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End-expiratory lung impedance change enables bedside monitoring of end-expiratory lung volume change

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Abstract *Objective:* The aim of the study was to investigate the effect of lung volume changes on end-expiratory lung impedance change (ELIC) in mechanically ventilated patients, since we hypothesized that ELIC may be a suitable parameter to monitor lung volume change at the bedside. *Design:* Clinical trial on patients requiring mechanical ventilation. *Settings:* Intensive care units of a university hospital. *Patients:* Ten mechanically ventilated patients were included in the study. *Intervention* Patients were ventilated in volume-controlled mode with constant flow and respiratory rate. In order to induce changes in the end-expiratory lung volume (EELV), PEEP levels were increased from 0 mbar to 5 mbar, 10 mbar, and 15 mbar. At each PEEP level EELV was measured by an open-circuit nitrogen washout manoeuvre and ELIC was measured simultaneously using Electrical Impedance Tomography (EIT) with sixteen electrodes placed on the circumference of the thorax and connected with an EIT device. Cross-sectional electro-tomographic measurements of the thorax were performed at each PEEP level, and a modified Sheffield back-projection was used to reconstruct images of the lung impedance. ELIC was calculated as the average of the end-expiratory lung impedance change. *Results:* Increasing PEEP stepwise from 0 mbar to 15 mbar resulted in an linear increase of EELV and ELIC according to the equation: $y = 0.98 \times -0.68$, $r^2 = 0.95$. *Conclusion:* EIT is a simple bedside technique which enables monitor lung volume changes during ventilatory manoeuvres such as PEEP changes.

Keywords Thoracic electrical impedance tomography · End-expiratory lung impedance change · End-expiratory lung volume

Abbreviations *ARF* acute respiratory failure · CO_2 carbon dioxide · *EIT* Electrical Impedance Tomography · *EELV* end-expiratory lung volume · FiO_2 inspiratory oxygen concentration · *PEEP* positive end-expiratory pressure · N_2 nitrogen · O_2 oxygen

Introduction

The monitoring of end-expiratory lung volume (EELV) could be an important tool to assess the pulmonary status and the effects of ventilator settings in critically ill patients [1]. The use of positive end-expiratory pressure (PEEP) is considered part of the standard therapy for patients with acute respiratory failure (ARF) requiring mechanical ventilation [2]. PEEP improves arterial oxygenation due to alveolar recruitment and is thereby associated with an increase in EELV. Consequently, techniques for the bedside measurement of EELV are desirable, but not yet available.

Information of alveolar recruitment can be obtained from CT scanning [3], but this is not a bedside method.

Table 1 Patient characteristics

Patient	Age (years)	Weight (kg)	Height (cm)	Diagnosis	Lung diagnosis	Lung injury score	FiO_2
1	37	80	178	Skull brain injury	Atelectasis	1.0	0.40
2	78	65	165	Hemicolektomie	Atelectasis	1.0	0.40
3	30	80	182	Skull brain injury	Atelectasis	1.3	0.55
4	78	60	167		Pneumonia	3.0	0.60
5	62	90	180	Subarachnoid hemorrhage	ARDS	3.3	0.60
6	58	65	168	Lung cancer	Pneumonia	1.0	0.35
7	33	80	170	Polytrauma	ARDS	2.0	0.40
8	69	115	185		ARDS	2.3	0.40
9	61	85	175		Pneumonia	3.0	0.45
10	51	92	183		Pneumonia	2.0	0.40
Mean±SD	58±16	81±16	175±7			2.0±0.9	

Another approach to measure alveolar recruitment is an open-circuit multibreath nitrogen-washout manoeuvre, first described by Darling et al. in 1940 [4].

Electrical Impedance Tomography was developed in 1984 by Barber and Brown [5]. EIT generates cross-sectional images of the impedance distribution within a transverse slice of the thorax. The basic principle of EIT is based on an alternate current injection and voltage measurement via surface electrodes placed around the thorax. Since the electrical properties of the chest varies depending on variations in the air content, ventilation-induced impedance changes can be measured by an EIT device [6]. Consequently, this method offers the possibility of continuously measuring lung volume changes at the bedside.

The aim of this study was to investigate the effects of lung volume changes induced by different PEEP levels on electrical impedance tomography and to compare changes in electrical impedance with changes in the EELV as measured by the multibreath nitrogen-washout manoeuvre.

Patients and methods

Study protocol

After approval by the local ethics committee, the investigation was performed in the intensive care unit of the Department of Anaesthesiology, Emergency and Intensive Care Medicine, University Hospital Göttingen, Germany.

Informed written consent to participate in this study was obtained from the nearest relatives of ten mechanically ventilated patients (mean±standard deviation: age 58±16 years, weight 81±16 kg, lung injury score 2±0.9 [7], days on mechanically ventilation 7±3 days) were included into the study (for patient characteristics see Table 1).

Inclusion criteria were:

- Mechanically ventilated patient with acute respiratory failure (PaO_2/FiO_2 <300 mmHg).
- Mechanical ventilation >24 h before onset of the study.
- Age ≥18 years.
- Informed written consent of the next kin.
- Clinically indicated arterial blood pressure measurement.

Exclusion criteria were:

- Inappropriate inclusion criteria.
- Pregnancy.
- Terminal illness.
- Unstable hemodynamics.

All patients were ventilated using an Evita2 ventilator (Dräger, Lübeck, Germany) in a volume-controlled mode with constant flow and a respiratory rate of 10·min^{-1}). Tidal volume, inspiratory oxygen concentration and the level of positive end-expiratory pressure (PEEP) were set by the attending physician in order to achieve normocapnia ($PaCO_2$ 35–45 mmHg) and an oxyhemoglobin saturation (SaO_2) >95%. At the beginning of the study the PEEP level was decreased to 0 cmH_2O and occasionally the FiO_2 was increased so that the SaO_2 remained above 90%. Thereafter, PEEP was increased stepwise to 5 mbar, 10 mbar, and 15 mbar after intervals of approximately 40 min when a steady state condition had been achieved. EIT measurements were performed continuously during the total observation period. At the end of each study period end-expiratory lung volume (EELV) was measured by an open-circuit multibreath nitrogen-washout manoeuvre and simultaneously recording of the end-expiratory lung impedance change was performed by electrical impedance tomography (EIT). We investigated the change of EELV and end-expiratory lung impedance change against baseline values with PEEP 0 mbar.

Open-circuit multibreath nitrogen-washout manoeuvre

An open-circuit multibreath nitrogen-washout manoeuvre was performed in similar way to the method described by Darling et al. [4], with modifications which have been described in detail elsewhere [8]. Briefly, gasflow was measured with a pneumotachograph (Fleisch No. 2, Fleisch, Lausanne, Switzerland) and a differential pressure transducer (Huba Control, Würenlos, Switzerland) directly connected to a heat and moisture exchanger (Humid-Vent 2, Gibeck Respiration, Väsby, Sweden) at the endotracheal tube. Inspiratory gas and expiratory gas was continuously sampled via a capillary (length: 3.09 m, flow: 1 ml·s^{-1}) connected to the y-piece of the breathing circuit. Nitrogen (N_2), oxygen (O_2), and carbon dioxide (CO_2) were measured by a mass spectrometer (MGA 1100, Perkin Elmer, Pomona, Calif., USA) which delivered gas concentrations as fractions excluding water vapour. All data were sampled online by an analogue/digital converter (DT2801-A, Data Translation, Marlboro, Mass., USA) at a rate of 40 Hz and processed by an IBM AT compatible personal computer. The data ac-

quisition and processing software was programmed with a commercially available software program (Asyst 4.0, Keithley Asyst, Taunton, Mass., USA).

The flow measuring system was calibrated with a gas mixture of known gas concentrations (65% N_2, 30% O_2, and 5% CO_2) and definite viscosity using a precision calibration pump (Engström Megamed 05, Engström, Stockholm, Sweden) that generates a sinusoidal flow pattern. During calibration measurements the instantaneous gas viscosity was determined from the actual gas fraction in order to correct the measured flow signal for the changing gas composition as described by Brunner et al. [9]. Volume was then obtained from the corrected flow signal by offline analysis. To minimize the drift of the flow signal by an offset, the pressure transducer was meticulously adjusted during zero-flow conditions before each measurement.

Determination of end-expiratory lung volume (EELV)

Calculation of EELV was performed offline. The multibreath nitrogen-washout manoeuvre was started by changing the FiO_2 at end-expiration from baseline to 1.0. Fractional nitrogen concentration (FN_2) at baseline was determined as average N_2-concentration before the start of washout. The EELV calculation procedure was started at end-expiration with the first oxygen washin breath. As the first breath usually still contains a certain amount of N_2, this inspired N_2-volume was subtracted from the cumulative N_2-volume calculated from the washout procedure. To reduce the influence of signal noise to N_2 washed out, direct calculation from the measurement was finished at 3% of the baseline FN_2. Additionally, a correction for tissue N_2 as described by Cournand et al. [10] was done in all patients. EELV were calculated from the measured N_2 volume divided by N_2 at baseline. For further details of determination and accuracy of the multibreath nitrogen-washout manoeuvre see [8].

Electrical Impedance Tomography

An Applied Potential Tomography System (APT System MK1, IBEES, Sheffield, UK) was used for the electrical impedance measurements. Sixteen surface electrodes (Blue sensor BR-50-K, Medicotest A/S, Olstyke, Denmark) were placed around the thorax of the patients in one transversal plane corresponding to the 6th intercostal parasternal space. An alternating current (5 mA p–p, 50 kHz) was injected between a pair of adjacent electrodes. The resulting surface potentials were measured between the remaining adjacent electrode pairs. In turns, all 16 adjacent electrode pairs were used as injecting electrodes. When all pairs of adjacent electrodes had been used as injecting electrodes, one data collection cycle consisting of 208 surface potential data was completed. We performed 1,000 data collection cycles per measurement with a sampling rate of 10 cycles per second. Thus, the mean acquisition time was 100 s, corresponding to 14 respiratory cycles during mechanical ventilation. The surface potentials were used to compute a sequence of the cross-sectional distribution of impedance changes within the thorax using a modified Sheffield back-projection [11] for tomographic reconstruction of an EIT image. The back-projection generates images which show the impedance changes as compared to a reference dataset. This method, therefore, allows the visualization of physiological or pathological phenomena, which induce impedance changes [12]. As the reference dataset we used 1,000 data recording cycles at PEEP zero for each individual patient.

End-expiratory lung impedance change (ELIC)

For every EIT image mean relative impedance change was calculated. The sequence of EIT images over time was used to calculate

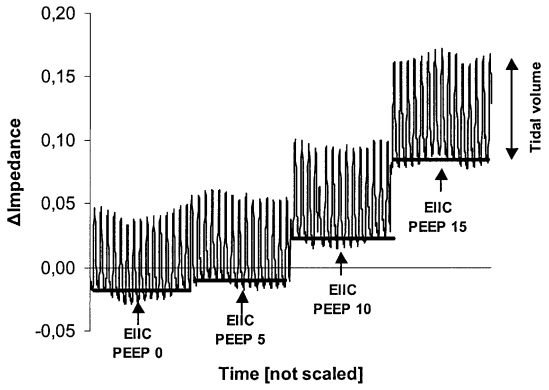

Fig. 1 Analysis of EIT measurement during mechanical ventilation with identical tidal volume at different PEEP-levels in one patient. The diagram shows four examples of the global time course of relative lung impedance change (impedance) at different PEEP levels. Each PEEP level was analysed for 100 s, corresponding to 14 respiratory cycles. Measurements of the end-expiratory lung impedance change (end-expiratory lung impedance change) and end-expiratory lung volume were performed simultaneously

mean lung impedance time course (LITC) within the observed part of the thorax along the time. End-expiratory impedance change, indicating EELV, was subsequently calculated by averaging minimal LITC values of 14 consecutive breaths. An example of LITC is shown in Fig. 1. Data were stored for offline evaluation on a personal computer (Pentium II 233 MHz, Microsoft Windows 95).

Hemodynamics and gas exchange

Arterial blood sampling was performed via a 20-gauge catheter which was inserted in the radial or femoral artery for clinical reasons. Arterial blood gas samples were analyzed by ABL 300 and OSM 3 Hemoximeter (Radiometer, Copenhagen, Denmark).

ECG, systemic arterial, and central venous pressures were displayed on a bedside monitor together with the oxyhemoglobin saturation (Datex AS/3, Datex Divison Instrumentarium, Helsinki, Finland) and recorded with reference to atmospheric pressure at the mid-thoracic level at end-expiration.

Statistics

Calculations were performed using the STATISTICA software package (Statistica 5.1, StatSoft Inc, Tulsa, USA) on a personal computer (Pentium II 233 MHz, Microsoft Windows 95).

All data are presented as Min-Max (Median) unless stated otherwise. Since the data were not normally distributed, as tested by the Shapiro-Wilk W-test, we subsequently applied a Wilcoxon matched-pair test to test the significance between different end-expiratory lung volumes and end-expiratory lung impedance time courses against reference at PEEP 0.

Linear regression analysis using the least square method was applied to correlate EELV and end-expiratory lung impedance change changes, respectively, against the different PEEP levels. Pearson's correlation analysis was used to detect any correlation between EELV and end-expiratory lung impedance change. In addition, EELV and end-expiratory lung impedance change data were compared using the statistical methods described by Bland and Altman [13], except for the bias which could not be compared due to the process of normalization. The standard deviation (SD) of the mean differences is considered to represent the random er-

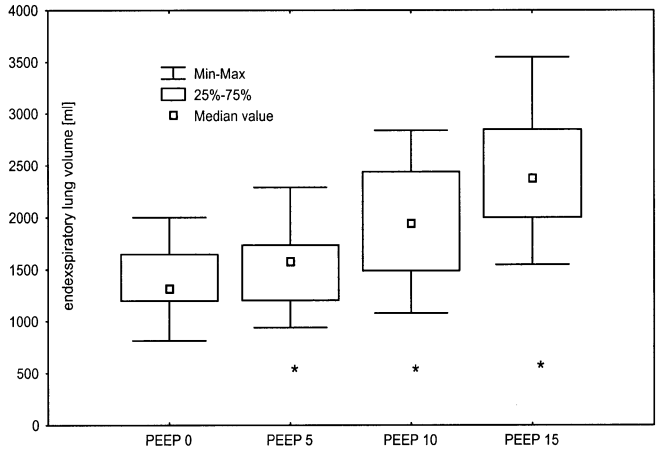

Fig. 2 Box-plots of end-expiratory lung volume at different PEEP-levels in ten mechanically ventilated patients. * P <0.05 against reference at PEEP 0 cmH_2O

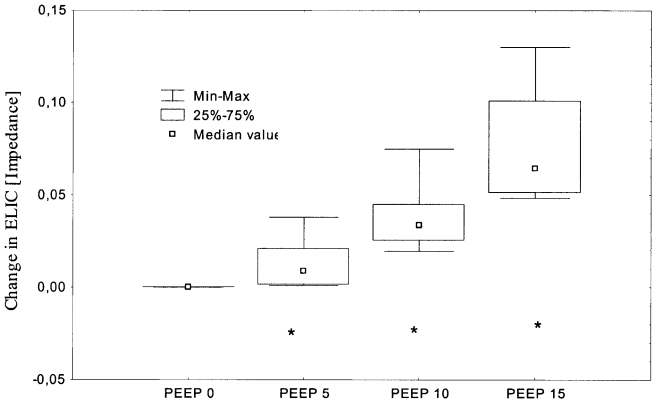

Fig. 3 Box-plots of change in end-expiratory lung impedance change (end-expiratory lung impedance change) at different PEEP levels in ten mechanically ventilated patients. * P <0.05 against reference at PEEP 0 cmH_2O

ror variability between both techniques. Mean difference±2SD was the limit of agreement of both methods. For all statistical tests P <0.05 was considered to be significant.

Results

Variation of end-expiratory lung volume (EELV)

EELV increased significantly from 815–2002(1316) ml at 0 cmH_2O PEEP, to 940–2291(1578) ml with a PEEP of 5 cmH_2O, to 1080–2841(1944) ml with a PEEP of 10 cmH_2O, and to 1546–3548(2379) ml with a PEEP of 15 cmH_2O (Min–Max(Median). All data are summarized in Fig. 2 and Table 2.

Variation of end-expiratory lung impedance change (ELIC)

According to our definition end-expiratory lung impedance change was 0.00–0.00(0.00) at a PEEP level of 0 cmH_2O (reference), it increased to 0.00–0.04(0.01) with a PEEP of 5 cmH_2O, increased further to 0.02–0.08(0.03) at a PEEP level of 10 cmH_2O, and reached a maximum value of 0.05–0.13(0.06) with a PEEP level of 15 cmH_2O [Min–Max(Median) of impedance change]. Similar to the changes of EELV, with each increase of PEEP a significant increase of end-expiratory lung impedance change was noted. All data are summarized in Fig. 3 and Table 3.

The long-term stability of the EIT signal, checked at PEEP 5 by comparison of the end-expiratory lung impedance change-values during the first minute, and after 10, 20, 30, and 40 min, showed a variation of 1.5–6.1% (3.1%).

Correlation of end-expiratory lung volume (EELV) and end-expiratory lung impedance change (ELIC)

Increasing PEEP stepwise from 0 mbar to 15 mbar resulted in an linear increase of EELV and end-expiratory lung impedance change (overall r^2=0.95). The within-subject r^2 were 0.96–0.99(0.99) [Min-Max (Median)]. The data are summarized in Fig. 4.

Table 2 End-expiratory lung volume at different PEEP-levels in ten mechanically ventilated patients. Data as range and median

Patient	PEEP 0 (ml)	PEEP 5 (ml)	PEEP 10 (ml)	PEEP 15 (ml)
1	2002	2291	2764	3482
2	1645	1736	2167	2574
3	1291	1546	2003	2547
4	1341	1720	2440	2849
5	815	940	1080	1546
6	1686	2035	2841	3548
7	1028	1054	1310	1573
8	1202	1206	1490	2079
9	1375	1414	1725	2000
10	1285	1610	1885	2211
	815–2002(1316)	940–2291 (1578)	1080–2841 (1944)	1546–3548 (2379)

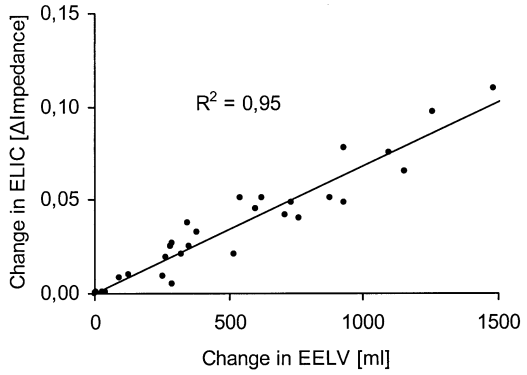

Fig. 4 Changes of the end-expiratory lung impedance change (end-expiratory lung impedance change: *y-axis*) measured by electrical impedance tomography versus changes of end-expiratory lung volume (EELV: *x-axis*) measured by multibreath nitrogen-washout manoeuvre during mechanical ventilation in ten patients. Changes of end-expiratory lung impedance change and EELV were calculated against end-expiratory lung impedance change and EELV values at PEEP 0 cmH_2O

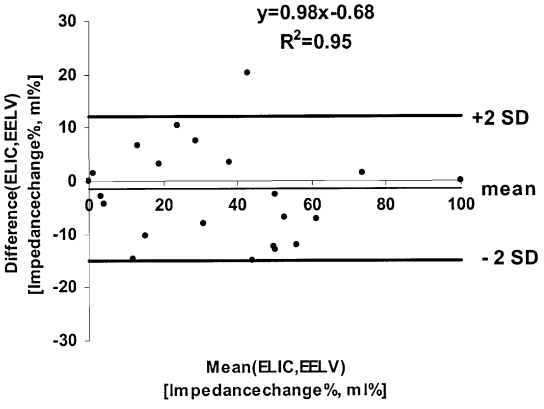

Fig. 5 Bland-Altman analysis. Comparison of end-expiratory lung impedance change (end-expiratory lung impedance change) measured with electrical impedance tomography and end-expiratory lung volume (EELV) measured by multiple breath nitrogen washout normalized to values at PEEP 15 cmH_2O in ten patients. The linear correlation is shown in Fig. 4. Since data were normalized relative to PEEP 0 and PEEP 15, the bias (mean) will invariably be close to zero. Thus, a bias analysis is not meaningful. However, the random error (±2SD) is not affected by the normalization process

The back-projection used generates relative change of impedance compared to a reference dataset at PEEP 0. Therefore, after normalizing the change of EELV and end-expiratory lung impedance change to data at PEEP 15, a linear correlation and a Bland-Altman analysis was performed (Fig. 5). When all comparisons from the ten patients studied were pooled, a highly significant linear correlation between end-expiratory lung impedance change measured by EIT and EELV measured by multibreath nitrogen-washout manoeuvre was found, according to the equation $y = 0.98 \times -0.68$, $r^2 = 0.95$.

Discussion

This study was performed to compare end-expiratory lung volume measured by multibreath nitrogen-washout (multibreath nitrogen-washout manoeuvre) with the end-expiratory lung impedance change as measured by EIT. Multibreath nitrogen-washout manoeuvre has been thoroughly validated to measure EELV at the bedside in ICU patients [8].

EIT is a new technique, which in previous studies under laboratory conditions has been shown to identify lung volume changes [14, 15, 16] with the potential of non-invasive monitoring lung volume changes in mechanically ventilated patients. The experimental studies have demonstrated the ability of EIT to identify incremental lung volume changes.

Our results show that a PEEP-induced increase of EELV is accompanied by a proportional increase of end-expiratory lung impedance change, but that end-expiratory lung impedance change slightly underestimates lung volume changes.

Several authors proposed the monitoring of end-expiratory lung volume as a tool to detect alveolar recruitment during mechanical ventilation [1, 3, 17].

Methodological aspects

The basic principle of EIT is based on the measurement of relative changes of impedance compared to a refer-

Table 3 Change in end-expiratory lung impedance change (end-expiratory lung impedance change) at different PEEP-levels against reference at PEEP 0 cmH_2O in ten mechanically ventilated patients. Data as range and median

Patient	PEEP 0 (Impedance)	PEEP 5 (Impedance)	PEEP 10 (Impedance)	PEEP 15 (Impedance)
1	0.000	0.005	0.040	0.110
2	0.000	0.008	0.021	0.048
3	0.000	0.010	0.042	0.097
4	0.000	0.033	0.075	0.101
5	0.000	0.010	0.020	0.049
6	0.000	0.038	0.065	0.120
7	0.000	0.001	0.025	0.051
8	0.000	0.001	0.027	0.051
9	0.000	0.001	0.025	0.051
10	0.000	0.021	0.045	0.078
	0.000–0.000 (0.000)	0.001–0.038 (0.009)	0.020–0.075 (0.034)	0.048–0.130 (0.065)

ence dataset within an observed object. Impedance changes within the lung are generated either by variations of the air content or changes of the central blood volume due to the pulsatile blood flow [12]. Thus, pulsatile changes of the central blood volume may interfere with lung volume measurements and may thereby increase the random error. In addition, pulmonary air content and impedance change may not correlate linearly, if stretching of lung parenchyma itself causes impedance changes. Since aeration of the lungs as well as the distribution of ventilated tidal volumes are not distributed homogeneously within the lungs, this will surely cause regional differences of lung parenchyma stretch. Furthermore, Holder and Khan [18] determined the linear operating range of impedance changes using different polyacrylamide gels and a saline-filled tank as a model together with the MarkIsystem (APT System MK1, IBEES, Sheffield, UK) for EIT measurements. They found that the measured impedance was linearly correlated to the impedance of the polyacrylamide gel, up to an increase of 20% of the reference. If gels with a higher impedance were used, the changes were underestimated by the MarkIsystem. This result may either depend on the electrical properties of the MarkI system [19] or on the image reconstruction algorithm [20] which is identical to the one we used in this study. The image reconstruction algorithm, is based on the following assumptions: the measured object has to be two-dimensional and circular, its resistivity distribution should initially be uniform, and changes in resistivity should be rather small. Finally, the electrodes have to be located equidistant around the object. The applied respiratory settings used in our study caused an end-expiratory lung impedance change of up to 0.12, which is 12%. Although all these assumptions are in fact violated during EIT measurements it has repeatedly been shown that meaningful results can be obtained with this method [21, 22, 23, 24, 6, 25, 26].

End-expiratory lung impedance change reflects impedance variations in one cross-section of the thorax, while EELV is a global parameter of the whole lung. Therefore, regional heterogeneity of the pulmonary compliance may cause slightly different results depending on the transverse slice monitored with EIT (e.g., apical versus basal region).

Nevertheless, the increase of EELV induced by stepwise increases of PEEP was proportional to end-expiratory lung impedance change, so that end-expiratory lung impedance change seems to reflect regional volume changes. In the future, the development of three-dimensional EIT [27] may provide helpful information not only about the regional volume redistribution but also about aeration and ventilation of the whole lung.

In conclusion, this study shows that EELV changes induced by PEEP during mechanical ventilation can be identified at the bedside and monitored continuously by end-expiratory lung impedance change using EIT. Thus, the method described here has the potential to be used as a simple bedside technique for the measurement of pulmonary aeration and ventilation distribution.

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