Sabine Krueger-Ziolek*, András Lovas, Fatime Hawchar, Bernhard Laufer and Knut Moeller for the Digital Clones in Personalized Medicine (DCPM) study team

EIT based intrathoracic pulsatile impedance measurements during apnea: a case study

Abstract: Intrathoracic ventilation related and pulsatile (perfusion) impedance changes can be measured by the non-invasive and radiation-free imaging method Electrical Impedance Tomography (EIT). Ventilation monitoring is still the key research area in EIT, whereby perfusion monitoring gain more and more in interest. However, there are still many unknown influencing factors concerning pulsatile impedance measurements which have to be investigated. Hence, in this observational case study the impact of prolonged apnea periods on pulsatile impedance changes was examined in a patient with suspected brain death undergoing several apnea tests. In addition, the correlation between changes in pulsatile impedance and certain blood gas parameters (carbon dioxide partial pressure, pCO_2; oxygen partial pressure, pO_2; pH; bicarbonate, HCO_3^-) were explored. Results show that the pulsatile impedance signal changes over time during apnea. An increase in the area under the curve (Mean AuC) and the maximum amplitude (Mean Max) of heart beat associated impedance signals was observed (Mean AuC: up to 65 %; Mean Max: up to 57 %). Furthermore, a positive correlation between the increase in impedance and pCO_2 and HCO_3^- was assessed (both: up to 0.99), whereas pO_2 and pH show a negative correlation (both: up to -0.99). These preliminary results indicate that pulsatile EIT monitoring may be applied to get additional information regarding cardio-pulmonary interactions sustaining diagnosis or treatment of lung diseases.

***Corresponding author: Sabine Krueger-Ziolek:** Institute of Technical Medicine, Furtwangen University, Jakob-Kienzle-Straße 17, Villingen-Schwenningen, Germany, krue@hs-furtwangen.de
András Lovas, Fatime Hawchar: Department of Anaesthesiology and Intensive Therapy, University of Szeged, Szeged, Hungary
Bernhard Laufer, Knut Moeller: [4]Institute of Technical Medicine, Furtwangen University, Villingen-Schwenningen, Germany
DCPM study team: Balázs Benyó[1], Geoff Chase[2], Thomas Desaive[3], Knut Moeller[4]
[1]Department of Control Engineering and Information, Budapest University of Technology and Economics, Budapest, Hungary.
[2]Centre for Bioengineering, University of Canterbury, Christchurch, New Zealand.
[3]GIGA Cardiovascular Science, University of Liege, Liege, Belgium.

Keywords: Electrical impedance tomography, pulsatile impedance changes, apnea, blood gas analysis

https://doi.org/10.1515/cdbme-2020-3014

1 Introduction

Respiratory failure is the third most common cause of death worldwide clarifying the necessity of innovative methods of lung function monitoring. Electrical impedance tomography (EIT), a still relatively unknown imaging technique, which is characterized by non-invasiveness, no radiation exposure, bedside application and a high temporal resolution (up to 50 Hz), depicts such a novel lung function monitoring tool [1].

In EIT, intrathoracic impedance changes, resulting from air and blood volume variations, can be determined by circumferentially attaching surface electrodes on the thorax, applying small alternating currents and measuring differences in surface potentials. These potential differences are used to reconstruct impedance images which can be employed to assess ventilation and perfusion distribution [2].

The main research area of EIT is ventilation monitoring during mechanical ventilation. However, since EIT is capable of measuring ventilation based as well as cardiovascular related (pulsatile) impedance changes, perfusion monitoring comes more and more into research focus. Several previous studies introduced different ways of measuring and separating ventilation associated and pulsatile impedance signals, for instance by injecting saline solution, applying frequency filtering or principal component analysis [3]. Despite all this, the easiest way to measure pulsatile impedance changes is holding the breath, which is of course not always feasible depending on the clinical situation (e.g. artificial respiration or spontaneous breathing).

In a previous study, we assessed changes in the pulsatile impedance signal depending on lung volume during breath holding (approx. 10 seconds) in a spontaneously breathing subject [4]. It was indicated that shape and amplitude of the pulsatile impedance signal varied based on changes in lung volume. However, there are still a lot of unknown influencing

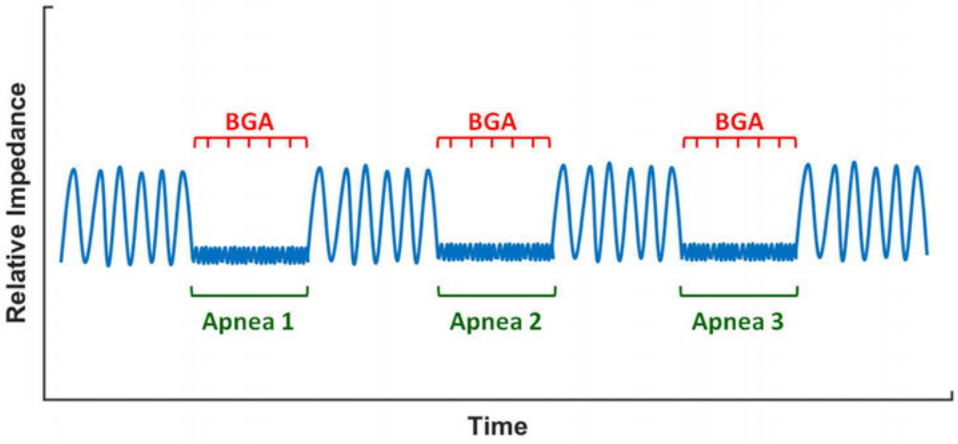

Figure 1: Schematic illustration of the measurement procedure. Ventilation related and pulsatile impedance changes within the observational period (blue). Apnea test 1 to 3 (green) and concurrent blood gas analyses (BGA, red).

factors which need to be explored. Thus, in this present case study, we evaluate changes in the pulsatile impedance signal in dependency on the duration of apnea and on variations in blood gas parameters in a mechanically ventilated patient with suspected brain death undergoing several apnea tests.

2 Methods

2.1 Study protocol and data collection

A female patient (51 years, 60 kg, 157 cm) with suspected brain death was observed over a period of 12 hours from one and at the final apnea test from three independent doctors at the university hospital of Szeged (Hungary) to determine a potential brain death. The patient suffered a subarachnoid haemorrhage, which is assigned to primary brain damages. All three doctors exhibited the required licence to do this examination and followed the standard procedure, which is strictly prescribed by the Hungarian law [5]. This standard procedure contains various required examinations, such as an apnea test, which has to be repeated every 4 hours during the observation period.

During these apnea tests, the patient was disconnected from the ventilator (after approx. 10 minutes of 1.0 FiO_2 preoxygenation, pCO_2 of 38-42 mmHg) and the doctors were looking for any respiratory movement as well as taking regularly arterial blood samples for blood gas analyses (every 2 to 3 minutes) until the patient reached a pCO_2 level of 60 mmHg. According to the Hungarian law, the patient must be oxygenated during this time span, which was done by administering 6 L/min O_2 into the endotracheal tube via a cannula.

EIT measurements were conducted simultaneously at the 5^{th} intercostal space (8.4 mA, 93 kHz) with a frame rate of 50 Hz to measure intrathoracic pulsatile impedance changes (PulmoVista®500, Dräger Lübeck, Germany). Figure 1 shows a schematic illustration of the measurement procedure.

2.2 EIT Data processing

The acquired EIT data were reconstructed into images of intrathoracic impedance changes (32 × 32 pixels) applying the manufacturer's software (EIT Analysis Tool 6.3, Dräger, Germany) which employs a FEM-based linearized Newton-Raphson algorithm. Further calculations were conducted with MATLAB (R2017a, The Mathworks® Inc., Natick, USA).

To preclude image artefacts and impedance changes based on other tissue than lung tissue as well as the ventricular region, a region of interest (ROI) was defined by using a linear regression fit [6]. Hence, linear regression was applied between the signal of each pixel (regional signal) and the signal of the sum of all pixels (global signal). Afterwards, a functional EIT (fEIT) image was generated in which each pixel represents the slope of the individual linear regression fit. Pixels values of the fEIT image higher than 15 % of the maximum value of the fEIT image were included in the ROI.

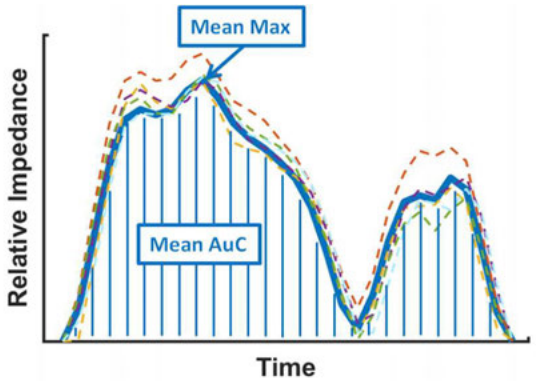

Figure 2: Schematic presentation of a mean impedance signal segment corresponding to one heart beat during apnea (blue). Exemplarily, five individual impedance signal segments are shown (colored dashed lines).

2.3 EIT and blood gas analysis

2.3.1 EIT data analysis

The intrathoracic pulsatile EIT signal measured during an apnea test was divided into signal sections of 2 to 3 minutes depending on the time points of the arterial blood sampling (Figure 1). Additionally, each EIT signal section was separated into smaller signal segments corresponding to one heart beat (Figure 2).

A linear trend between the start and end point of each signal segment was removed as well as an interpolation of each signal segment to the mean length of all signal segments was conducted (refer to [4]). Subsequently, for each 2 to 3 minutes section, the mean signal of all signal segments was calculated (Figure 2). The area under the curve and the maximum of the mean signal (Mean AuC and Mean Max) were calculated for each interval, respectively.

2.3.2 Blood gas analysis

During an apnea test, arterial blood samples were taken every 2 to 3 minutes to e.g. observe the carbon dioxide partial pressure (pCO_2) concentration (refer to 2.1). However, several other blood components were determined such as pH, oxygen partial pressure (pO_2) or minerals like sodium (Na^+). In this observational study the following analysis was restricted to pH, pCO_2, pO_2 and bicarbonate (HCO_3^-).

Since the mean EIT signal between two time points of subsequent blood samplings was studied, the average of pH, pCO_2, pO_2 and HCO_3^- of the corresponding two time points were calculated. Additionally, the correlation between the EIT based parameters (Mean AuC and Mean Max) and the averaged blood gas parameters was examined.

3 Results

Figure 3 presents the Mean AuC and Mean Max values as well as the corresponding averaged pH, pCO_2, pO_2 and HCO_3^- values of all predefined time sections within the three apnea periods. An increase of Mean AuC, Mean Max and pCO_2 could be observed within all three apnea phases (Mean AuC: up to 65 %; Mean Max: up to 57 %; pCO_2: up to 24 %). On the other hand, a decrease over the course of all apnea periods could be seen for pO_2 and pH (pO_2: up to 9 %; pH: up to 0.9 %). The averaged HCO_3^- values were inconsistent within the three different apnea periods. During apnea phases 2 and 3 HCO_3^- values showed a slightly ascending trend (HCO_3^-: up to 6 %), whereas within apnea period 1 HCO_3^- values remained almost constant.

Table 1 shows the accompanying correlation coefficients of the EIT based parameters (Mean AuC and Mean Max) and the corresponding average blood gas values (pH, pCO_2, pO_2 and HCO_3^-).

Table 1: Correlation coefficients of EIT (Mean AuC, Mean Max) and blood gas (pH, pCO_2, pO_2, BE, HCO_3^-) parameters for all three apnea periods.

		Mean AuC	Mean Max
Apnea 1	**pH**	-0.9183	-0.9209
	pCO_2	0.8884	0.8912
	pO_2	---	---
	HCO_3^-	-0.1037	-0.1007
Apnea 2	**pH**	-0.7582	-0.9775
	pCO_2	0.7601	0.9743
	pO_2	-0.8426	-0.9833
	HCO_3^-	0.7991	0.9651
Apnea 3	**pH**	-0.9905	-0.9893
	pCO_2	0.9916	0.9900
	pO_2	-0.9971	-0.9983
	HCO_3^-	0.9939	0.9915

4 Discussion

Results of this observational case study demonstrate that the EIT based parameters Mean AuC and Mean Max show a positive or negative correlation with certain blood gas parameters. During the apnea phases a clear increase in the area under the curve (Mean AuC) and the amplitude of the pulsatile impedance signal (Mean Max) was observed, which was accompanied with a decline in pO_2 and pH as well as with a rise in pCO_2.

Since the patient was disconnected from the ventilator for several minutes and no gas exchange was taking place, O_2 was used up and CO_2 was enriched within the body, which on the other hand could result in respiratory acidosis (pH<7.35).

Furthermore, no gas exchange might have provoked to less blood volume within the lung tissue which might have led to a decrease in conductivity, and thus to an increase in impedance (implied by higher Mean AuC and Mean Max).

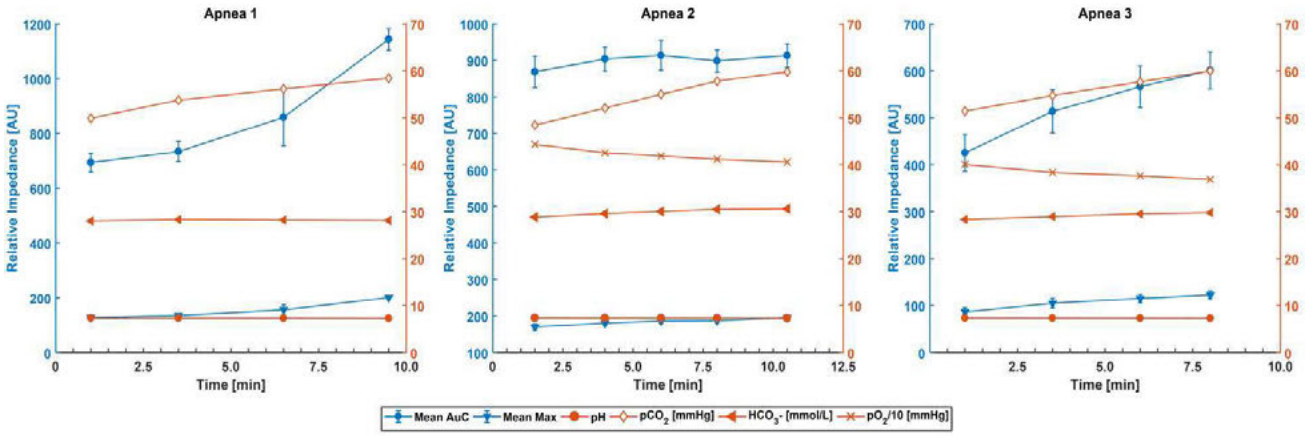

Figure 3: EIT based measures (blue) and blood gas parameters (red) of the predefine time sections of all three apnea periods.

HCO_3^- showed an inconsistent behaviour during the three apnea tests. No removal of CO_2 during apnea leads to an accumulation of bicarbonate within the body, which corroborates with the slightly increase in HCO3- in apnea period 2 and 3. During apnea period 1 HCO_3^- remained almost the same which might be based on the flatter increase of pCO_2 in comparison to apnea phase 2 and 3.

However, these first results indicate that the pulsatile EIT signal might change in amplitude and shape over time during apnea. Furthermore, results suggest that changes in the pulsatile EIT signal correlate with certain blood gas parameters, such as pO_2 or pCO_2, which might provide additional information in EIT lung monitoring.

Nevertheless, this observational case study represents only one patient. To confirm these observations, additional studies including more patients need to be undertaking. In addition, other influencing factors of pulsatile EIT monitoring, such as changes in cardiac activity (e.g. changes in heart beat volume), have to be considered and investigated.

5 Conclusion

This observational case study shows that the pulsatile EIT signal changes in height during a longer period of apnea. Furthermore, it was observed that EIT pulsatile changes correlate with blood gas parameters pCO_2, pO_2, pH and HCO_3^-. Hence, pulsatile EIT monitoring might be used to gain further information concerning cardio-pulmonary interactions supporting the diagnosis or treatment of lung diseases.

Acknowledgement

This work was partially supported by the German Federal Ministry of Education and Research (MOVE, Grant 13FH628IX6) and has received funding from EU H2020 R&I programme (MSCA-RISE-2019 call) under grant agreement #872488 — DCPM.

Author Statement

Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study. Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

References

[1] Gong B, Krueger-Ziolek S, Moeller K, Schullcke B, Zhao Z. Electrical impedance tomography: functional lung imaging on its way to clinical practice? Expert Rev Respir Med 2015; 9 (6): 721-37.

[2] Bodenstein M, David M, Markstaller K. Principles of electrical impedance tomography and its clinical application. Crit Care Med 2009; 37 (2): 713-24.

[3] Nguyen DT, Jin C, Thiagalingam A, McEwan AL. A review on electrical impedance tomography for pulmonary perfusion imaging. Physiol Meas 2012; 33 (5): 695-706.

[4] Krueger-Ziolek S, Gong B, Laufer B, Moeller K. Impact of lung volume changes on perfusion estimates derived by Electrical Impedance Tomography. Current Directions in Biomedical Engineering 2019; 5 (1): 199-202.

[5] 1. melléklet a 12/2012. (VIII. 6.) EMMI rendelethez. Magyar Közlöny 2012;(105): 17688-89.

[6] Frerichs I, Pulletz S, Elke G, Reifferscheid F, Schadler D, Scholz J, Weiler N. Assessment of changes in distribution of lung perfusion by electrical impedance tomography. Respiration 2009; 77 (3): 282-91.