Efficacy of Different Recruitment Maneuvers for Improved Lung Inhomogeneity in a Pig Model of ARDS

CURRENT STATUS: UNDER REVISION

Feiping Xia
Southeast University

Chun Pan
Southeast University Zhongda Hospital

Lihui Wang
Southeast University

Ling Liu
Southeast University Zhongda Hospital

Songqiao Liu
Southeast University Zhongda Hospital

Fengmei Guo
Southeast University Zhongda Hospital

Yi Yang
Southeast University Zhongda Hospital

Yingzi Huang
Southeast University Zhongda Hospital

yz_huang@126.com Corresponding Author

DOI:
10.21203/rs.2.21361/v1

SUBJECT AREAS
Anesthesiology & Pain Medicine

KEYWORDS
electrical impedance tomography, global inhomogeneity, acute respiratory distress syndrome
Abstract
Background: In acute respiratory distress syndrome (ARDS), lung recruitment maneuvers can recruit collapsed alveoli in gravity-dependent lung regions, improving the homogeneity of ventilation distribution. This study used electrical impedance tomography (EIT) to investigate the efficacy of different recruitment maneuvers for alveolar recruitment in a pig model of ARDS.

Methods: ARDS was induced in ten healthy male pigs with repeated bronchoalveolar lavage until the arterial partial pressure of oxygen (PaO₂) /fraction of inspired oxygen (FiO₂) (P/F ratio) was < 100 mmHg and remained stable for 30 minutes (TARDS). ARDS pigs underwent three sequential recruitment maneuvers, including sustained inflation (SI), increments of positive end-expiratory pressure (PEEP) (IP), and pressure-controlled ventilation (PCV) applied in random order, with 30 mins at a PEEP of 5 cmH₂O between maneuvers. Respiratory mechanics, hemodynamics, arterial blood gas, and EIT were recorded at baseline, TARDS, and before and after each recruitment maneuver.

Results: In all ten pigs, ARDS was successfully induced with a mean 2.8±1.03 (2800±1032.80ml) bronchoalveolar lavages. PaO₂, SO₂, P/F, and compliance were significantly improved after recruitment with SI, IP or PCV (all p<0.05), and there were no significant differences between maneuvers. Global inhomogeneity (GI) was significantly decreased after recruitment with SI, IP, or PCV. There were no significant differences in GI before or after recruitment with the different maneuvers. The decrease in GI (ΔGI) was significantly greater after recruitment with IP compared to SI (p=0.023), but there was no significant difference in ΔGI between IP and PCV.

Conclusion: SI, IP, and PCV increased oxygenation, regional compliance and lung compliance, and decreased inhomogeneous gas distribution with no adverse effects on hemodynamics in ARDS pigs. IP significantly improved inhomogeneity of the lung compared to SI.

Background
Acute respiratory distress syndrome (ARDS) is a clinical syndrome characterized by a decrease in functional lung size¹. The pathophysiology of ARDS includes diffuse alveolar collapse³ and acute exudative lesions distributed in a gravitationally dependent gradient⁴. Although this disease was first defined almost 50 years ago, the hospital mortality rate for patients with severe ARDS remains high,
estimated at 46%. 

Lung recruitment maneuvers, including sustained inflation (SI), increments of positive end-expiratory pressure (PEEP) (IP), and pressure-controlled ventilation (PCV), can improve oxygenation and increase lung compliance in patients with ARDS. Recruitment maneuvers can recruit collapsed alveoli in gravity-dependent lung regions and improve the homogeneity of ventilation distribution, but may cause alveolar overdistention and lead to ventilator-associated lung injury in non-dependent regions. A randomized controlled trial showed that SI and PCV improved the arterial partial pressure of oxygen (\(\text{PaO}_2\))/fraction of inspired oxygen (\(\text{FiO}_2\)) (P/F ratio) in 40 patients with ARDS, and the P/F was significantly increased after PCV compared to SI. However, dynamic regional information on changes in lung ventilation after recruitment maneuvers has not been reported.

Recruitment and overdistention during lung recruitment have been evaluated by chest X-ray, computed tomography, and lung ultrasound. Electrical impedance tomography (EIT) is a non-invasive, radiation-free technique that can be used for bedside monitoring of lung tissue aeration during breathing. EIT allows semi-continuous, real-time measurement of changes in electrical resistivity within lung tissue and provides information on regional ventilation distributions. Domenighetti reported that EIT can be used to measure impedance changes and assess regional ventilation distribution during tidal breathing. The EIT-based global inhomogeneity (GI) index has been developed as a tool to quantify tidal volume distribution within the lung.

Previous research has focused on the effect of recruitment maneuvers on gas exchange and hemodynamics. To the authors’ knowledge, no study has explored the influence of recruitment maneuvers on regional ventilation distribution. This study used EIT to investigate the efficacy of different recruitment maneuvers that achieve the same maximum pressure for alveolar recruitment in a ARDS porcine model, excluding a possible risk of barotrauma for ARDS individuals.

Methods

The protocol for this study was approved by the Science and Technological Committee and the Animal Use and Care Committee of the University School of Medicine, Nanjing, China. The domestic pigs (Sus
scrofa domesticus) were purchased from a local farmer (Qinglongshan animal breeding farm, JiangShu, China). Animal experiments were performed in accordance with the Guidance for the Care and Use of Laboratory Animals\textsuperscript{11}.

Animal Preparation

The pigs housed on straw in cage were fed with standard diet. Prior to the study, the animals were fasted overnight, and premedication was conducted under intramuscular injection of ketamine hydrochloride (3 mg/kg), atropine (2 mg/kg) and fentanyl citrate (2 mg/kg) and an intravenous infusion of propofol (1-2 mg/kg·h), fentanyl citrate (0.5-1 μg/kg·h), midazolam (0.1 mg/kg·h), and atracurium (0.4 mg/kg·h). Ten healthy male pigs (body weight 50.3±1.5 kg) were placed in the supine position on a thermo-regulated operating table after being anesthetized with an intramuscular and an intravenous infusion. During surgery, pigs received balanced electrolyte solution (5 ml/kg/h), pigs’ body temperature was maintained at 37.5°C, and pigs’ mean arterial pressure (MAP) was maintained > 60 mmHg with rapid infusions of 0.9% saline (20 ml/kg), as needed.

Following anesthesia, tracheotomy was performed, and pigs were mechanically ventilated (Servo-i ventilator, Solna, Sweden) using volume-control mode at a tidal volume (VT) of 6 mL/kg, a respiratory rate of 30 breaths/min, FiO\textsubscript{2} of 1.0, a inspiration-to-expiration time ratio (I:E) of 1:2, and PEEP of 5 cmH\textsubscript{2}O. Cardiac output (CO) and MAP were monitored, and arterial blood samples were collected using a thermistor-tipped PiCCO catheter (Pulsion Medical System, Munich, Germany) inserted in the right femoral artery. Central venous pressure (CVP) and pulmonary arterial wedge pressure (PAWP) were measured using a Swan–Ganz catheter (Arrow International, Reading, PA, USA) inserted in the internal jugular vein.

Experiment Protocol

Baseline measurements (TBaseline) were made after pigs had stabilized for 30 minutes. Subsequently, a pig model of ARDS was established using bilateral lung lavage with isotonic saline (30 ml/kg; 38°C) infused through a funnel. Negative pressure was applied to the proximal portion of an endotracheal tube to remove excessive fluid. Alveolar lavage was repeated every 10 min until the
P/F ratio decreased to < 100 mmHg and remained stable for 30 min (TARDS).

ARDS pigs underwent three sequential recruitment maneuvers, including SI, IP and PCV applied in random order according to a random number table, with 30 mins at a PEEP of 5 cmH₂O between maneuvers (Figure 1). SI was performed using continuous positive airway pressure (CPAP) held at 40 cmH₂O for 40 secs\(^1\). For IP, PEEP was increased from 5 cmH₂O to a maximum of 40 cmH₂O in 5 cmH₂O increments, with each increment lasting 30 secs, and retuned to 5 cmH₂O in the reverse process. For PCV, peak pressure was 40 cmH₂O, inspiratory to expiratory ratio was 1:2, and PEEP was 20 cmH₂O for 2 min. Respiratory mechanics, hemodynamic parameters, arterial blood gas, and EIT were recorded at TBaseline, TARDS, and before and after each recruitment maneuver. MAP, CVP, and PAWP were monitored using calibrated pressure transducers. Blood gases were evaluated with an automated blood gas analyser (Nova M; Nova Biomedical, Waltham, MA, USA).

EIT Measurements and Analysis

EIT measurements (PulmoVista 500; Dräger Medical GmbH, Lübeck, Germany) were performed for 3 minutes each at TBaseline, TARDS, and before and after each recruitment maneuver as previously described\(^1\)\(^3\). EIT data were generated by applying small alternate electrical currents through 16 electrodes located equidistant apart on a belt positioned around the pigs’ thorax, 5cm above the xyphoid process. A reference electrocardiogram (ECG) electrode was positioned on the abdomen. Current applications and voltage measurements were automaticity selected to be compatible with the image reconstruction algorithm. The images were continuously recorded and reconstructed at 40 Hz (Draeger EIT Data Analysis Tool 61).

Four regions of interests (ROI) of the same size and shape consisting of contiguous pixels were identified within EIT images obtained during tidal breathing.\(^1\)\(^4\) Tidal volume distribution within the lung was quantified using the GI, as previously described.\(^1\)\(^5\) For each breathing cycle, the median value of a tidal image, in which each pixel represented the difference in impedance between end-inspiration and end-expiration, was calculated. The absolute difference between the median value
and every pixel value was summed to indicate the variation in the tidal volume distribution. The GI index was adjusted by normalization to the sum of the impedance values. A smaller GI index represented a more homogeneous distribution, and a larger GI index indicated a more inhomogeneous ventilation. Change in GI (ΔGI) with each recruitment maneuver was calculated as the difference in GI before and after recruitment.

General anesthesia was maintained to prevent suffering during the study. After completion of the medical experiments, the animals were euthanized in deep anesthesia by an intravenous injection of thiopental.

Statistical Analyses

Statistical analyses were performed using SPSS v20 (Chicago, IL, USA). Differences in global inhomogeneity and changes in global and regional end-expiratory lung impedance among different recruitment maneuvers were investigated. Comparisons were made between values obtained before and after each recruitment maneuver. For non-normally distributed data, results are expressed as median and interquartile range, and comparisons were made with the Wilcoxon rank test. For data that was normally distributed, results are expressed as mean and standard deviation, and comparisons were made with paired samples t tests and Bonferroni correction. p < 0.05 was considered statistically significant.

Results

In all ten pigs, ARDS was successfully induced with a mean 2.8±1.03 (2800±1032.80ml) bronchoalveolar lavages. Mean P/F was significantly decreased after the final lavage (81.69±55.79mmHg) compared to baseline (362.48±117.38mmHg). The recruitment maneuvers did not cause hemodynamic instability, and there were no significant differences in hemodynamic parameters during recruitment with the different maneuvers. No animals died during the experiments.

PaO₂, SO₂, and P/F were significantly improved after recruitment with SI, IP or PCV (all p<0.05), and there were no significant differences between maneuvers. The recruitment maneuvers had no obvious
effect on PaCO₂ and pH (Table 1).

Overall lung compliance was significantly increased after recruitment with SI, IP, or PCV (p< 0.05) (Table 1). The recruitment maneuvers had no obvious effect on compliance in non-gravity-dependent lung regions. Compliance was significantly increased in gravity-dependent lung regions after lung recruitment with IP or PCV, and there were no significant differences between maneuvers (Figure 2).

GI was significantly decreased after recruitment with SI, IP, or PCV (GIpreSI 0.55±0.14u vs. GIpostSI 0.42±0.040; GIpreIP 0.62±0.19u vs. GIpostIP 0.42±0.07u; GIprePCV 0.60±0.09u vs. GIpostPCV 0.4431±0.05u; all p<0.001) (Figure 3). There were no significant differences in GI before or after recruitment with the different maneuvers. The decrease in GI (ΔGI) was significantly greater after recruitment with IP compared to SI (p=0.023), but there was no significant difference in ΔGI between IP and PCV (Figure 4).

Discussion
This study used EIT to investigate the efficacy of different recruitment maneuvers that achieve the same maximum pressure, including SI, IP and PCV, for alveolar recruitment in a pig model of ARDS. Findings showed that these recruitment maneuvers increased oxygenation and overall and regional compliance, and decreased inhomogeneous gas distribution in the ARDS lung, with no adverse effects on hemodynamics.

Patients with ARDS can suffer from inhomogeneous gas distribution, which leads to ventilation-perfusion mismatching, a high dead-space fraction, and the potential for ventilator-induced lung injury (VILI). Recruitment maneuvers open collapsed alveoli and improve oxygenation and lung compliance. However, recruitment maneuvers can over-distend aerated alveoli, and ventilation at high inflation pressures can lead to VILI.

Heterogeneous lung structure (i.e, collapsed and overexpanded contiguous lung regions) is increasingly recognized as a key factor for inhomogeneous gas distribution, VILI, and mortality in mechanically ventilated patients. Recent studies showed that the extent of lung inhomogeneities
increase with the severity of ARDS\textsuperscript{20}, and a protective ventilatory strategy may not be sufficient to minimize VILI in patients with ARDS whose disease process is characterized by an inhomogeneous distribution of pulmonary lesions that includes a small, nondependent, normally aerated compartment and a large, dependent, nonaerated compartment\textsuperscript{21,22}.

In the present study, the inhomogeneous distribution of lung alterations in the pig model of ARDS was directly assessed using EIT. EIT has several advantages compared to established imaging techniques such as CT as it is radiation free and applicable at the bedside. In previous studies, Zhao\textsuperscript{15} et al developed the global inhomogeneity index to quantify the spatial extent and dispersion in the distribution of tidal breath. A tidal EIT image is generated and variations in pixel values are used as an indicator of the inhomogeneity of air distribution during tidal ventilation\textsuperscript{15}. In the present study, we used the GI index as a direct representation of global inhomogeneity in tidal ventilation in ARDS pigs.

We assessed the change in inhomogeneity (ΔGI) with various recruitment maneuvers. We showed that recruitment maneuvers were able to decrease the spatial inhomogeneity of ventilation, possibly because of their unique ability to couple regional recruitment with preserved diaphragm activity, both of which are able to increase homogeneity of ventilation\textsuperscript{14,23,24}. Previous studies have shown different recruitment maneuvers are associated with differences in oxygenation, lung compliance, hyperinflation, and hemodynamics\textsuperscript{16,17,18,25}. However, a ventilation strategy with aggressive lung recruitment may increase mortality in patients with ARDS\textsuperscript{26}. The present study showed that IP significantly improved inhomogeneity of the lung compared to SI and PCV in ARDS pigs. These data suggest that evaluating the effect of recruitment maneuvers with EIT could play a role in minimizing VILI.

Our study was associated with several limitations. First maximal recruitment of the lung was not achieved with any maneuver. A peak pressure of 40 cmH\textsubscript{2}O may not have been sufficient for opening certain alveoli in ARDS pigs. Borges\textsuperscript{27} et al. reported that when PEEP was set to 25 cm H\textsubscript{2}O in patients with ARDS, producing peak airway pressures of 40 cm H\textsubscript{2}O, lung recruitment was approximately 67%.
When peak airway pressures of 60 cm H$_2$O were reached, lung recruitment was approximately 87%.

Failure to achieve maximal recruitment of the lung would affect monitoring of end-expiratory lung impedance. Second, the relative impedance changes monitored by EIT may have been affected by cardiac movement and errors in the reconstruction algorithm. Last, the duration of the recruitment maneuvers may have been too short to recruit the majority of the alveoli.

Conclusions
This study used EIT to show that different recruitment maneuvers that achieve the same maximum pressure, including SI, IP, and PCV, increased oxygenation and overall and regional compliance, and decreased inhomogeneous gas distribution with no adverse effects on hemodynamics in ARDS pigs. IP significantly improved inhomogeneity of the lung compared to SI and PCV. Further studies are needed to confirm the clinical significance of these findings.

Abbreviations
ARDS: acute respiratory distress syndrome; EIT: electrical impedance tomography; PaO2: arterial partial pressure of oxygen; FiO2: fraction of inspired oxygen; P/F ratio: arterial partial pressure of oxygen /fraction of inspired oxygen; SI: sustained inflation; PEEP: positive end-expiratory pressure; IP: increments of positive end-expiratory pressure; PCV: pressure-controlled ventilation; GI: Global inhomogeneity; ΔGI: decrease in GI; MAP: mean arterial pressure; VT: tidal volume; I:E: inspiration-to-expiration time ratio; CO: Cardiac output; CVP: Central venous pressure; PAWP: pulmonary arterial wedge pressure; TBaseline: Baseline measurements; TARDS: remained stable for 30 min; CPAP: continuous positive airway pressure; ECG: electrocardiogram; ROI: regions of interests; VILI: ventilator-induced lung injury

Declarations
Acknowledgments
We thank the Critical Care Institute for Laboratory Animal Science, Southeast University School of Medicine, Nanjing, namely Prof. Songqiao Liu, Dr. Qing Sun and Li Tan. We thank Prof. Songqiao Liu
for his financial support.

Funding
A grant (81370180, Beijing, China) from the National Natural Science Foundation of China. The funding bodies had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Availability of data and materials
The datasets used during the current study are available from the corresponding author on reasonable request.

Authors’ contributions
XFP was responsible for conception and design of the study; acquisition, analysis and interpretation of data; and drafting and revising the article for final approval before publication. PC and WLH was responsible for design of the study; acquisition and analysis of data; and revising the article. LL and LSQ participated in data analysis and interpretation of the results. GFM participated in interpretation of the results and writing the article. YY participated in data analysis; interpretation of the results; and writing the article. HYZ was responsible for the conception and design of the study; analysis and interpretation of data; drafting and revising the article, providing important intellectual content; and final approval before publication. All authors read and approved the manuscript.

Ethics approval
The study was approved by the Science and Technological Committee and the Animal Use and Care Committee of the Southeast University School of Medicine, Nanjing, China.

Consent for publication
Not applicable.
Competing interests

The authors declare that they have no competing interests

References

1. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. Lancet 1967;2(7511):319-323.

2. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, Patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA 2016;315(8):788-800.

3. Gattinoni L, Mascheroni D, Torresin A, Marcolin R, Fumagalli R, Vesconi S, et al. Morphological response to positive end expiratory pressure in acute respiratory failure. Computerized tomography study. Intensive Care Med 1986;12(3):137–142.

4. Pelosi P, D'Andrea L, Vitale G, Pesenti A, Gattinoni L. Vertical gradient of regional lung inflation in adult respiratory distress syndrome. Am J Respir Crit Care Med 1994;149(1):8-13.

5. Meier T, Luepschen H, Karsten J, Leibecke T, Grossherr M, Gehring H, et al. Assessment of regional lung recruitment and derecruitment during a PEEP trial based on electrical impedance tomography. Intensive Care Med 2008;34(3):543-550.

6. Iannuzzi M, De Sio A, De Robertis E, Piazza O, Servillo G, Tufano R. Different patterns of lung recruitment maneuvers in primary acute respiratory distress syndrome: effects on oxygenation and central hemodynamics. Minerva Anestesiologica 2010;76(9):692-698.

7. Frerichs I. Electrical impedance tomography (EIT) in applications related to lung and ventilation: a review of experimental and clinical activities. Physiol Meas
8. Nopp P, Rapp E, Pfützner H, Nakesch H, Ruhsam C. Dielectric properties of lung tissue as a function of air content. Phys Med Biol 1993;38(6):699-716.

9. Domenighetti G, Maggiorini M. Electrical impedance tomography to guide ventilation in ALI-ARDS patients: a research tool for zealous physiologists or an imminent support for the real world intensivist? Minerva Anestesiol 2010;76(12):986-988.

10. Zhao Z, Pulletz S, Frerichs I, Müller-Lisse U, Möller K. The EIT-based global inhomogeneity index is highly correlated with regional lung opening in patients with acute respiratory distress syndrome. BMC Res Notes 2014;7: 82-88.

11. Garber J C. Guide for the Care and Use of Laboratory Animals. National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. 2011. 8th edition. Washington (DC); National Academies Press (US). 11-154.

12. David M, Karmrodt J, Bletz C, David S, Herweling A, Kauczor HU, et al. Analysis of atelectasis, ventilated, and hyperinflated lung during mechanical ventilation by dynamic CT. Chest 2005; 128(5):3757-3770.

13. van der Burg PS, Miedema M, de Jongh FH, Frerichs I, van Kaam AH. Cross-sectional changes in lung volume measured by electrical impedance tomography are representative for the whole lung in ventilated preterm infants. Crit Care Med 2014;42(6):1524-1530.

14. Mauri T, Bellani G, Confalonieri A, Tagliabue P, Turella M, Coppadoro A, et al. Topographic distribution of tidal ventilation in acute respiratory distress syndrome: Effects of positive end-expiratory pressure and pressure support. Crit Care Med 2013;41(7):1664-1673.

15. Zhao Z, Möller K, Steinmann D, Frerichs I, Guttmann J. Evaluation of an electrical
impedance tomography-based global inhomogeneity index for pulmonary ventilation
distribution. Intensive Care Med 2009;35(11):1900-1906.

16. Santos RS, Moraes L, Samary CS, Santos CL, Ramos MB, Vasconcellos AP, et al. Fast
versus slow recruitment maneuver at different degrees of acute lung inflammation
induced by experimental sepsis. Anesth Analg 2016;122(4):1089-100.

17. Odenstedt H, Lindgren S, Olegård C, Erlandsson K, Lethvall S, Aneman A, et Slow
moderate pressure recruitment maneuver minimizes negative circulatory and lung
mechanic side effects: evaluation of recruitment maneuvers using electric impedance
tomography. Intensive Care Med 2005;31(12):1706-1714.

18. Richard JC, Maggiore SM, Jonson B, Mancebo J, Lemaire F, Brochard L. Influence of
tidal volume on alveolar recruitment respective role of peep and a recruitment
aneuver. Am J Respir Crit Care Med. 2001;163(7):1609-1613.

19. Mead J, Takishima T, Leith D. Stress distribution in lungs: A model of pulmonary
elasticity. J Appl Physiol 1970;28(5):596-608.

20. Cressoni M, Cadringher P, Chiurazzi C, Amini M, Gallazzi E, Marino A, et al. Lung
inhomogeneity in patients with acute respiratory distress syndrome. Am J Respir Crit
Care Med 2014;189(2):149-158.

21. Bellani G, Guerra L, Musch G, Zanella A, Patroniti N, et al. Lung regional metabolic
activity and gas volume changes induced by tidal ventilation in patients with acute
lung injury. Am J Respir Crit Care Med 2011;183(9):1193-1199.

22. Terragni PP, Rosboch G, Tealdi A, Corno E, Menaldo E, Davini O, et al. Tidal
hyperinflation during low tidal volume ventilation in acute respiratory distress
syndrome. Am J Respir Crit Care Med 2007;175(2):160-166.

23. Blankman P, Van Der Kreeft SM, Gommers D. Tidal ventilation distribution during
pressure-controlled ventilation and pressure support ventilation in post-cardiac
surgery patients. Acta Anaesthesiol Scand 2014;58(8):997-1006.

24. Halter JM, Steinberg JM, Schiller HJ, DaSilva M, Gatto LA, Landas S, et al. Positive End-Expiratory Pressure after a Recruitment Maneuver Prevents Both Alveolar Collapse and Recruitment /Derecruitment. Am J Respir Crit Care Med 2003;167(12):1620-1626.

25. Kheir JN, Walsh BK, Smallwood CD, Rettig JS, Thompson JE, Gómez-Laberge C, et al. Comparison of 2 lung recruitment strategies in children with acute lung injury. Respir Care 2013;58(8):1280-1290.

26. Cavalcanti AB, Suzumura ÉA, Laranjeira LN, Paisani DM, Damiani LP, Guimarães HP, et al. Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. JAMA 2017;318(14):1335-1345.

27. Borges JB, Okamoto VN, Matos GF, Caramez MP, Arantes PR, Barros F, et al. Reversibility of lung collapse and hypoxemia in early acute respiratory distress syndrome. Am J Respir Crit Care Med 2006;174(3):268-278.

Tables
Table 1 Hemodynamic parameters and oxygenation with recruitment
|                | SI                      | IP                      | p   | SI                      | IP                      | p   |
|----------------|-------------------------|-------------------------|-----|-------------------------|-------------------------|-----|
| HR (BPM)       | 89.1±25.32              | 97.5±31.17              | 0.517 | 90.4±39.40             | 96.9±46.84              | 0.951 |
| MAP (mmHg)     | 102.1±23.14             | 92.7±17.71              | 0.321 | 109.2±19.00            | 96.8±23.93              | 0.452 |
| CVP (mmHg)     | 7.62±3.37               | 8.81±3.12               | 0.420 | 7.45±2.91              | 9.10±4.72               | 0.526 |
| PAWP (mmHg)    | 8.81±4.94               | 10.72±4.40              | 0.376 | 9.34±4.08              | 11.62±4.88              | 0.346 |
| CO (L/min)     | 4.74±1.55               | 4.45±1.35               | 0.664 | 4.74±2.11              | 4.46±1.63               | 0.736 |
| PH             | 7.28±0.12               | 7.29±0.12               | 0.95  | 7.27±0.13              | 7.30±0.12               | 0.62  |
| PaCO2 (mmHg)   | 52.56±13.82             | 48.24±13.20             | 0.484 | 55.82±17.49            | 45.94±13.82             | 0.201 |
| PaO2 (mmHg)    | 81.62±22.36             | 145.83±26.86<sup>a</sup> | 0.000 | 78.22±24.28            | 167.98±36.85<sup>a</sup> | 0.000 |
| SO₂            | 86.77±8.28              | 96.46±2.05<sup>a</sup>  | 0.002 | 84.91±8.25             | 97.57±1.96<sup>a</sup>  | 0.000 |
| P/F (mmHg)     | 81.62±22.36             | 145.83±26.86<sup>a</sup> | 0.000 | 78.22±24.28            | 167.98±36.85<sup>a</sup> | 0.000 |
| Cr (ml/cmH2O)  | 13.34±3.66              | 24.26±8.00<sup>a</sup>  | 0.001 | 12.88±3.20             | 27.51±7.99<sup>a</sup>  | 0.000 |
| HCO3-(mmol/L)  | 24.13±2.99              | 23.02±3.25              | 0.437 | 24.8±3.73              | 22.08±3.79              | 0.14  |

HR, heart rate; MAP, mean arterial pressure; CVP, central venous pressure; PAWP, pulmonary artery wedge pressure; CO, cardiac output; SI, sustained inflation; IP, increments of PEEP; PCV, pressure-controlled ventilation

<sup>a</sup> Significantly different versus Before
Flowchart of study design. ARDS pigs underwent three sequential recruitment maneuvers applied in random order according to a random number table, with 30 mins at a PEEP of 5 cmH2O between maneuvers. Respiratory mechanics, hemodynamic parameters, arterial blood gas and EIT were recorded at TBaseline, TARDS, and before and after each recruitment maneuver.

Figure 2

Compliance in non-gravity-dependent (A) and gravity-dependent (B) lung regions. ap<0.05, comparison between before and after recruitment maneuver SI, sustained inflation; IP, increments of PEEP; PCV, pressure-controlled ventilation.
EIT-based global inhomogeneity (GI) index with recruitment A: SI; B: IP; C: PCV. Recruitment maneuvers were performed in the same pig SI, sustained inflation; IP, increments of PEEP; PCV, pressure-controlled ventilation

Figure 3

Change in EIT-based global inhomogeneity (GI) index with recruitment *p<0.05 SI vs. IP

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.
NC3Rs ARRIVE Guidelines Checklist 2014.docx