High-speed visualization of tissue-perfusion dynamics

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Optical coherence tomography enhances clinical diagnosis and could increase our understanding of major disease progression.

Quantitative knowledge about blood flow in tissues is crucial for evaluating health, and different methods have been applied to assess blood-tissue perfusion, such as Doppler ultrasound and laser-Doppler imaging.

Doppler optical coherence tomography (DOCT), a sophisticated non-invasive technique based on optical interferometry which can capture detailed images of biological tissues, provides the best available spatial and temporal resolution to localize and quantify blood flow. The first DOCT systems date back to the late 1990s, but the method has yet to find its way into clinical practice.

This may have been because of the limited reproducibility of quantitative Doppler readings caused by the early and relatively slow image acquisition rates. However, after 2003, high-speed spectral or Fourier-domain OCT (SD-OCT) started to gradually replace time-domain OCT, and comprehensive volumetric in vivo imaging allowed better diagnosis and treatment monitoring.

Retinal perfusion is uniquely accessible through the highly transparent ocular (eye) tissue. Blood flow velocity data is contained in the phase of the reconstructed sample signal and can be obtained through differential phase analysis of scans at successive depths. Detectable flow speeds are in the order of millimeters per second, and after a typical recording time of 10µs, blood has moved a distance of just 10nm. Such incredibly small distances can only be assessed in vivo using a fast and phase-stable interferometric method such as SD-OCT.

Figure 1 shows a Doppler tomogram (single image) compiled from a time-series of human retina tomogram images and demonstrates the ability of DOCT to extract perfusion-relevant parameters. Precise knowledge of the temporal behavior of blood flow allows the calculation of parameters such as the pulsatility index, which can be an early indicator of pathological changes.

Applying novel complementary metal-oxide semiconductor (CMOS) detector imaging technology, we recently captured retinal bed flow dynamics at a line rate of 200kHz and a volume repetition rate of 13 per second, as shown in Figure 2. The high speed is a drawback because the higher the speed, the less sensitively flow can be quantified. This is important for flat vessel beds perpendicular to detection direction, and for

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assessing flow in small capillaries. To quantitatively visualize flow dynamics of full retinal volumes, we developed a method that takes advantage of the pulsatile behavior of blood flow. Using a plethysmograph, an instrument for measuring changes in volume, we recorded several tissue volumes synchronously with the heartbeat at a line-rate of 60kHz. During post-processing, we were able to re-order the tomograms that constitute a single volume according to the heartbeat phase at which they were acquired, and obtained several new volume-flow maps for each given pulse phase. Such a map now allows investigation of flow dynamics within full tissue volumes. Figure 3 demonstrates the retinal projections of volume flow at the systolic and diastolic phase of the heart cycle.

Today, a variety of methods exist to measure quantitative and qualitative tissue perfusion that await clinical validation. Blood flow imaging gives direct access to tissue physiology and pathophysiology, as well as the dynamic interplay between tissue structures. Our continuing research, and that of several other international research groups, should enhance and refine existing diagnostics instrumentation in the near future.

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References