Optical coherence tomography measurements of biological fluid flows with picolitre spatial localiztion

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Keywords: Microcirculation, optical coherence tomography, speckle, phase-sensitive interferometry, rheology

Interest in studying the human and animal microcirculation has burgeoned in recent years. In part this has been driven by recent advances in volumetric microscopy modalities, which allow the study of the 3-D morphology of the microcirculation without the limitations of 2-D intra-vital microscopy. In this talk I will highlight results from my lab and others which show the power of optical coherence tomography (OCT) to image the normal and pathological microcirculation with picolitre voxel sizes. Both phase-resolved and speckle-variance methods are employed to characterize complex rheological flows both in-vitro and in-vivo.

1 Optical coherence tomography

Optical coherence tomography is an optical analogue of ultrasound imaging, with limited depth penetration into biological tissues (< 2mm) but offering high spatial resolution (picolitre voxels) and high voxel acquisition rates (up to 1 Gigavoxel per second). First generation time-domain OCT (TD-OCT) was superceded in 2003 by Fourier domain OCT (FD-OCT), bringing a 100-fold improvement in acquisition speed with no SNR penalty. OCT combines readily with Doppler velocimetry to provide 3-D flow mapping with excellent spatial, temporal and velocity resolution.

2 Doppler OCT and Doppler amplitude OCT

First generation time-domain OCT can be given velocity sensitivity by processing the low-coherence interferogram using joint time-frequency techniques such as the short-time Fourier Transform (STFT). We used this technique to study the rheology of whole blood in capillary vessels and demonstrated measurements of non-parabolic flow profiles characteristic of biphasic flows. Measuring the amplitude as well as the centre frequency within an STFT window allows mapping of the local concentration of moving scatterers. We used this to demonstrate the phenomenon of red-blood cell “tubular pinch” aggregation at high shear rates in whole blood.

3 Phase-resolved DOCT

STFT analysis leads to an undesirable trade-off between velocity resolution and spatial resolution. This can be overcome by moving to phase-resolved measurements, with the only disadvantage being aliasing at high flow speeds. This can be overcome using high A-scan acquisition rates and/or the method of synthetic phase. The technique can be readily adapted to FD-OCT. We used phase-resolved TD-OCT to demonstrate oscillatory flow dynamics described by Womersley theory in a highly scattering liquid and used phase-resolved FD-OCT to image blood flow in-vivo in the cerebral tissue of small animals. The technique has been very successfully applied to animal and human retinal blood flow imaging, and has great potential in studying neurovascular coupling in the brain, the response of the tumour microcirculation to therapeutic interventions and the presence of non-melanoma and melanoma epithelial cancer.

4 Speckle-variance and correlation mapping OCT

A limitation of phase-resolved FD-OCT is its sensitivity to motion artefacts. The high B-scan acquisition rates of FD-OCT systems makes dynamic speckle imaging a viable proposal. Speckle-variance OCT is less sensitive to motion artefacts than phase-resolved OCT but lacks quantification of flow velocity. The long acquisition times of speckle-variance imaging can be reduced by correlation-mapping, where the statistics are accumulated over a kernel in the image rather than a pixel time-series.

We used correlation-mapping OCT to detect the presence of the superficial blood vessels in the human nailfold. Such microangiography applied clinically could offer new ways to detect skin and oral cancer, with improved specificity due to the rejection of confounding influences such as inflammation.

5 Conclusions

High-speed volumetric imaging of the microcirculation is now a reality. Further improvements in acquisition speeds can be expected due to advances in swept-laser light sources and the promise of wafer-scale fabrication of electrically-pumped VCSEL lasers could drive down costs by orders of magnitude. Novel contrast mechanisms based on photothermal and photoacoustic interactions promise to supplement flow information with oxygenation information, providing a complete description of tissue oxygen transport at the capillary level. New clinical insights are promised by these advances.