EXPERIMENTAL

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Multislice spiral computed tomography to determine the effects of a recruitment maneuver in experimental lung injury

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Abstract Although recruitment of atelectatic lung is a common aim in acute respiratory distress syndrome (ARDS), the effects of a recruitment maneuver have not been assessed quantitatively. By multislice spiral CT (MSCT), we analyzed the changes in lung volumes calculated from the changes in the CT-values of hyperinflated (V_{HYP}), normally (V_{NORM}), poorly (V_{POOR}) and nonaerated (V_{NON}) lung in 8 mechanically ventilated pigs with saline lavage induced acute lung injury before and after a recruitment maneuver. This was compared to single slice analysis near the diaphragm. The increase in aerated lung was mainly for V_{POOR} and the less in V_{NORM}. Total lung volume and intrathoracic gas increased. No differences were found for tidal volumes measured by spirometry or determined by CT. The inspiratory-expiratory volume differences were not different after the recruitment maneuver in V_{NON} (from 62±18 ml to 43±26 ml, p=0.114), and in V_{NORM} (from 216± 51 ml to 251±37 ml, p=0.102). Single slice analysis significantly underestimated the increase in normally and poorly aerated lung. Quantitative analysis of lung volumes by whole lung MSCT revealed the increase of poorly aerated lung as the main mechanism of a standard recruitment maneuver. MSCT can provide additional information as compared to single slice CT.

Keywords Acute respiratory distress syndrome · Acute lung injury · Diagnosis · Recruitment · Computed tomography · Measurement

Introduction

In acute lung injury (ALI) and in the acute respiratory distress syndrome (ARDS) severe impairment of oxygenation is caused by an inhomogenous ventilation-perfusion $\dot{V}_A/\dot{Q}$ distribution and an increase in shunt fraction resulting from atelectasis formation. The amount of aerated lung is markedly reduced due to alveolar collapse and flooding [1, 2], which is found predominately in the dependent parts of the lungs [1, 3]. Mechanical ventilation has been shown to further aggravate the $\dot{V}_A/\dot{Q}$ mismatch [4]. One of the commonly used treatment concepts in such situations is to open up atelectasis, aiming at recruitment and maintenance of ventilated lung volume to improve oxygenation[5].

Although significant controversy exists over the optimal maneuver to achieve alveolar recruitment, no gold standard exists as how to measure the success of such a maneuver. Computed tomography (CT) has been used to detect recruitment [6] with the distributions of the CT-values as measured in Hounsfield units (HU) assigned to lung tissue ventilation [7]. In these early studies, only single slices had been analyzed and the results were extrapolated to the whole lung. This had been demonstrated to be unreliable due to the uneven distribution of aerated and nonaerated lung from apical to basal [8]. Therefore, images of the whole lung by multiple exposures have been evaluated for this purpose [9–11]. Recruitment was assessed by the increase of intrathoracic gas and by histograms showing CT-value distributions. However, long exposure times

with a single slice CT scanner and gross calculation of differently aerated lung volumes have prevented subtle analysis in the quantitative distribution of ventilation volumes for transition into clinical practice [9]. The aim of this study was to investigate, whether the effects of a standard recruitment maneuver on the volumes of differently aerated lung parenchyma in acute lung injury could be determined more easily and faster by use of a multislice CT scanner in static conditions of acute lung injury.

Materials and methods

After governmental approval, eight anesthetized and paralyzed female pigs (31.3±1.9 kg) were orotracheally intubated and ventilated in constant flow mode with an inspiratory oxygen concentration (FiO_2) of 100%, a tidal volume of 8 ml/kg and a positive end-expiratory pressure (PEEP) of 10 cmH_2O throughout the study. Handling of animals conferred to the guidelines laid out in the Guide for the Care and Use of Laboratory Animals [12]. Anesthesia was maintained with continuous infusions of propofol (Fresenius Kabi, Bad Homburg, Germany), fentanyl (Janssen-Cilag, Neuss, Germany) and pancuronium (Schwabe-Curamed, Karlsruhe, Germany) and a continuous infusion of Ringer's solution maintained at 5 ml/kg h^{-1}.

Gas flow and airway pressure were measured between the tracheal tube and the Y-piece of the ventilator circuit by a membrane differential pressure transducer, connected to the ventilator (Galileo Gold, Hamilton Medical, Rhäzüns, CH, accuracy ±5%). Tidal volume (V_T) was derived from the integrated flow signal. Expiratory volumes were corrected as proposed by Jonson et al [13].

Experimental protocol

Acute lung injury was induced through repeated lavages with saline warmed to 38°C and allowed to stabilize until the PaO_2 was constantly below 13,3 kPa for 60 min [14]. Afterwards, the animals were placed supine on the CT table and MSCT was performed during end-expiratory and end-inspiratory breath-hold of approximately 5.5 sec [1, 15]. Between scans tidal ventilation was resumed for 30 seconds. Then the actual recruitment maneuver was performed by inflating the lungs three times with a pressure of 45 cmH_2O for 40 seconds [7, 16–18] ,with 10 normal tidal breaths in-between inflations. Fifteen minutes after the recruitment maneuver a second set of MSCT scans was obtained. After the experiment the animals were killed with a barbiturate overdose.

Fig. 1 One exemplary slice near the diaphragma of a pig with saline lavage induced acute lung injury. Upper panel (**a**): before the recruitment maneuver and Lower panel (**b**): after the recruitment maneuver. I: inspiratory breath hold; E: expiratory breath hold
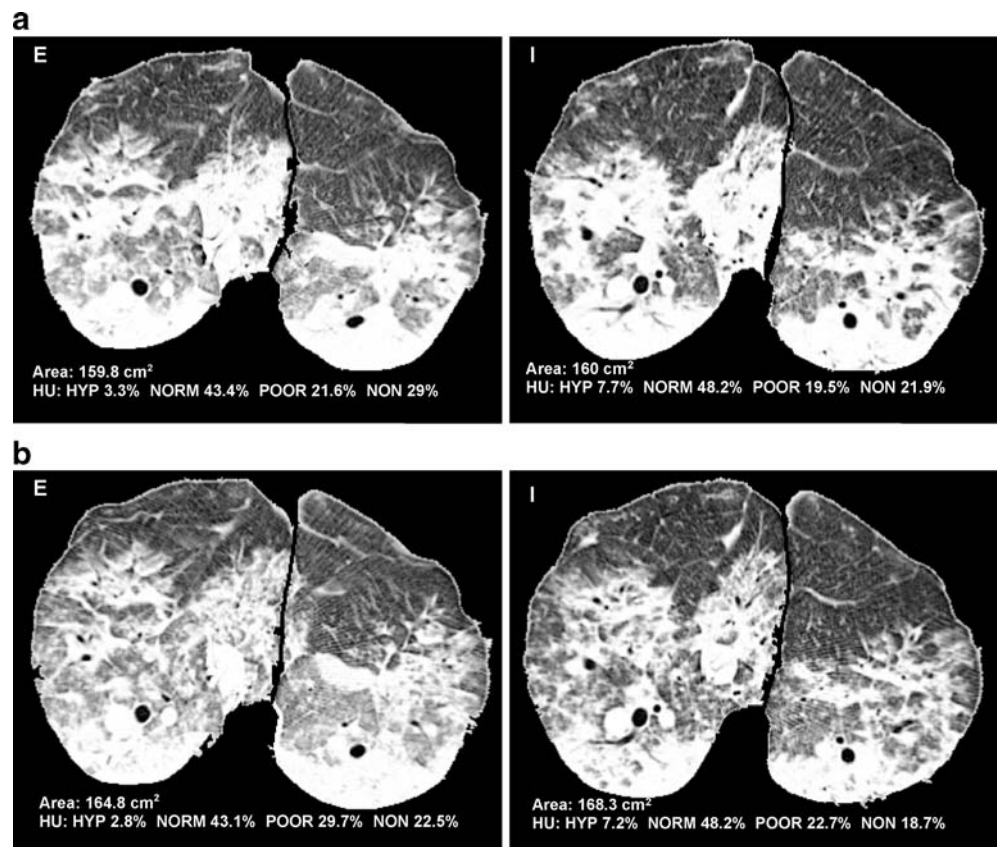
CT measurements

MSCT of the whole lung was performed with a 16 slice CT scanner (SOMATOM Sensation 16 Siemens, Forchheim, Germany). Scan parameters were chosen as follows: 16×1.5-mm collimation, 120 kV tube voltage with an effective tube current-time product of 100 mAs$_{eff}$, a gantry rotation time of 500 milliseconds and 36 mm table feed per rotation. For image reconstruction an effective slice thickness of 2 mm and a reconstruction increment of 1 mm were used. An optimized sharp kernel (B50f) and a field-of-view of 280×280 cm^2 with a 512×12 matrix were applied. All images were assessed at a window width of 1200 HU and a window center of −600 HU. For analysis of MSCT images a commercially available software was used (Pulmo Option, Syngo, Siemens). First the lung parenchyma was automatically delineated at the inner pleura and then corrected by hand by an experienced reader (DH). CT-values within a range from −1000 to +100 HU were assigned to lung parenchyma, representing the range from air only to totally de-aerated lung tissue. The fractions of density distributions were automatically calculated by the CT software in steps of 100 HU. From this data the area covered by each HU interval per slice was calculated. The values of the different lung volumes were calculated by multiplying the resulting areas with the slice thickness'. Lung parenchyma was characterized as hyperinflated (V_{HYP}) from −1000 to −900 HU, as normally aerated (V_{NORM}) from −900 to −500 HU, as poorly aerated (V_{POOR}) from −500 to −100 HU and as non-aereated (V_{NON}) from −100 to +100 HU [15]. The gas content was calculated as $V_{GAS} = \frac{V \times HU_{MEAN}}{-1000}$ and the tissue mass was calculated as $V_{TISS} = V_{TOT} - V_{GAS}$. The lung volumes consisted of $V_{GAS} + V_{TISS}$, e.g. a mean HU of −500 representing 50% gas and 50% tissue [15]. All volumes were calculated for end-inspiratory and end-expiratory scans separately. The tidal distribution was calculated by subtracting end-expiratory from end-inspiratory values.

Fig. 2 Volumes for each 100 HU compartment from −1000 to +100 HU. Upper panel: Values at inspiratory hold; lower panel: Values at expiratory hold. ☆ denotes p<0.05 for comparison between "before" and "after" the recruitment maneuver. Boxplot: Parameter median, interquartile range, standard deviation
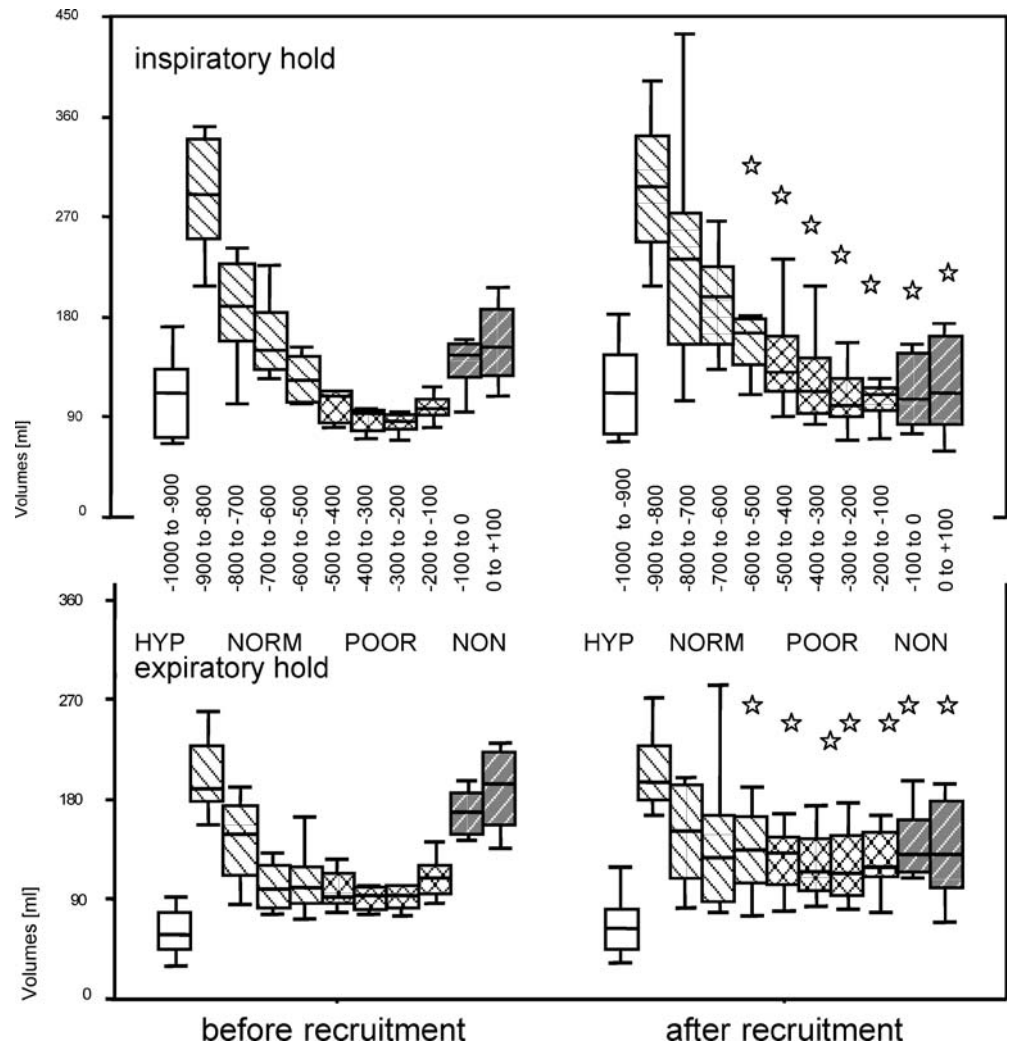
Fig. 3 Distributions of differently aerated lung volumes [in ml] during a tidal breath before (left side) and after (right side) a recruitment maneuver, obtained by inspiratory-expiratory differences. Positive values represent an increase, negative values a decrease of the respective volume during inspiration. The shown data represent the absolute values for hyperinflated, normally, poorly and non aerated lung volumes. The range from −400 to −300 HU not shown due to very small values (−1±7 ml before and 2±17 ml after recruitment). Data presented as mean±SD
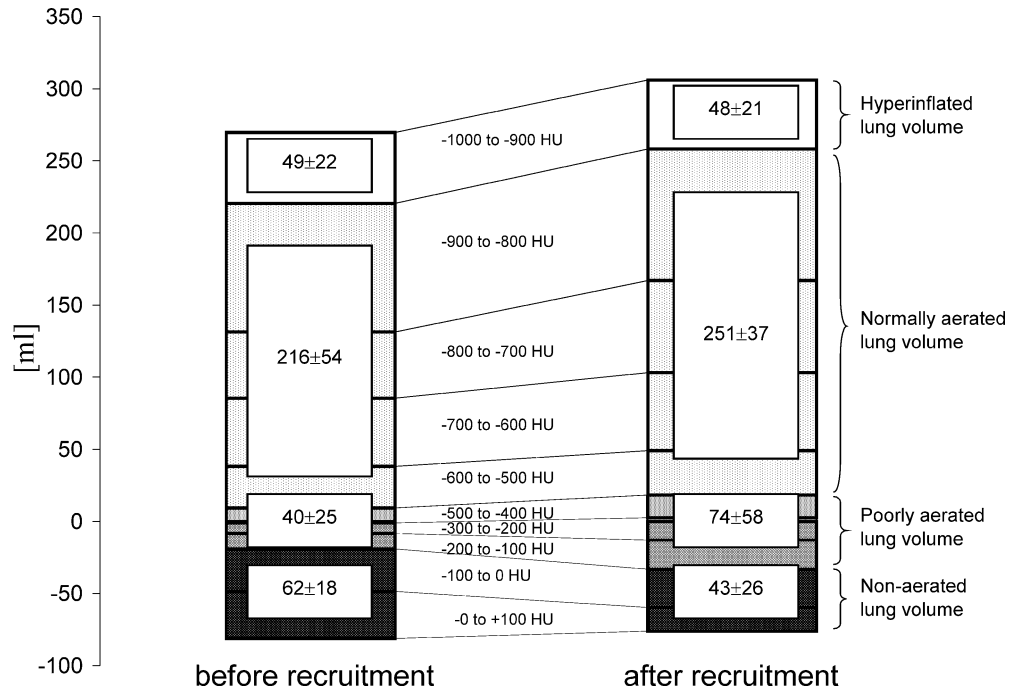
For each slice from apical to basal the total cross-sectional area and the mean area taken by the particular increments in HU were calculated.

To compare the results with those obtained by just single slice analysis, the same procedure was applied to the single slice cranial to the diaphragma with the greatest cross-sectional area in the expiratory exposure before the recruitment maneuver. The slices at the same position were then analyzed for the other exposures also. Instead of volumes, data are given as fractions of the total cross-sectional area.

All data are reported as mean±standard deviation (SD). "Before" and "after" recruitment maneuver values were compared using Wilcoxon's signed ranks test. Recruitment was defined as the increase in aerated and the decrease in non-aerated volumes after the recruitment maneuver. Statistical significance was accepted at $p<0.05$ (SPSS 11.0, Chicago, USA).

Results

Comparison of breath-hold volumes before and after the recruitment maneuver During end-inspiratory and end-expiratory breath hold there was a significant increase in the poorly aerated lung volumes (V_{POOR}) and a decrease in nonaerated volumes (V_{NON}) (Fig. 1). This was associated with an increase in the PaO_2 from 9.5±2.7 to 12,6±3,8 kPa ($p=0.017$). Total end-inspiratory lung volume increased from 1589±139 ml before to 1713±150 ml after the recruitment maneuver ($p=0.01$), while V_{GAS} increased from 838±84 ml before to 939±128 ml after the recruitment maneuver ($p=0.012$). The distribution of this gas went

preferentially to poorly aerated and normally aerated lung, which was more pronounced in the regions of −700 to −500 HU (Fig. 2). No significant changes in the better ventilated regions of V_{NORM} from −900 to −700 HU were observed. V_{TISS} did not change (819±56 ml before vs. 838±64 ml after, $p=0.263$).
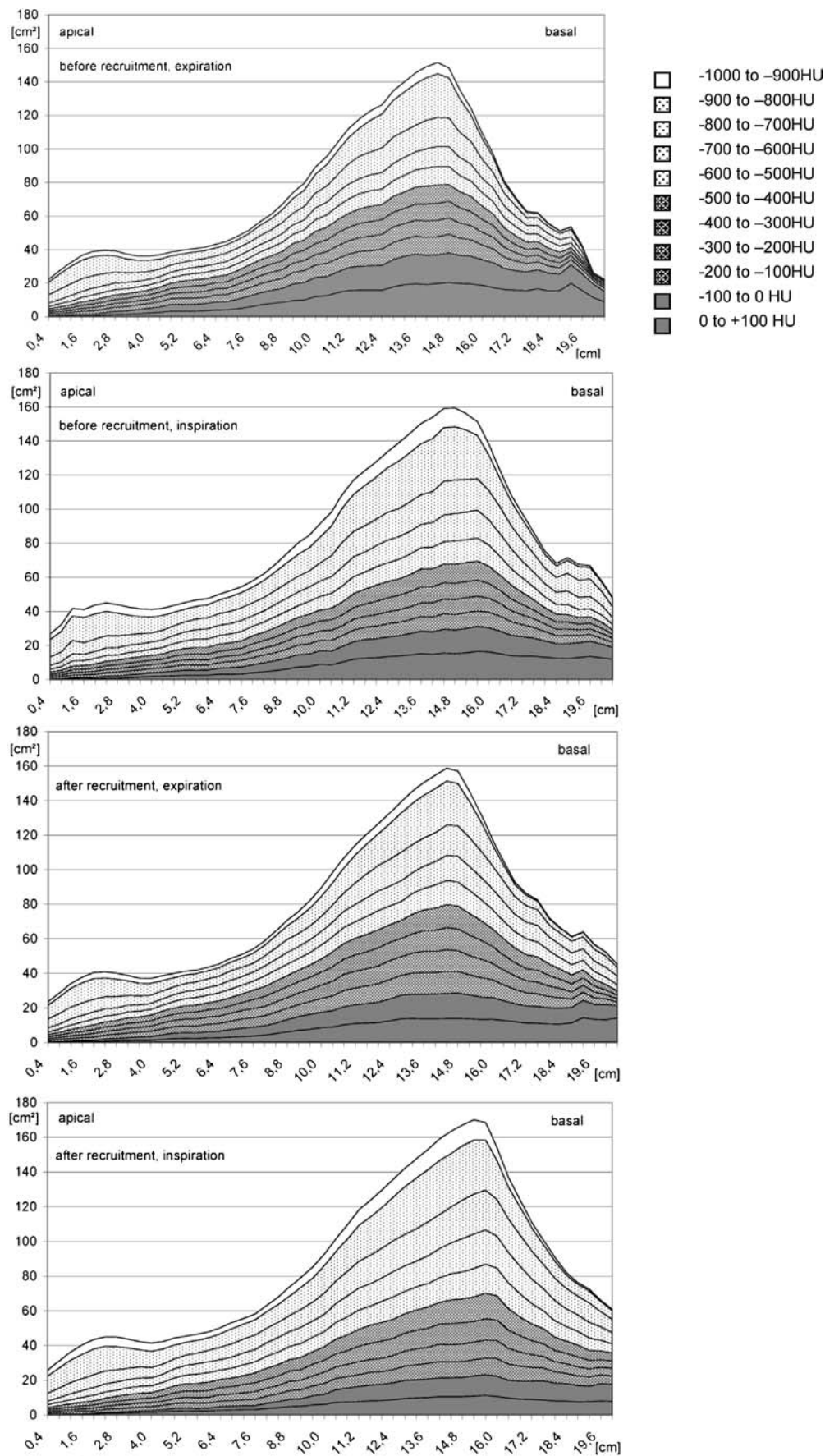
Comparison of inspiratory-expiratory differences, resembling tidal ventilation The distribution of tidal ventilation to differently aerated regions is shown in Fig. 3. No significant differences were found for tidal volumes measured by spirometry (230±16 ml) or determined by MSCT (209± 52 ml, $p=0.10$). Tidal volume was not significantly increased after the recruitment maneuver, which can be expected in volume controlled ventilation, but inspiratory plateau pressure decreased from 31±3 cmH_2O to 27± 3 cmH_2O ($p=0.03$). For other ventilatory parameters see Table 1. A significant portion of the tidal breath is distributed to nonaerated and poorly aerated parenchyma,

Table 1 Ventilation parameters

	Before	After
	The recruitment maneuver	
V_E [l/min]	9.8±0.9	10.1±1.1*
RR [min^{-1}]	39.8±2.3	39.8±2.3
PIP [cmH_2O]	36.6±4	31.1±3.7*
P_{PLAT} [cmH_2O]	30.7±3.1	27.2±2.8*
$T_{i/TOT}$	0.5±0.01	0.5±0.01

V_E=expiratory minute ventilation; RR=ventilatory rate; PIP=peak inspiratory pressure; P_{PLAT}=plateau pressure; $T_{i/TOT}$=inspiratory to total time ratio. *$p<0.05$ before vs. after recruitment maneuver

Fig. 4 Cross-sectional area of each slice from apical to basal and the parts of it taken by nonaerated, poorly aerated, normally aerated and hyperinflated lung. **a)** Before recruitment, expiration; **b)** inspiration; **c)** after recruitment, expiration; **d)** inspiration
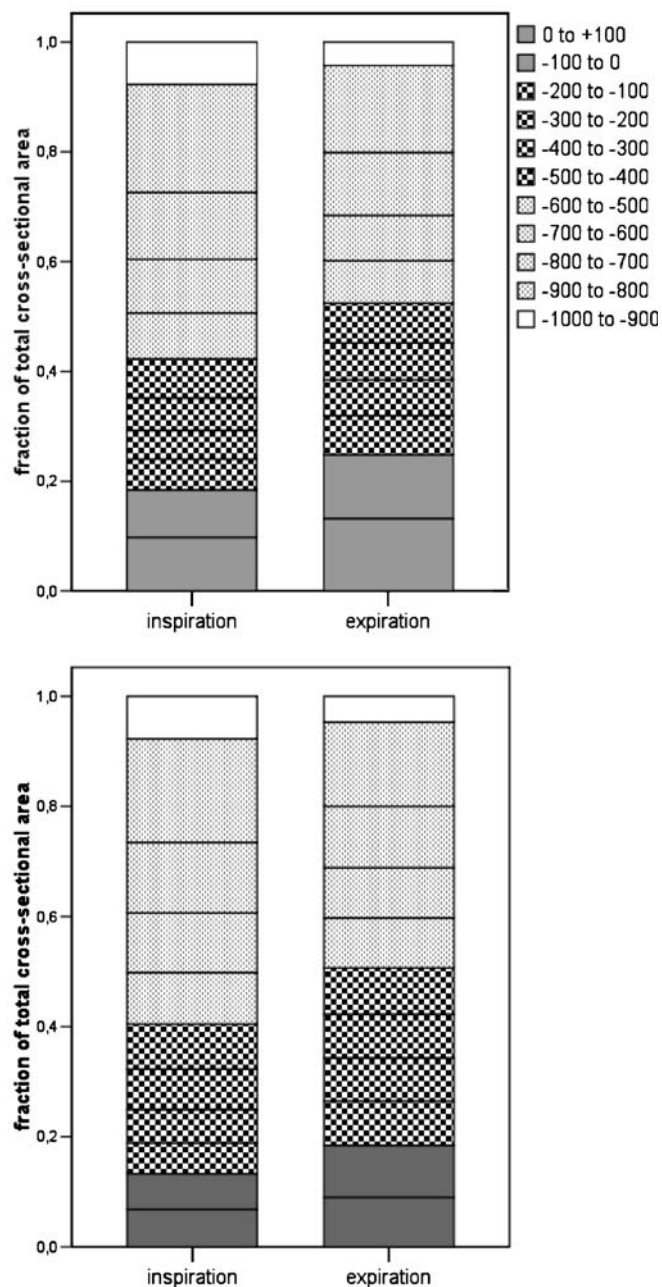
Fig. 5 Distribution of differently aerated lung **a**) before recruitment: **b**) after recruitment

representing expiratory collapse and inspiratory re-opening of alveoli. The inspiratory-expiratory volume change in all non-aereated regions (62 ± 18 ml) was not significantly reduced after the recruitment maneuver (43 ± 26 ml, p=0.114). On the other hand, the distribution of ventilation to normally aerated regions appeared to be increased, but did not reach statistical significance (p=0.102).

Comparison of single slice with whole lung MSCT analysis Great differences in the cross-sectional area and the distributions of HU can be observed from apical to basal (Fig. 4). In the analysis of a single slice just cranial to the diaphragma, the recruitment maneuver resulted in a decrease in non-aerated lung and an increase in poorly and normally aerated lung (Fig. 5). The percent changes correlated highly significant (r=0.96, p=0.001) with those observed with whole lung analysis, but significantly underestimated the increase in normally and poorly aerated lung (Table 2).

Discussion

In a porcine model of saline lavage induced acute lung injury we calculated the volumes of differently aerated lung parenchyma by attenuations of HU. Thereby it is possible to observe the differential distribution of ventilation induced by a lung recruitment maneuver (Fig. 2). Mainly, the intrathoracic gas volume increased and there was a shift from non-aerated to poorly and normally aerated lung volumes. The broad availability and improved performance of MSCT scanners have increased the acceptance of lung CT scanning in the treatment of ARDS [19] and have led to routine use in specialized centers.

Experimental limitations To investigate, whether changes in the amount of aerated and nonaerated lung volumes could be assessed quantitatively, we have chosen a model of acute lung injury which is known to be easily recruitable. Furthermore, the preferential distribution of atelectasis to the dependent lung could also be demonstrated in patients with ARDS by use of CT scanning [15]. Even though the general limitations of transferring experimental animal results into human pathology have to be applied, the pig lavage model has been used for several investigations [11, 20, 21]. To investigate the effects on the whole

Table 2 Percent changes in lung volumes (whole lung analysis) or cross-sectional area (single slice) of differently aerated lung after a recruitment maneuver

P-value given for whole lung vs. single slice analysis of changes

	Inspiratory hold		Expiratory hold		P-value
	whole lung [%]	single slice [%]	whole lung [%]	single slice [%]	whole vs. single
Hyperinflated	5±6	1±16	10±10	11±17	0.619
Normally aerated	12±12	4±7	11±13	3±8	<0.001
Poorly aerated	21±18	13±15	22±18	17±20	<0.001
Non aerated	−22±16	−27±17	−23±15	−25±20	0.066

lung we employed static conditions, even though dynamic studies of tidal ventilation have shown that a dynamic component of tidal recruitment might not be adequately reflected during breath-hold exposures of inspiration and expiration [21, 22]. However, to our knowledge no software is available to analyze dynamic studies of the whole lung.

The understanding of the pathology of the ARDS has improved considerably since the introduction of CT [1]. The characterization of the disease severity was mainly done by looking at different gray scaling densities interpreted as infiltrates, consolidation or atelectasis during the acute phase [15] and after the resolution of ARDS [23]. The measurement of lung and intrathoracic gas volumes by CT has been validated previously [24, 25], but has not been used for as a routine procedure due to complicated and time-consuming exposure and analysis techniques. More recently, from the distribution of frequencies distributions it was attempted to describe changes within the lung induced by certain interventions [7] with regard to the distribution of ventilation. Also, the lavage model in pigs has been used to describe changes seen in CT [22, 26–28], but mostly single slice analysis had been used. The use of MSCT has enabled to look at the lung as a whole [29], acknowledging that interventions might induce changes in lung aeration at the apex differently from basal lung regions [9]. In a study by Malbouisson et al [8] a single slice CT scanner was used requiring an exposure time of >15 seconds. This however can interfere with ventilation and induce additional atelectasis formation in ARDS patients with highly unstable lungs [30]. In addition, recruitment was defined as the increase of intrathoracic gas, which could have also resulted from overdistended alveoli within the area marked as poorly or non-aerated lung. In contrast to previous investigations we calculated actual volume shifts within regions of differently aerated lung parenchyma. As a consequence we could demonstrate that the main mechanism of a standard recruitment maneuver is not an increase in normally aerated lung, but mainly an increase in poorly aerated lung, representing unstable units with low ventilation/perfusion distribution. Since we observed a significant improvement in oxygenation, the dependency of gas exchange on the amount of normally aerated lung volume has to be questioned in severe hypoxemic lung injury. Possibly poorly aerated regions with low ventilation-perfusion distribution and shunt perfusion are the main determinant of the relatively small changes in oxygenation, depending on regional perfusion alterations [31]. Since the interpretation of these results depends on the definition of the differently aerated lung compartments, the assignment of different density ranges to normally, poorly and non aerated lung might lead to other results [22]. However, we have demonstrated that the main increases in aerated lung were in the range from −500 to −200 HU, whether this be called still normally or already poorly aerated. On the other hand, hardly any changes could be observed in the clearly good aerated ranges from −900 to −700, representing normally aerated lung.

Most importantly, though the amount of intrathoracic gas (and thereby the functional residual capacity) increased, the tissue amount [11] (also representing lung edema) and the distribution of the tidal breath to the differently aerated regions was unchanged. One of the known mechanisms of potentially harmful ventilation is the repeated collapse and re-opening of alveoli during tidal breath [32], characterized as tidal ventilation occurring in non-aerated and poorly aerated lung regions. On the other hand, the hyperinflated lung volume has been stable. This observation is important since a recruitment maneuver had been suspected to lead to hyperinflation and overdistension of certain areas of the lung. This study provides data which demonstrate that this is not true in a lavage model of ARDS, at least in volume controlled ventilation. With pressure-controlled mode, the changes after the recruitment maneuver would have been different, with a significant increase in tidal volumes. Instead, we have observed a decrease in inspiratory distending pressure, which will further reduce the potentially injurious mechanisms of artificial ventilation. The question, whether volume or pressure controlled ventilation is best for optimal recruitment is still unsolved [14], therefore both modes should be regarded as equal from this point of view. However, we have shown the importance of analyzing the whole lung, since the amount of recruited lung has been underestimated from the analysis of a single slice near the diaphragm. In this area the atelectasis commonly is found to be at its greatest and the lung is additionally compressed by a superimposed vertical gradient and increased abdominal pressure [16]. To recruit these areas, extremely high pressures might be necessary, leading to overstretching of the non-atelectatic lung, which however was not observed in our study with an inspiratory plateau pressure around 30 cmH$_2$O. Dynamic investigations have been used to characterize the effects of ventilation modalities on the distribution ventilation within the lung [28, 33], and in the future these could aid in the adjustment of ventilator settings.

In conclusion, we have shown that quantitative analysis of the whole lung by use of a MSCT scan is able to provide important insights into the consequences of a therapeutic intervention, e.g. a standard recruitment maneuver, as compared to a single slice analysis. Regions especially prone to atelectasis, e.g. the dependent lung, may be investigated in further studies with this technique. Further developments towards reduction of the radiation dose [34] and improved analysis software could promote MSCT as a routine investigation in acute lung injury and ARDS.

References

1. Gattinoni L, Caironi P, Pelosi P, Goodman LR (2001) What has computed tomography taught us about the acute respiratory distress syndrome? Am J Respir Crit Care Med 164:1701–1711
2. Hubmayr RD (2002) Perspective on lung injury and recruitment: a skeptical look at the opening and collapse story. Am J Respir Crit Care Med 165:1647–1653
3. Rouby JJ, Puybasset L, Cluzel P, Richecoeur J, Lu Q, Grenier P (2000) Regional distribution of gas and tissue in acute respiratory distress syndrome. II. Physiological correlations and definition of an ARDS Severity Score. CT Scan ARDS Study Group. Intensive Care Med 26:1046–1056
4. Tokics L, Hedenstierna G, Strandberg A, Brismar B, Lundquist H (1987) Lung collapse and gas exchange during general anesthesia: effects of spontaneous breathing, muscle paralysis, and positive end-expiratory pressure. Anesthesiology 66:157–167
5. Lachmann B (1992) Open up the lung and keep the lung open. Intensive Care Med 18:319–21
6. Gattinoni L, Pelosi P, Vitale G, Pesenti A, D'Andrea L, Mascheroni D (1991) Body position changes redistribute lung Computed-Tomographic density in patients with acute respiratory failure. Anesthesiology 74:15–23
7. Crotti S, Mascheroni D, Caironi P, Pelosi P, Ronzoni G, Mondino M, Marini JJ, Gattinoni L (2001) Recruitment and derecruitment during acute respiratory failure: a clinical study. Am J Respir Crit Care Med 164:131–140
8. Malbouisson LM, Muller JC, Constantin JM, Lu Q, Puybasset L, Rouby JJ (2001) Computed tomography assessment of positive end-expiratory pressure-induced alveolar recruitment in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 163:1444–1450
9. Wrigge H, Zinserling J, Neumann P, Defosse J, Magnusson A, Putensen C, Hedenstierna G (2003) Spontaneous breathing improves lung aeration in oleic acid-induced lung injury. Anesthesiology 99:376–384
10. Vieira SR, Puybasset L, Richecoeur J, Lu Q, Cluzel P, Gusman PB, Coriat P, Rouby JJ (1998) A lung computed tomographic assessment of positive end-expiratory pressure-induced lung overdistension. Am J Respir Crit Care Med 158:1571–1577
11. Luecke T, Roth H, Herrmann P, Joachim A, Weisser G, Pelosi P, Quintel M (2003) PEEP decreases atelectasis and extravascular lung water but not lung tissue volume in surfactant-washout lung injury. Intensive Care Med 29:2026–2033
12. Drummond JC, Todd MM, Saidman LJ (1996) Use of neuromuscular blocking drugs in scientific investigations involving animal subjects. The benefit of the doubt goes to the animal. Anesthesiology 85:697–699
13. Jonson B, Beydon L, Brauer K, Mansson C, Valind S, Grytzell H (1993) Mechanics of respiratory system in healthy anesthetized humans with emphasis on viscoelastic properties. J Appl Physiol 75:132–140
14. Dembinski R, Max M, Bensberg R, Rossaint R, Kuhlen R (2002) Pressure Support Compared with Controlled Mechanical Ventilation in Experimental Lung Injury. Anesth Analg 94:1570–1576
15. Puybasset L, Cluzel P, Gusman P, Grenier P, Preteux F, Rouby JJ (2000) Regional distribution of gas and tissue in acute respiratory distress syndrome. I. Consequences for lung morphology. CT Scan ARDS Study Group. Intensive Care Med 26:857–869
16. Pelosi P, Goldner M, McKibben A, Adams A, Eccher G, Caironi P, Losappio S, Gattinoni L, Marini JJ (2001) Recruitment and derecruitment during acute respiratory failure: an experimental study. Am J Respir Crit Care Med 164:122–130
17. Marini JJ (2001) Recruitment maneuvers to achieve an "open lung"— whether and how? Crit Care Med 29:1647–1648
18. Grasso S, Mascia L, del Turco M, Malacarne P, Giunta F, Brochard L, Slutsky AS, Marco RV (2002) Effects of recruiting maneuvers in patients with acute respiratory distress syndrome ventilated with protective ventilatory strategy. Anesthesiology 96:795–802
19. Kopp R, Kuhlen R, Max M, Rossaint R (2002) Evidence-based medicine in the therapy of the acute respiratory distress syndrome. Intensive Care Med 28:244–255
20. Grasso S, Terragni P, Mascia L, Fanelli V, Quintel M, Herrmann P, Hedenstierna G, Slutsky AS, Ranieri VM (2004) Airway pressure-time curve profile (stress index) detects tidal recruitment/hyperinflation in experimental acute lung injury. Crit Care Med 32:1018–1027
21. Bink A, Markstaller K, Birkenkamp K, Karmrodt J, Stepniak A, Heussel CP, Eberle B, Thelen M, Kauczor HU (2001) Multi-rotation CT and acute respiratory distress syndrome. Animal experiment studies. Radiologe 41:195–200
22. Markstaller K, Kauczor HU, Eberle B, Weiler N, Siebertz D, Birkenkamp K, Heinrichs W, Thelen M (1999) Multi-rotation CT during continuous ventilation: comparison of different density areas in healthy lungs and in the ARDS lavage model. Rofo 170:575–580
23. Nobauer-Huhmann IM, Eibenberger K, Schaefer-Prokop C, Steltzer H, Schlick W, Strasser K, Fridrich P, Herold CJ (2001) Changes in lung parenchyma after acute respiratory distress syndrome (ARDS): assessment with high-resolution computed tomography. Eur Radiol 11:2436–2443
24. Wandtke JC, Hyde RW, Fahey PJ, Utell MJ, Plewes DB, Goske MJ, Fischer HW (1986) Measurement of lung gas volume and regional density by computed tomography in dogs. Invest Radiol 21:108–117
25. Verschakelen JA, Van fraeyenhoven L, Laureys G, Demedts M, Baert AL (1993) Differences in CT density between dependent and nondependent portions of the lung: influence of lung volume. AJR Am J Roentgenol. 161:713–717
26. Markstaller K, Eberle B, Kauczor HU, Scholz A, Bink A, Thelen M, Heinrichs W, Weiler N (2001) Temporal dynamics of lung aeration determined by dynamic CT in a porcine model of ARDS. Br J Anaesth 87:459–468
27. Markstaller K, Kauczor HU, Weiler N, Karmrodt J, Doebrich M, Ferrante M, Thelen M, Eberle B (2003) Lung density distribution in dynamic CT correlates with oxygenation in ventilated pigs with lavage ARDS. Br J Anaesth 91:699–708

28. David M, Bletz C, David S, Karmrodt J, Herwelling A, Heussel CP, Markstaller K (2005) Analysis of the static pressure volume curve of the lung in experimentally induced pulmonary damage by CT-densitometry. Rofo 177:751–757

29. Puybasset L, Gusman P, Muller JC, Cluzel P, Coriat P, Rouby JJ (2000) Regional distribution of gas and tissue in acute respiratory distress syndrome. III. Consequences for the effects of positive end-expiratory pressure. CT Scan ARDS Study Group. Adult Respiratory Distress Syndrome. Intensive Care Med 26:1215–1227

30. Brochard L (2001) Watching what PEEP really does. Am J Respir Crit Care Med 163:1291–1292

31. Musch G, Harris RS, Vidal Melo MF, O'Neill KR, Layfield JD, Winkler T, Venegas JG (2004) Mechanism by which a sustained inflation can worsen oxygenation in acute lung injury. Anesthesiology 100:323–330

32. Ranieri VM, Suter PM, Tortorella C, De Tullio R, Dayer JM, Brienza A, Bruno F, Slutsky AS (1999) Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. JAMA 282:54–61

33. Bletz C, Markstaller K, Karmrodt J, Herweling A, Melvan M, Goetz R, Stepniak A, Eberle B, Kauczor HU, Heussel CP, Thelen M (2004) Quantification of atelectases in artificial respiration: spiral-CT versus dynamic single-slice CT. RoFo 176:409–416

34. Wildberger JE, Max M, Wein BB, Mahnken AH, Weiss C, Dembinski R, Katoh M, Schaller S, Rossaint R, Gunther RW (2003) Low-dose multi-slice spiral computed tomography in acute lung injury: animal experience. Invest Radiol 38:9–16