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Patterns of pulsatile impedance change during the apnea test detected by electrical impedance tomography

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Abstract: The apnea test (AT) is a critical procedure in determining brain death. It temporarily disconnects the patient from the ventilator for 7 to 10 minutes. This study explores pulsatile Electrical Impedance Tomography (EIT) during AT in 10 patients suspected of brain death to discern physiological changes. Analysis revealed three distinct patterns of pulsatile EIT signal changes: increasing; fluctuating; and decreasing. These findings show the potential of pulsatile EIT monitoring to provide novel insight into cardio-pulmonary dynamics during AT.

Keywords: Apnea test; brain death; electrical impedance tomography; intrathoracic pulsatile signal

1 Introduction

The apnea test (AT) is a crucial and standard procedure in medical determination of brain death [1]. Its underlying principle lies in the induction of hypercapnia, which stimulates the medullary respiratory center. However, protocols for conducting AT vary between countries. In Hungary, national regulations stipulate an elevation of the partial pressure of carbon dioxide ($PaCO_2$) levels exceeding 60 mmHg or in case of pre-existing chronic hypercarbia, surpassing a baseline by more than 20 mmHg. This protocol mandates restoration of a $PaCO_2$ level between 38-42 mmHg and a preoxygenation period of 10 minutes with an inspired oxygen fraction (FiO_2) of 100%. Subsequently, the patient is disconnected from the ventilator. Oxygen supplementation is provided at a rate of 6 L/minute through a cannula inserted into the endotracheal tube. The duration of an AT is 7 to 10 minutes. Monitoring $PaCO_2$ levels is via arterial blood gas (ABG) to ensure development of hypercapnia. The absence of spontaneous respiration during AT is a crucial determinant in the diagnosis of brain death.

Electrical Impedance Tomography (EIT) is a promising monitoring tool for lung function, notable for its low cost, bedside operability, and temporal resolution reaching up to 50 Hz. It is an optimal approach for real-time lung monitoring, particularly in critical care settings. EIT operates by mapping intrathoracic impedance fluctuations caused by changes in air and blood volume, by placing surface electrodes around the thorax, injecting minor alternating currents, and recording the induced surface potential variations. Measurements are then reconstructed into impedance images of the distribution of ventilation and perfusion within the lungs [2].

EIT has been primarily applied in the context of ventilation monitoring, particularly beneficial during mechanical ventilation to optimize patient care. Nevertheless, the technique's capability extends to quantifying both ventilation-associated and cardiovascular-induced (pulsatile) impedance changes, broadening its applicability to perfusion monitoring. Despite advancements in methodologies, such as saline solution injection, frequency filtering, and principal component analysis, the most straightforward approach to ascertain pulsatile impedance changes is through an introduced apnea phase, which remains impractical in many clinical scenarios.

Previously, we examined temporal variations in pulsatile impedance signals during AT in a single patient suspected of brain death [3]. Findings indicated the potential application of EIT monitoring as a supplementary diagnostic tool during AT to provide more details of the patients. Consequently, 9 more patients suspected of brain death were recruited, and the identical protocol was implemented during the AT.

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2 Methods

2.1 Study protocol and data collection

This study was approved by the Human Investigation Review Board of the University of Szeged with approval number 87/2020-SZTE. The trial was pre-registered on ClinicalTrials.gov under NCT04857242. A cohort of 10 patients (4 females, 6 males; mean age 46.4±9.7 years) with suspected brain death were enrolled. The AT were administered under the supervision of an independent physician at the University Hospital of Szeged, Hungary, in accordance with the established protocol for determining brain death. The physician possessed the requisite licensure mandated by Hungarian law for conducting such evaluations, adhering strictly to the standardized procedures outlined therein. The AT may be repeated at intervals of every 4 hours throughout the observation period.

During the AT, patients were disconnected from ventilator following 10 minutes of preoxygenation with FiO_2 of 100% and achieving a target $PaCO_2$ of 38-42 mmHg. The supervising physician monitored for any signs of spontaneous respiratory movement, while obtaining arterial blood samples for ABG analysis at regular intervals of every 2 to 3 minutes until the patient attained a $PaCO_2$ level of 60 mmHg. Under Hungarian regulations, oxygen supplementation was provided throughout AT, facilitated by administering oxygen at a rate of 6 *L*/min via a cannula inserted into the endotracheal tube.

Simultaneously, EIT measurements were performed at the 5th intercostal space following a standardized protocol, using a PulmoVista 500 (Dräger AG, Lübeck, Germany) with a frame rate of 50 Hz. Fig. 1 depicts an example of EIT measurement and corresponding AT procedure.

2.2 EIT data processing

EIT measurements were reconstructed into EIT images depicting intrathoracic impedance variations at a resolution of 32 × 32 pixels using the proprietary software provided (EIT Analysis Tool 6.3, Dräger AG, Lübeck, Germany). The software utilizes a finite element method (FEM)-based linearized Newton-Raphson algorithm to reconstruct these images. Further data processing and analysis were performed using MATLAB R2023b (The MathWorks, Natick, MA, USA).

To exclude the potential influence of image artifacts and impedance changes arising from non-lung tissue and ventricular regions, a region of interest (ROI) was defined through linear regression analysis [3].

The intrathoracic pulsatile EIT signals acquired each AT period (T_a in Fig. 1) were segmented into 2 to 3-minute intervals, aligning with ABG sampling. However, some intervals exceeded 4 minutes between ABG measurements. Despite this variability, EIT signals were consistently partitioned into 2-minute intervals for analysis, with ABG parameters marked as 'N/A' (not applicable), where an interval has no ABG value.

Each EIT signal section was subdivided into smaller segments corresponding to individual heartbeats (t_a in Fig. 1). A linear trend between the start and end points of each segment was removed, and interpolation was performed to adjust each segment to the mean length of all segments within a signal section [4]. Subsequently, the averaged impedance signal across all segments within each signal section was computed, as illustrated in Fig. 2. The area under the curve (Mean AuC) and the maximum value of the averaged impedance signal (Mean Max) were determined for each signal section, respectively. Considering the intervals between subsequent ABG, the average values of $PaCO_2$ and PaO_2 at the corresponding time points were calculated for analysis.

3 Results and Discussion

Figure 3 displays the Mean AuC and Mean Max values alongside the averaged values of $PaCO_2$ and PaO_2 values for the corresponding intervals within individual apnea periods. Notably, only three ATs from Patient 1, Patient 2, and Patient 5 are depicted to exemplify distinct trends observed in Mean AuC and Mean Max relative to the duration of the AT, as identified in our study: increasing trend (Patient 0, Patient 1, Patient 4), fluctuating trend (Patient 2, Patient 8, Patient 9), and decreasing trend (Patient 3, Patient 5, Patient 6, Patient 7). A comprehensive summary of results is in Tab. 1.

In Tab. 1, numerical values are presented in black to denote baseline conditions for the respective ATs. Values displayed in green signify an increase compared to the baseline, while those in red indicate a decrease. The designation "N/A" is employed to denote instances where results are unavailable, such as when ABG data is not obtained or when Mean AuC and Mean Max calculations cannot be performed.

Physiologically, Mean AuC is correlated with global stroke volume, representing the volume of blood ejected from the right and the left ventricle during systolic contraction. MeanMax value shows the largest changes, which could be correlated with contractility. During the AT, as patients are disconnected from the ventilator, the rise in $PaCO_2$ levels prompts physiological responses, including increased heart rate and vasodilation, potentially augmenting stroke volume. Consequently, a decrease in Mean AuC, reflecting a reduction in impedance, is expected in EIT measurements, as observed in 40% of recruited patients. However, AT procedure

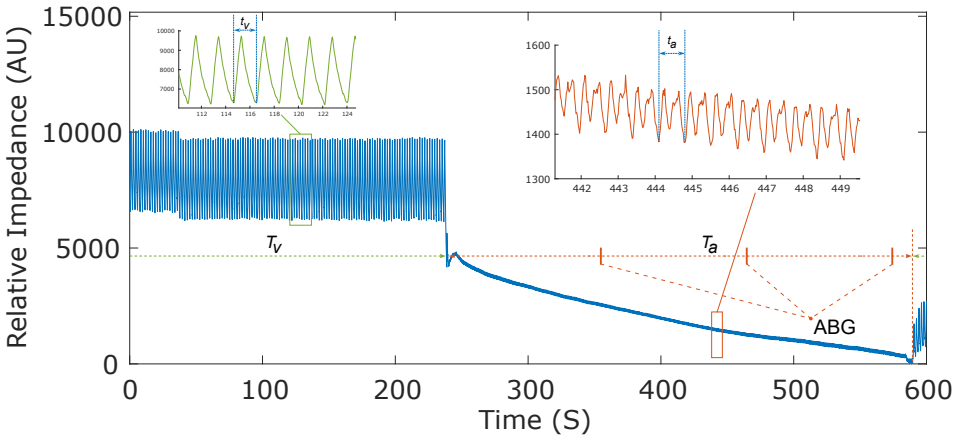

Fig. 1: EIT waveforms and the corresponding AT procedure. The green plot illustrates a brief period of mechanical ventilation support, while the orange plot depicts a brief period of the AT. ABG analysis is performed every 2 or 3 minutes during the AT.

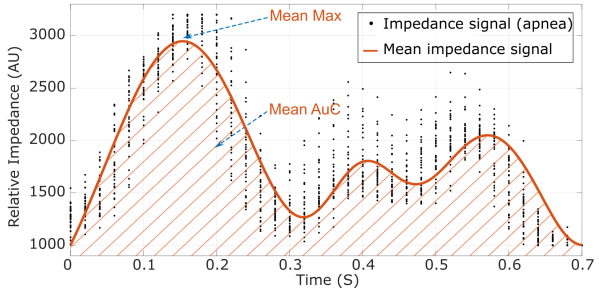

Fig. 2: The averaged impedance signal across all segments within each signal section. The black dots denote the relative impedance variation within a single signal section.

inherently imposes physiological stress and risks [5], leading to potential complications, e.g., hypoxemia and related hypoxemic pulmonary vasoconstriction, consecutive increase in pulmonary vascular resistance, and hypotension, which could introduce confounding influences on EIT measurements. These factors may account for the varying trends observed.

Furthermore, the intervals between consecutive ATs often exceed 4 hours, during which the EIT belt is removed, and the device is disconnected, introducing additional uncertainty into EIT measurements. Despite these challenges, this study shows the potential of EIT to be used as a monitoring tool during the AT. To validate these findings, future studies should explore additional factors influencing pulsatile EIT monitoring, such as alterations in stroke volume.

4 Conclusion

This follow-up study reveals three distinct patterns of pulsatile EIT signal changes observed during the AT. This shows the potential of EIT monitoring of pulsatile signals in providing additional insights into cardio-pulmonary interactions and supporting the assessment of physiological changes during AT.

Author Statement

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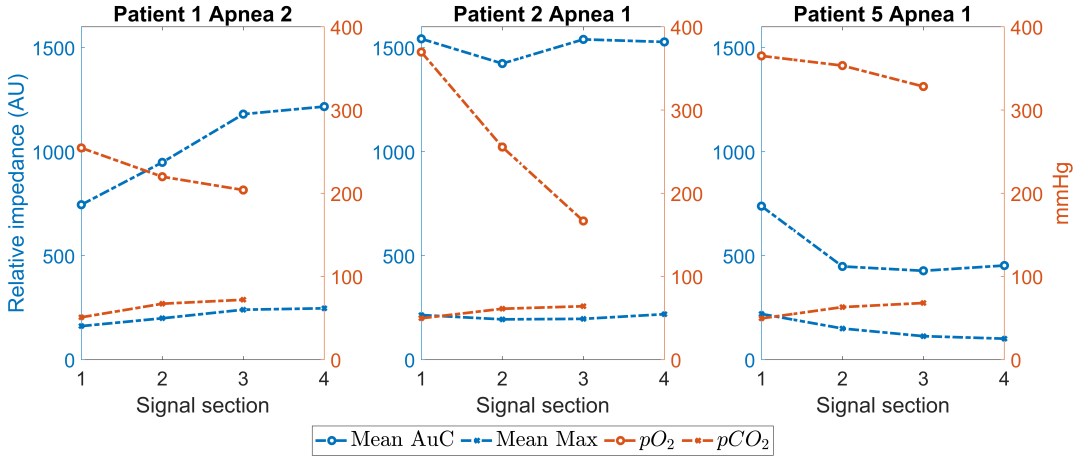

Fig. 3: Mean AuC and Mean Max values, accompanied by the averaged $PaCO_2$ and PaO_2 values, depicted across all predefined time sections within individual apnea periods for Patient 1, Patient 2, and Patient 5.

Tab. 1: Summary of AT results of 10 subjects, including Mean AuC and Mean Max values, alongside corresponding changes in $PaCO_2$ and PaO_2 levels. Baseline conditions are indicated in black, while increases and decreases relative to baseline are denoted in green and red, respectively. "N/A" denotes instances where data are unavailable or calculations cannot be performed.

Patient No.	Signal Section	Apnea 1				Apnea 2				Apnea 3			
		PCO_2	PO_2	MeanAuC	MeanMax	PCO_2	PO_2	MeanAuC	MeanMax	PCO_2	PO_2	MeanAuC	MeanMax
Patient 0	1	41.20	N/A	693.41	128.33	40.10	127.70	868.80	170.22	41.20	413.10	425.36	86.18
	2	+6.80	N/A	+40.48	+6.57	+6.10	+328.70	+34.91	+10.24	+8.80	+4.20	+88.24	+18.96
	3	+10.60	N/A	+165.46	+27.28	+10.60	+302.80	+44.86	+16.73	+11.60	-28.90	+140.72	+29.16
	4	+14.50	N/A	+450.21	+72.57	+13.30	+292.80	+29.76	+17.40	+15.50	-29.90	+175.68	+36.72
	5	+15.40	N/A	N/A	N/A	+16.50	+289.20	+44.59	+25.35				
	6					+18.90	+278.40	N/A	N/A				
Patient 1	1	42.20	306.00	1565.30	214.38	39.40	273.10	744.91	161.39				
	2	+21.50	-82.40	+210.50	+27.13	+23.10	-37.20	+203.74	+37.57				
	3	+29.90	-119.00	+216.20	+35.88	+32.60	-69.20	+435.49	+78.87				
	4					N/A	N/A	+471.89	+85.48				
Patient 2	1	41.30	395.00	1542.50	214.53								
	2	+16.90	-50.60	-118.80	-20.70								
	3	+22.90	-228.30	-2.70	-18.31								
	4	N/A	N/A	-14.90	+4.06								
Patient 3	1	41.10	584.20	1074.00	208.04	39.40	92.20	771.00	170.89	41.60	110.70	1009.90	193.56
	2	+12.30	-68.30	-120.77	-8.08	+13.40	+325.50	-95.00	-12.84	+17.90	+354.40	-354.31	-25.46
	3	+18.00	-76.00	-183.93	-8.37	+19.30	+334.10	-74.58	-9.04	+22.70	+331.60	-456.85	-17.52
	4	+22.70	-64.20	-279.24	-11.75	+22.10	+327.20	-94.32	-19.92	+27.50	+309.30	-376.89	-28.33
Patient 4	1	36.20	437.40	573.78	155.01	39.80	359.80	511.62	166.34	36.20	217.00	554.92	162.67
	2	+16.40	-59.70	+36.05	+3.27	+18.10	-13.90	-39.62	+0.65	+14.70	-12.10	+42.56	+4.16
	3	+24.20	-86.00	+75.74	+4.08	+23.20	-13.30	-32.90	+0.92	+25.10	+27.80	+75.32	+7.58
	4	+25.40	-75.00	+67.03	+6.68	N/A	N/A	-45.38	+3.06	N/A	N/A	+124.49	+11.09
	5	+30.90	-59.20	+77.61	+5.61								
Patient 5	1	40.90	351.60	738.08	219.84	40.80	210.40	219.51	78.63	38.90	140.60	550.44	156.02
	2	+17.40	+27.00	-289.89	-69.98	+11.60	+42.50	-3.01	+4.67	+13.90	+165.20	+39.58	+4.07
	3	+27.20	-23.30	-310.76	-106.84	+18.30	+11.00	+4.56	+11.52	+20.70	+173.80	+36.59	+7.19
	4	N/A	N/A	-285.41	-118.81	+22.90	-8.20	+30.94	+20.75	+26.30	+191.30	-35.76	-2.18
	5									N/A	N/A	-38.63	-3.12
Patient 6	1	42.00	606.00	2451.60	402.34	41.60	524.10	2509.00	457.32				
	2	+10.30	-27.00	-466.50	-25.33	+8.20	-49.60	-187.50	-27.71				
	3	+16.70	-46.10	-711.10	-61.56	+13.40	-28.90	-437.20	-36.21				
	4	+23.00	-58.50	-884.40	-82.11	+17.30	-58.20	-590.30	-51.15				
	5					+21.60	-38.50	-713.90	-73.59				
	6					N/A	N/A	-822.40	-100.54				
	7					N/A	N/A	-893.70	-117.19				
Patient 7	1	40.20	156.60	1720.40	244.24	40.80	165.50	1085.70	239.80				
	2	+15.50	+97.40	+15.60	-6.25	+14.40	+44.30	-297.12	-58.61				
	3	+21.90	+106.30	+13.50	-24.77	+20.50	+19.20	-372.97	-36.25				
	4	N/A	N/A	-36.30	-39.34	+23.50	+1.70	-398.16	-46.91				
Patient 8	1	36.10	148.80	839.00	129.23	39.60	77.40	1081.10	197.48	N/A	N/A	901.22	189.38
	2	N/A	N/A	+31.22	-16.36	N/A	N/A	-112.01	-38.97	N/A	N/A	+167.08	-10.91
	3	N/A	N/A	+182.10	+2.24	+17.50	+15.90	-196.63	-46.64	N/A	N/A	+63.57	-40.01
	4	+21.90	-44.60	+319.90	-0.79					+54.70	+67.10	+247.68	-7.09
	5									+12.80	+73.50	+281.38	-3.95
Patient 9	1	39.10	497.70	806.19	186.45								
	2	N/A	N/A	-102.36	-13.67								
	3	+18.80	-161.80	-131.79	-20.57								
	4	+24.80	-188.00	-101.45	-16.36								
	5	+29.20	-204.70	-101.00	-4.49								
	6	+35.50	-202.70	-51.72	+10.29								