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Optical Doppler tomography and spectral Doppler imaging of localized ischemic stroke in a mouse model

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Abstract:

We present a combined optical Doppler tomography/spectral Doppler imaging modality to quantitatively evaluate the dynamic blood circulation and the artery blockage before and after a localized ischemic stroke in a mouse model. Optical Doppler Tomography (ODT) combines the Doppler principle with optical coherence tomography for noninvasive localization and measurement of particle flow velocity in highly scattering media with micrometer scale spatial resolution. Spectral Doppler imaging (SDI) provides complementary temporal flow information to the spatially distributed flow information of Doppler imaging. Fast, repeated, ODT scans across an entire vessel were performed to record flow dynamic information with high temporal resolution of cardiac cycles. Spectral Doppler analysis of continuous Doppler images demonstrates how the velocity components and longitudinally projected flow-volume-rate change over time for scatters within the imaging volume using spectral Doppler waveforms. Furthermore, vascular conditions can be quantified with various Doppler-angle-independent flow indices. Non-invasive in-vivo mice experiments were performed to evaluate microvascular blood circulation of a localized ischemic stroke mouse model.

Keyword: Doppler, tomography, interferometry

Introduction

Ischemic stroke is the most common kind of stroke and is known to be related to the blockage of an artery (arteries). It can affect people of all ages. The artery brings fresh blood of oxygen and nutrients to the brain and supplies the neurons with sufficient energy to function properly. Ischemic stroke occurs whenever an artery to the brain is blocked. Several different techniques have been used to study the blood flow within localized regions of brain activity, such as Positron Emission Tomography (PET), Near Infrared Spectroscopy, Blood-Dye Imaging, Intrinsic Signal optical Imaging (ISI), Laser Doppler Perfusion Imaging (LDPI), functional Magnetic Resonance Imaging (fMRI), and two-photon microscopy. High spatial resolution, on the order of micrometers, is necessary to distinguish different vascular components (arterioles, capillaries, venules) and individual columns of brain, which are about 100–200 square micrometers in tangential size. The current resolutions of PET, LDPI, and fMRI are too low to distinguish these components. Although ISI can map out *en face* cortical hemodynamics and columns, depth resolution is not available [1]. Two-photon microscopy has been used for mapping cortical activity. However, flow measurement requires fluorescent dye injection, which can be problematic, if the objective is to image blood flow changes induced by pharmacological agents [2]. The noninvasive high resolution tomographic capabilities of Optical coherence/Doppler tomography make it a promising technique for mapping depth resolved cortical blood flow.

Optical coherence tomography [3] (OCT) has recently emerged as a fundamentally new type of optical imaging modality. OCT performs high resolution, cross-sectional tomographic imaging of internal microstructure in materials and biological systems by measuring backscattered light. Optical Doppler tomography (ODT), also named Doppler optical coherence tomography (Doppler OCT), combines Doppler principle with OCT for tomographic imaging of tissue structure and blood flow, simultaneously [4-9]. Given the noninvasive nature and exceptional high spatial resolution, ODT has found a number of potentially important clinical applications, such as evaluating the efficiency of laser treatment of port wine stains and photodynamic therapy, screening vasoactive and antiangiogenic drugs, skin cancer diagnosis, monitoring cortical activity and brain injury.

Method and Experiments

By implementing the spectral Doppler imaging concept developed in Doppler ultrasound, we have been able to quantify the pulsatile blood flow pattern from blood vessels with the spectral Doppler imaging mode of our Fourier-domain Doppler OCT [10]. The schematic of the FDOCT system used in this study is shown in Fig. 1. Low-coherence light having a 1310 nm center wavelength with a full width at half maximum of 95 nm was coupled into the source arm of a fiber-based Michelson interferometer. Back-reflected lights from the reference and sample arms were guided into a spectrometer. The dispersed spectrum by a diffraction grating (500g/mm) was sampled by the spectrometer with a 1×1024 InGaAs detector array (SU1024-1.7T, Sensors Unlimited) at 7.7 kHz. The wavelength range on the array was 130 nm, corresponding to a spectral resolution of 0.13 nm and an imaging depth of 3.6 mm in air.

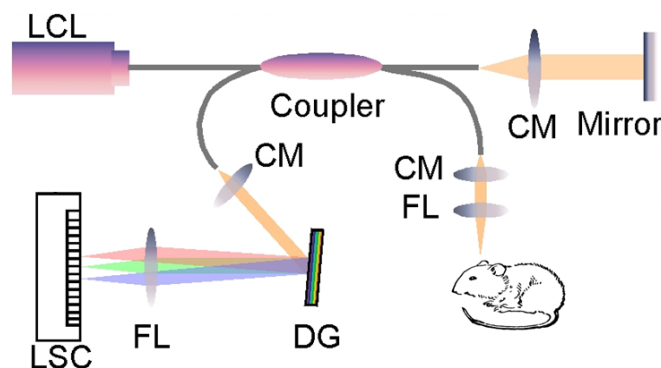


Fig. 1. Schematic of the OCT system (FL, focusing lens; DG, diffraction grating; CM, collimator; LSC, line-scan camera; LCL, low coherent laser).

Repeated color Doppler scans across an entire vessel were performed instead of an M-mode scan in order to enhance the temporal resolution of cardiac cycles. Fast, repeated, color Doppler scans are able to provide an accurate estimation of flow dynamics compared to the single line information acquired from an M-mode scan without compromising laser safety and system sensitivity. Spectral Doppler analysis of continuous color Doppler images demonstrates how the velocity components and longitudinally projected flow-volume-rate change over time for scatters within the imaging volume using spectral Doppler waveforms. Various velocity envelope curves can be derived from spectral Doppler waveforms and used to extract the corresponding pulsatility index, resistance index (RI) and several other indices that can provide interpretable Doppler-angle-independent information needed to quantify the pulsatile

nature of ocular blood flow. Successful application of Doppler ultrasound devices for medical imaging has demonstrated that spectral Doppler imaging is valuable in clinical settings by providing complementary information for Doppler imaging. The RI measurements have been widely used in Doppler ultrasound medicine. In vitro experiment conducted with ultrasound has demonstrated the higher vascular resistance value is associated with the higher RI measured assuming the constant compliance of vascular tube [11]. In this study, a mouse model was used as a platform to investigate the microvasculature change before and after photochemical induction of a localized ischemic stroke.

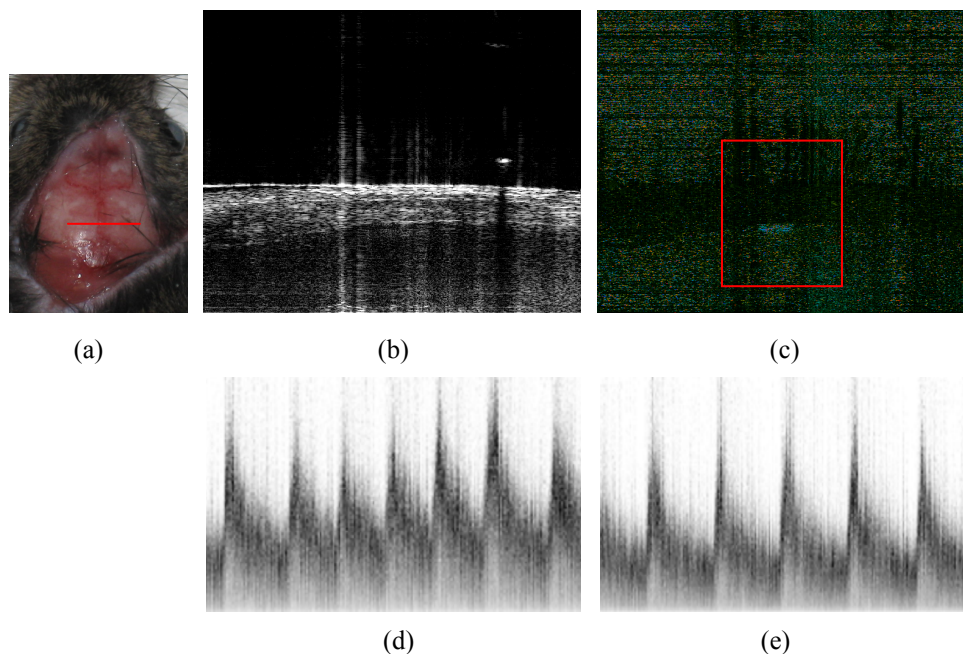


Figure 2 (a) mouse intact skull under imaging, (b) one typical OCT snapshot and (c) ODT snapshot. Figures (d) and (e) show the Doppler waveforms of the picked vessel (red window in Fig. (c)) before and after localized ischemic stroke.

Figure 2 shows the spectral Doppler waveforms acquired with the spectral Doppler imaging method. RI of ~ 0.4 was measured before the photochemical induced ischemic stroke. RI of 0.50 was measured after the stroke. The increased RI is in accordance with the laser speckle imaging results. The increased RI can be explained as the increased vascular resistance that was caused by the localized ischemic stroke. The above results agree with the spectral Doppler ultrasound literature. It suggests that by measuring the RI of an upstream artery with spectral Doppler imaging of DOCT, it is possible to find out the resistance change of its downstream vascular beds. The Resistive indices changes clearly showed the blockage of the cortical blood vessels.

Conclusion

In summary, we correlated the RI measurements by spectral Doppler imaging method of Doppler OCT with the micro-vasculature change due to a photochemical induced localized ischemic stroke. Laser speckle imaging instrument was also used to monitor the whole process. The higher RI is associated with higher resistance state that was accompanied by the localized ischemic stroke. The lower RI is associated with lower resistance state without any occlusion of the vessels.

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