharie Auray[a], Olivier Martinache[a], Marius Dubosc[a], Noé Topeza[a], Chloé Magnier[a], Maxime Boy-Arnould[a], Michael Atlan[a*]

[a] Langevin Institute. Centre national de la recherche scientifique (CNRS). Paris Sciences & Lettres (PSL) University. École Supérieure de Physique et de Chimie Industrielles (ESPCI) Paris. 1 rue Jussieu, 75005 Paris, France

**Presenting author; contact: micatlan@gmail.com*

1. Introduction

Real-time Doppler holography reveals local blood flow contrasts in the eye fundus [1]. We conducted a quantitative analysis of hemodynamics in primary in-plane retinal arteries using a prototype device capable of recording at 24,000 frames per second, equipped with a streaming camera (Ametek Phantom S711, Euresys Coaxlink QSFP+ frame grabbers). This device is designed for large-scale patient screenings. Leveraging near-infrared high-speed digital holographic imaging, this non-invasive angiography technique offers the potential for reliable estimation of local blood flow in retinal vessels. Doppler holography in ophthalmology has advanced through the integration of a co-designed optical interferometry system and high-performance computing, with the goal of identifying new biomarkers for enhanced non-invasive pathology classification and therapeutic monitoring. In this study, we performed image acquisition of the eye fundus, focusing on the optic disc of a volunteer. The optic nerve head and surrounding areas prominently display the primary branches of the central retinal artery, which supplies the retina, and the central retinal vein, which drains the retinal tissue. Monitoring retinal vascular supply is crucial for assessing eye health and may provide valuable insights into the systemic vascular system, as the central retinal artery originates from the ophthalmic branch of the internal carotid artery.

2. Methods and results

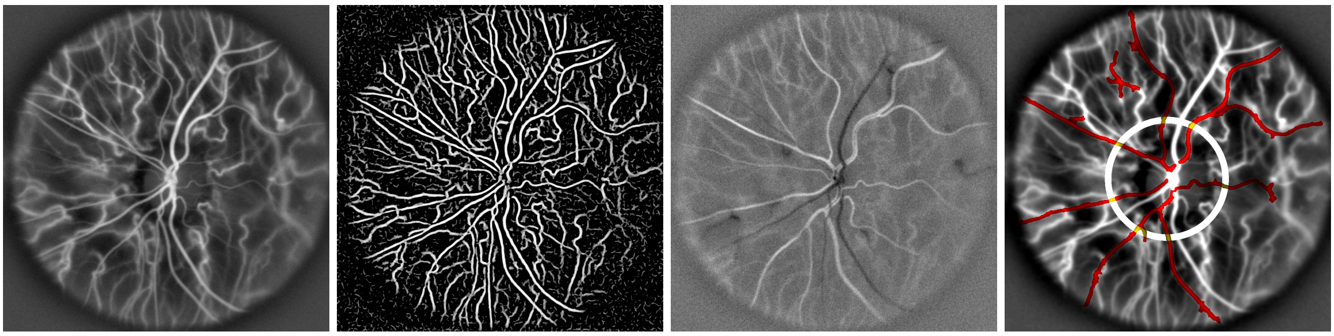

Fig. 1. From left to right : Power Doppler image averaged over three cardiac cycles, revealing retinal and choroidal blood flow contrasts. Frangi segmentation (https://github.com/edggjames/FrangiVesselnessSegmentation). Temporal correlation map with spatially-averaged signal revealing retinal arteries. Segmented retinal arteries (in red).

Image rendering was achieved through Fresnel transformation, singular value decomposition filtering, and short-time Fourier transform applied within 128-frame windows to generate power Doppler images [1]. Segmented retinal arteries (Fig. 1) were analyzed by measuring differential Doppler frequency broadening relative to surrounding areas. This locally increased broadening in retinal arteries, denoted as Δf, was estimated by calculating the square root of the absolute difference between the local normalized second-order moments of the Doppler spectrum within the 5 kHz to 12 kHz band across the field of view. The result was then multiplied by +1 or -1, depending on whether the sign of this difference was positive or negative, to account for instances where the signal from the local neighborhood does not accurately estimate Doppler broadening in the arterial background. This approach yielded estimated velocity distributions with a negative component (Fig. 2, right).

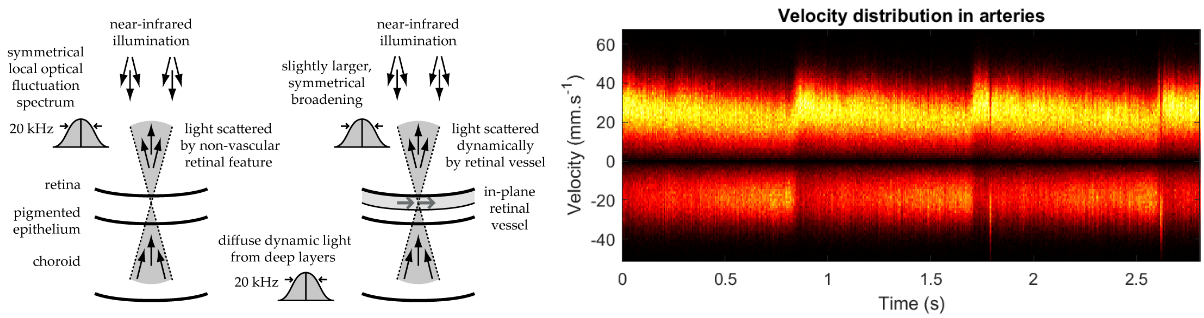

Fig. 2. Left: A simplified model illustrating the forward scattering of light from a diffuse, Doppler-broadened secondary source within the deep choroid, used to estimate blood flow in in-plane retinal vessels [2]. Right: The estimated velocity distribution of blood flow in segmented arteries shows a range from positive to negative values, revealing a statistical discrepancy: the measured local Doppler spectrum within a retinal artery can be narrower than that of its surrounding neighborhood.

We assume that the discrepancy introduced by local artery neighborhood measurements is statistically negligible. A forward scattering physical model, based on a diffused secondary light source in deeper retinal layers, was employed to derive the local root mean square blood flow velocity in in-plane retinal arteries [2]. The velocity $v = \lambda\, \Delta f / NA$ was calculated as the product of the optical wavelength (852 nm) and the local differential Doppler broadening (Δf), divided by the numerical aperture (NA) of the eye, estimated to be 0.124. The local absolute blood volume rate was determined by multiplying the local velocity by the cross-sectional area of the vessels, at arbitrary locations within a given radius from the centroid of the segmented vessels (Fig. 1, right; Fig. 3, left). The total arterial blood volume rate and arterial resistivity index were estimated by summing the measurements across the principal retinal arteries (Fig. 3).

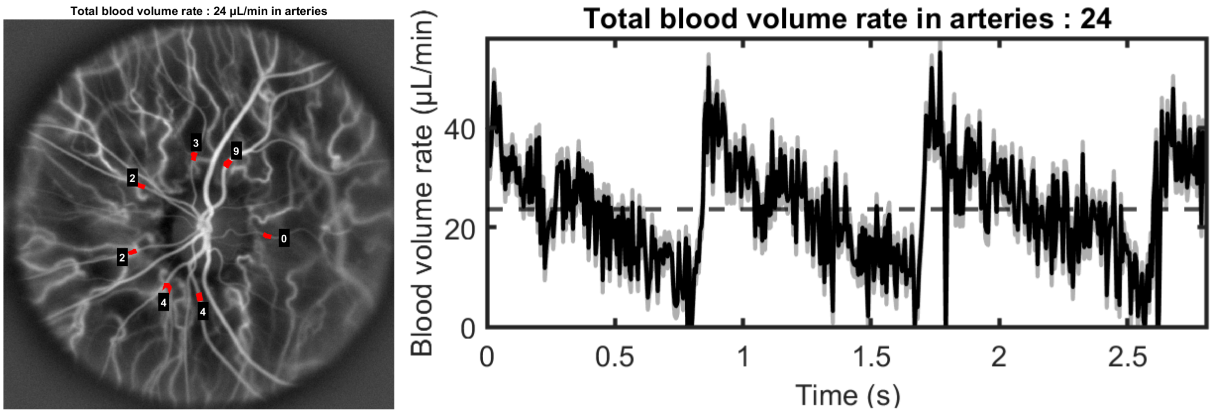

Fig. 3. Arterial blood volume rate estimated in a volunteer from 2.7 s of interferograms recorded at 24,000 frames per second.

3. Software and data

All the software used for the quantitative estimation of total retinal arterial blood flow using real-time Doppler holography is open-source and available on GitHub:

- Real-time, concurrent image rendering and raw image saving : https://github.com/DigitalHolography/Holovibes
- Offline image rendering and Doppler lineshape measurement : https://github.com/DigitalHolography/HoloDoppler
- Offline segmentation and retinal blood flow estimation : https://github.com/DigitalHolography/PulseWave

Image rendering and analysis were performed using the following software versions: Holovibes Release 13.2.3, HoloDoppler Release 1.1, and Pulsewave Release 1.2. The raw dataset used for the reported results is available upon request.

4. Conclusion

The average total retinal blood volume rate observed in our control subject is 24 µL/min (Fig. 3). It is notably lower than the range previously established by laser Doppler flowmetry and Doppler OCT. According to the literature, the average total arterial and venous volumetric flow rates were 33 ± 9.6 µL/min and 34 ± 6.3 µL/min, respectively, as measured in 12 eyes using bidirectional laser Doppler velocimetry [3]. Additionally, Doppler FD-OCT measurements in eight out of ten subjects reported a mean (SD) total retinal blood flow of 45.6 (3.8) µL/min, with a range of 40.8 to 52.9 µL/min [4]. We hypothesize that our deterministic blood flow analysis routine, utilizing real-time Doppler holography at 24,000 frames per second, may underestimate the total retinal blood volume rate compared to state-of-the-art methods. This discrepancy likely arises because the current recording frame rate is insufficient to fully capture the local Doppler broadening, leading to some signal clipping beyond the Nyquist frequency. Increasing the image recording and processing frame rates could potentially resolve this issue. Doppler holography now holds significant promise for monitoring retinal health by detecting blood supply variations during glaucoma treatments. This technique could also potentially become a routine examination for individuals with cardiovascular conditions, providing enhanced insights into their treatment response and overall vascular health.

5. Funding

ANR LIDARO ANR-22-CE19-0033-01.

6. References

[1] Puyo, Leo, Loic Bellonnet-Mottet, Antoine Martin, Francois Te, Michel Paques, and Michael Atlan. "Real-time digital holography of the retina by principal component analysis." arXiv preprint arXiv:2004.00923 (2020).

[2] Atlan, Michael. "Doppler holography for ophthalmology." arXiv preprint arXiv:2403.08849 (2024).

[3] Riva CE, Grunwald JE, Sinclair SH, Petrig BL. Blood velocity and volumetric flow rate in human retinal vessels. Invest Ophthalmol Vis Sci. 1985 Aug;26(8):1124-32. PMID: 4019103.

[4] Wang Y, Lu A, Gil-Flamer J, Tan O, Izatt JA, Huang D. Measurement of total blood flow in the normal human retina using Doppler Fourier-domain optical coherence tomography. Br J Ophthalmol. 2009 May;93(5):634-7. doi: 10.1136/bjo.2008.150276. Epub 2009 Jan 23. PMID: 19168468; PMCID: PMC2743389.