FLUORESCENT BLOOD pCO_2 SENSOR WITH NO DIRECT BLOOD–FLUOROPHORE CONTACT: REAL-TIME MONITORING AND COMPARISON WITH A COMMERCIAL DEVICE

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Abstract – Continuous monitoring of blood pCO_2 in extracorporeal circulation (ECC) would significantly support clinical decisions. Unfortunately, this is generally not possible during routine ECC. One of the aspects that limits the possibility of monitoring blood pCO_2 in real-time is biocompatibility. This study investigates the performance of a "prototype" fluorescent pCO_2 sensor (MS2), designed exploiting a blood-compatible gas-permeable membrane to isolate the sensing chemistry from the patient's blood and, the "off-label" use of a commercial optical CO_2 sensor, namely, the MCR-O1P1C1 by PreSens. Unlike the PreSens sensor, which requires direct contact between the sensing element and the blood, the gas-permeable membrane of the MS2 creates a measuring chamber that isolates the sensing chemistry from the patient's blood. During a 6.5-hour test with bovine blood, both sensors demonstrated suitable accuracy, matching the reference hemogas analyzer. While at present the MCR-O1P1C1 sensor provides shorter response times, the MS2 sensor potentially offers superior safety and biocompatibility compared to sensors that require contact between the sensing element and the patient's blood. These results position the MS2 as a promising solution for real-time, in-line blood gas monitoring in ECC procedures.

Keywords: Blood pCO_2, biomedical monitoring, biomedical measurement, optical sensors, extracorporeal circulation (ECC), hemodialysis, extracorporeal membrane oxygenation (ECMO), extracorporeal carbon dioxide removal (ECCO2R), heart-lung machine, severe acute respiratory syndrome (SARS).

1. INTRODUCTION

Continuous and accurate monitoring of critical blood parameters, also known as critical care analytes (CCAs), which include blood electrolytes, metabolites, and blood gasses (O_2 and CO_2), is essential during blood extracorporeal circulation (ECC) procedures to support timely and informed clinical decisions. In this work, we focus on optical sensors designed to measure the partial pressure of carbon dioxide (pCO_2). One of the primary challenges in the development of sensors for use in ECC systems is the need to achieve complete and sustained biocompatibility. Preventing direct exposure of the patient's blood to the sensing element is generally recognized not only to improve the safety and functionality of the device but also its long-term operational stability, reliability, and suitability for continuous clinical use. Systems like the Terumo CDI 550 Blood Parameter Monitoring System, which employs optical fluorescence technology to continuously measure pCO_2—as well as pH, pO_2, K^+, and other critical blood parameters—in-line within the extracorporeal circuit, have been extensively used during cardiopulmonary bypass procedures to support real-time clinical decision-making [1].

In this paper, we investigate and compare the performance of a new disposable sensor prototype hereafter referred to as the MS2 sensor, and an optical commercial measuring system, the MCR-O1P1C1 model from PreSens GmbH, (Germany) equipped with the CO_2 sensor spot SP-CD1 (PreSens GmbH). The reference instrument was a hemogas analyzer, the actual golden standard in clinical contexts.

2. METHODS AND PROCEDURES

The MS2 sensor features a blood-compatible, gas-permeable membrane like those currently used for Extracorporeal Membrane Oxygenation (ECMO) treatments. The use of such a membrane not only ensures patient safety but also guarantees a duration of use of several days in continuous contact with the patient's blood. In the MS2 sensor, such a membrane is used to prevent the passage of blood components, realizing a separation between the blood on one side of the membrane and the chemistry in the measuring chamber created on the other side [2,3]. The measuring chamber is filled with a buffer solution, whose pH is influenced by the pCO_2, and a ratiometric pH-sensitive fluorophore [2,3]. The CO_2 contained in blood diffuses through the gas-permeable membrane, determining the pH in the measuring chamber. The fluorescence of the pH-sensitive fluorophore thus allows continuous and precise optical monitoring of the pCO_2 in blood [2,3]. On the contrary, the PreSens sensor uses a sensing element that must be in direct contact with the measurand throughout the operation. This design, while effective in terms of metrological performances, may introduce significant complications in terms of long-term biocompatibility, including risks associated with potential interactions with blood components that could affect both patient safety and sensor performance over time. In this regard, it is important to note that the MCR-O1P1C1 sensor is not intended for use with human blood and, even less, for monitoring ECC. On the contrary, by preventing direct contact between the sensing element and blood MS2 sensor ensures patient safety by design and offers enhanced stability and long-term accuracy, making it suitable for continuous, real-time blood gas monitoring in clinical settings.

Both sensors were tested over a 6.5-h test using bovine blood maintained at 36.8 °C flowing in simulated ECC at a nominal flow of 1 L/min. As shown in Fig. 1, the main blood circuit was split into two branches to allow simultaneous, interference-free pCO_2 measurements by both the MS2 and PreSens sensors. Blood pCO_2 was varied using an oxygenator with alternating gas inputs (CO_2, N_2, and air). To obtain an estimate, although approximate, of sensors response, blood pCO_2 was subjected to sudden variations, much greater than those that a patient could experience in a real ECC treatment. During the test, readings were taken from both sensors by

setting the sampling frequencies at 0.3 Hz for MS2 and at 0.5 Hz for PreSens. The measurements obtained from both sensors were compared with the measurements obtained by the reference instrument, i.e., the blood gas analyzer (GEM PREMIER 4000, Werfen, Italy) through blood samples taken at the sites "A", "B" and, "C" shown in Fig. 1.

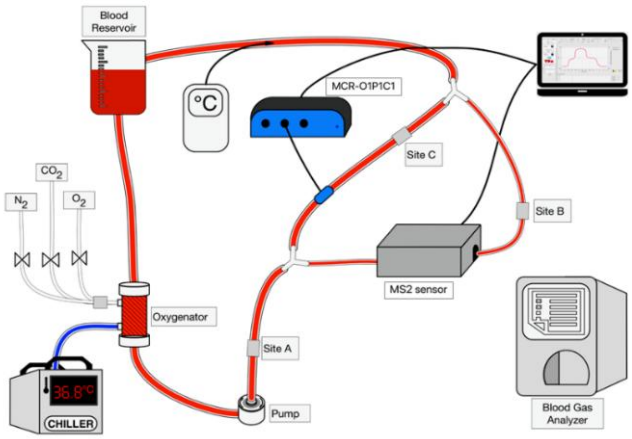

Figure 1: Schematic of the blood circuit employed during the test. The oxygenator and the valves for regulating the N_2, CO_2, and O_2 flows, allowed to change blood pCO_2. The chiller kept the blood temperature at about 36.8 ◦C. The pump allowed to control the blood flow in the circuit. Blood samples were taken from sites A, B, and C and then analyzed by the blood gas analyzer.

3. Results and Discussion

Fig. 2 summarizes the test results. As shown in Fig. 2, while the PreSens sensor can follow the sudden (and unnatural) changes in pCO_2 imposed by the oxygenator, the MS2 sensor prototype suffers longer response and rise times. This is probably since the current MS2 sensor prototype is made up of a limited number of fibers, which results in a reduced exchange surface. Therefore, longer response and rise times. Furthermore, the reduced number of fibers also realizes a significant hydraulic resistance. This meant that the blood flow in the branch that included the MS2 sensor was about 1/10 of the flow in the branch that included the PreSens sensor, introducing an additional delay due to the time required for the blood whose pCO_2 was modified by the oxygenator to reach the sensor.

As shown in Fig. 2, the blood samples analysed using the blood gas analyzer were taken few minutes after the sudden variations in pCO_2 imposed by the oxygenator. Under these conditions, the average root mean square error (RMSE) between the measures provided by the blood gas analyzer and the respective measurements provided by the MS2 sensor was 5.7 mmHg.

Regarding the MCR-O1P1C1 sensor, although PreSens provides each sensor with its own calibration coefficients, it is not designed to be used with blood. The use of such calibration coefficients led the MCR-O1P1C1 sensor to provide estimates that were up to tens of mmHg distant from the measures provided by the blood gas analyzer. Thus, the data shown in Fig. 2 were obtained by performing an adjustment based on the measurements provided by the blood gas analyzer. After this adjustment, the average RMSE between the measurements provided by the blood gas analyzer and the respective measurements provided by the MCR-O1P1C1 sensor was 2.5 mmHg.

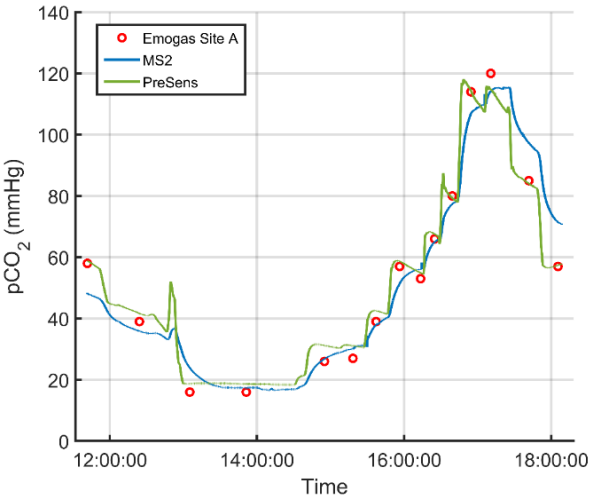

Figure 2: Obtained results. The red dots represent the measures obtained by the blood gas analyzer from the samples taken at "site A". The green and blue lines represent the measures recorded by the PreSens sensor (after adjustment) and the MS2 sensor, respectively.

4. Conclusions

In conclusion, although the limited number of fibers available for the realization of the MS2 sensor prototype limits its performance in terms of response and rise times, the results obtained in this experiment highlight how such a sensor allows obtaining an estimate of the pCO_2 in the blood in extracorporeal circulation. All this, using a blood-compatible gas-permeable membrane that, preventing any contact between the patient's blood and the sensing elements, guarantees patient safety and offers the long-term operational compatibility that these ECMO membranes have already widely demonstrated in the field. Therefore, the results obtained suggest that the MS2 sensor could be well-suited for integration into clinical workflows, with the potential to improve patient safety and reduce monitoring costs during ECC.

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References

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