Regional Ventilation by Electrical Impedance Tomography* 
A Comparison With Ventilation Scintigraphy in Pigs

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Study objective: The validation of electrical impedance tomography (EIT) for measuring regional ventilation distribution by comparing it with single photon emission CT (SPECT) scanning.

Design: Randomized, prospective animal study.

Settings: Animal laboratories and nuclear medicine laboratories at a university hospital.

Participants: Twelve anesthetized and mechanically ventilated pigs.

Interventions: Lung injury was induced by central venous injection of oleic acid. Then pigs were randomized to pressure-controlled mechanical ventilation, airway pressure-release ventilation, or spontaneous breathing.

Measurements and results: Ventilation distribution was assessed by EIT using cross-sectional electrotomographic measurements of the thorax, and simultaneously by single SPECT scanning with the inhalation of 99mTc-labeled carbon particles. For both methods, the evaluation of ventilation distribution was performed in the same transverse slice that was approximately 4 cm in thickness. The transverse slice then was divided into 20 coronal segments (going from the sternum to the spine). We compared the percentage of ventilation in each segment, normalized to the entire ventilation in the observed slice. Our data showed an excellent linear correlation between the ventilation distribution measured by SPECT scanning and EIT according to the following equation: $y = 0.82x + 0.7$ ($R^2 = 0.92$; range, 0.86 to 0.97).

Conclusion: Based on these data, EIT seems to allow, at least in comparable states of lung injury, real-time monitoring of regional ventilation distribution at the bedside.

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Key words: regional ventilation; thoracic electrical impedance tomography

Abbreviations: APRV = airway pressure release ventilation; CPAP = continuous positive airway pressure; EIT = electrical impedance tomography; f-EIT = functional electrical impedance tomography; EVLWI = extravascular lung water index; $F_{\text{io}}_2$ = fraction of inspired oxygen; PCV = pressure-controlled ventilation; SPECT = single photon emission CT; $V_{\text{reg}}$ = registered volume; $V_t$ = tidal volume

Electrical impedance tomography (EIT), which was developed in the early 1980s by Barber and Brown,1 generates cross-sectional images of the impedance distribution within a measured object. The basic principle of EIT is based on an alternate-current injection and voltage measurement via sur-
face electrodes. If surface electrodes are placed around the thorax, changes in the electrical impedance during ventilatory maneuvers parallel to changes of aeration within the lungs can be measured. This enables the measurement of regional ventilation. EIT has been used increasingly as an experimental, noninvasive, lung-imaging technique.2–14 EIT has been shown to detect physiologic events related to anatomic settings.2,5,8,15 Validation of the technique by an established clinical method,
however, has not been obtained. The aim of this study was therefore to validate the measurement of regional ventilation, assessed by a newly developed high-performance EIT device, with ventilation scintigraphy. Since EIT may have the potential to be a bedside technique in the intensive care setting, we performed the tests in a porcine lung damage model, during different ventilatory support modes.

MATERIALS AND METHODS

Study Protocol

After approval by the local animal ethics committee, 12 pigs of mixed breed (i.e., Hampshire, Yorkshire, and Swedish country breed) [mean (± SD) weight, 30 ± 4 kg] were anesthetized and mechanically ventilated. Acute lung injury was induced in all pigs by IV injections of oleic acid (Apoteksbolaget; Göteborg, Sweden) that was suspended in 20 mL isotonic saline solution. The dosing of the oleic acid was guided by intermittently taken arterial blood samples in order to achieve a PaO2/fraction of inspired oxygen (FiO2) ratio of about 200 mm Hg. After the induction of lung injury, a stabilization period of at least 2 h was allowed before we proceeded with the experimental protocol, so that lung injury was stable, as assessed by oxygenation and respiratory mechanics. Another hour later, the pigs were transferred to the nuclear medicine laboratories, the animals were placed in the supine position, with the front legs stretched cranially, and simultaneous measurements of regional ventilation distribution using EIT16 and single photon emission CT (SPECT) scanning17 were performed. The ventilation distribution was assessed in an approximately 4 cm-thick transverse slice of the lung. The slice then was divided into 20 equally thick coronal segments going from the sternum to the spine. For both methods, the percentage of ventilation in each coronal segment was calculated and compared, as shown in Figure 1.

The investigation was performed in the experimental laboratories of the Department of Clinical Physiology at the University Hospital of Uppsala, Sweden.

Anesthesia

Azaperone (Stresnil; Janssen Pharmaceutica; Beerse, Belgium), 40 mg IM, were administered as premedication. General anesthesia was induced with remifentanil (Ultiva; Glaxo Wellcome; Hamburg, Germany) [0.04 mg/kg/min] and ketamine (Ketanest; Parke-Davis; Berlin, Germany), followed by a constant IV infusion of both drugs to maintain either controlled ventilation or spontaneous breathing. The animals received tracheotomies and were either spontaneously breathing or mechanically ventilated through auffed tube. Prior to measurements, 1,000 mL Ringer-acetate (Pharmacia AB; Stockholm, Sweden) at body temperature was infused.

Ventilation

Mechanical ventilation was provided with a ventilator (EVITA 4; Dräger; Lübeck, Germany). Respirator settings were initially in the pressure-controlled mode with a peak airway pressure of 15 cm H2O, a positive end-expiratory pressure of 5 cm H2O, a respiratory rate of 20 breaths/min, an inspiratory/expiratory ratio of 1:2, and an FiO2 of 0.5.

After oleic acid administration and a stabilization period of approximately 2 h, the pigs were randomized to pressure-controlled ventilation (PCV) without spontaneous breathing, PCV with spontaneous breathing (i.e., airway pressure release ventilation [APRV]), or spontaneous breathing (i.e., continuous positive airway pressure [CPAP]). The pigs also were studied for other purposes, which are reported on elsewhere. Another hour later, the pigs were moved to the gamma camera for the study, keeping the ventilator settings constant in the PCV group, and

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**Figure 1.** Analysis procedure. For each pig, simultaneous transversal measurements from SPECT scanning and EIT were performed in a 4-cm slice of the thorax. Each slice was divided into 20 anterior-posterior segments (going from the sternum to the spine). Ventilation for both methods was calculated by the percentages of either regional minute volume for SPECT scanning or by the percentages of regional impedance change for EIT. The correlation of ventilation in each segment was calculated, \( A = \Delta \).

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adjusting the ventilator support in the APRV and CPAP groups so that spontaneous breathing was resumed. Arterial blood gas samples were analyzed (ABL 300 and OSM 3 Hemoximeter; Radiometer; Copenhagen, Denmark).

**Hemodynamics**

For arterial blood gas sampling, an 18-gauge catheter was inserted into the carotid artery, together with a thermistor-tipped fiberoptic catheter (Pulsiocath 4F PT PV 2024; Pul tion Medical System; Munich, Germany), which was advanced into the descending aorta for measurements of extravascular lung water index (EVLWI). EVLWI was calculated automatically (Pulsion COLD Z-021; Pulsion Medical System) after injecting 8 to 10 mL 1 mg/mL indocyanine green (ICG-Pulsion, Pulsion Medical System), which was mixed in sterile water (temperature range, 5°C to 7°C) randomly within the respiratory cycles. The generation of f-EIT is monitored continuously during mechanical ventilation over a period of 3 to 5 min from a 2-L syringe that was connected to the Y-piece. During the injection of the carbon particles, a pressure of approximately 31 cm H₂O was maintained within the syringe, as controlled by a manometer connected to the syringe via a three-way stopcock, resulting into a continuous flow of carbon particles into the Y-piece during the whole respiratory cycles. Images were acquired on a dual-head gamma camera (Munich; General Electric Systems; Milwaukee, WI) that was equipped with all-purpose low-energy collimators. The SPECT acquisitions were performed in 64 projections (32 projections per head) and were stored in a 64 × 64 matrix. The acquisition time was 15 s for each projection.

The data were reconstructed on a computer workstation (HERMES; Nuclear Diagnostics; Stockholm, Sweden). The acquired data were prefiltered with a two-dimensional Butterworth filter (cutoff frequency, 0.14; filter order, 10). Filtered back-projection reconstruction was performed without applying attenuation correction. After corrections for the background, the number of counts was measured in each volume element of the lungs.

Minute ventilation was assessed by pneumotachography (as described above). Ventilation in the 4-cm-thick slice near the EIT electrodes was calculated as the number of counts within the slice, times minute ventilation, divided by the total number of counts within the whole lung. By adding coronal planes, the slices were divided into 20 equally thick segments in the ventral-dorsal direction going from the sternum to the spine. The ventilation of each segment finally was calculated as the fractional activity in each segment times minute ventilation.

Since animals with varying degrees of pulmonary edema and damage were studied, the risk of carbon particles being trapped in the edematous airways was considered to be possible. The intrapulmonary distributions of the carbon particles therefore were compared with a reference technique, the inhalation of radioactive krypton gas, in four pigs. 81mKr was produced as a gas in a 133Ba/129IKr generator (KryptoScan; Mallinckrodt Medical BV, Petten, the Netherlands). The krypton was continuously administered directly into the ventilator during the whole acquisition time. The scintigraphic acquisition of carbon particles and 81mKr was performed simultaneously in two separate windows of 140 keV (± 10%) and 186 keV (± 10%), respectively, for technetium and krypton. Except for an extension of the acquisition time per projection to 35 s, the same camera and acquisition settings were used as described above. After correction for crossover into the 140-keV window, reconstruction was performed as described above.

**Statistical Analysis**

Calculations were performed with a statistical software package (Statistica, version 5.1; StatSoft Inc; Tulsa, OK) on a personal computer.
computer (Pentium II 233 MHz processor; Intel; Santa Clara, CA; and Windows 95; Microsoft; Redmond, WA). All data are presented as the minimum to maximum (median). A p value of < 0.05 was chosen as the level of significance.

The Pearson correlation analysis was used to calculate the correlation between the ventilation distribution assessed by the two methods. In addition, EIT and SPECT data were compared using the statistical analysis method of Bland and Altman. Bias was defined by the mean differences between EIT and SPECT, and it represented the systematic error. The SD of the mean differences is considered to represent the random error variability between the two techniques. Bias ± 2 SDs was the limit of agreement of both methods.

Results

Four pigs each were ventilated in the PCV, APRV, and CPAP modes, and the median values of the PaO₂/FIO₂ ratio were 176, 197, and 212 mm Hg, respectively. Respirator settings, blood gas data, and respiratory compliance are summarized in Table 1.

Correlation of Inhaled Krypton and Nebulized Carbon Particles

A good correlation between the distributions of inhaled krypton and nebulized carbon particles was obtained, according to the following equation: VregTc = 0.97 × VregKr + 4.3 (R² = 0.98; mean Vreg, approximately 350 mL), where Vreg is registered volume, Tc is technetium, and Kr is krypton. This was considered proof that the carbon particles could be used for the subsequent comparisons between EIT and SPECT could also be use in the present pigs with oleic acid-induced pulmonary edema.

Pooled Data for Regional Ventilation Distribution

A highly significant linear correlation between regional ventilation measured by EIT and SPECT scanning was found, according to the equation y = 0.82x + 0.73 (R² = 0.92; range, 0.86 to 0.97) [Fig 2]. However, the regression coefficient was < 1.0 (p < 0.001), and we found a positive intercept (p < 0.001).

As can be seen from a Bland-Altman analysis, EIT tended to overestimate ventilation in regions that were poorly ventilated and to underestimate ventilation in well-ventilated regions (Fig 3). Thus, the magnitude of the regional ventilation affected the correlation between EIT and SPECT scanning values. However, the difference between EIT and SPECT scanning did not exceed 10% and was mostly much less than that.

Influence of Spontaneous and Mechanical Ventilation

The same correlation between EIT and SPECT data was seen whether the pigs were receiving continuous mechanical ventilation (ie, PCV) or were breathing spontaneously (ie, CPAP). A combination of mechanical and spontaneous ventilation (approximate ratio, 80:20) [ie, APRV] also resulted in a similar correlation (Fig 4). Thus, the respiratory mode had no effect on the relationship between EIT and SPECT scanning. Figure 5 shows the spatial ventilation distribution in the dorsoventral orientation (going from the sternum to the spine) of the different ventilatory modes as examined with EIT and SPECT scanning.

Influence of Lung Edema, Minute Ventilation, and PaCO₂

Since the distribution of the oleic acid-induced edema is gravity-dependent, dorsal lung regions are more severely affected than anterior regions. Therefore, an analysis was made about whether this (ie, the upper, healthier lung regions vs the lower, sicker lung regions) had an effect on the relationship between EIT and SPECT scanning, but no such effect was found (Fig 6). Moreover, the compliance of the respiratory system as well as of the EVLWI were compared with the correspondence between EIT and SPECT scanning. No correlation was found between compliance or EVLWI, either in absolute numbers or in terms of the relative change from baseline, and the difference between EIT and SPECT scanning.

Minute ventilation and PaCO₂ varied considerably between pigs, with several pigs displaying hypovo

Discussion

EIT is a noninvasive technique with the potential to monitor regional ventilation distribution. Since its introduction, the hardware and software have been improved continuously. Hahn and coworkers developed more advanced algorithms for the analysis of dynamic physiologic phenomena with low amplitudes than was initially supplied (Mark I or DAS-01P; Royal Hallamshire Hospital; Sheffield, UK). Thus, they introduced the fEIT and the averaging technique. These improvements, together with
Table 1—Results of Randomization to Various Respiratory Modes*

<table>
<thead>
<tr>
<th>Pig</th>
<th>Pig</th>
<th>PaO₂/FiO₂, mm Hg</th>
<th>PaCO₂, mm Hg</th>
<th>Airway Pressure, cm H₂O</th>
<th>Respiratory Rate, breaths/min</th>
<th>Minute Volume, L</th>
<th>Compliance, mL/cm H₂O</th>
<th>EVLWI, mL/kg/m²</th>
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<tr>
<td>PCV†</td>
<td>4</td>
<td>264</td>
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<td>40</td>
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<tr>
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<td>47</td>
<td>7.2</td>
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</table>

*BL = dynamic lung compliance at baseline; ALI = acute lung injury. NA = not applicable. Values in parentheses are for the spontaneous respiratory rate.
†Airway pressure values given as peak airway pressure and positive end-expiratory pressure.
‡Airway pressure values given as upper airway pressure level and lower airway pressure level.
§Airway pressure values given as CPAP.
other refinements of the technique, have resulted in a higher cycle rate and a better signal-to-noise ratio, which enable the system to monitor impedance changes during for example respiration. The major advantages of EIT are thereby that it is noninvasive, it is easy to use at the bedside, and data collection can be performed with a high time resolution.

**EIT vs SPECT**

The validation of the EIT technique has so far been based on correlation analysis with global parameters or on the reproduction of known physiologic phenomena or anatomic settings. A partitioning of ventilation between the right and left lung by EIT and a comparison with radionuclide scanning was performed by Kunst and coworkers. However, they needed to average 10 data collection cycles to obtain one EIT image. Although the time resolution was rather poor, they found a good correlation between the EIT and radionuclide methods for separate lungs. With the advanced hardware and software used in the present study, the technique also should be suitable for the regional analysis of...
ventilation within the lungs. We obtained an excellent linear correlation between f-EIT and ventilation scintigraphy (ie, SPECT scanning). Whether breathing was spontaneous or mechanically delivered did not affect the correlation. Moreover, we did not see any influence of the severity of lung damage in this correlation on a global level (ie, no correlation to respiratory compliance and EVLWI) and on a regional level (ie, no difference in the relationship between EIT and SPECT in dependent, more severely affected lung regions or upper, nondependent regions).

However, a regression coefficient of 0.82 and the positive intercept between SPECT scanning (independent variable) and EIT (dependent variable) showed that EIT slightly underestimated ventilation compared to SPECT scanning in rather well-ventilated regions and overestimated it in poorly ventilated areas. The difference in regional ventilation as measured by both methods was < 10%, and this is comparable to the coefficient of variation of most physiologic methods. The EIT method thus seems to be acceptable as a monitoring device in, for example, the intensive care setting. Potential causes of the measured differences between EIT and SPECT are discussed in the following paragraph.

**Linearity of EIT**

Holder and Khan determined the linear operating range of the impedance change caused by various polyacrylamide gels with different impedance char-
Characteristics. As a physiologic model, they used a saline solution-filled tank and an EIT system (APT System Mark I; IBEES; Sheffield, UK). Impedance changes increased in a linear fashion up to 20%. Impedance changes of \( \geq 20\% \) were underestimated by the EIT system. This effect may depend on the electrical properties of the EIT system \(^{27}\) or on the image reconstruction algorithm, \(^{28}\) which is the same as the one that we have used. The algorithm for image reconstruction is based on the assumptions that the object is two-dimensional and circular. Furthermore, the distribution of resistivity initially has to be uniform, the changes in resistivity should be small, and the electrodes should be spaced equally around the thorax. Nevertheless, EIT images can be acquired even if these assumptions are violated. The respiratory patterns in the present study included \( V_t \) values \( \leq 15 \) mL/kg, which confined impedance changes to a maximum of 25%. This may be the reason for the underestimation of larger regional volume changes, as seen in the present study.

Possibilities and Limitations of EIT

Value of Information: Although we calculated only 20 regions of interest from one f-EIT image, the spatial resolution allows the calculation of a maximum of 912 regions of interest per image. According to Hahn et al., \(^{29}\) the minimal detectable lung volume by EIT is in the range of 9 to 29 mL, whereas the spatial resolution using SPECT scanning is approximately 1 mL. Thus, regional ventilation of well-ventilated lung areas, which are located close to poorly or nonventilated lung regions, may be underestimated by EIT and vice versa. By measuring EIT over time, this spatial resolution combined with the time resolution of \( \leq 44 \) Hz offers the possibility of following regional ventilation. A lower sampling rate of 1 Hz is sufficient to monitor slow events like stepwise changes in lung volume during breathholding procedures. \(^{30}\) Higher sampling rates may be suitable for rapid physiologic events, like a forced expiration in spontaneously breathing subjects.

Since EIT images are generated by relatively small local impedance changes, whereas absolute impedance values may vary considerably among different subjects, EIT is most suitable for intraindividual monitoring, with each subject serving as his own reference.

Clinical Application: As it is noninvasive and easily transportable, EIT might be suitable for monitoring regional lung function in mechanically ventilated patients at the bedside. It may be used to acquire information, such as regional lung ventilation, regional distribution of \( V_t \), regional lung volume, and functional residual capacity. \(^{31}\) Furthermore, fluid accumulation, redistribution of ventilation inside the lungs, \(^{32}\) and regional compliance curves \(^{11}\) may be reconstructed from EIT data. Thus, EIT could be used, for example, to monitor atelectasis and hyperinflation during different ventilatory strategies or in opening procedures. In patients with COPD, EIT measurement of regional lung function during therapeutic interventions such as bronchodilator administration or noninvasive ventilation also might be possible. In neonates, for whom radiation exposure is undesirable, EIT potentially may replace radiographic investigations in certain situations. \(^{7}\) However, EIT should not be applied to obtain morphologic information similar to CT scanning or MRI, since the latter diagnostic methods provide anatomic information with a much higher spatial and morphologic resolution compared to EIT.

Conclusion

EIT data of regional ventilation correlated closely to ventilation distribution by SPECT scanning in a porcine, oleic acid-lung damage model. Whether breathing was spontaneous or mechanical had no effect on the relationship between EIT and SPECT scanning, and the severity of lung damage on a global scale.
or a regional level did not influence the relationship either. A slight overestimation of ventilation in well-ventilated areas and a slight underestimation in poorly ventilated areas was seen, but the difference was always <10% of ventilation measured by SPECT scanning. Thus, EIT appears to be an interesting monitoring technique for use in the intensive care setting.

**REFERENCES**