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Assessment of Endothelial Functions in ICU Patients by Diffuse Optics

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Abstract: We assessed in 14 healthy volunteers and 10 intensive care unit (ICU) patients low and very low frequency oscillations in hemodynamic parameters of thenar eminence by studying their power spectral density exploiting time domain near-infrared and diffuse correlation spectroscopies. © 2025 The Author(s)

1. Introduction

Endothelium plays a critical role in regulating key physiological processes, including vasoregulation, homeostasis, and in maintaining the barrier function of blood vessels. However, endothelial dysfunction is a hallmark of various diseases, such as septic shock and acute respiratory distress syndrome. Recent advancements have demonstrated that combining near-infrared spectroscopy (NIRS) with vascular occlusion tests (VOT) can effectively monitor the progression of these conditions. This approach assesses the severity of endothelial dysfunction by analyzing the reoxygenation rate and hyperemic response following VOT [1,2].

As part of the VASCOVID project (Horizon 2020 European project, https://vascovid.eu), we investigated an alternative method for evaluating microvascular function. This approach relies on stationary diffuse optical (DO) monitoring of peripheral muscles, eliminating the need for a potentially uncomfortable intervention like VOT. Drawing on insights from laser Doppler flowmetry (LDF) and photoplethysmography (PPG), we explored the feasibility of analyzing frequency spectra derived from hemodynamic parameters measured in the microcirculatory system using DO.

Previous LDF studies have shown that blood flow oscillations correlate with various physiological processes, depending on their frequency range [3]: [0.6–2.0 Hz] cardiac activity; [0.145–0.6 Hz] respiratory activity; [0.052–0.145 Hz] (I_3) myogenic activity;[0.021–0.052 Hz] (I_2, low frequency or LF) neurogenic (sympathetic) activity; [0.0095–0.021 Hz] (I_1, very low frequency or VLF) endothelial activity mediated by nitric oxide (NO).

While LDF and PPG are useful for studying superficial tissues like the skin, they do not provide insights into deeper tissues such as skeletal muscles.

In this study, we utilized a hybrid time-domain NIRS (TD-NIRS) and diffuse correlation spectroscopy (DCS) device to measure hemodynamic spectra during rest on the thenar eminence. We compared measurements from healthy subjects with those obtained from 10 ICU patients in the intensive care unit, highlighting the potential of this method in discerning differences in microvascular functions across health states.

2. Methods

Two hybrid TD-NIRS and DCS devices were used in this study to monitor the hemodynamics of the thenar muscle of 14 healthy volunteers [4] and 10 ICU patients [5] at rest. They allow simultaneous measurements of hemoglobin concentrations and blood flow.

For TD-NIRS measurements, a semi-infinite homogeneous model for photon migration was applied to determine the optical properties at 670 nm and 830 nm. Using the Beer-Lambert law, the concentrations of oxygenated hemoglobin (HbO_2) and deoxygenated hemoglobin (HHb) were calculated. The blood flow index (BFI) was derived from the diffusion equation for the electric field autocorrelation function, measured at 784 nm. The device exploited

in clinic to measure ICU patients differs only for the source-detector separation, that was 2.5 cm for both modules, from that used to measure healthy volunteers [4, 5].
The time traces of the hemodynamic parameters were normalized using a third-order polynomial fit to remove long-term trends, andprocessed to eliminate the continuous component. Then, the power spectral density (PSD) for each signal was computed using the Welch algorithm, employing Hamming windows of 300 seconds with a 50% overlap. Finally, the average PSD and standard error were calculated across all subjects of the two groups for each hemodynamic parameter.

3. Results and discussion

The PSD of BFI was significantly higher (more than 2 order of magnitude) compared to those of hemoglobin concentrations, indicating the presence of stronge oscillatory components in the recorded DCS signal. Thus, we compared the PSD of BFI measured on the thenar eminence of the septic patients in ICU with the ones of the healthy volunteers (Figure 1a): the septic patients showed lower spectra at VLF, suggesting a different endothelial activity. As reported in Fig 1b), the absolute area in the endothelium related frequency range (I_1) is significantly ($p<0.01$) lower in ICU patients compared to healthy volunteers.

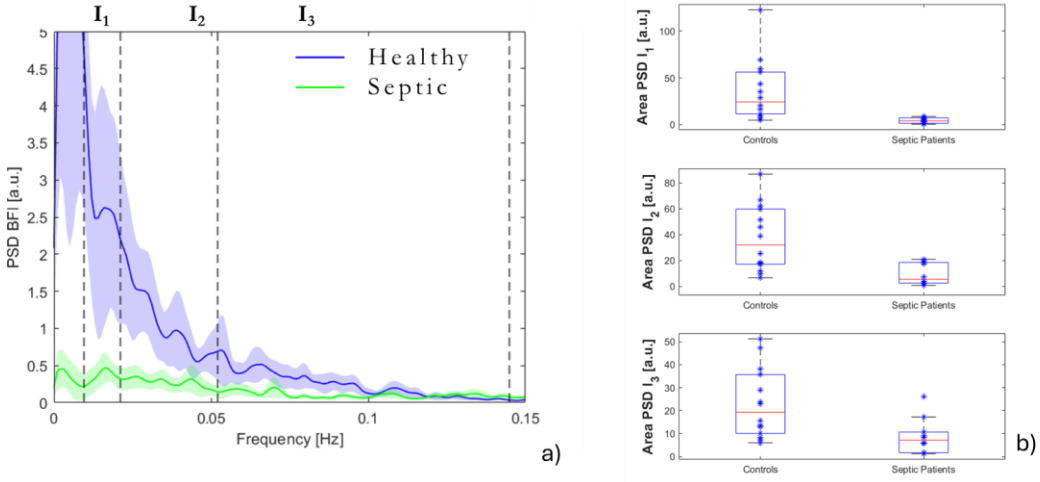

Figure 1 Panel a): comparison of the PSD of BFI measured on healthy volunteers and ICU patients, on the thenar eminence. Panel b): Absolute areas of PSD BFI in the three frequency ranges considered, I_1, I_2, I_3, of healthy volunteers and ICU patients.

4. Conclusions

We explored the feasibility of non-invasively assessing LF and VLF spontaneous oscillations in the microvasculature through resting-state measurements of skeletal muscle hemodynamics using DO methods. Frequency analysis revealed that both TD-NIRS (data not shown) and DCS techniques are effective in detecting LF and VLF oscillations, with an observed larger PSD for the BFI compared to hemoglobin concentrations.
This study represents a significant step toward the evaluation of the endothelial activity in skeletal muscles using DO technologies, without the need for additional interventions. Our results are promising, even if they suffer from two main limitations: the age mismatch between the two groups (27.1 years old for healthy volunteers against 62.9 years old for ICU patients), and the limited number of ICU patients, who also underwent different therapies that might affect endothelial functions. Thus, we aim to extend this research by including a larger cohort of healthy volunteers and ICU patients, matching their age, to further validate and refine the method.

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