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In vivo Time-Domain Diffuse Correlation Spectroscopy of the human muscle above 1000 nm

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ABSTRACT

Time-domain diffuse correlation spectroscopy (TD-DCS) is an emerging optical technique with the potential to resolve the blood flow (BF) in depth. The first *in vivo* measurements have been shown recently on humans, however improvements in terms of signal-to-noise ratio (SNR) and depth sensitivity would be beneficial for biological applications. In this contribution, we explore the possibility of *in vivo* TD-DCS measurements above 1000 nm, and discuss its possible advantages compared to standard wavelengths (i.e. 700-800 nm). In our experimental setup, we exploited a tunable pulsed laser source extended more to the infrared and an InGaAs photomultiplier. Here, we report the results of a cuff occlusion on the forearm of a healthy adult subject at a wavelength of 1000 nm. Compared to the same experiment at standard wavelength (785 nm), the electric-field auto-correlation functions show a slower decay rate during all the experiment (both during and after the occlusion) as expected, suggesting a higher SNR. Even longer wavelengths, for diminishing water absorption, can be obtained through optimization of the laser source and the use of more efficient detectors.

Keywords: Time-domain techniques, speckle imaging, blood flow

1. INTRODUCTION

Diffuse correlation spectroscopy (DCS) is a well established optical technique which, studying the intensity fluctuations of diffuse light multiply scattered through biological media, is able to measure the blood flow (BF)[1]. Light produced from a long coherence length, typically continuous wave (CW), laser is injected in the tissue and produces a speckle pattern on the surface of the media, which fluctuates over time due to scatterers motion, its fluctuation being quantified by the measured intensity auto-correlation function. When using a pulsed yet coherent laser source, using the physical relation between photon time-of-flight (TOF) and mean penetration depth[2], a depth-resolved BF measurement is enabled[3,4], by selectively measure the auto-correlation function of photons belonging to a given temporal gate (i.e. window). This method is the principle of time-domain (TD) DCS. TD-DCS has been demonstrated experimentally on liquid phantoms and small animals[3], then recently extended to in vivo experiments on humans[4]. Very recently, a hardware gating scheme was also proposed enabling measurements at quasi-null source-detector (SD) separations[5].

In this work, we evaluate the feasibility of performing *in vivo* TD-DCS measurements at long wavelengths (λ), in particular beyond water peak (i.e. $\lambda > 970$ nm). In that spectral region, the slower decay time of the auto-correlation functions could increase the signal-to-noise ratio (SNR) compared to wavelengths used in previous works (i.e. 700-800 nm)[3,4]. At the same time, ANSI standards for maximum permissible exposure allow more light to be delivered, as photons carry less energy at this wavelength. Both these factor contribute to a higher expected SNR. In addition, the lower scattering would increase the depth penetration[2].

2. EXPERIMENTS AND DISCUSSION

In our experimental setup, we have modified the TD-DCS setup already described in detail in reference[4] as shown in Fig. 1. We used a custom-made mode-locked Ti:Sapphire laser, repetition rate 100 MHz, and mounted a set of cavity mirrors designed for operation up to 1000-1050 nm. We delivered light to the tissue with a multi mode graded-index fiber (MMF), and recollected the photons diffused in the tissue at a source-detector separation ρ = 1 cm with a single-mode 5 μm core fiber (SMF). We delivered the diffused light to an InGaAs photomultiplier (PMT) (Hamamatsu Photonics, Japan) and

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acquired the time of arrival (time-stamps) of each photon with a time-correlated single-photon module (TCSPC) (TH260 nano, PicoQuant, Germany). The pulse-sync signal (SYNC) is obtained by splitting off a small fraction of the laser light with a beam splitter (BS) and delivering it to a photo-diode (PD), removing one signal every two with a custom-made electronic comparator to stay below maximum sync rate of the TCSPC module.

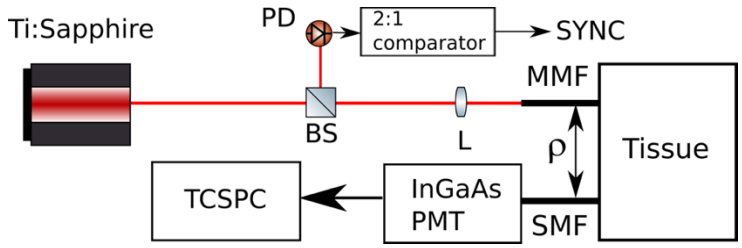

Figure 1: Experimental setup

An adult healthy subject (male, 53 years) underwent a cuff occlusion experiment of the left arm. The protocol was composed of 3 minutes of rest (baseline), 3 minutes of occlusion by inflation of a tourniquet at 200 mmHg, and 4 minutes of recovery. We placed a soft black probe, with the source and detection fibers, below the tourniquet on the brachioradialis muscle of the subject, where we estimated with a plicometer a thickness of the superficial layer of 3 mm. We tuned the laser to $\lambda = 1000$ nm and set the optical power on the tip of the source fiber to 30 mW with a variable attenuator, obtaining an average count rate of 151 kcps. The following day, for comparison, we repeated the experiment tuning the laser to $\lambda = 785$ nm, using the same input power. After the experiments, from the measured time-stamps, we computed with an integration time of 1 s the auto-correlation curves with the software correlator already deployed in our previous works[4,5].

In Fig. 2 we compare the ungated electric-field auto-correlation functions g_1, computed using the Siegert relation[1] from the intensity auto-correlation function g_2, measured at $\lambda = 785$ nm and 1000 nm. The curves and their fit using the correlation diffusion equation[1] are shown in three physiological conditions: before the occlusion, during the occlusion, and 20 s after the release of the tourniquet, in correspondence of the hyperemic peak.

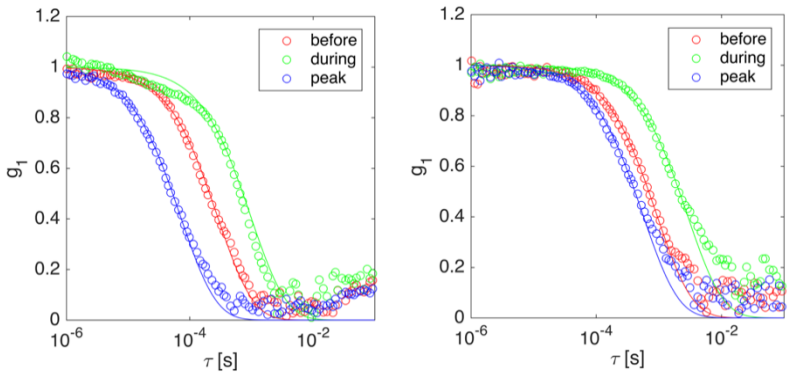

Figure 2: Ungated g_1 auto-correlation functions and their fit for the cuff occlusion experiments performed at $\lambda = 785$ nm (left plot) and 1000 nm (right plot) in three conditions: before the occlusion, during the occlusion and at the hyperemic peak.

From Figure 2 it is possible to see that during and after the occlusion, the auto-correlation function decay rate differs from its baseline value, as expected by the large BF changes induced by the occlusion itself. In addition, the auto-correlation decay rates at 1000 nm (right plot) are significantly different from the ones at 785 nm (left plot), as expected by to the lower value of the wave-vector and the scattering coefficient. Then, for the 1000 nm experiment, we computed the auto-correlation functions for two temporal gates of the distribution of time-of-flights (DTOF) curve: an early gate, opening before the rise of the curve and closing when the curve reached 50 % of its peak value on the rising side, and a late gate, from 50 % of the peak value on the falling side to the point where the curve reached the noise floor. The gated auto-correlation functions were fitted for retrieving the blood flow index (BFI) with the model that can be found in references[4,5],

assuming an absorption coefficient $\mu_a = 0.25\ cm^{-1}$ and a reduced scattering coefficient $\mu'_s = 5\ cm^{-1}$ for estimating the path length distribution in the theoretical expression of $g_1(\tau)$. The BFI was then normalized to the first 3 minutes.

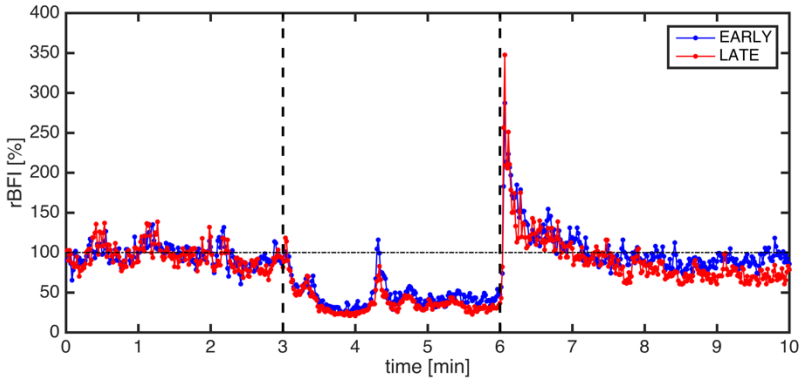

Figure 3: Relative BFI (rBFI) for the 1000 nm cuff occlusion experiment for early (blue) and late (red) gates. The two vertical dashed lines enclose the 3 minutes occlusion window.

As can be seen from Figure 3, the system is able to follow the BF changes induced by the occlusion for both the temporal gates considered. In addition, the rBFI traces show a slightly different temporal trends in the early and late gate, as expected by the layered structure of the forearm. The small superficial thickness of the subject may prevent a full disentanglement of the different BF responses of upper (skin/fat) and lower (muscle) tissue layers.

To conclude, in this contribution we have reported a TD-DCS cuff occlusion experiment at 1000 nm on an adult healthy subject. The BFI from gated auto-correlations showed the expected temporal trend and, compared to 785 nm, showed a slower decay rate, suggesting a higher SNR useful for biological applications. Through improvement of the experimental system it may be possible to optimize the wavelength, especially in terms of tissue absorption, for human studies.

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