Quantitative functional retinal angiography via real-time Doppler holography. Effects of moderate intraocular pressure elevation

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1. Introduction

Intraocular pressure (IOP) plays a critical role in retinal blood flow regulation. While retinal circulation normally autoregulates against changes in ocular perfusion pressure [1], even moderate IOP elevations (12 to 20 mmHg) can impair this mechanism. Experimental studies show increased retinal vascular resistance, endothelial dysfunction, and lasting autoregulatory deficits at these levels[2, 3]. Clinically, raising IOP to 20 mmHg reduces retinal blood flow velocity and raises the central retinal artery resistive index (RI), indicating elevated downstream resistance [4]. As IOP nears the autoregulatory threshold, perfusion declines and pulsatile dynamics deteriorate, contributing to ischemia in glaucoma and other optic neuropathies[3]. Studying retinal hemodynamics and autoregulation has long been difficult, with no established gold-standard method [3]. Techniques like laser Doppler velocimetry (LDV) and its combination with vessel diameter measurement enabled point estimates of absolute blood flow [3]. Laser Doppler flowmetry (LDF) and scanning laser systems (e.g., Heidelberg Retina Flowmeter) allowed 2D perfusion mapping [3]. More recent methods include laser speckle flowgraphy (LSFG), which assesses relative flow via speckle blur, and the retinal vessel analyzer, which tracks diameter changes to evaluate vascular reactivity [3]. Real time high-speed digital holography has recently emerged as a powerful tool for quantitative retinal blood flow imaging in ophthalmology [5]. The approach provides direct access to absolute hemodynamic parameters.

2. Methods

Real-time data acquisition was performed with Holovibes at 37,000 frames per second on the retina of a volunteer. Automated extraction of absolute blood flow metrics was performed from Doppler holography measurements. This fully automated process is integrated into the open-source signal analysis pipelines HoloDoppler and EyeFlow, enabling robust hemodynamic monitoring. The signal analysis pipeline has three major steps: 1- Vessel segmentation and Doppler linewidth measurement: The primary retinal arteries are segmented in the imaging plane. Local Doppler frequency broadening in retinal vessels is extracted by subtracting a smooth background estimated from the Doppler linewidth in surrounding tissues, across the field of view. All Doppler spectra were analyzed within the 6–18 kHz frequency band. 2- Velocity estimation (mm/s): A forward light diffusion model accounts for multiply scattered light from the sclera and choroid, allowing calibration-free estimation of absolute velocity using known parameters (optical wavelength, numerical aperture). 3- Volumetric flow calculation (μL/min): The Doppler broadening profile is fitted to a laminar flow model, enabling estimation of vessel cross-sectional area with micrometer accuracy. Multiplying this area with the local velocity yields absolute blood flow per retinal vessel. Spatial consistency and low variability across repeated acquisitions support the validity of this approach for clinical use. Key hemodynamic biomarkers were quantified, including : stroke volume (nL), end-diastolic volume (nL), pulse waveform timings (ms), local arterial and venous luminal flow cross-sectional area (μm^2), modulation depth of the spontaneous venous pulsation (0–1), resistivity, pulsatility, and systole-over-diastole indexes from blood velocity and volume rate in retinal arteries and veins (0-1), and arteriovenous pulse delay (ms) (Fig. 1).

3. Results

Key findings in a healthy subject under modest IOP elevation (from 12 to 20 mmHg) reveal significant and quantifiable changes in retinal hemodynamics (Fig. 1). Arterial resistivity index increased from 0.55 to 0.87, indicating elevated downstream resistance and reduced diastolic flow. Arteriovenous phase delay doubled from 27 ms to 54 ms, reflecting slower capillary transit, possibly due to increased venous pressure or impaired outflow. Arteriovenous blood volume rate decreased by approximately 40–50%, suggesting compromised autoregulation and reduced perfusion capacity. Vessel lumen diameter decreased by 10–20% in both major retinal arteries and veins, consistent with increased vascular tone or mechanical compression. These results demonstrate that even mild elevations in IOP can induce pronounced, measurable disruptions in retinal perfusion—now accessible in real time through Doppler holography. Notably, all parameters returned to baseline immediately upon restoration of normal IOP.

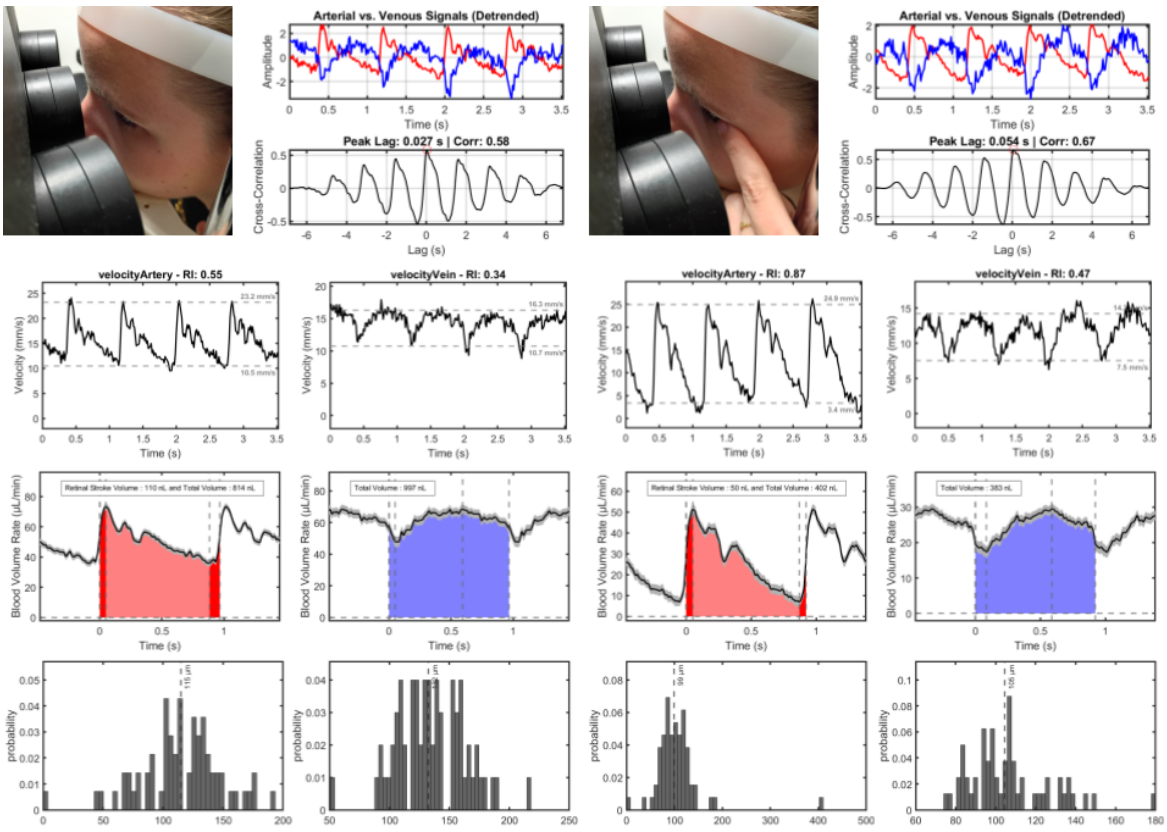

Fig. 1. Arteriovenous pulse delay, velocity profiles, blood volume rate, and lumen diameter statistics under IOP elevation from $\sim$ 12 (left) to $\sim$ 20 mmHg (right)

4. Conclusion

Real-time Doppler holography enables precise quantification of retinal hemodynamic responses to moderate IOP elevation, offering absolute, dynamic measurements of vascular function. This approach sets a new standard for assessing autoregulation and microperfusion in both health and disease. While static hemodynamic biomarkers already provide valuable insight into microvascular status, their response to controlled IOP provocation reveals autoregulatory impairments that may remain hidden under resting conditions. Future tests will include hypercapnia, the Valsalva manoeuver, and flicker stimulation.

5. Acknowledgment

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6. References

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