NON-INVASIVE EVALUATION OF MICROVASCULAR AND ENDOTHELIAL FUNCTION WITH HYBRID NEAR-INFRARED SPECTROSCOPIES

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Near-infrared diffuse optical spectroscopies, in particular, time-resolved near-infrared spectroscopy (TR-NIRS) and diffuse correlation spectroscopy (DCS) allow for the non-invasive measurement of microvascular blood oxygen saturation, blood flow and the derivation of the metabolic rate of oxygen extraction. We have been developing these technologies for inclusion in increasingly high technology readiness level (TRL) instrumentation and utilizing them in multi-center clinical studies.

Recently, there has been an increasing amount of interest and publications indicating that more traditional and clinically approved continuous-wave near-infrared spectroscopy (CW-NIRS) instruments could be utilized in the critical-care to assess the microvascular and endothelial function at a systemic level by measuring the peripheral muscles. These publications have demonstrated by measuring the dynamics of the tissue/blood oxygenation during an extended vascular occlusion test (VOT), it is possible to evaluate the severity of microvascular impairment due to conditions such as sepsis and more recently due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, to guide the process of weaning from mechanical ventilation and more. They have also highlighted several major shortcomings; (a) CW-NIRS instruments that are clinical approved suffer from poor accuracy and poor precision and do not provide identical results between different instruments, (b) the VOT procedures lack standardization, and (c) blood perfusion should be measured simultaneously in order to get a more reliable and complete assessment.

In this talk, I will present our recent efforts working with clinicians around the world and with the industry to develop and test a new platform combining TR-NIRS, DCS with automated VOT, a smart probe, built-in pulse-oximetry and remote control for evaluating the resting state oxygen metabolism as well as the microvascular and endothelial function. I will detail the new procedures (phantoms, laboratory procedures as well as *in vivo* protocols) what have developed in order to standardize the testing and the operation of these platforms, describe the physiological and clinical relevance of this evaluation and present the clinical results from both the HEMOCOVID-19 (ten testing sites in five countries) and the VASCOVID projects. I will speculate about other potential applications beyond critical care and VOT such as those in neurology, endocrinology, aging and others with illustrative examples and results. As a whole, this will involve results from nearly thousand patients. Finally, I will place all these activities with the context of regulatory approvals for medical devices and the identification of clinical indications to target.

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