Temporal dynamics of lung aeration determined by dynamic CT in a porcine model of ARDS

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We used dynamic CT to identify two different time constants of lung aeration and their individual contribution to the total increase in cross-sectional lung area in healthy and experimentally damaged lungs. In five healthy pigs, inflation and deflation between 0 and 50 cm H₂O was imposed during dynamic (250 ms/image) CT acquisition, and repeated after experimental lung injury by saline lavage. The fractional areas of density ranges, which represent aerated lung parenchyma, were determined planimetrically, and their time for expansion during the manoeuvre was fitted using a bi-exponential model. Thus, two compartments, their sizes, i.e. their relative contributions to lung area aerated by the manoeuvre, and their specific time constants (τ) were sought. Healthy lungs were characterized best by a one-compartmental behaviour with one τ only, both during inflation (median τ=0.5 s; range 0.4–0.6 s) and deflation (1.2 s; 1.1–1.3 s). In damaged lungs two compartments were found both during inspiration and expiration, with 86% (78–87%) of the recruitable lung area following a short τ of 0.5 s (0.5–0.6), and 14% (13–22%) following a longer τ of 9.1 s (8–16.8 s) during inflation. During expiration, damaged lungs had a short τ of 0.8 s (0.5–1.0 s) for 94% (84–100%) of deflated lung area, and a longer τ of 26.5 s (7.1–34.3 s) for 6% (0–16%). We conclude that dynamic CT indicates the relative size and temporal behaviour of functional compartments in normal and abnormal lungs. Our findings suggest that after lung damage, cyclic ventilation with inspiratory periods of <10 s duration will not achieve maximum recruitment for a chosen inspiratory pressure. In ARDS, the short expiratory τ predisposes to atelectasis formation if expiratory times are >1 s.

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In acute lung injury, maldistribution of ventilation and perfusion is the most frequent cause of gas exchange impairment. The best settings for mechanical ventilation are based on empirical rules and trials of treatment such as the response of gas exchange to PEEP. Clinical progress is followed by measurement of blood gases, respiratory mechanics and by chest x-ray. Static chest CT can be used to stage ARDS and detect complications (e.g. barotrauma), but is not used to adjust ventilation.¹

A recent CT acquisition technique, called dynamic multiscan CT, allows continuous image acquisition with a temporal resolution of 250 ms. This superior resolution allows changes in radiologic attenuation of the lung during mechanical ventilation to be followed. Neumann and colleagues investigated the temporal behaviour of poorly aerated lung regions and atelectases during inspiration and expiration in pigs with experimental lung damage. Using a monoexponential relationship, they described the kinetics of mean radiologic density of the lung (mean lung density, MLD) and of two density ranges describing poorly aerated lung and atelectasis.² We considered that although aeration of the healthy lung may have one-compartmental behaviour,
aeration of damaged lungs may be better described by considering more than one compartment. To obtain maximum sensitivity for ventilation-induced changes in aeration, we analysed those lung density ranges which had shown the greatest area change with inspiratory and expiratory manoeuvres in a previous study of similarly treated animals (see Fig. 5). To prove our hypothesis, we used an experiment to allow us to discriminate different 
(1) the repeated lavage model, which has been described as a model for lung collapse and recruitment phenomena; and (2) rectangular airway pressure steps between ZEEP and 50 cm H2O, in order to allow both atelectasis formation and nearly complete recruitment.

Materials and methods

Instrumentation

With Animal Care Committee approval, five pigs (26.8 (SD 1.6) kg) were anaesthetized (piratramide 1.2 mg kg⁻¹ i.v.; thiopentone 10–15 mg kg⁻¹ i.v.) and ventilated via a tracheal tube (ID 7.0 mm), in volume-controlled mode with 15 cycles min⁻¹, a ratio of inspiration:plateau:expiration=25:10:65%, a PEEP of 5 cm H2O, and a fractional inspiratory oxygen (FIO₂) of 1.0 (Servo 900C, Siemens, Germany). The expired tidal volume was set to 12 ml kg⁻¹ and adjusted to keep the end-tidal carbon dioxide concentration between 35 and 40 mm Hg. Anaesthesia was maintained by continuous i.v. infusion of piratramide (2 mg kg⁻¹ h⁻¹) and thiopentone (10 mg kg⁻¹ h⁻¹). We measured ECG, and the femoral vessels were exposed to insert arterial central venous and pulmonary artery catheters. Intravascular pressures (Sirecust 404-1, Siemens, Germany), arterial blood gases and acid–base status (Paratrend 7, Diamectrics Medical Ltd, UK) were measured continuously. For calibration of the Paratrend Monitor routine blood gas measurements from arterial and mixed venous blood were made (ABL 500/OSM 3, Radiometer Copenhagen, Germany). After instrumentation was completed, the animals were positioned in supine position in the CT scanner (Somatom Plus 4, Siemens, Germany).

Study procedure

Baseline values of haemodynamics, blood gases, and acid–base status were obtained. Two scout views were taken during end-inspiratory and end-expiratory breathholds and a transverse, supradiaphragmatic slice was defined by a reference scan. Thus, a fixed table position was defined which allowed the visualization of lung parenchyma between the apex of the heart and the diaphragm, both during inspiration and expiration.

Airway pressure step manoeuvres were performed with healthy lungs and again after surfactant-depletion by repeated lavage of the lungs. Lung lavages were performed 9±1 times with 1 litre of isotonic Ringer’s solution. Inotropic support was provided by continuous infusion of 3±2 µg kg⁻¹ h⁻¹ epinephrine after lung lavages.

To generate a quasi-rectangular increase or decrease in airway pressure, the respirator was switched to its CPAP mode, and the CPAP level was increased swiftly in one step from end expiration (ZEEP=0 cm H2O) to 50 cm H2O or from CPAP of 50 cm H2O to ZEEP, respectively. The CT acquisition was started 5 s before the airway pressure step and continued for at least 30 s after the step change. Volume-controlled ventilation was resumed afterwards, until baseline haemodynamics and blood gases were restored.

CT acquisition parameters

In all dynamic multiscan CT acquisitions, the tube voltage was set to 120 kV and the tube current to 110 mA. A matrix of 512×512 and a slice thickness of 1.0 mm was used. Images were reconstructed using the high-resolution algorithm. Total rotation time of the x-ray tube was 750 ms allowing for an overlapping temporal increment, i.e. an effective temporal resolution, of 250 ms.

Quantitative analysis of CT scans

In each lung image, the total lung area was determined semi-automatically using a dedicated software (Pulmo-Software®, Siemens, Germany). An interactive correction was carried out if the total lung area resulting from the automatic segmentation did not represent the anatomical lung area. Such errors occurred predominantly in damaged lungs. The boundaries of the lung were defined by the ribs, the aorta, and the heart. All segmentations were performed by one investigator to avoid operator-related variation. The total lung area (density range from –1024 to +200 HU) was automatically divided into fractional areas of defined densities. The density range from –910 to –700 HU was used to describe aerated lung parenchyma in healthy porcine lungs. The range from –910 to –300 HU represented aerated tissue in the lavaged lungs model. For each density range, the corresponding relative lung area was evaluated planimetrically.

Radiological interpretation

To verify the quantitative analysis by density ranges, every image series was evaluated by a board-certified radiologist (H.-U.K.) for the following criteria: general lung aeration, presence of atelectasis, and a ventral-to-dorsal gradient. An image-by-image evaluation was done to describe the temporal evolution of these criteria.

Identification of lung compartments, their time constants (τ) and fractional sizes (A)

The time behaviour of a specific density range during inflation or deflation was analysed under the a priori
assumption of two-compartmental behaviour. The change in aeration (air content) of one homogeneous compartment in response to a rectangular airway pressure increase or decrease can be described by a mono-exponential wash-in or wash-out function, respectively:\[ V(t) = V_0 \times e^{-(t/\tau)} \]

($V$, expired volume; $\tau$, time constant).

In this study, $\tau$ was derived from the temporal dynamics of the area of a defined density range in subsequent CT images. In the following, $\Delta A$ denotes the lung area, which becomes aerated by the airway pressure increase from ZEEP, or collapses during the airway pressure decrease to ZEEP. The lung area at ZEEP was defined as the baseline for the aeration manoeuvre (and as the endpoint of collapse, respectively), and was not taken into account for this analysis. To separate the two time constants $\tau$, the increase or decrease of aerated lung area in response to the airway pressure change was fitted by a least-squares fitting procedure using a bi-exponential relationship, i.e.,

$$\Delta A(t) = \Delta A_1 \times e^{-(t/\tau_1)} + \Delta A_2 \times e^{-(t/\tau_2)}$$

In this relationship, $\Delta A_1$ represents the fraction of $\Delta A$, which follows a time constant $\tau_1$. $\Delta A_2$ represents the fraction of $\Delta A$ with a temporal behaviour characterized by $\tau_2$.

First, the temporal behaviour of the area of the predefined density range was plotted. The bi-exponential equation (above) was then introduced as user-defined fitting function. Data points were fitted with the software package Origin® (Origin 4.0, Microcal Software Inc., USA). As the fitting procedure requires a selection of starting values for the parameters, we chose the following parameters, which gave reproducible results in simulation curves: $\Delta A_1=80\%$, $\Delta A_2=20\%$, $\tau_1=1$ s, and $\tau_2=10$ s. These settings were applied to all data sets, i.e. before and after lung damage, and gave a satisfactory goodness of fit (chi-squared=2.06 (0.75); mean (SD) for all fits performed). An example of a fit result is given in Figure 1.

Depending on the individual contribution of each compartment to the aeration process, a one- or a two-compartmental behaviour of lung aeration was defined. Two compartments were considered present if $\Delta A_2$ exceeded 5% of $\Delta A$, whereas a compartment size of $\leq5\%$ was neglected.

**Haemodynamics and gas exchange measurements**

Before lung damage and after stabilization after repeated lung lavages, we recorded aortic and central venous pressures, and cardiac output. For assessment of gas exchange, arterial and mixed venous blood gases were measured.

**Results**

We measured five animals with healthy lungs and four animals with lavaged lungs. One animal died during lung damage. Haemodynamic and gas exchange values before and after lavage of the lungs are shown in Table 1. Lavage caused a mean oxygenation index ($P_{aO_2}/F_{iO_2}$) of 61. Haemodynamic measurements after lung damage were made during low-dose inotropic support.

**Radiological interpretation**

**Healthy lungs**

At end-expiration, an antero-posterior increasing gradient of attenuation was seen, and only a small amount of atelectasis could be observed, whereas at end-inspiration the lung

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Healthy lungs (n=5)</th>
<th>Lavage-ARDS (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{aO_2}$ (mm Hg)</td>
<td>513 (5.1)</td>
<td>61 (13.4)</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mm Hg)</td>
<td>37 (2.9)</td>
<td>53 (15.5)</td>
</tr>
<tr>
<td>pH</td>
<td>7.49 (0.04)</td>
<td>7.19 (0.19)</td>
</tr>
<tr>
<td>$HCO_3^-$ (mmol litre$^{-1}$)</td>
<td>27.6 (3.59)</td>
<td>18.2±7.35</td>
</tr>
<tr>
<td>Base excess (mmol litre$^{-1}$)</td>
<td>6.25 (4.03)</td>
<td>$-11$ (8.77)</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>85 (14)</td>
<td>65 (7)</td>
</tr>
<tr>
<td>Diastolic arterial pressure</td>
<td>4.3 (3)</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Systolic arterial pressure</td>
<td>109 (12)</td>
<td>94 (9)</td>
</tr>
<tr>
<td>Central venous pressure</td>
<td>4.6 (1)</td>
<td>4.7 (3)</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>69 (12)</td>
<td>46 (9)</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>85 (14)</td>
<td>65 (7)</td>
</tr>
<tr>
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<td>Cardiac output</td>
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<td>46 (9)</td>
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</tbody>
</table>
parenchyma appeared completely aerated (see Fig. 2A–C). Only a very small amount of over-expansion was noticed. During airway pressure changes, lung density changed homogeneously.

*Lavage ARDS*
At end-expiration, large portions of the lung were atelectatic, predominantly in the dependent lung regions. During inflation, lung density in already aerated lung areas decreased first, followed by a reduction of atelectasis (see Fig. 3A–C). At end-inspiration, a marked and antero-posterior gradient of increasing density gradient was accompanied by a significant number of regions with signs of over-expansion. During deflation, a fast reappearance of atelectasis paralleled the increase of lung density over the entire cross-sectional slice. Some atelectasis persisted throughout all images.

*Aeration process in healthy lungs*

**Inflation**
Healthy lungs had a one-compartmental behaviour, with a median $\tau$ of 0.5 (range 0.4–0.6 s).

**Deflation**
A deflation process with a single fast compartment was present in all animals, with a time constant of 1.2 s (range 1.1–1.3 s). In only one of five animals a second, longer $\tau$ of 4.5 s was evident, which comprised 7% of the total ventilated lung area. In four of five healthy animals, the deflation process fulfilled the prospectively defined criterion of a fast one-compartmental behaviour.

*Lavaged lungs*

**Inflation**
Here, a short time constant of 0.5 s (range 0.5–0.6 s) was detected in 86% (range 78–87%) of the lung area inflated by the manoeuvre. The second, longer $\tau$ of 9.1 s (range 8–16.8 s) was found in 14% (range 13–22%) of the inflation area (see Fig. 4A).

**Deflation**
A short $\tau$ of 0.8 s (range 0.5–1.0 s) was found in 94% (84–100%) of lung area deflated during the manoeuvre, and a longer $\tau$ of 26.5 s (7.1–34.3 s) governed a slow compartment, which comprised 6% (0–16%) of the deflated area. Thus, during expiration, ARDS lungs showed a bi-compartmental behaviour in three of four animals, whereas

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**Fig 2** Transverse supradiaphragmatic CT scans of healthy lungs during airway pressure increase from 0 to 50 cm H$_2$O. (A) At end-expiration, an antero-posteriorly increasing density gradient is visible. (B) After 3 s of CPAP maintained at 50 cm H$_2$O, lung parenchyma appears almost homogeneous, with only slightly increased lung density in basal lung areas. (C) Lung parenchyma appears homogeneously aerated 31 s after the airway pressure increase to 50 cm H$_2$O CPAP.
only one of four animals showed a fast, one-compartmental deflation behaviour.

Individual data for all animals are listed in Table 2.

### Discussion

We wished to compare ventilation and recruitment processes in healthy lungs and in the lavage model of ARDS using a dynamic CT-based method. We hypothesized that we might identify two different compartments, on the basis of their temporal behaviour, and their contribution to total lung aeration (i.e. distension of already open as well as recruitment of collapsed alveoli) after lung damage by lavage.

In healthy lungs, the inflation and deflation processes are characterized best by a one-compartmental behaviour, whereas after lavage the co-existence of two compartments with clearly different τ was observed. A short inspiratory τ was found for 86% of the total lung area ventilated or recruited by the manoeuvre. The remaining 14% of finally aerated lung area inflated quite slowly with a τ of about 10 s. In contrast, during expiration, 94% of the damaged lung collapsed very quickly with a τ of less than 1 s, compared with slower deflation with a τ of more than 1 s in the healthy lungs.

Radiological interpretation of the dynamic series of CT scans gave a more descriptive assessment of the temporal dynamics of lung aeration with ventilation and recruitment phenomena in ARDS.

During inflation, areas that were already filled expanded first, followed by a slow recruitment of atelectasis. Thus, the short τ in inspiration appeared to represent ventilation of already aerated alveoli, whereas the longer τ reflects recruitment of atelectatic areas.

During deflation, rapid collapse of large portions of lung parenchyma, with a rapid increase of atelectatic and hypoventilated dense lung areas, causes the short expiratory τ. The long expiratory τ in ARDS represents expiration from lung areas, which remain air-filled even at ZEEP.

In a similar animal model of ARDS, Wegenius and colleagues described a quantal behaviour of atelectatic lung detectable by CT. This behaviour is because surfactant-depleted alveoli are either fluid-filled and thus collapsed, or air-filled and open, but almost no intermediate states are present. This theory is supported by our observation that only after lung damage, i.e. after development of widespread expiratory alveolar collapse, two-compartmental behaviour appears. During inflation, the short τ reflects inflation of open alveoli (i.e. a ventilation process), and the longer τ represents the slower opening of collapsed alveoli at their respective opening pressures, for example the recruitment process. During deflation, fast expiration of air is accompanied by the rapid formation of large atelectatic areas, which explains the large compartment with a short τ of <1 s.

As we aimed to develop a diagnostic method to characterize compartments of lung aeration in ARDS, we chose a lavage-induced form of lung damage to reproduce the ventilation and recruitment processes after surfactant-depletion according to Wegenius and colleagues. The lavage model simulates only one aspect of ARDS, i.e. loss of surfactant. In our study, the appearance of the CT images

### Table 2

Lung compartments assessed by multiscan CT before and after lavage ARDS induction: co-existing time constants and correspondent compartment size. τ 1, short time constant in s; τ 2, long time constant in s; fractional area 1, compartment size of τ 1 in per cent which becomes aerated by the airway pressure increase from ZEEP; or collapses during the airway pressure decrease to ZEEP; fractional area 2, compartment size of τ 2 in per cent which becomes aerated by the airway pressure increase from ZEEP, or collapses during the airway pressure decrease to ZEEP.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Inflation</th>
<th>Deflation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>τ 1</td>
<td>τ 2</td>
</tr>
<tr>
<td>Healthy lungs (n=5)</td>
<td></td>
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<tr>
<td>Animal</td>
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<tr>
<td>Animal</td>
<td>Inflation</td>
<td>Deflation</td>
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<tr>
<td></td>
<td>τ 1</td>
<td>τ 2</td>
</tr>
<tr>
<td>ARDS lungs (n=4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animal</td>
<td>τ 1</td>
<td>τ 2</td>
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<tr>
<td>ARDS lungs (n=4)</td>
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</table>
was consistent with the well-described radiological criteria for healthy lungs during general anaesthesia, and for lungs in an early stage of ARDS, respectively.\(^8\)\(^9\) Images also closely resembled those published by Neumann and co-workers, who compared saline-lavage in pigs with ARDS induced by oleic acid and endotoxin administration, using dynamic CT.\(^2\)

Various definitions of ‘lung aeration’, defined by densitometry of CT images, co-exist in the radiology literature. Neumann and co-workers used the increase or decrease of MLD to quantify the changing air content in serially acquired CT images.\(^10\) MLD reduces the entire distribution function of density values, for example the attenuation histogram, in the lung to a single-number descriptor. Therefore, it will reflect not only the change of aeration in a lung region of interest, but also varying contributions of intravascular and extravascular water content. Temporal dynamics of MLD are, therefore, determined not by the processes of aeration (or collapse) alone, but by the net temporal behaviour of all density domains or compartments of a region together. A decrease in MLD may thus represent effects as different as recruitment, ventilation, overdistension, or even barotrauma. Such processes are, however, clearly discernible if, within the spectrum of attenuations, a density range is selected which is known to specifically reflect the effects of interest. We wished to detect rapid changes in parenchymal aeration, for example recruitment and ventilation, with high sensitivity, and not to compare absolute gas content of healthy and diseased lungs. Therefore, we studied aeration changes by following the temporal behaviour of specific density windows, which we had tuned to our animal model and imaging parameters in a previous study.\(^3\) In the literature, a density range of \(-910\) to \(-500\) HU is used to detect aerated lung areas. In this previous study, airway pressure was increased and decreased in a stepwise manner (5 cm H\(_2\)O every 5 s) during dynamic multiscan CT. In healthy and lavaged lungs, the fractional area change of attenuation ranges of increasing bandwidth (constant lower threshold of \(-910\) HU, higher threshold increasing from \(-800\) HU to \(-200\) HU in steps of 100 HU) was determined planimetrically and compared. We found a density window from \(-910\) HU to \(-700\) HU for healthy lungs, and from \(-910\) HU to \(-300\) HU for lavage ARDS to be most sensitive to airway pressure-dependent changes in lung aeration.\(^3\) These response curves are shown

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Fig 3 Transverse supradiaphragmatic CT scans of lavage-ARDS lungs during airway pressure increase from 0 to 50 cm H\(_2\)O. (A) At end-expiration, large areas of atelectasis and a marked antero-posterior density gradient can be observed. (B) After 3 s of CPAP maintained at 50 cm H\(_2\)O, a reduction of atelectasis is visible, although a marked density gradient remains. (C) At end-inspiration, 31 s after increase to 50 cm H\(_2\)O CPAP, the entire cross-sectional lung area appears aerated, although to a variable degree. Nevertheless, ground-glass opacities caused by increased lung water content persist. In the scans acquired subsequently, a slightly varying slice position can be noted as a result of a cranio-caudal motion of the lung during the manoeuvre.
in Figure 5. They are explained by the fact that after lavage a greater parenchymal water content causes ground-glass opacities which nevertheless respond strongly to aeration. Another way to assess aeration of lung tissue, which also avoids the shortcomings of regional analysis of MLD, is to calculate the total amount of air on a pixel-by-pixel basis as described by Puybasset and colleagues. This approach translates, in a strictly proportional fashion, x-ray attenuation (in Hounsfield Units) into fractional gas content, and calculates absolute FRC from this and from the volume of voxels. To obtain volumetric data that are meaningful to the clinician, this technique requires static thin-section CT acquisition of the entire lung volume. At present, however, fast dynamic assessment of multiple slices or even the entire lung volume is not yet technically possible. Once this is achieved, our technique will allow calculation of the compartmental distribution of the tidal volume and the pertinent time constants, similar to that of Puybasset and colleagues.

Fig 4 (a) Relative increase of aerated lung area after airway pressure increased from 0 to 50 cm H2O in lavage ARDS. Aerated lung area (pixels with densities ranging from −910 to −300 HU) is expressed as fraction (in per cent), which becomes aerated from the airway pressure increase from ZEEP. (b) Relative decrease of aerated lung area after airway pressure decreased from 50 to zero cm H2O in lavage ARDS. Aerated lung area (pixels with densities ranging from −910 to −300 HU) is expressed as fraction (in per cent), which collapses from the airway pressure step-down to ZEEP. Individual animals are represented by different symbols.
colleagues. However, as our study was restricted to a fast dynamic but two-dimensional analysis of only one large transverse lung slice, attenuation was not transformed further into gas content in that slice, particularly because relative compartmental size and time constants are independent of such a transformation.

Neumann and colleagues evaluated the temporal dynamics of lung inflation and collapse with a fast CT technique, assuming a priori a one-compartmental behaviour of the lung. They found that both recruitment and collapse of lungs damaged with saline lavage, oleic acid and endotoxin-induced ARDS occurred mainly during the first 4 s. In lavage-ARDS, a longer $t_1$ ($\approx 2.0$ s) was observed in expiration than in inspiration ($\approx 0.7$ s). Our results support these findings. These authors fitted their data to follow a mono-exponential relationship, and the contribution of our ‘slow’ compartment may have been underestimated by their choice of an upper CPAP level of $\approx 40$ instead of the 50 mbar we used. They concluded that in their experimental settings, expiratory times $< 0.6$ s would be necessary to avoid cyclic alveolar collapse during mechanical ventilation, which is also supported by the findings of our study for the lavage-ARDS model.

In a related study of porcine oleic-acid-induced ARDS, Neumann and co-workers used several PEEP levels ranging from 10 to 25 cm H$_2$O and an inspiratory peak pressure of 15 cm H$_2$O above PEEP to determine the minimum PEEP level as well as the critical inspiratory and expiratory time to avoid lung collapse. They found that a PEEP level $> 20$ cm H$_2$O or an expiration time $= 0.6$ s were required to largely prevent expiratory lung collapse. As the short deflation $t_1$ in our ARDS series ranged between 0.4 and 1.0 s, we predict that reducing expiration time to $< 0.6$ s would allow deflation of only about 60% of the fast compartment, causing FRC to increase, and would completely prevent collapse of the ‘slow’ compartment ($t_2 > 7$ s). However, whereas titration of PEEP or expiration times takes time and requires repeated assessments by blood gas analysis or CT, the technique to derive compartmental time constants of lung aeration from one rectangular CPAP manoeuvre may reduce the time to optimize the ventilation pattern in an individual ARDS patient.

Recently, electrical impedance tomography (EIT) has been introduced as another image-based technique to quantify regional lung aeration. Kunst and colleagues showed, that the lower and upper inflection point can be determined with EIT in porcine lavage ARDS lungs. In contrast with dynamic CT, EIT can be used as a bedside technique without any radiation exposure. CT, on the other hand, allows much better temporal and spatial resolution. Further studies are necessary to compare these methods and their potential roles for clinical decision-making.
A current limitation of our technique is that the resolution of the CT data is only achieved in one cross-sectional slice of the lung. We selected a slice between apex of the heart and diaphragm, which allows a fair approximation of total ventilated lung area. To reduce consecutive errors in planimetry and densitometry, the cross-sectional slice for image acquisition was determined by a scout view and a reference scan before each experiment. This slice definition was important to ensure that in every CT image only the lung parenchyma between the apex of the heart and the diaphragm was measured. Also, as the scanner table is immobile during the dynamic multiscan acquisition, this slice cannot be followed during inspiration or expiration although the lung area of interest moves slightly over time with the cranio-caudal respiratory motion of the lung. This may explain the occasional, counterintuitive observation in our series as well as in others, that ventral lung regions actually appear to become smaller again during late inspiration (compare Fig. 3B and C), or that density in ventilated (subcardial accessory lobe of the pig lung. Deviation from a two-compartmental behaviour, i.e. existence of a third compartment, is another possibility yet to be studied. In the near future, multislice CT scanners will allow simultaneous acquisition of several slices. These image series, acquired at different cranio-caudal levels, may also allow dynamic lung volume changes to be calculated during ventilation.

The temporal resolution of the CT scanner was limited to 250 ms in this study. This resolution allows 6 data points to be obtained during 1.5 s; for example, a $\tau$ of 0.5 s is the minimum to be determined by least-squares fitting. Scanning at even better temporal resolution would be necessary if $\tau < 0.5$ s are expected. Fast dynamic CT acquisitions with an effective temporal resolution up to 100 ms are already available, and further improvement may come soon. An even better temporal resolution of about 50 ms is already obtainable by electron beam scanners (EBCT), but this technology is not widely available for clinical use, and causes increased radiation exposure compared with spiral CT scanners.

Even dynamic CT uses a lot of radiation. Although dosimetry was not performed in this study, preliminary data on humans show a dose of 47 mGy for a 10 s dynamic CT measurement, using the same scanner and similar acquisition parameters, compared with a dose of approximately 30–40 mGy when undergoing a spiral CT of the thorax.

**Clinical consequences**

Different respiratory time constants and their individual contributions to lung ventilation and alveolar recruitment can be found by dynamic CT acquisition using clinical spiral CT scanners. Such analyses may help to rapidly and individually optimize ventilator settings in ARDS patients, avoid cyclic alveolar collapse and reopening, maximize ventilated lung, and reduce respirator-induced lung injury. Dynamic CT techniques open a new diagnostic field, providing a regional analysis of lung function with correlation to the underlying pathology. Further studies are necessary to establish the clinical value of this method.

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