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Abstract

Measuring Exhaled Propofol in an Ex Vivo Lung Model with Low-Cost Metal Oxide Gas Sensors †

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† Presented at the XXXV EUROSENSORS Conference, Lecce, Italy, 10–13 September 2023.

Abstract: Herein, commercially available MOS gas sensors running in temperature cycling operations are studied for the online monitoring of propofol in an ex vivo ventilation and perfusion lung model. A porcine lung was connected to a heart–lung machine and propofol was added into the blood reservoir. The MOS sensor was able to quantitatively detect exhaled propofol in the very low ppb range. The results are in accordance with those obtained by a propofol-sensitive ion mobility spectrometer.

Keywords: MOS sensors; ex vivo; propofol detection; ion mobility spectrometer; TCO

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Citation: Bur, C.; Karst, K.; Schütze, A.; Maurer, F.; Radermacher, S.; Hoffmann, K.; Kreuer, S. Measuring Exhaled Propofol in an Ex Vivo Lung Model with Low-Cost Metal Oxide Gas Sensors. *Proceedings* **2024**, *97*, 108. https://doi.org/10.3390/proceedings2024097108

Academic Editors: Pietro Siciliano and Luca Francioso

Published: 27 March 2024

1. Introduction

The non-invasive detection of drugs in exhaled air is of great therapeutic relevance in the pursuit of precise and individual dosing. For intravenous anesthetic propofol, a reasonable correlation between plasma and the exhaled concentration measured by ion mobility spectrometry (on a minute-by-minute basis) has been reported [1]. Metal oxide semiconductor (MOS) gas sensors are promising candidates for low-cost online measurements, especially when using temperature-cycling operations, as they have sensitivity as good as analytical systems [2]. In a previous work, the sensitivity of commercially available MOS sensors to propofol under lab conditions has been shown [3]. In this work, these sensors are studied in an ex vivo lung model for the detection of propofol in exhaled air.

2. Materials and Methods

In order to avoid animal testing, an ex vivo ventilation and perfusion lung model (VPM) was applied. Heart, lungs, and blood from a slaughtered pig were used in a heart–lung machine with a blood flow of 300 mL/min combined with an oxygenator. The ventilation rate was set to 14/min, and we used a tidal volume of 700 mL, a basic pressure of 8 mbar, and a 35 mbar peak. Propofol (12 mg) was injected every 30 min into a reservoir with 1.2 L blood. Figure 1 shows the experimental setup.

The exhaled air was analyzed by commercially available metal oxide semiconductor gas sensors, i.e., ZMOD4510 (Renesas, Dresden, Germany) in the bypass of the expiratory path. The MOS sensor was run in a temperature-cycled operation (TCO) with a sampling period of 25 ms. The temperature cycle consists of three high-temperature (450 °C) and three low-temperature phases (250 °C, 275 °C, and 300 °C). The total length of the temperature cycle was 1.125 s. The sensors were calibrated in the lab with different propofol concentrations in pseudo-random order and a simulated breath atmosphere. A partial least

square regression (PLSR) model was calculated based on the calibration data as well as data sampled from the VPM without propofol. The root meat squared error (RMSE) of a group-based leave-one-out cross-validation (LOOCV) was 0.8 ppb when using 4 PLSR components in the range of 0–9.8 ppb. As a reference, a propofol-sensitive ion mobility spectrometer (P-IMS), which has successfully been used and validated in previous studies [1], was used as a monitor parallel to the MOS sensors.

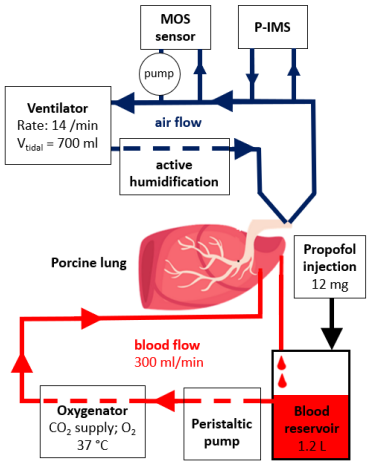

Figure 1. Schematic of the experimental setup.

3. Discussion

Porcine lung, heart, and blood were transported from the slaughterhouse to the laboratory and were immediately connected to the heart lung machine and ventilator. Figure 2 shows the peak intensity of the P-IMS in the lower panel, the MOS sensor response at 450 °C at the top, and the model estimate in the middle. The ventilation started at 22:00 (green line) and the first propofol injection (red line) into the blood reservoir took place at 22:15. The P-IMS detected propofol for the first time around 22:45. The response of the ZMOD4510 at 250 °C showed a small reaction at 22:35. Further propofol injections (red lines) only led to a small increase in the propofol intensity due to severe adsorption effects on the plastic parts of the system (the blood reservoir, oxygenator, etc.). The prominent peak observed at 23:07 in both detector signals is due to the removal of some blood/foam from the tubing system causing the ventilation to stop (black line). The system was open for approximately 4 min while the perfusion with blood continued. The experiment was stopped at 1:10.

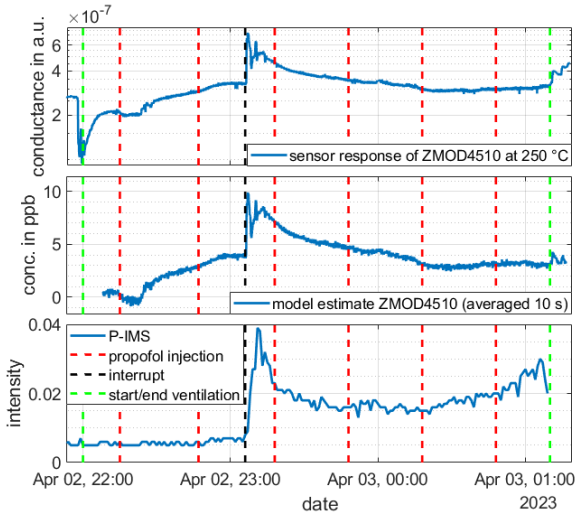

Figure 2. Sensor response of the ZMOD4510 (**top**), model estimate (**middle**), and P-IMS (**bottom**).

The model estimate allows for reliable propofol quantification, with a response comparable to the reference instrument (P-IMS).

In summary, MOS sensors are promising candidates for online drug monitoring in exhaled air, as demonstrated in an ex vivo lung model for propofol. Further validation experiments are planned.

Author Contributions: Conceptualization, C.B., S.R., K.H., F.M. and S.K.; methodology, C.B., F.M. and S.K.; software, K.K. and C.B.; validation, K.K., F.M. and S.R.; formal analysis, K.K.; investigation, K.K., S.R. and K.H.; resources, S.K.; data curation, K.K. and F.M.; writing—original draft preparation, C.B. and K.K.; writing—review and editing, A.S.; visualization, K.K.; supervision, C.B. and S.K.; project administration, S.R.; funding acquisition, S.K. All authors have read and agreed to the published version of the manuscript.

Funding: The project was funded by a research grant from the government of Saarland (Ministry of Finance and for Science, Saarbrücken, Saarland, Germany).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data available on request.

Conflicts of Interest: The authors declare no conflicts of interest.

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