Tidal recruitment assessed by electrical impedance tomography and computed tomography in a porcine model of lung injury*

Thomas Muders, MD; Henning Luepschen, MSc, PhD; Jörg Zinserling, MSc, PhD; Susanne Greschus, MD; Rolf Fimmers, MSc; Ulf Guenther, MD; Miriam Buchwald, Daniel Grigutsch, Steffen Leonhardt, MD, PhD; Christian Putensen, MD, PhD; Hermann Wrigge, MD, PhD

Objectives: To determine the validity of electrical impedance tomography to detect and quantify the amount of tidal recruitment caused by different positive end-expiratory pressure levels in a porcine acute lung injury model.

Design: Randomized, controlled, prospective experimental study.

Setting: Academic research laboratory.

Subjects: Twelve anesthetized and mechanically ventilated pigs.

Interventions: Acute lung injury was induced by central venous oleic acid injection and abdominal hypertension in seven animals. Five healthy pigs served as control group. Animals were ventilated with positive end-expiratory pressure of 0, 5, 10, 15, 20, and 25 cm H₂O, respectively, in a randomized order.

Measurements and Main Results: At any positive end-expiratory pressure level, electrical impedance tomography was obtained during a slow inflation of 12 mL/kg of body weight. Regional-ventilation-delay indices quantifying the time until a lung region reaches a certain amount of impedance change were calculated for lung quadrants and for every single electrical impedance tomography pixel, respectively. Pixel-wise calculated regional-ventilation-delay indices were plotted in a color-coded regional-ventilation-delay map. Regional-ventilation-delay inhomogeneity that quantifies heterogeneity of ventilation time courses was evaluated by calculating the scatter of all pixel-wise calculated regional-ventilation-delay indices. End-expiratory and end-inspiratory computed tomography scans were performed at each positive end-expiratory pressure level to quantify tidal recruitment of the lung. Tidal recruitment showed a moderate inter-individual (r = .54; p < .05) and intra-individual linear correlation (r = .46 up to r = .73 and p < .05, respectively) with regional-ventilation-delay obtained from lung quadrants. Regional-ventilation-delay inhomogeneity was excellently correlated with tidal recruitment intra- (r = .90 up to r = .99 and p < .05, respectively) and inter-individually (r = .90; p < .001).

Conclusions: Regional-ventilation-delay can be noninvasively measured by electrical impedance tomography during a slow inflation of 12 mL/kg of body weight and visualized using ventilation delay maps. Our experimental data suggest that the impedance tomography-based analysis of regional-ventilation-delay inhomogeneity provides a good estimate of the amount of tidal recruitment and may be useful to individualize ventilatory settings. (Crit Care Med 2012; 40:903–911)

Key Words: acute lung injury; electrical impedance tomography; mechanical ventilation; positive end-expiratory pressure; regional ventilation delay inhomogeneity; tidal recruitment

*See also p. 1015.

From the Department of Anesthesiology and Intensive Care Medicine (TM, HL, JZ, UG, MB, DG, CP, HW), University of Bonn, Bonn, Germany; Philips Chair for Medical Information Technology (HL, SL), Helmholtz-Institute for Biomedical Engineering, RWTH Aachen University, Aachen, Germany; Department of Radiology (SG), University of Bonn, Bonn, Germany; Institute for Medical Biometry, Informatics, and Epidemiology (RF), University of Bonn, Germany; Department of Anesthesiology and Intensive Care Medicine (HW), University of Leipzig, Germany.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s Web site (http://journals.lww.com/ccmjournal).

Part of these data has been presented in form of abstracts at the ATS International Conference 2009 (San Diego) and at the EIT conference 2009 (Manchester), and in the form of an extended abstract at the IFMBE World Congress on Medical Physics and Biomedical Engineering 2009 (Munich).

Supported, in part, by a grant of the German Research Council “Deutsche Forschungsgemeinschaft,” DFG (WR47-1-1). Draeger Medical provided an EIT device and the ventilator was supplied by GE Healthcare without any restrictions. The University Hospitals of Bonn and Leipzig were supported by research funding from Draeger Medical not related to this study.

Prof. Leonhardt, Prof. Putensen, and Prof. Wrigge received honoraria/speaking fees and grants from Dräger Medical AG. These grants were not related to the currently submitted study. Further, our study was supported by the DFG granted to Prof. Wrigge. The remaining authors have not disclosed any potential conflicts of interest.

For information regarding this article, E-mail: t.muders@uni-bonn.de

Copyright © 2012 by the Society of Critical Care Medicine and Lippincott Williams & Wilkins

DOI: 10.1097/CCM.0b013e318236f452

Crit Care Med 2012 Vol. 40, No. 3

903
proved outcome (16). Thus, individual setting of PEEP appears reasonable (17, 18) and should aim to reduce tidal recruitment (15).

Whereas CT provides insights into regional aeration heterogeneities (7, 19, 20) but cannot be used at bedside, global indices of lung function such as blood gases and respiratory mechanics that are used to titrate ventilator settings do not allow conclusion of regional ventilation distribution and, hence, of regional tidal recruitment (21).

Electrical impedance tomography (EIT) of the lungs measures relative impedance changes in lung tissue during tidal breathing and creates images of the local ventilation distribution at bedside (22–33). An EIT-based index (regional-ventilation-delay [RVD]) describing the scatter of impedance time courses has recently been shown to be able to detect recruitment during a vital capacity inflation maneuver (30). In this experiment, we studied the hypotheses that RVD can be measured by EIT during a slow inflation maneuver of only 12 mL/kg of body weight (BW) and can be used to estimate the amount of tidal recruitment and its PEEP-associated changes.

**MATERIALS AND METHODS**

**Animals, Lung Injury and Ventilatory Settings.** After approval of the local animal ethics committee, 12 healthy pigs (29–35 kg) were anesthetized, tracheotomized, and instrumented in supine position as previously described (34–36). Pigs were mechanically ventilated (Engström Carestation; GE Healthcare, Helsinki, Finland) in a volume-controlled mode with a tidal volume (VT) set to 6–8 mL/kg BW, a respiratory rate of 15 min⁻¹, and PEEP of 5 cm H₂O. After preparation, ALI was induced in seven animals by intravenous injection of oleic acid (0.1 mL/kg) in combination with intra-abdominal hypertension of 20 cm H₂O caused by intraperitoneal infusion of saline (34). Five animals served as controls. Then, respiratory rate was increased up to 30 min⁻¹ to avoid hypercapnia (Paco₂ >50 torr), and FiO₂ was increased to maintain a Paco₂ of >80 torr. Intrinsic PEEP was excluded by observation of end-expiratory zero flow patterns at the ventilator.

**Measurement and Interventions.** After 3 hrs, animals were transferred to the CT scanner without interrupting ventilation. Then, PEEP was changed to 0, 5, 10, 15, 20, and 25 cm H₂O in a randomized order, whereas all other ventilatory settings remained unchanged. Lungs were derecruited (by disconnection of the respirator) and then recruited by a continuous positive airway pressure of 50 cm H₂O for 40 secs before PEEP settings were changed, respectively.

After 30 mins of ventilation on the selected PEEP level blood gases, respiratory mechanics and hemodynamics were measured (34–36). EIT measurements were performed during a single slow inflation maneuver with a constant gas flow by setting respiratory rate to 4 min⁻¹, which resulted in an inflation time of 7.5 secs and a VT of 12 mL/kg BW. Then, spiral CT scans were performed at end-expiration and end-inspiration (with a clamped tube) to measure amount of gas, nonaerated lung tissue, and regional tidal recruitment.

**EIT and CT Imaging.** An EIT system (EIT evaluation KIT II; Dräger Medical GmbH, Lübeck, Germany) was used. It reconstructs images of ventilation distribution by comparing impedance changes to a reference state applying a modified Newton-Raphson algorithm (37). Regional and global time courses of impedance changes were recorded with a temporal resolution of 20 Hz during a single slow inflation maneuver (Fig. 1). The global impedance time curve, ΔZ(t), was calculated as the sum over the impedance changes of all pixels.

RVD time (ΔtRVD) (30) was determined between the start of inspiration defined as first increase of the global ΔZ(t) curve and the time when the respective regional curve ΔZi(t) reaches a threshold of 40% of the maximal local impedance change (Fig. 24 and 2B). To address the fact that ΔtRVD depends on inflation time, it was normalized by dividing by inflation time (Δtmax–min):

\[
\text{RVD} = \frac{\Delta t_{\text{RVD}}}{\Delta t_{\text{max–min}}}
\]

Thus, RVD index describes the delay given in percent of inflation time until the respective regional impedance change exceeds a certain threshold (30). RVDs were obtained for lung quadrants (Fig. 2A) (30) and for any single EIT pixel.

A color-coded map was plotted to visualize the pixel RVD indices (Fig. 2B). To quantify RVD inhomogeneity (SDRVD), the SD over all single-pixel RVDs (Fig. 2B) was calculated after filtering and masking. A more detailed description of EIT data acquisition and processing is given in the Supplemental data (SDC-1, Supplemental Digital Content 1, http://links.lww.com/CCM/A361).

**CT Scanning and Analysis.** Spiral CT scans (120 kV, 120 mA) of the total lungs were performed during end-expiration and end-inspiration holds using a Brilliance 64 CT scanner (Philips Healthcare, Hamburg, Germany). Images were reconstructed in 8-mm slices using a standard filter.

We performed densitometric analysis of all pulmonary CT slices using a computer program (Osiris; University of Geneva, Geneva, Switzerland) as described previously (34–36). From four CT slices covering the EIT belt and from all CT slices, the amounts of hyperinflated, normally, poorly, and nonaerated lung tissue and tidal recruitment (19, 38, 39) were calculated for lung quadrants (30) and for the total lung, respectively (SDC-2 for details; Supplemental Digital Content 1, http://links.lww.com/CCM/A361).

**Statistical Analysis.** After confirming normal distribution (Shapiro-Wilk W test), data
were compared between ALI and control group (factor ALI) and between the different PEEP levels (factor PEEP) using a two-way repeated measures analysis of variance (Statistica 6.0; StatSoft, Tulsa, OK). Differences were separated by post hoc tests (Newman-Keuls test) comparing three groups of low PEEP (0 and 5 cm H₂O), moderate PEEP (10 and 15 cm H₂O), and high PEEP (20 and 25 cm H₂O) within and between groups, respectively.

Tidal recruitment (calculated from four EIT-covering CT slices as well as from total lung CT) was linearly correlated with quadrant RVD and sRDV, respectively. Linear correlations were calculated between these parameters for single animals (intra-individually) and between these parameters for all animals (inter-individually) by taking data points from all PEEP levels. Data are given as mean ± SD; p < .05 was considered significant.

RESULTS

Gas Exchange, Respiratory, and Hemodynamic Parameters

Detailed tables of cardiorespiratory and gas exchange variables are given in the Supplemental data (SDC-3, Tables S1–S3; Supplemental Digital Content 1, http://links.lww.com/CCM/A361). Briefly, PaO₂/FiO₂ was significantly higher in the control group when compared to injured pigs (p < .05) and increased significantly with higher PEEP (p < .001) (SDC-3, Fig. S3A, Supplemental Digital Content 1, http://links.lww.com/CCM/A361). Respiratory system compliance (SDC-3, Fig. S3A, Supplemental Digital Content 1, http://links.lww.com/CCM/A361) was always lower (p < .05) in ALI pigs and increased when PEEP was increased (p < .001) but decreased with highest PEEP levels in control animals (p < .001). Increasing PEEP decreased cardiac output and mean arterial blood pressure in the control group but not in the ALI group (p < .001; Table S1; Supplemental Digital Content 1, http://links.lww.com/CCM/A361).

Lung Aeration, Gas Volume, and Tidal Recruitment

In ALI animals, 52% ± 29% of the lung was nonaerated at end-expiration at zero end-expiratory pressure (Table 1). Tidal recruitment amounted 13% ± 7% of the total lung (Table 1). When PEEP was increased, end-expiratory lung volume significantly increased up to fourfold (p < .001), whereas the amount of nonaerated lung tissue and tidal recruitment decreased (p < .001, respectively; Table 1).

In control animals, end-expiratory amount of nonaerated lung tissue and tidal recruitment were much lower when compared to the ALI group (p < .05; Table 1) and not detectable at PEEP > 5 cm H₂O (p < .001; Table 1). The increase in end-expiratory lung volume paralleled PEEP (p < .001). Compared to the ALI group, end-expiratory lung volume was approximately doubled at every PEEP step (p < .001; Table 1). Hyperinflated lung tissue amounted <1% of the lungs.

RVD Index and RVD Inhomogeneity

RVD indices (Fig. 3) were higher in dependent quadrants when compared to nondependent quadrants (p < .001), and they decreased with increasing PEEP (p < .001). At higher PEEP levels, differences between dependent and nondependent quadrants were reduced. Accordingly, RVD maps (Fig. 4, fourth row) showed early aeration (i.e., low RVD values) in the nondependent and delayed aeration (i.e., high RVD values) in the dependent lung regions at low PEEP. When PEEP increased, the number of pixels with early and delayed aeration decreased. At the highest PEEP levels, all
Correlation of EIT Parameters and Tidal Recruitment

Inter-individual and intra-individual RVD indices and tidal recruitment correlated only moderately when obtained in lung quadrants (Tables 2 and 3). In contrast, for single animals, RVD inhomogeneity (measured by EIT) and the amount of tidal recruitment (calculated by CT) with changes in PEEP showed similar courses (Fig. 4). ALI pigs showed high RVD inhomogeneities when the amount of tidal recruitment was high at lower PEEP levels, but reached small RVD inhomogeneities at highest PEEP levels, when tidal recruitment was minimized. Increasing PEEP from 20 to 25 cm H₂O did not further reduce tidal recruitment and RVD inhomogeneity reached a plateau. Both parameters showed good to excellent linear within-subject correlation (Fig. 4, Table 2) and for all animals (Fig. 5B, Table 2). In control animals showing no or minimal tidal recruitment, RVD inhomogeneity was always low (Fig. 5A and 5B) and, thus, data showed a moderate but still significant correlation (Fig. 4, Table 2). At the highest PEEP levels, when tidal recruitment was comparable for control and ALI pigs (Table 1), both groups could not be further distinguished by means of RVD inhomogeneity (Fig. 5A). Calculating tidal recruitment from only four CT slices covering the EIT belt did not relevantly change these results (Table 3).

**DISCUSSION**

The main findings of our animal study are that RVD indices can be measured by EIT during a 12-mL/kg slow inflation maneuver and can be regionally visualized by RVD maps. The SD of pixel-wise-defined RVD values quantifies RVD inhomogeneity (SDRVD) that is highly linearly correlated to tidal recruitment and its PEEP-associated changes.

**Detection of Tidal Recruitment**

It is worth noting that our study was not designed to compare different strategies of PEEP titration, but rather to determine the value of EIT in measuring changes in tidal recruitment at different PEEP levels. Our data show that the amount of tidal recruitment can be reliably estimated by RVD inhomogeneity, as suggested by a good intra-individual and inter-individual linear correlation of both parameters (Table 2, Figs. 4 and 5B). When compared to global parameters of lung mechanics and gas exchange, RVD inhomogeneity was the most robust parameter quantifying tidal recruitment in our model (Table 2, Fig. 5, SDC-3 Figure S3 [Supplemental Digital Content 1, http://links.lww.com/CCM/A361]). Although measurement of lung and chest wall compliance using an esophageal pressure catheter (17) and determination of dynamic compliance (40) may be useful to individually titrate PEEP, our findings confirm the theoretical model of lung mechanics in ARDS proposed by Hickling (21), demonstrating that the presence of different opening pressures of ventilator units might remain undetected when focusing on the global pressure/volume curve only. In this respect, the method presented here seems to be fea-

---

**Table 1. Lung aeration, recruitment, and ventilation delay inhomogeneity**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>Positive End-Expiratory Pressure in [cm H₂O]</th>
<th>Analysis of Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>End-expiratory lung volume</td>
<td>Control</td>
<td>131 ± 37</td>
<td>174 ± 35</td>
</tr>
<tr>
<td>(mL)</td>
<td>ALI</td>
<td>72 ± 25</td>
<td>93 ± 32</td>
</tr>
<tr>
<td>Poorly aerated lung tissue</td>
<td>Control</td>
<td>40 ± 11</td>
<td>37 ± 10</td>
</tr>
<tr>
<td>(% lung)</td>
<td>ALI</td>
<td>37 ± 11</td>
<td>36 ± 10</td>
</tr>
<tr>
<td>Non-aerated lung tissue</td>
<td>Control</td>
<td>2 ± 1</td>
<td>2 ± 3</td>
</tr>
<tr>
<td>(% lung)</td>
<td>ALI</td>
<td>52 ± 29</td>
<td>45 ± 42</td>
</tr>
<tr>
<td>Tidal recruitment</td>
<td>Control</td>
<td>3 ± 3</td>
<td>2 ± 1</td>
</tr>
<tr>
<td>(% lung)</td>
<td>ALI</td>
<td>13 ± 7</td>
<td>12 ± 8</td>
</tr>
<tr>
<td>Hyperinflated lung tissue</td>
<td>Control</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>(% lung)</td>
<td>ALI</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>SD_RVD</td>
<td>Control</td>
<td>4 ± 1</td>
<td>5 ± 1</td>
</tr>
<tr>
<td>(% ALI)</td>
<td></td>
<td>14 ± 4</td>
<td>13 ± 5</td>
</tr>
</tbody>
</table>

ALI, acute lung injury.
possible and may complement global measurement of respiratory mechanics and gas exchange to individually improve ventilatory settings.

**Methodologic Aspects**

We have recently shown that the RVD index is able to detect lung recruitment during a vital capacity inflation maneuver (30). The present study aimed to refine this method by reducing the slow inflation time. Outlined symbols indicate control pigs; filled symbols, acute lung injury pigs. Different markers indicate different levels of PEEP: circles, 0 cm H₂O; downward triangles, 5 cm H₂O; upwards triangles, 10 cm H₂O; squares, 15 cm H₂O; diamonds, 20 cm H₂O; hexagons, 25 cm H₂O. A linear regression analysis shows mean (solid line) and 95% confidence intervals. $r$ = Pearson linear correlation coefficient. Statistics: repeated-measures analysis of variance with factors “acute lung injury” (for differences between healthy and lung-injured animals) and “PEEP” (for differences between PEEP levels). Post hoc tests (Newman-Keuls test) to separate differences between low (0 and 5 cm H₂O), moderate (10 and 15 cm H₂O), and high (20 and 25 cm H₂O) PEEP within one group (a: $p < .05$ vs. low PEEP; b: $p < .05$ vs. middle PEEP; c: $p < .05$ vs. high PEEP) and between both groups (d: $p < .05$ vs. control low PEEP; e: $p < .05$ vs. control moderate PEEP; f: $p < .05$ vs. control high PEEP). Box plots show median and quartiles.
tion breath from 40 mL/kg BW to 12 mL/kg BW to ensure feasibility of repeated RVD measurements in patients during PEEP titration. Further, we studied whether RVD measurements are suitable to estimate changes in tidal recruitment at different PEEP levels. After this modification, correlation between RVD indices and tidal recruitment was merely moderate when calculated from lung quadrants (Tables 2 and 3), because reducing inflation volume decreased the signal to be measured and thereby disproved signal-to-noise ratio of this measurement (19). Therefore, RVD inhomogeneity provides one single “global” number, it derives from a plenteous of regionally measured RVDs and thus still reflects regional information. Additionally, RVD maps may help to regionally visualize delayed alveolar aeration (Fig. 6).

The methodology used aimed at maximizing the strength of the linear relationship between tidal recruitment assessed by CT and RVD obtained from EIT. Using different thresholds or several numerical curve-fitting methods with different model functions to quantify the ventilation delay did not improve our results (SDC-5 and Table S4; Supplemental Digital Content 1, http://links.lww.com/CCM/A361).

It is important to note that EIT scans were obtained during 12 mL/kg BW slow inflation breath, whereas tidal recruitment was measured by CT during subsequent “regular” tidal volume breaths of 6–8 mL/kg BW (Fig. 1). We also calculated RVD indices and inhomogeneity from EIT signals of regular 6–8 mL/kg breaths that were recorded immediately before the slow inflation was performed (SDC-4, Supplemental Digital Content 1, http://links.lww.com/CCM/A361). These were not well-correlated with tidal recruitment, always underestimated RVD inhomogeneity when compared to slow inflation, and did not discriminate between different PEEP levels, suggesting that slow inflations with slightly increased tidal volume are required (SDC-4, Supplemental Digital Content 1, http://links.lww.com/CCM/A361). Our study aimed at the development of a diagnostic maneuver to characterize the regional mechanical behavior of the lung. Slow inflation maneuvers, however, are commonly used in respiratory mechanics with even higher inflation volumes and pressures (41). If PEEP titration using this EIT-based method will be proven in patients in the future, then a possible benefit from that may surely exceed the potential harm of a single low-flow breath with a limited inflation volume. Hence, although obtained during an artificial maneuver with different flow and inflation volume, measurement of RVD inhomogeneity delineates heterogeneity in regional lung mechanics at certain PEEP levels that, in turn, are affecting tidal recruitment during regular breaths. This regional heterogeneity may mainly reflect differences in alveolar opening pressures (21), resulting in different aeration times during slow inflation. Therefore, RVD inhomogeneity is not a direct measure of tidal recruitment, but rather a surrogate that was strongly related to tidal recruitment in our experiment.

### Table 2. Linear correlation coefficients, global lung

<table>
<thead>
<tr>
<th>Group</th>
<th>Control</th>
<th>Acute Lung Injury</th>
<th>SD&lt;sub&gt;RVD&lt;/sub&gt;</th>
<th>SD&lt;sub&gt;RVD&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadrant Regional Ventilation Delay</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inter-individually</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>0.54&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.50&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.90&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.92&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Within group</td>
<td>0.49&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.49&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 3. Linear correlation coefficients, electrical impedance tomography-covered lung region

<table>
<thead>
<tr>
<th>Group</th>
<th>Control</th>
<th>Acute Lung Injury</th>
<th>SD&lt;sub&gt;RVD&lt;/sub&gt;</th>
<th>SD&lt;sub&gt;RVD&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadrant Regional Ventilation Delay</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inter-individually</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>0.67&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0.66&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0.87&lt;sup&gt;ac&lt;/sup&gt;</td>
<td>0.88&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>Within group</td>
<td>0.55&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.66&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

<sup>a</sup> All measurements were obtained using a single-breath maneuver with different flow and inflation volume. The methodology used aimed at maximizing the strength of the linear relationship between tidal recruitment assessed by CT and RVD obtained from EIT. Using different thresholds or several numerical curve-fitting methods with different model functions to quantify the ventilation delay did not improve our results (SDC-5 and Table S4; Supplemental Digital Content 1, http://links.lww.com/CCM/A361).

<sup>b</sup> The methodology used aimed at maximizing the strength of the linear relationship between tidal recruitment assessed by CT and RVD obtained from EIT. Using different thresholds or several numerical curve-fitting methods with different model functions to quantify the ventilation delay did not improve our results (SDC-5 and Table S4; Supplemental Digital Content 1, http://links.lww.com/CCM/A361).

<sup>c</sup> The methodology used aimed at maximizing the strength of the linear relationship between tidal recruitment assessed by CT and RVD obtained from EIT. Using different thresholds or several numerical curve-fitting methods with different model functions to quantify the ventilation delay did not improve our results (SDC-5 and Table S4; Supplemental Digital Content 1, http://links.lww.com/CCM/A361).
inflection points (51) derived from groups found a large heterogeneity of or in animal models (47–50). Other lung regions were found to be described “inflation delay” in dependent standard. Victorino et al (28) already described aeration and ventilation time courses. To temporally resolve, allowing analysis of lapse (33) were quantified at different volume (25, 26, 31, 33, 44, 45), and collapse (33) were quantified at different PEEP levels.

A major advantage of EIT is its high temporal resolution, allowing analysis of aeration and ventilation time courses. To our knowledge, our study is the first focusing on regional distribution and inhomogeneity of ventilation time courses (as opposed to the amount and distribution of ventilation) to quantify tidal recruitment and the influence of different PEEP levels with EIT and CT as the gold standard. Victorino et al (28) already described “inflation delay” in dependent zones during mechanical ventilation. Regional filling characteristics of different lung regions were found to be inhomogeneous in patients with ARDS (46) or in animal models (47–50). Other groups found a large heterogeneity of inflection points (51) derived from global pressure-volume and regional pressure-impedance curves.

However, these studies are limited by several restrictions (42) because no reference methods were used (31, 44, 47, 48, 50) or because combined measurements of EIT and lung mechanics during tidal capacity maneuvers were required (33, 51). Nevertheless, our results support the findings that global parameters differ from regional impedance curves (46, 48–50).

Limitations

Our study clearly has several limitations. The EIT belt only covers a limited section of the lung. However, calculating tidal recruitment only from the EIT belt covering CT slices did not affect our results, indicating that the lung section analyzed by the EIT was representative.

Even though the oleic acid injection model of lung injury is widely used (52), as this model mimics the pathologic features of ARDS (53), comparisons with patients with ALI or ARDS should be made with caution. The amount of nonaerated lung tissue found in our animals (Table 1) was comparable to that described in a mixed population of patients with ARDS (16). The amount of recruitable lung tissue (Table 1), however, was higher in our animals, which might be explained by the increased abdominal pressure used in our model. In patients with a more focal loss of lung aeration and low potential for alveolar recruitment, regional mechanical characteristics may differ from those in our model. Reanalyzes of previously published data showed that adding a pulmonary ALI group would not expand our findings (SDC-6, Supplemental Digital Content 1, http://links.lww.com/CCM/A361). Finally, the value of our method has yet to be proven in clinical studies.

From our data, we cannot define a SDRVD value that should be targeted during PEEP titration. However, a certain RVD inhomogeneity is present in even healthy and fully recruited lungs, and clinical studies have to identify a normal range in patients. It is supposable that a predefined SDRVD number does not have to be reached, but individually minimizing this parameter might be appropriate.

Currently, a scientific debate concentrates on the possible underlying mechanisms of tidal recruitment (5–7, 54, 55), which goes far beyond the scope of this article. We have intensively discussed this issue previously (56). However, without doubt, these processes on the alveolar scale will lead to the development of ventilator-induced lung injury (1–4) and, regardless of the mechanisms involved, will lead to impaired patient outcome (16). Consequently, the quantification of tidal recruitment by EIT at the bedside may help to individualize ventilator management.

Changes in lung fluid and blood volume might also influence impedance, especially when comparing impedance information over a longer period. Our method, however, only takes tidal changes in impedance into account, minimizing the influence of fluid change (33).

In single pigs, we found RVD values of ventral regions to increase again by a further increase in PEEP (as deducible from the yellow to orange pixels in ventral regions at higher PEEP levels; Fig. 4, third row). Higher RVD values may also result from delayed filling attributable to alveolar hyperdistention that is also supposed to cause ventilator-associated lung injury. Even though the current use of CT in detecting hyperdistention might be matter of discussion (SDC-2, Supplemental Digital Content 1, http://links.lww.com/CCM/A361) (57), we did not observe CT
densities <−900, which should represent hyperinflated regions; thus, based on our data, we were unable to systematically examine this phenomenon. Therefore, conclusions have to be restricted to detection of tidal recruitment. However, it recently has been shown that the benefit of reducing tidal recruitment by increasing PEEP prevails over the effect of increasing alveolar strain in patients with high lung recruitability (16), suggesting that minimizing cyclic tidal recruitment is a critical matter.

CONCLUSION

In conclusion, our study suggests that analyzing the scatter of aeration times of regional ventilation during a slow inflation maneuver as measured by EIT allows assessing temporal inhomogeneity of tidal ventilation. Delayed regional aeration as measured by EIT allows analyzing the scatter of aeration times of tidal ventilation. However, higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. A randomized controlled trial. JAMA 2008; 299: 637–645.


We thank Dr. Dirk Varelmann, Boston, MA, and Dr. Andreas Reske, Leipzig, Germany, for their helpful review of the manuscript and stimulating discussions.

REFERENCES


