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VASCOVID: An integrated platform to evaluate endothelial and microvascular impairment in severe COVID-19 patients

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Abstract: The VASCOVID project aims to develop an hybrid diffuse optical device with a vascular occlusion protocol for evaluating endothelial and microvascular health in severe COVID-19 patients admitted to the ICU.

1. VASCOVID project

Worldwide, up to 25% of patients affected by the coronavirus disease-19 (COVID-19) that are admitted to intensive care unit (ICU), suffer from severe oxygenation impairment in the lungs driven by acute respiratory distress syndrome (ARDS) with an associated high mortality rate [1, 2]. Despite many years of clinical research, therapy options are still limited and supportive mechanical ventilation (MV) is still considered a keystone in the management of patients affected by respiratory failure. The virus that causes COVID-19, not only can seriously damage the lungs due to ARDS, but it also severely affects blood, causes clots, impairs the function of endothelium and the microvasculature.

Within this context, the Horizon 2020 project VASCOVID, is developing a portable, cost-effective, non invasive and real time health monitoring platform for the stratification and management of severe COVID-19 patients at the ICU, within 2 years starting from December 2020. The VASCOVID consortium will benefit from the experience gained in the sister HEMOCOVID-19 project which is running an international clinical study using standard near-infrared spectroscopy (NIRS) (https://hemocovid19-project.org/).

HEMOCOVID-19 deploys commercial continuous wave NIRS that is indeed less accurate and reproducible than the one proposed in VASCOVID, representing a limiting factor regarding possible outcomes. On the other hand, in the early stages of the ongoing pandemic this technology was the only one available and quickly ready-to-use fast. More importantly, this will link VASCOVID ongoing research activities in the ICU for best adaptations of this soon-to-be-ready technology.

VASCOVID device combines state-of-the-art bio-photonics technologies, time-resolved near infrared spectroscopy (TR-NIRS) and diffuse correlation spectroscopy (DCS), alongside artificial intelligence (AI). TR-NIRS and DCS have been separately validated in laboratories and many clinical applications on subjects of all ages and in animal models.

In fact, such hybrid optical platforms reached their maturity in other two European projects: LUCA and Baby-Lux, that are currently exploited in clinical trials for thyroid nodule cancer screening and premature neonatal care, respectively. In particular, TR-NIRS can resolve the pathlengths of photons that have propagated through the tissue, which allows the separation of absorption from scattering using a single source-detector separation. Also, time-gating of pathlengths emphasizes signal from deeper tissues [6]. These features make the retrieval of absolute

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values microvascular blood oxygen saturation (StO_2) and total hemoglobin concentration (THC) possible.

On the other hand, NIRS alone is not sufficient to estimate oxygen delivery to the tissue since results can vary between individuals depending on previous clinical conditions, level of exercise etc. DCS investigates blood flow index (BFi), which can be considered a more truthful parameter for microvascular compliance, by quantifying temporal fluctuations of NIR light scattered by red moving cells into the tissue. The time scale of these fluctuations is defined by the intensity autocorrelation [7]. The combination of the previously mentioned biomarkers makes the evaluation of microvascular blood/tissue oxygen availability and perfusion possible in a robust and accurate way. Also, tissue oxygen extraction (TOE$\sim$ SpO_2-StO_2, where SpO_2 is pulse oxymetry saturation), and the metabolic rate of oxygen extraction ($MMRO_2$ $\sim$TOE$\cdot$ BFi) can be assessed.

This automated device will consist of TR-NIRS and DCS sub-systems with integrated pulse-oximetry and an automated inflatable tourniquet. The latter is included because the protocol will use a vascular occlusion test (VOT) to evaluate endothelial and microvascular function. In a VOT, the tourniquet is inflated well above the systolic pressure to induce an extended period of ischemia to the target muscle. In a healthy tissue, oxygen is extracted during ischemia while blood flow is stopped, then, upon release it rapidly recovers to the baseline and show an overshoot of both blood flow and oxygenation. Endothelial and microvascular dysfunction alter these dynamics. VOT monitored with NIRS was shown to be a clinically relevant biomarker in sepsis, ARDS and other critical conditions. Thenar muscle of the palm is used as an indicator of systemic endothelial and microvascular function.

The entire system is controlled via the on-board single board computer (SBC), which is commanded wireless with a tablet and can be battery operated for about six hours at the ICU. Both DCS and TRS source and detection fibers will be hosted in a bio-compatible probe and attached to the thenar muscle of the subject. Finally, the whole set of VASCOVID data will be loaded on cloud and analyzed by AI algorithms for better extraction of relevant biomarkers based on machine-learning and time-series predictions.

The project consortium combines academia, industry and clinical research/practice as well as medical device regulatory expertise. The platform and the project structure is outlined in Figure 1.

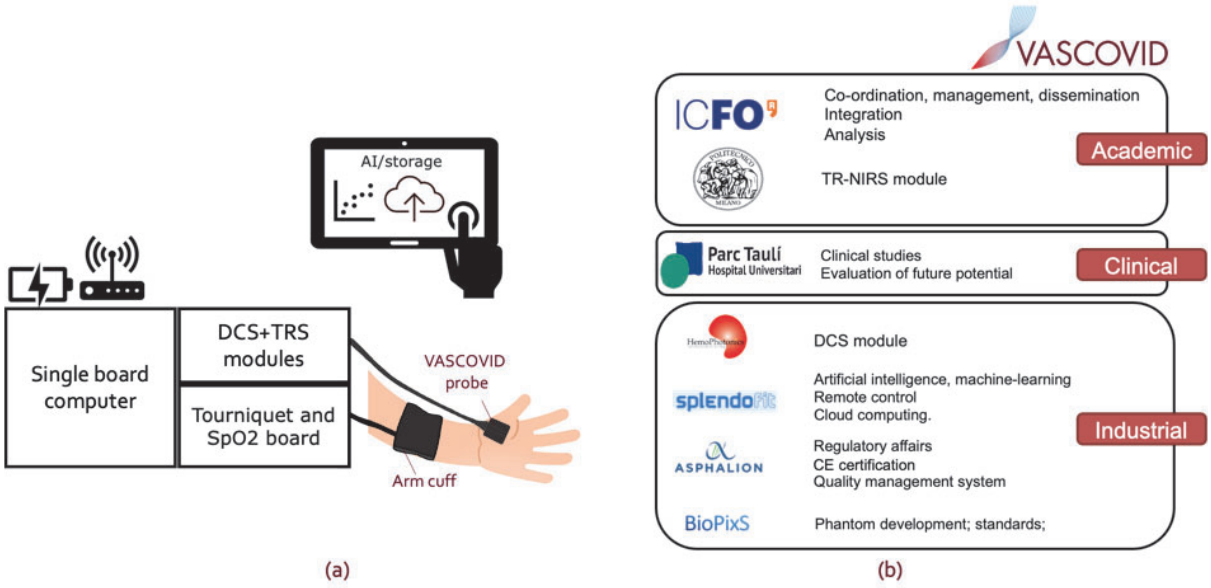

Fig. 1. Schematic of the VASCOVID device (a) and project structure (b).

2. Clinical aims of the project

VASCOVID project will carry out pilot testing on two fronts.

I. Stratification derived from endothelial function evaluation. It has been proven that microvascular endothelial dysfunction during the early stages of ARDS (within 24 h) is correlated with the illness severity and that StO_2 measured at the thenar eminence, can be a better predictor of poor outcome due to ARDS than the commonly used PaO_2/FiO_2 ratio, where PaO_2 is arterial oxygen partial pressure and FiO_2 is fractional inspired oxygen [3]. This means that there is room for improvement in the stratification methods of severe ARDS cases with poor outcome.

II. Personalized management based on the evaluation of cardiopulmonary interaction. MV along with additional strategies, such as prone positioning [5], is often required to support respiratory failure avoiding ventilator-

induced lung injury (VILI). Such strategies have effects on the cardiovascular performance which impact both PaO_2/FiO_2 and final oxygenation of the tissues. This procedure can be too aggressive for the patient but also time consuming for the clinicians, impacting heavily on the clinical resources in COVID-19 scenario. Furthermore, all patients receiving MV have to face a disconnection process from the ventilator which is divided into two phases: (1) spontaneous breathing without support of the ventilator through a spontaneous breathing trial (SBT); (2) extubation and definitive disconnection from MV. Extubation failure is defined when the patient needs reconstitution of ventilatory support within 48-72 h from extubation.

3. Conclusion

We will present the VASCOVID project's technological and clinical goals and present its current status.

4. Acknowledgments & Disclosures

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