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Bioimpedance technology for detection of thoracic injury

Ruben Buendia[1,2,3,4], **Stefan Candefjord**[1,2,3], **Benjamin Sanchez**[5], **Hans Granhed**[6], **Bengt-Arne Sjöqvist**[1,2,3], **Per Örtenwall**[6] **and Eva-Corina Caragounis**[6]

[1] Department of Electrical Engineering, Chalmers University of Technology, Gothenburg, Sweden
[2] MedTech West, Sahlgrenska University Hospital, Gothenburg, Sweden
[3] SAFER Vehicle and Traffic Safety Centre at Chalmers, Gothenburg, Sweden
[4] Department of Information Technology, University of Borås, Borås, Sweden
[5] Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, United States of America
[6] Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

E-mail: Ruben.Buendia@gmail.com

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Abstract

Objective: Thoracic trauma is one of the most common and lethal types of injury, causing over a quarter of traumatic deaths. Severe thoracic injuries are often occult and difficult to diagnose in the field. There is a need for a point-of-care diagnostic device for severe thoracic injuries in the prehospital setting. Electrical bioimpedance (EBI) is non-invasive, portable, rapid and easy to use technology that can provide objective and quantitative diagnostic information for the prehospital environment. Here, we evaluated the performance of EBI to detect thoracic injuries. *Approach*: In this open study, EBI resistance (R), reactance (X) and phase angle (PA) of both sides of the thorax were measured at 50 kHz on patients suffering from thoracic injuries ($n = 20$). In parallel, a control group consisting of healthy subjects ($n = 20$) was recruited. A diagnostic mathematical algorithm, fed with input parameters derived from EBI data, was designed to differentiate patients from healthy controls. *Main results*: Ratios between the X and PA measurements of both sides of the thorax were significantly different ($p < 0.05$) between healthy volunteers and patients with left- and right-sided injuries. The diagnostic algorithm achieved a performance evaluated by leave-one-out cross-validation analysis and derived area under the receiver operating characteristic curve of 0.88. *Significance*: A diagnostic algorithm that accurately discriminates between patients suffering thoracic injuries and healthy subjects was designed using EBI technology. A larger, prospective and blinded study is thus warranted to validate the feasibility of EBI technology as a prehospital tool.

Keywords: bioimpedance, thoracic injuries, prehospital care, diagnostics, trauma, injury prevention

(Some figures may appear in colour only in the online journal)

1. Introduction

Ten percent of worldwide deaths (approximately five millions per year) are caused by trauma (Lozano *et al* 2012). Injury also accounts for 10% of the global burden of disease as measured in disability-adjusted life years (DALY), causing 250 million DALY in 2013 (Haagsma *et al* 2016). Death from transport injury is most common (1.48 million per year), followed by intentional injury (interpersonal violence and self-harm, 1.25 million) and falls (0.56 million) (Haagsma *et al* 2016). The number of potentially preventable prehospital deaths is high (Oliver *et al* 2017). To mitigate the injury outcome for trauma casualties, it is essential to provide adequate medical treatment with minimal delay after incident. A key to achieve this is to make an accurate diagnosis at the prehospital stage, typically on-scene or in the ambulance, so that patients can have time-critical interventions immediately performed and be transported directly to the most suitable medical facility.

For severely injured patients treated at a trauma center the risk of death is reduced by 25% as compared to treatment at a non-trauma center (MacKenzie *et al* 2006). Delayed care at a trauma center due to transfer from a non-trauma center is associated with increased mortality of 25% (Haas *et al* 2010). Unfortunately, many patients with severe injuries receive definitive care at non-trauma centers, or reach a trauma center via secondary transfer causing long delays of treatment (Leach *et al* 2007, Xiang *et al* 2014, Candefjord *et al* 2016). For example, Xiang *et al* (2014) showed that more than one third of patients with severe injuries (Injury Severity Score, ISS > 15) in the US emergency departments were undertriaged. To decrease the rate of undertriage while maintaining overtriage at acceptable levels is a major challenge (Leach *et al* 2007, Haas *et al* 2010, Nakahara *et al* 2010, Rehn *et al* 2012, Xiang *et al* 2014, Candefjord *et al* 2016).

Thoracic trauma has a high incidence rate and is a common cause of death. It directly causes around 25% of traumatic deaths, and contributes to death in additionally 25% of cases (Baker 1980, Demetriades *et al* 2004). Many severely injured patients with severe thoracic injuries (Abbreviated Injury Scale, AIS $\geqslant 3$) are transported to non-trauma centers (Haas *et al* 2010, Candefjord *et al* 2016). For example, Candefjord *et al* (2016) found that, for transport trauma in Sweden, over 50% of AIS 3+ thorax injuries were transported to non-trauma centers. Severe thoracic injuries are often occult and difficult to diagnose in the field (Hunt 1999). Ultrasound might be a suitable technology for diagnosing thoracic injuries such as pneumothorax (PTX); however, it is challenging to quantify and the accuracy depends on the experience of the operator. Therefore, a non-operator dependent method would be valuable for detection and continuous monitoring of thoracic injuries (Oveland *et al* 2012, 2015, O'Dochartaigh and Doumab 2015).

Electrical bioimpedance (EBI) is a non-invasive, portable, rapid and easy to use technology suitable for the prehospital environment, with potential for accurate detection of thoracic injuries (Costa *et al* 2008). EBI measures the opposition of biological tissue to the flow of a low-amplitude alternating electrical current and thus it is sensitive to morphological and

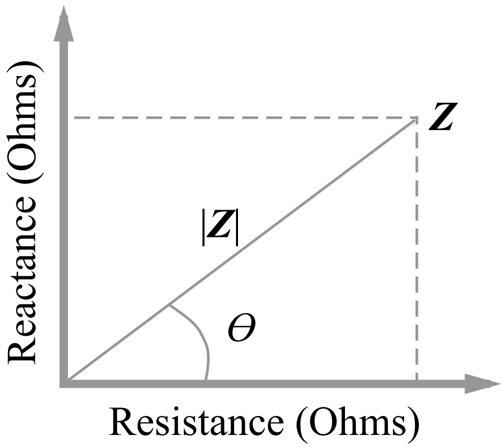

Figure 1. Schematic representation of EBI data in the complex plane at a single frequency. *The standard notation for EBI is Z, and* is determined by the resistance (*R*) and reactance (*X*) components. The phase angle *PA* (Θ) and the magnitude |*Z*| can be calculated from *X* and *R* by applying trigonometry.

physiological changes occurring in the tissues, e.g. due to edema, inflammation or injury. EBI data are determined by two components, resistance (*R*) and reactance (*X*). From *R* and *X* the phase angle (*PA*) can be derived as $\theta = \tan^{-1}\left(\frac{X}{R}\right)$, see figure 1. EBI is typically measured at 50 kHz because it is close to the characteristic frequency, i.e. frequency at which the reactance is maximum.

EBI is sensitive to changes of the permeability of cell membranes, which reflect membrane integrity and can be changed due to disease or injury (Lukaski 2013). A decrease in *PA* reflects impaired membrane function (Lukaski 2013). Both *X* and *PA* decrease with tissue damage and cell loss (Lukaski 2013, Nescolarde *et al* 2013, 2015). Further, a decrease of *R* is associated with interstitial edema and loss of muscle function in injured muscle tissue (Nescolarde *et al* 2013, 2015, Sanchez *et al* 2017a). Localized EBI have also been proven valuable in prognosis of diseases affecting skeletal muscle (Sanchez *et al* 2017b).

The aim of this study is to evaluate the potential of using EBI measurements in conjunction with a diagnostic mathematical algorithm for detection of thoracic injuries. To do so, we developed a support vector machine (SVM) algorithm using EBI data and evaluated its performance in terms of sensitivity and specificity. The thoracic injuries were confirmed by the gold standard computed tomography (CT) scan.

2. Materials and methods

2.1. Study subjects

This was an open and non-blinded study, approved by the Regional Ethical Review Board at the University of Gothenburg, Sweden. Twenty patients and 20 healthy volunteers were recruited. All participants were measured between October 2015 and October 2016. All subjects provided written informed consent prior to the measurements. Patients were recruited after admission to the trauma unit at Sahlgrenska University Hospital, Gothenburg, Sweden. Table 1 shows the inclusion and exclusion criteria.

Table 1. Inclusion and exclusion criteria for patients and healthy volunteers.

Patients		Healthy volunteers	
Inclusion	Exclusion	Inclusion	Exclusion
⩾18 years of age Admitted to trauma unit Thorax injury confirmed on CT Signed a written informed consent	Pregnant women Patient has pacemaker or other device generating electric current implanted	⩾18 years of age Healthy, i.e. no significant medical history Signed a written informed consent	Pregnant women Subject has pacemaker or other device generating electric current implanted

Table 2. Subject characteristics.

	Healthy subjects			Patients suffering thoracic injuries		
	Male	Female	All	Male	Female	All
No. of subjects	11	9	20	15	5	20
Age (years)	44.2 ± 16.4	33.1 ± 9.2	38.2 ± 14.2	59.5 ± 17.5	46.4 ± 15.0	56.2 ± 17.8
Height (cm)	181.1 ± 5.9	163.3 ± 6.1	175.2 ± 9.0	180.8 ± 5.5	168.2 ± 6.2	177.7 ± 7.9
Weight (kg)	77.7 ± 5.7	61.2 ± 5.9	70.3 ± 10.0	86.0 ± 14.9	72.6 ± 10.9	82.6 ± 15.1
BMI (kg m^{-2})	23.7 ± 1.8	21.8 ± 1.7	22.9 ± 2.0	26.3 ± 4.2	25.7 ± 4.0	26.1 ± 4.1

Mean and standard deviation of age, height, weight and body mass index (BMI) for patients and healthy controls are shown in table 2. There were statistically significant differences between patients and healthy controls for age and weight, whereas proportion of males versus females and BMI were not significant, as tested by unpaired Student's *t*-test.

Patient injury characteristics are shown in table 3. The majority of patients had multiple injuries from blunt trauma. All patients but one had ISS $\geqslant 9$ and thoracic AIS $\geqslant 3$. Further, 14 patients had predominant injury on the left side, five on the right side, and one had bilateral injuries.

2.2. EBI device and measurements

The measurement device used was the *BIA 101 Anniversary* (Akern SRL, Pontassieve, Italy), see figure 2. The device measures EBI at 50 kHz and the data is then visualized in the display. A calibration test was performed prior to each measuring session using the supplied test circuit, which ensures data accuracy within the tolerance range by compensating for the effect from cables and connections. In order to ensure the correct operation of the device within the measurement range and accuracy, we performed 40 measurements on the test circuit. For each test all four connections were disconnected and connected again, with the device turned off and on. The connections were interchanged for the five tests performed, i.e. current and voltage crocodile clips were connected to a different current and voltage input of the circuit each five tests. The results were $R = 384.4 \pm 0.1$ Ohms and $X = 47.0 \pm 0.2$ Ohms, whereas the test circuit nominal values are $R = 383 \pm 10$ Ohms and $X = 45 \pm 5$ Ohms. The device was considered to operate correctly, i.e. within the range of specifications determined by the manufacturer. For the measurements on human subjects, we used gel adhesive electrodes supplied together with the device (Biatrodes, AKERN SRL, Pontassieve, Italy).

Table 3. Patient injury characteristics. Abbreviations: MOI = mechanism of injury; MC = motorcycle, PTX = pneumothorax, HTX = hemothorax. L = left, R = right.

Patient	MOI	ISS	Thorax AIS	PTX	HTX	Rib fractures
1	Fall	9	3	—	L	L 6–10
2	Go-kart	4	2	—	—	R 7–8
3	Fall	9	3	L	—	L 8–11
4	Fall	9	3	—	R	R 9–12
5	Fall	10	3	—	—	R 3–9
6	Bike	10	3	L	L	—
7	Fall	9	3	—	L	L 6–12
8	Horse	17	3	L	L	L 4–8
9	Horse	16	4	R, major	R	R 6
10	MC	13	3	L	L + R	L 1–8, R 1–2
11	Bike	11	3	L	L	L 5–9
12	Moped	13	3	L	L	L 5
13	Stab	16	4	R	R, major	—
14	MC	14	3	—	—	L 10
15	MC	41	4	R	L, major + R	L 6–12, R 3–9
16	Fall	27	3	—	—	L 8, 10, 11
17	Violence	17	3	L	L	L 2–4
18	MC	27	3	L	L	L 4–6
19	MC	9	3	—	L	L 4–8
20	Fall	25	5	L, major	L	L 5, 8

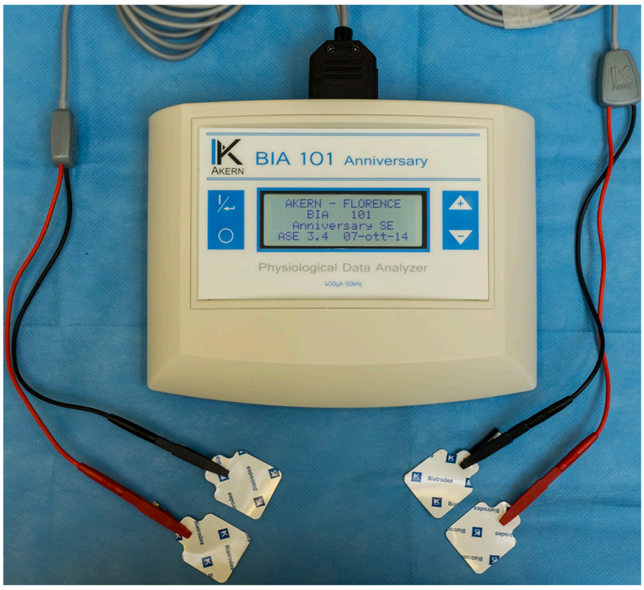

Figure 2. The measurement device *BIA 101 Anniversary* (AKERN SRL, Pontassieve, Italy). The red and black cables lead to the current injecting and voltage measuring electrodes, respectively.

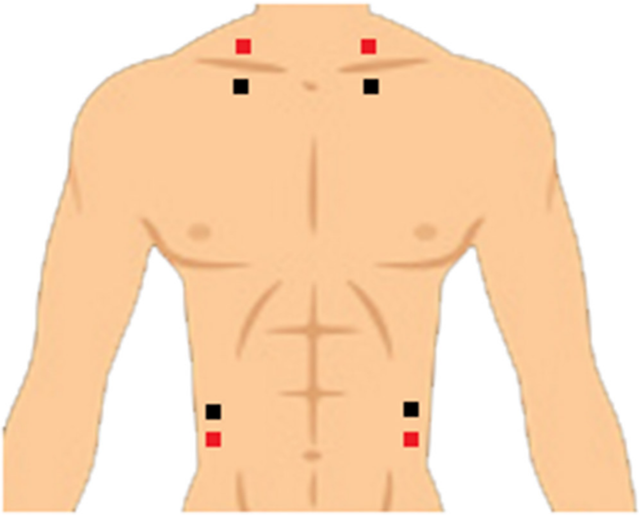

Figure 3. Schematic representing the electrode locations. For each side of the thorax, an electrical current at 50 kHz is passed between the two outer current electrodes (shown in red), and the resulting voltages are recorded using the two inner electrodes (shown in black).

To avoid electrode polarization effects (Schwann and Ferris 1968), tetrapolar measurements were performed for all subjects using new electrodes each time. All measurements were performed by the same operator (author RB). Measurements on patients were performed at the trauma unit of Sahlgrenska University Hospital, under the supervision of a trauma physician and/or a nurse. Repeated measurements were performed to test repeatability. In some patients, however, that was not possible because it would have interfered with the clinical standard of care. For this reason, only the first measurement on each subject was used for the data analysis (except for repeatability assessment). Subjects were measured in supine position when possible. Eight of the patients could not be examined in complete horizontal position due to pain or discomfort. They needed an inclination angle of between 30 and 45 degrees, elevating their upper body including the thorax. No statistically significant differences for patients that were measured in a reclined position were identified for any of the EBI parameters as assessed by unpaired Student's *t*-test.

For each measurement, four electrodes were first placed on the right side of the thorax and then the left side (see schematic in figure 3). For each side, one pair of electrodes was located on the upper thorax and one pair on the lower thorax. Upper and lower current electrodes were positioned on the mid-supraclavicular area and the mid-axillar line just over the umbilicus level, respectively; upper voltage sensing electrodes were positioned at the mid-infraclavicular area, while the lower voltage sensing electrodes were positioned at distance center-to-center between electrodes of 5 cm above the lower current electrodes. This electrode configuration is similar to the one used with the EBI device NICOM (Cheetah Inc., Tel Aviv, Israel) (Keren *et al* 2017). Right and left thoracic measurements were performed on all subjects.

This measurement configuration was designed to obtain contralateral measurements in order to reduce inter-individual variability of baseline (healthy state) using EBI ratios (right side/left side). Then, the quotients between the *R*, *X* and *PA* of the right and the left sides were computed. The hypothesis is that quotients of EBI data will change when either side of the thorax is injured. For bilateral injuries, there is usually a difference in the type or extent of injuries on each side, which is expected to produce a change in the quotient as compared to the uninjured state. Hereafter, the *R*, *X* and *PA* quotients between the right and left sides of the thorax are labelled *R_Ratio*, *X_Ratio* and *PA_Ratio*.

2.3. Data analysis

Data were analysed using MATLAB (versions 2013b and R2016b, The Mathworks, Natick, MA, USA). The LIBSVM package (version 3.21) implemented for MATLAB was used for SVM classification (Chang and Lin 2011). Algorithms included in MATLAB/LIBSVM were used when possible, and other algorithms were programmed ad hoc.

Investigators conducting the data analysis (authors RB and SC) were not blinded to subject diagnosis. A diagnostic mathematical algorithm for differentiating patients from healthy controls was developed by using principal component analysis (PCA) and an SVM classifier. In SVM a so-called kernel function needs to be chosen and appropriate values of the penalty parameter C and kernel parameters need to be selected. For this study the recommendations by Hsu *et al* (2003) were followed. Thus, the radial basis function (RBF) kernel, and a two-step process were used. Firstly, the best values for the kernel parameters penalty C and width γ were found by means of grid search and cross-validation (CV). Thereafter, the best parameter values were used to train the whole training dataset. Grid search was performed in the intervals $C = 2^{-5}$–2^{15} and $\gamma = 2^{-15}$–2^{3} using five-fold CV. Training data was scaled to the interval (0, 1) for each variable, and test data was scaled using training data scaling values (Hsu *et al* 2003). Performance of the model was calculated as area under the receiving operative characteristic (ROC) curve (AUC) using leave one out cross-validation (LOO-CV), with fixed values of the kernel parameters identified from the preceding grid search.

Because the EBI data was distributed differently for patients with thoracic injury as compared to healthy controls depending on the side of the injury, i.e. towards lower and higher values, respectively, the EBI data was preprocessed by subtracting the mean of healthy volunteers from the training set from all subjects, and subsequently deriving the absolute value.

First, the algorithm was fed with all possible combinations of EBI parameters, i.e. the seven possible combinations of *R_Ratio*, *X_Ratio* and *PA_Ratio*. Additionally, because right and left measurements might contain valuable information despite different individuals presenting different baseline EBI values, right and left EBI parameters were used as input to the algorithm. However, not all predictors could be used simultaneously to avoid over-fitting (nine predictors, i.e. three each from *R*, *X* and *PA* for both sides plus the three ratios, versus a sample size of 40 subjects). We then used PCA to reduce the number of predictors. PCA is a suitable method to extract the maximum independent information in a reduced set of parameters.

One-way ANOVA was used to assess the relation between injury status and the different parameters considered (significance $p < 0.05$), i.e. EBI parameters and principal components (PC), as recommended in Tronstad and Pripp (2014). Patients were categorized into two groups: (1) patients with predominant right side injury; and (2) patients with predominant left side injury. The side of injury has a profound influence on the EBI parameter. Thus, EBI parameters of injured patients cannot be expected to follow a normal distribution, rather two normal distributions, i.e. one for each side of predominant injury. The patient with bilateral injuries was considered to have right side predominant injury because it exhibited a PTX only in the right side.

Patients were, on average, significantly older and heavier than healthy subjects, ($p < 0.05$, unpaired Student's *t*-test). For this reason, in order to control for confounders, the correlation coefficients between the input predictors, i.e. parameters used for classification, and healthy

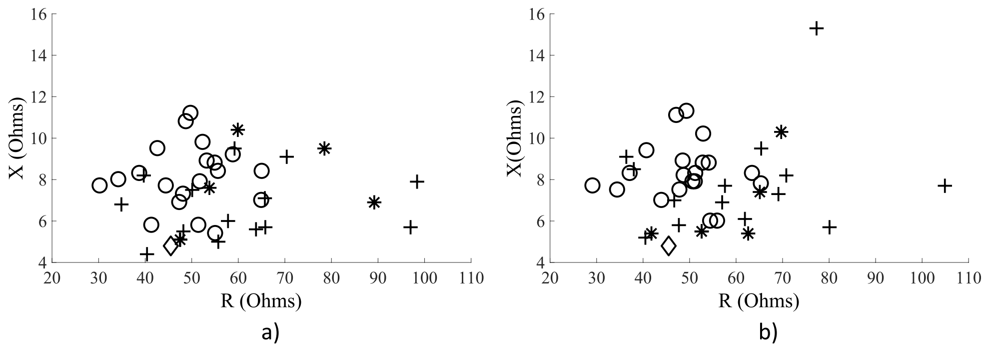

Figure 4. Resistance and reactance data measured, (a) on left side and (b) right side of the thorax. Circles represent healthy controls, crosses predominant left side injury, asterisks predominant right side injury, and a black diamond represents the only bilaterally injured subject.

controls' age and weight were calculated. This method can be used to determine whether differences in subjects' characteristics may affect the performance of the model, i.e. if any predictor would correlate with age and weight the algorithm could use the influence of these two factors on the predictors to distinguish patients and healthy controls, because the patient group included heavier and older subjects. Additionally, repeatability of measurements was tested by calculating the correlation coefficients of repeated measurements, and within-subject standard deviations S_w, and repeatability coefficients (Bland and Altman 1999), i.e. $2.77 \times S_w$ as recommended in Tronstad and Pripp (2014).

3. Results

3.1. Thoracic EBI

EBI data of both sides of the thorax are shown in figure 4.

3.2. Discrimination between patients and controls using EBI parameters as input predictors

Box plots and outcome of one-way ANOVA tests of *R_Ratio*, *X_ Ratio*, and *PA_ Ratio* for healthy controls and patients with predominant right and left side injuries are shown in figure 5.

Classification performance measured as AUC estimated on LOO-CV was tested for all possible combinations of *R_Ratio*, *X_ Ratio*, and *PA_ Ratio* (see table 4). Using the *PA_Ratio* alone resulted in the highest performance, i.e. AUC = 0.87. The best kernel parameter values ranged from $C = 0.25$–32 768 and $\gamma = 3.1 \times 10^{-5}$–3.5.

3.3. Discrimination between patients and controls using PCs as input predictors

The PCA produced nine components, whereof the first five containing $> 99.6\%$ of the variability of the dataset, were retained (figure 6). In order to compare the values of PC for the three groups, i.e. healthy controls, patients with predominant right and left side injuries, box plots and results for one-way ANOVA tests are shown in figure 7.

The best performance was obtained using PCs 3 and 4 as predictors, with kernel parameter values $C = 294$ and $\gamma = 8$. The ROC can be observed in figure 8. The AUC was 0.88.

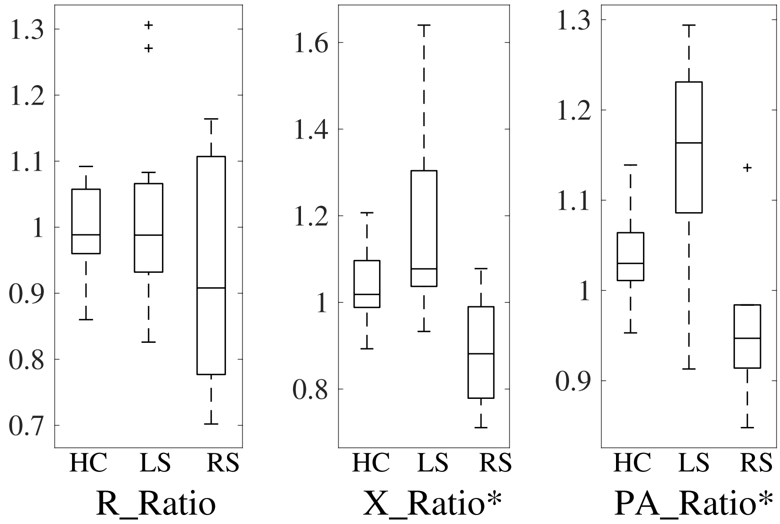

Figure 5. Box plots of *R_Ratio*, *X_ Ratio* and *PA_Ratio* for healthy controls (HC) and patients with predominant right (RS) and left side (LS) injuries. Differences between *X_Ratio* and *PA_Ratio* were statistically significant (marked with asterisk), $p < 0.005$ and $p < 0.0001$, respectively.

Table 4. Classification performance measured as AUC estimated using LOO-CV for all possible combinations of resistance ratio (*R_Ratio*), reactance ratio (*X_ Ratio*), and phase angle ratio (*PA_Ratio*).

Predictors	AUC
R_Ratio	0.49
X_Ratio	0.54
PA_Ratio	0.87
R_Ratio + *X_Ratio*	0.73
R_Ratio + *PA_Ratio*	0.85
X_Ratio + *PA_Ratio*	0.85
R_Ratio + *X_Ratio* + *PA_Ratio*	0.84

3.4. Controlling for confounders

Correlation coefficients between the subjects' characteristics that presented a significant difference between healthy and injured subjects, i.e. age and weight, and utilized parameters, i.e. *PA_Ratio* and PCs 3 and 4, are shown in table 5. None of the correlation coefficients were statistically significant. Furthermore, the *PA_Ratio* for healthy women was 1.034 ± 0.05 (mean ± std) and for healthy men was 1.037 ± 0.04; the PCs 3 and 4 for healthy women were respectively 1.96 ± 3.41 and 0.13 ± 0.32 and for healthy men were respectively -0.07 ± 2.30, and 0.23 ± 0.36. None of the differences were statistically significant. Additional classification tests removing the two participants on the extremes of age and weight were performed, i.e. two subjects exhibiting highest age and weight for patients and opposite for controls. The AUC using only the *PA_Ratio* was 0.86 for the age case and 0.85 for the weight case.

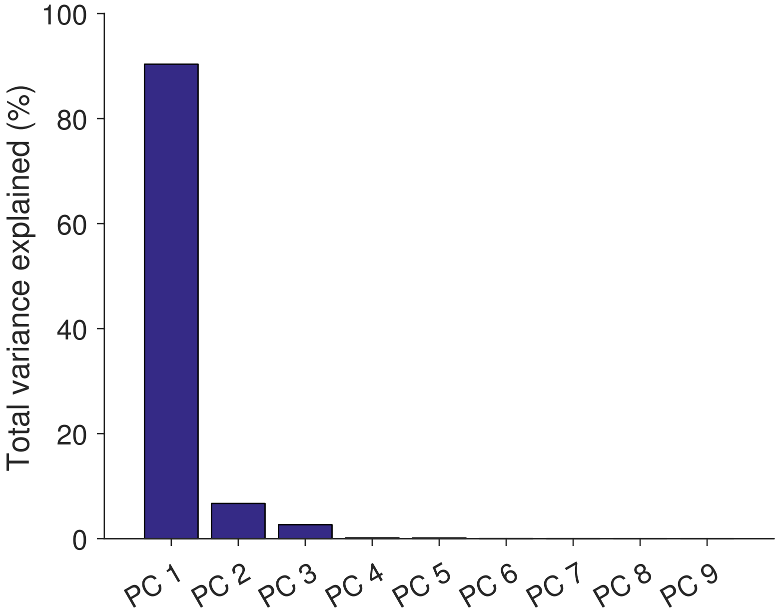

Figure 6. Total variance percentage explained for each PC. The values of total variance for each PC were: PC1 = 90.36, PC2 = 6.70, PC3 = 2.66, PC4 = 0.14, PC5 = 0.13, PC6–PC9 < 0.01.

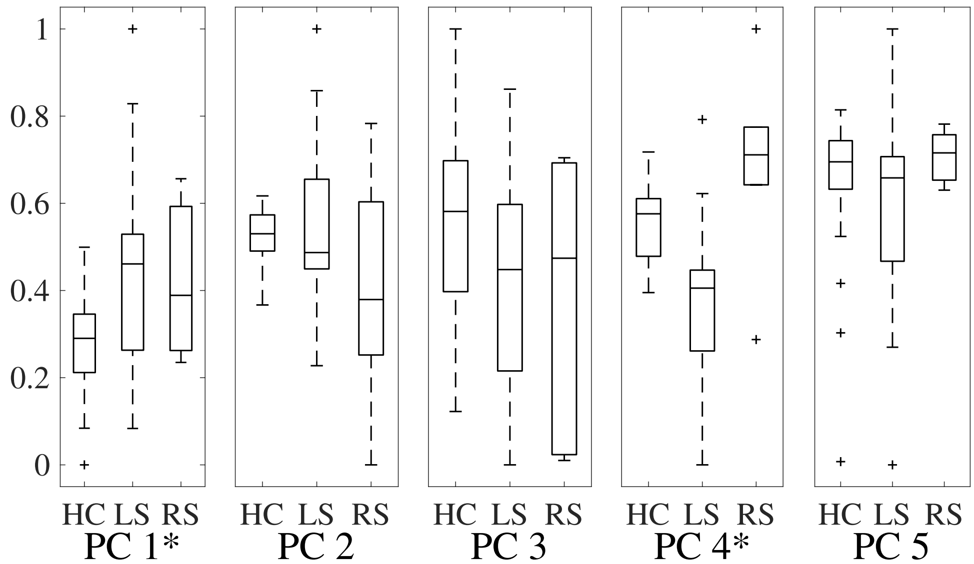

Figure 7. Box plots of the five first PCs for healthy controls (HC) and patients with predominant right (RS) and left side (LS) injuries. Statistical significance was set as $p < 0.05$ (marked with $*$) and calculated using one-way ANOVA test.

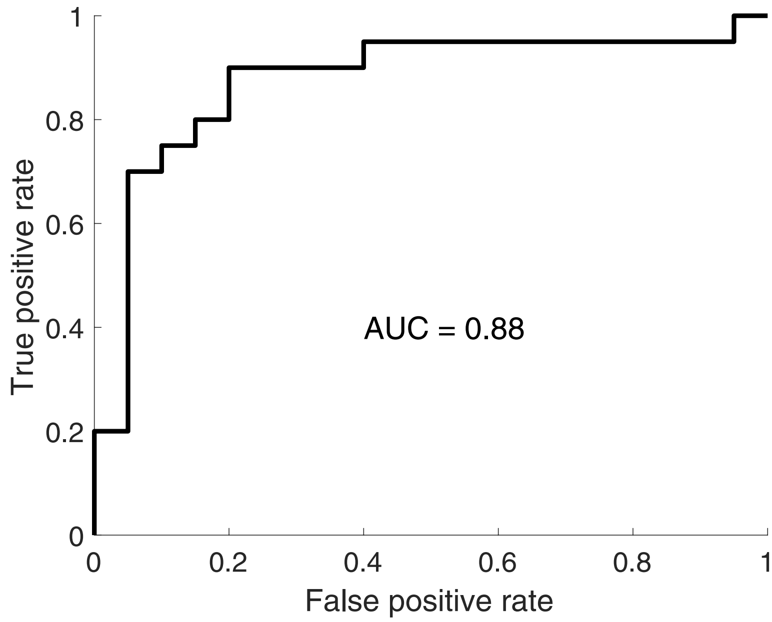

Figure 8. Receiver operating characteristic (ROC) curve of an SVM using the third and fourth PC as input predictors (see figure 6). The area under the curve (AUC) is 0.88.

Table 5. Correlation between utilized parameters, i.e. *PA_Ratio* and PCs 3 and 4, and age and weight of healthy controls; none was statistically significant.

	PA_Ratio	PC3	PC4
Age	0.29	−0.32	−0.05
Weight	0.40	0.08	−0.38

Table 6. Repeatability of EBI measurements.

	R_RS	X_RS	PA_RS	R_LS	X_LS	PA_LS
r	0.97	0.83	0.96	0.97	0.93	0.98
S_w	2.79	1.06	0.66	2.50	0.47	0.44
Repeatability coefficient (Ω)	7.72	2.93	1.82	6.92	1.30	1.21

Abbreviations: r = correlation coefficient; S_w = within-subject standard deviation.

3.5. Repeatability of measurements

Correlation coefficients of repeated measurements, within-subject standard deviations (S_w), and repeatability coefficients, i.e. $2.77 * S_w$, reported in table 6 indicate high repeatability.

4. Discussion

This study represents an initial effort towards validating a prehospital tool for early detection of thoracic injury based on EBI. This tool is much needed because the undertriage of patients suffering thoracic injuries is high (Haas *et al* 2010). A tool based on EBI measurements that has already proven valuable and suitable in the prehospital environment is the device NICOM (Cheetah Inc., Tel Aviv, Israel) (Squara *et al* 2007, Dubost *et al* 2013, Dunham *et al* 2013). NICOM is a commercial system that estimates cardiac output using EBI technology with the same measurement setup as the one presented here. Therefore, we foresee in the future NICOM could also incorporate the capability of detecting patients that might suffer thoracic injuries.

A diagnostic algorithm was designed using SVM to discriminate between patients suffering thoracic injuries and healthy controls using parameters derived from EBI thoracic measurements. Two approaches for deriving EBI parameters were considered. First, we considered only contralateral ratios, i.e. *R_Ratio*, *X_Ratio* and *PA_Ratio*. Best performance was given when using just the *PA_Ratio* (see table 4). That performance evaluated as AUC estimated using LOO-CV was 0.87, which represents high classification accuracy. This result is consistent with *X* and *PA* changes reported by others in injured muscle (Nescolarde *et al* 2013, 2015, Sanchez *et al* 2017a). Importantly, an advantage of the *PA_Ratio* being the most sensitive parameter is that the *PA* is a robust indicator against the placement of the electrodes (Sanchez *et al* 2016). This may become important in a demanding environment such as prehospital settings. The second approach consisted of deriving PCs, which is an approach to reduce sets of parameters that are highly interrelated as in this study. Considering a space of as many dimensions as predictors, the PCs have the advantage of being in orthogonal planes; which means that each PC has information that is independent of the others (not interrelated like EBI parameters). Best performance resulted when using the third and fourth PCs together. The AUC estimated using LOO-CV was 0.88, representing high classification performance.

All three EBI parameters analysed here, i.e. *R*, *X* and *PA*, have been shown to decrease in injured muscle. Unlike here where the *PA* was the most sensitive parameter, Nescolarde *et al* (2013, 2015) found that *X* at 50 kHz was the most sensitive parameter to detect muscle injury in professional football players. This difference can be explained by Nescolarde *et al* performing localized measurements on injured leg muscles, whereas in this work we measured thoracic injuries. We hypothesize that while *X* could be more sensitive to muscle changes in morphology, *PA* could be decreased by deteriorated health in addition to morphological and physiological changes in muscle tissue. Supporting this hypothesis is that *PA*, as measured in conventional whole-body bioimpedance at 50 kHz, has been proven an excellent indicator of disease onset in many types of diseases (Lukaski 2013). *PA* is also a valuable vitality index in health and disease (Lukaski 2013). Importantly, *PA* is calculated using a non-linear operation of *R* and *X* (see figure 1), and therefore it is related to *R* and *X*. Thus, in some conditions, changes in *R* and *X* can be magnified when calculating the *PA*.

As 25% (Baker 1980) of fatalities after trauma are due to chest trauma it is important to diagnose life-threatening injuries early in order to avoid preventable deaths. Although only 15% of chest trauma require surgery and the remaining can often be treated conservatively, there are patients who require prompt treatment with chest drains. A rapid diagnosis of pneumothorax and/or hemothorax is therefore beneficial to the patient.

Among the limitations of this study, the data was recorded prospectively but analysed retrospectively. Moreover, the study was not blinded. Further, the fact that the best performance using EBI parameters was achieved with the *PA_Ratio* alone, indicates that EBI-based predictors were highly interrelated and that the model may be overfitted with more than one predictor. This is likely due to the relatively small size of the dataset, which may also have limited the usefulness of the PCA approach. Larger datasets evaluated in blinded studies are necessary in future studies, to verify the current findings and develop the methodology further. Indeed, having a larger sample size will allow to utilize all EBI parameters, potentially enhancing the performance and confidence of the model developed here.

Further, limitations from the physiological perspective were that patients were significantly older and heavier than the healthy subjects. However, non-significant correlation coefficients of age and weight against the utilized parameters suggest that the bias of the model, if any, would not be substantial. Additional tests were performed where the two youngest participants in the control group and the two oldest patients in the injured group were excluded. Analogously, we performed another test where the two lightest healthy controls and the two heaviest patients were excluded. The AUC using only the *PA_Ratio* (highest performance), decreased from 0.87 to 0.86 in the age case and to 0.85 in the weight case. This slight decrement in performance might be explained by a smaller training set. These tests were not performed on PCs because removing subjects would mean recalculating and changing PCs. Moreover, patients measured in reclined position did not show significant differences from patients measured in supine. On further complicating matters, other physiological factors could have impacted EBI parameters evaluated here. For example, changes occurring in the skin blood flow due to increased heat exposure are known to alter body composition outcomes (Caton *et al* 1988, Gudivaka *et al* 1996, Buono *et al* 2004). Further work is required to determine whether additional physiological factors such as skin temperature, sweat accumulation or hyperpnea influence the ability to detect thoracic injury. From the instrumentation perspective, low values of impedance as in this study might be less accurate. Fortunately, the frequency of 50 kHz is in the most robust part of the bioimpedance spectra (Buendia *et al* 2014).

We plan to address these limitations in the future conducting a larger study measuring EBI at multiple frequencies and not just 50 kHz. We believe that multi-frequency EBI data could potentially lead to a model with better performance. Finally, we also plan to target the injuries PTX and HTX specifically, the main concern in thoracic injury, extending the pilot results in a porcine model reported in Buendia *et al* (2016).

5. Conclusions

The results in this study indicate the possibility of accurately discriminating between healthy controls and patients suffering thoracic injuries using EBI. Future work is necessary including a larger blinded study in patients with PTX and HTX. Ultimately, EBI technology may be used as a prehospital tool for early detection of thoracic injuries.

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ORCID iDs

Stefan Candefjord https://orcid.org/0000-0001-7942-2190
Benjamin Sanchez https://orcid.org/0000-0002-1594-9847
Eva-Corina Caragounis https://orcid.org/0000-0001-5637-2637

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