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Publication Date

2009-02-12

DOI

10.1117/12.809692

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Peer reviewed

Spectral Doppler Imaging of Micro-vasculature Response to Laser Irradiation

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Abstract:

Doppler Optical Coherence Tomography (DOCT) imaging of in-vivo retinal blood flow was widely studied as efforts of research community to push this technology into clinic. Spectral Doppler imaging of DOCT has been demonstrated as a quantification method of in-vivo pulsatile retinal blood flow in human eye. This technology has the all the advantages inherited from OCT comparing to Doppler ultrasound. Comparing to normal spatial-distributed color Doppler imaging of DOCT, spectral Doppler imaging can reveal more haemodynamics details on the time dimension. Although resistance index (RI) of a micro-vascular can be measured in vivo from human retina, the clinical significance of RI measurements still needs to be investigated. 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. In this study, the rodent window-chamber model (RWCM) was used as a platform to investigate the RI change as the micro-vasculature response to laser irradiation. The higher RI was measured after the occlusion of two veins (should it be arterials) that was verified with laser speckle imaging in our preliminary experiment results.

1. Introduction

Although in-vivo human blood flow imaging with color Doppler OCT was demonstrated as early as 2000 with a time-domain system [1], there is still no commercial available Doppler OCT instrument for blood flow imaging in eye clinic. A few technology obstacles exist in applying the time-domain Doppler OCT into clinic. The first obstacle is eye movement, when there is no tracking device installed. The second obstacle is Doppler angle problem associated with all Doppler devices. The third obstacle is the limited velocity range that can be measured. The fourth obstacle lies in the difficulties of

recording and quantifying the pulsatile blood flow that varies along human cardiac cycle. The technology revolution in optical coherence tomography (OCT), triggered by the demonstration of sensitivity advantage of Fourier-domain configuration over time-domain configuration [2-4], also allows the researchers to overcome or alleviate the above obstacles in imaging human blood flow with Doppler OCT.

Doppler OCT relies on a dense scan to reduce the large phase variation caused by speckle noise; therefore, Doppler OCT is affected by moving artifacts. The eye movement problem has been greatly alleviated by the enhanced imaging speed of Fourier domain Doppler OCT. Bulk motion artifacts can be better corrected by the improved phase-resolved algorithm [5] than conventional histogram method [6]. Recently, a few researchers have utilized blood vessel orientation information to calculate the Doppler angle [7-9]. By using resonant Doppler technology, researchers have demonstrated imaging fast blood flow around the optical nerve head [9]. By implementing the spectral Doppler imaging concept developed in Doppler ultrasound, we have been able to quantify the pulsatile blood flow pattern from retinal blood vessels with the spectral Doppler imaging mode of our Fourier-domain Doppler OCT [5]. The blood flow pattern is observed by a series of blood flow snap shot images and analyzed with Doppler flow indices, such as resistive index (RI).

The RI measurements have been widely used in Doppler ultrasound medicine. However, the clinical significance of spectral Doppler imaging with Doppler OCT still needs to be investigated. 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 [10]. In this study, the rodent window chamber model (RWCM) was used as a platform to investigate the RI change as the micro-vasculature response to laser irradiation.

2. Material and methods

2.1 Non-invasive imaging modalities

The doppler retinal imaging system setup was shown in figure 1. The optical source is Broadligger D890 from Superlum Inc and the light source is protected by an optical isolator device. The sample arm was constructed with x-y Galvo scanning system from Cambridge technology. A 20/80 fiber coupler was used to construct the fiber based Michelson interferometer for the imaging system. A continuously adjustable attenuator was used in reference arm which included a static metal mirror. The detection arm employed a multi-element focusing lens after the transmissive grating which was illuminated by the collimated beam. The CCD line scan camera can operate as high as 28 KHz per second and has 2048 pixels. The line spectra information was acquired by a frame grabber and processed with Dell work station. The system software with multiple threads was developed to enhance the image processing speed. The optical power split from 20/80 coupler to the modified Zeiss patient module is $650 \mu\text{w}$. The integration time of CCD camera was set as $50 \mu\text{s}$. Spectral Doppler imaging scan protocol [5] includes a first 3D OCT scan over the sample, then selecting interested blood vessel from the OCT generated projection image and a final repeated Doppler scan over the selected vessel.

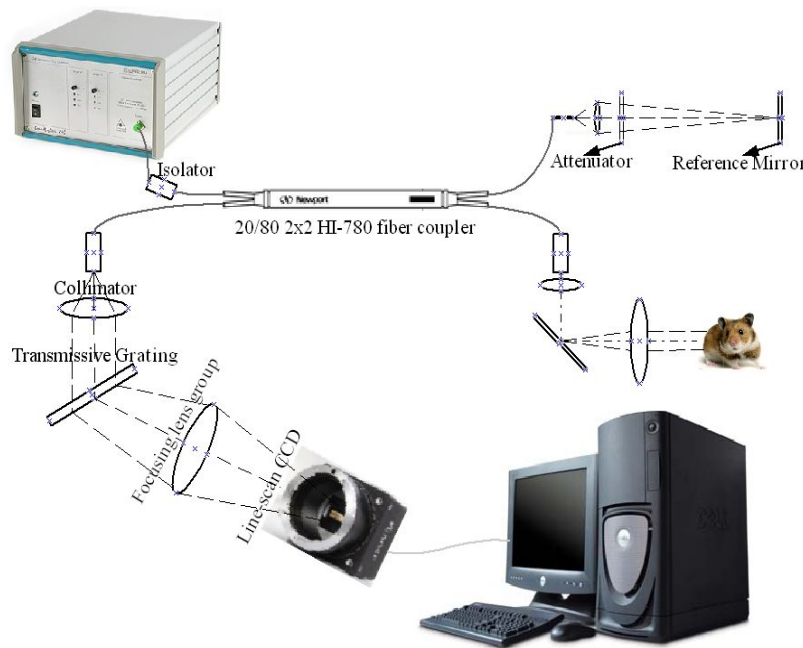


Figure 1 Spectral Doppler Imaging Setup

The Laser speckle imaging instrument has been previously used in monitoring micro-vascular blood flow response after pulsed laser irradiation [11]. In this study, it was used to verify the occlusion of irradiated vasculature.

2.2 Rodent window chamber model

Hamster was selected for the surgical installation of a dorsal skinfold window that permits optical imaging through the window. The animal was anesthetized with a combination of Ketamine and Xylazine (4:3 ratio, 0.1 g /100 g body weight) by intraperitoneal injection. A section for window placement on the back of the animal was selected, surgically scrubbed, shaved, and depilated. Sutures attached to a temporary mount retracted the dorsal skin away from the animal's body. A circular section with diameter of 1 cm was cut from one side of the symmetrical skinfold, thus exposing blood vessels in the underlying skin. An aluminum chamber was sutured to both sides of the skin and the sutures cut to release the skin from the mount. Saline was applied periodically to the subdermal skin to avoid dehydration. The above procedures were performed as defined in a protocol approved by the University of California, Irvine, Animal Use Committee.

2.3 Pulse laser irradiation

A commercial dermatology laser of 532 nm was used for this study. The pulse width is 1 ms. Five laser pulses with a repetition rate of 26 Hz and a total radiant exposure of 15 J/cm² were irradiated on blood vessels marked in photography.

2.4 Experimental design

One upstream artery was selected for spectral Doppler imaging to record and quantify the pulsatile blood flow before pulsed laser irradiation. The flow condition of the down stream vascular beds was recorded by the laser speckle imaging modality before the pulsed laser irradiation. After the laser irradiation, the same artery site was measure again with spectral Doppler imaging and the whole window chamber was also imaged with laser speckle imaging instrument.

3. Preliminary Results

3.1 Photograph and Laser speckle imaging before and after laser irradiation

Figure 2 showed the photography of the rodent dorsal skinfold window chamber and the location of laser irradiation area identified by the circle on the photography.

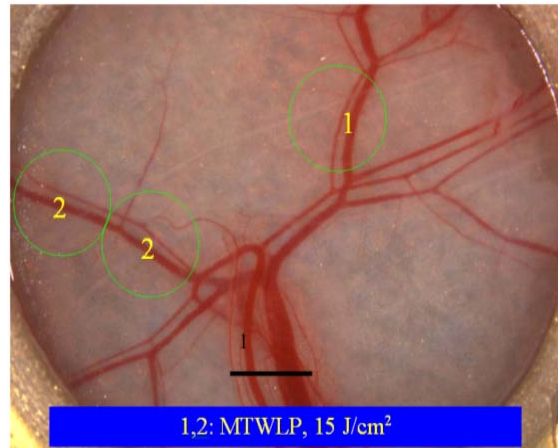


Figure 2 Photography of a rodent window chamber

Figure 3(a) shows the laser speckle imaging before the laser irradiation. Figure 3(b) shows the laser speckle image after the laser irradiation on sites 1, 2 and 3.

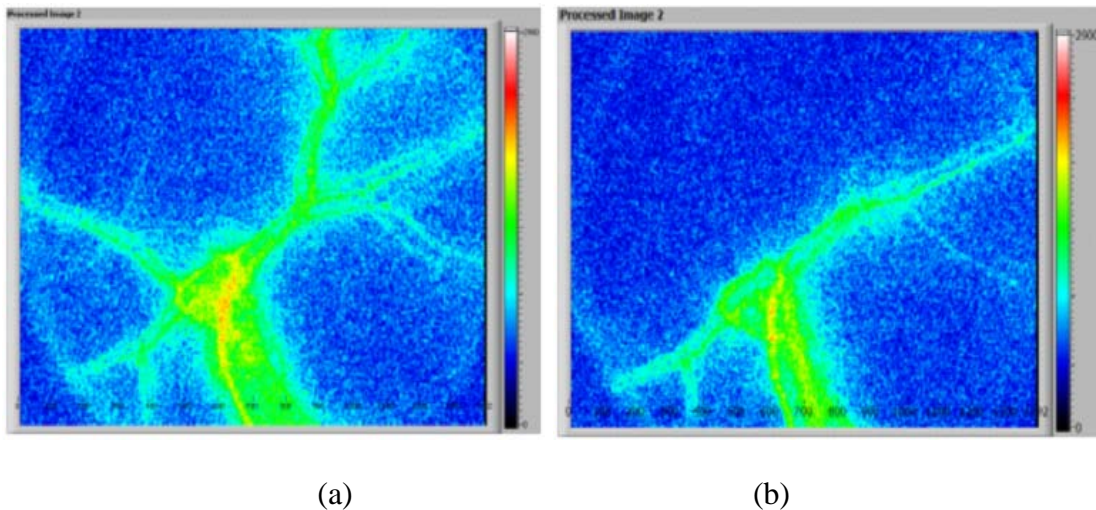


Figure 3 laser speckle image (a) before laser irradiation and (b) after laser irradiation. Blood flow in the two venule/arterial pairs identified by the circle 1 and circle 2 was seen in figure 3(a) and invisible in figure 3(b). That means the two venule/arterial pairs were occluded.

3.2 Spectral Doppler imaging results

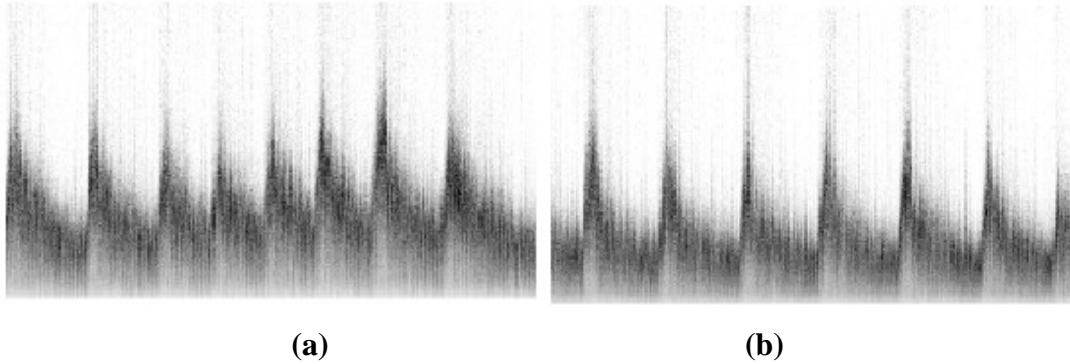


Figure 4 Spectral Doppler waveforms (a) before and (b) after laser irradiation

The spectral Doppler imaging sites was identified by the black bar in figure 2. Figure 4 shows the spectral Doppler waveforms acquired with the spectral Doppler imaging method. RI of **0.4089** was measured before laser irradiation. RI of **0.5561** was measured after laser irradiation. The increased RI is in accordance with the laser speckle imaging results. The increases RI can be explained as the increased vascular resistance that was caused by the occlusion of two venule/arterial pairs. 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 down stream vascular beds. This result also suggests that the spectral Doppler imaging method previously used in imaging pulsatile retinal blood flow may be used in monitoring the development of some vascular related eye diseases such as retinal vein occlusion or even in studying the pharmaceutical or surgical treatment outcome of these diseases.

4. Conclusion

In summary, we correlated the RI measurements by spectral Doppler imaging method of Doppler OCT with the micro-vasculature response for pulsed laser irradiation, that was monitored with laser speckle imaging instrument. The higher RI is associated with higher resistance state that was accompanied by the occlusion of two venule/arterial pairs. The lower RI is associated with lower resistance state without any occlusion of the vessels. The results agree with spectral Doppler ultrasound literature and suggest its further application in vascular related eye diseases.

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