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Assessment of PEEP-induced reopening of collapsed lung regions in acute lung injury: are one or three CT sections representative of the entire lung?

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On behalf of the ARDS CT Scan Study Group

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Abstract *Objectives*: To study whether PEEP-induced reopening of collapsed lung regions – defined as the decrease in nonaerated lung volume measured on a single or three computerized tomographic (CT) sections – is representative of the decrease in overall nonaerated lung volume.
Design: Review of 39 CT scans obtained in consecutive patients with Acute Lung Injury.
Settings: Fourteen-bed surgical intensive care unit of a University Hospital.
Measurements and results: PEEP-induced decrease in nonaerated lung volume was measured in 39 patients with ALI on a single juxtadiaphragmatic CT section, on three CT sections – apical, hilar, and juxtadiaphragmatic – and on contiguous apex-to-diaphragm CT sections. The percentage of decrease in nonaerated lung volume following PEEP, was compared between one, three and all CT sections using a linear regression analysis and Bland and Altman's method. The decrease in nonaerated lung volume measured on a single and three CT sections was significantly correlated with the decrease in nonaerated lung volume measured on all CT sections: $R = 0.83$, $P < 0.0001$ for one CT section and $R = 0.92$, $P < 0.0001$ for three CT sections. However, measurements performed on a single CT section were poorly representative of the overall lung: bias –6 %, limits of agreement ranging between –37 % and +25 %. Measurements performed on three CT sections overestimated by 11 % the overall decrease in nonaerated lung volume: bias –11 %, limits of agreement ranging between –29 % and +7 %.
Conclusions: PEEP-induced reopening of collapsed lung regions measured on a single or three CT sections sensibly differs from the reopening of collapsed lung regions measured on the overall lung. The inhomogeneous distribution of PEEP-induced reopening of collapsed lung regions along the cephalocaudal axis probably explains these discrepancies.

Keywords Acute lung injury · Computed tomography · Positive end-expiratory pressure · Alveolar recruitment

Introduction

Lung Computed Tomography (CT) became available in the critical care environment in the mid-1980s enabling the assessment of positive end-expiratory pressure (PEEP)-induced reopening of collapsed lung regions in Acute Respiratory Distress Syndrome (ARDS) [1, 2, 3]. The first generation of CT scanners that were available at that moment had a major limitation: the acquisition of a single CT section required 2–3 min rendering impossible the analysis of the entire lung because of the risk of high X-ray exposure [4]. As a consequence, the lung CT scan performed in patients with ARDS was limited to 1–3 CT sections supposed to be representative of the whole lung [5]. Later on, a comparison was made between a single basal CT section located 1–2 cm above the diaphragm and three CT sections corresponding to lung levels of apex, hilum, and base in patients with acute respiratory failure: a significant correlation was found between the CT number characterizing the single basal CT section and the average CT number characterizing the three CT sections, and the basal CT section was considered as representative of the entire lung [6].

The development of a new generation of helicoidal CT scanners in the 1990s gave the possibility of scanning the entire lung parenchyma in patients with ARDS. Using a specific software designed for measuring regional lung volumes of gas and tissue, we evidenced an inhomogeneous intrapulmonary distribution of gas and tissue in patients fulfilling the criteria of ARDS resulting in marked differences of lung morphology and radiological presentation [7, 8]. In addition, PEEP-induced reopening of collapsed lung regions was markedly influenced by the lung morphology feature at zero end-expiratory pressure (ZEEP). In patients with diffuse CT attenuations, the PEEP-induced reopening of collapsed lung regions was homogenously distributed along the cephalocaudal axis. In contrast, in patients with lobar and patchy CT attenuations whose upper lobes remained partially aerated, PEEP-induced reopening of collapsed lung regions decreased from the lung apex to the diaphragm whereas lung overdistension was observed in normally aerated lung regions at ZEEP [9, 10]. These results suggest that reopening of collapsed lung regions may not be correctly assessed when measured on a single or three CT sections.

The aim of the study was to compare the PEEP-induced reopening of collapsed lung regions measured on a single juxtadiaphragmatic and on three CT sections to the reopening of collapsed lung regions measured on all CT sections in a series of patients with acute lung injury (ALI).

Materials and methods

Patients

The CT scans of 39 consecutive patients with ALI who had been included in different therapeutic and investigational protocols [7, 8, 9, 10, 11, 12, 13, 14] were reviewed and analyzed for the present study. ALI was defined according to criteria proposed by the American-European Consensus Conference [15] and each patient underwent thoracic CT scans under ZEEP and PEEP conditions within the first 10 days of the acute lung disease. During the protocol, each patient was sedated and paralyzed, mechanically ventilated and monitored using a Swan-Ganz catheter. Clinical characteristics including the Lung Injury Severity Score (LISS) [16] and the ARDS Severity Score (ARDS-SS) [8] were recorded. Cardiorespiratory parameters including cardiac filling pressures, true pulmonary shunt, airway pressures, and blood gas were measured in ZEEP conditions. In each individual, a P-V curve was performed in ZEEP conditions according to a technique previously described [17] and PEEP was set according to the initial part of the P-V curve. In the absence of a detectable lower inflection point, a PEEP of 10 cmH_2O was administered. When a lower inflection point was identified, the PEEP was set 2 cmH_2O above. PEEP ranging between 10 cmH_2O and 17 cmH_2O were administered. In each individual, respiratory rate and tidal volume were adjusted by the physician in charge in order to achieve $PaCO_2$ values between 30 mmHg and 50 mmHg without exceeding a plateau inspiratory pressure of 35 cmH_2O and generating auto-PEEP [14]. An inspiratory time of 33 % and a FiO_2 of 1 were maintained throughout the study period.

Acquisition of the CT sections and measurement of lung volume

Each patient was transported to the Department of Radiology (Thoracic Division) by two intensivists. Mechanical ventilation was provided using an Osiris ventilator (Taema, France) delivering 100 % oxygen. Heart rate, pulse oxymetry, and systemic arterial pressure were monitored continuously using a Propaq 104 EL monitor (Protocol System, North Chicago, Ill., USA). Lung scanning was performed from the apex to the diaphragm using a fast spiral Tomoscan SR 7000 (Philips, Eindhoven, The Netherlands) as previously described [13]. All images were observed and photographed at a window width of 1,600 Hounsfield Units (HU) and a level of –700 HU. The exposures were taken at 120 kV and 250 mAs. The value of the pitch was 1. Contiguous axial CT sections 10-mm thick were reconstructed from the volumetric data. Acquisitions of spiral CT sections were first obtained at end-expiration in ZEEP (pulmonary volume equal to apneic functional residual capacity), the patient being disconnected from the ventilator and then, 15 min after applying PEEP, the connecting piece between the Y piece and the endotracheal tube being clamped at end-expiration. Airway pressure was monitored during the CT scan acquisition in PEEP to ensure that the selected pressure was actually applied. All CT scans were recorded on optical disks for later computerized analysis. In ZEEP and PEEP conditions, three CT sections were selected from all CT sections at three different lung levels (apex, hilum, and base) as previously recommended [3]: the apical CT section was selected 2 cm above the carina, the hilar CT section 1 cm below the carina, and the basal CT section 1 cm above the diaphragmatic cupola.

The lung volume was computed as the total number of voxels present in a given region times the volume of the voxel. The lung is composed of gas and tissue and it can be assumed that lung tissue has a density equal to water's density. The respective volumes of gas and tissue were measured using a specifically designed software (Lungview) according to a previously described analysis [9, 10], based on the tight correlation existing between CT attenuations and the physical density [18].

In order to differentiate the lung zones with different degrees of aeration, the entire lung was divided into four zones using a color encoding analysis provided by the software Lungview: lung zones with a CT attenuation between –1,000 and –900 HU were considered as overdistended [19], those between –900 and –500 HU as normally aerated, those between –500 and –100 HU as poorly aerated, and those between –100 and +100 HU as nonaerated (Fig. 1). Intraparenchymal pulmonary vessels were included in the analysis and considered as nonaerated lung regions. Mediastinal vessels were excluded from the analysis.

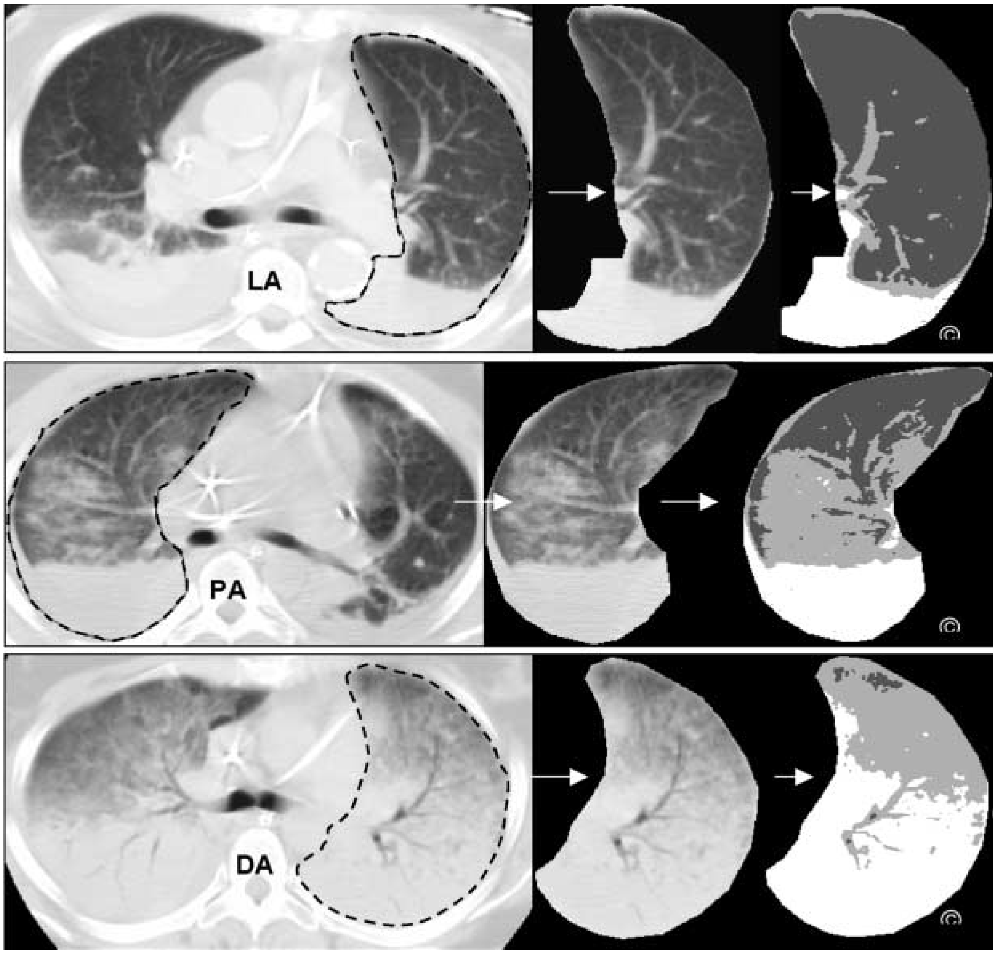

Fig. 1 Classification of the patients into three groups according to computed tomography lung morphology. Following manual delineation of lung parenchyma *(dashed line, first white arrow)*, a color encoding analysis was applied *(second white arrow)* allowing the visualization of the distribution of lung CT attenuation. Normally aerated lung parenchyma characterized by CT attenuations ranging between –500 and –900 Hounsfield Units (HU) appears in *dark gray*, poorly aerated lung parenchyma (–500 and –100 HU) in *light gray*, and nonaerated parenchyma (-100 and +100 HU) in *white*. *Group LA* lobar CT attenuations *(upper panels)*, *group PA* patchy CT attenuations *(middle panels)*, *group DA* diffuse CT attenuations *(lower panels)*

CT measurement of reopening of collapsed lung regions

PEEP-induced reopening of collapsed lung regions was assessed by the method proposed by Gattinoni et al. [20] and defined as the decrease in nonaerated lung volume between PEEP and ZEEP, and expressed in percentage of variation in order to allow for the comparison between alveolar recruitment measured on a single, three, and all CT sections:

Reopening of collapsed lung regions (%) =

$$\frac{V_{\text{nonaeratedPEEP}} - V_{\text{nonaeratedZEEP}}}{V_{\text{nonaeratedZEEP}}}$$

where $V_{\text{nonaerated ZEEP}}$ is the volume of the nonaerated lung tissue in ZEEP conditions and $V_{\text{nonaerated PEEP}}$ is the volume of the nonaerated lung tissue in PEEP conditions.

Classification of the patients according to CT lung morphology

The patients were classified into three groups on the basis of the distribution of CT attenuations as described by Puybasset et al. [7]. When areas of lung attenuation had a lobar or segmental distribution established on the recognition of anatomical structures, such as the major fissure or interlobular septas, the patient was classified as having a lobar pattern (group LA = lobar attenuations); when lung attenuations were diffusely distributed throughout the lungs, the patient was considered as having a diffuse pattern (group DA = diffuse attenuations); the patients presenting in some parts of the lungs lobar or segmental areas of lung attenuations, and in some other parts lung attenuations without recognized anatomical limits, were classified as having a patchy pattern (group PA = patchy attenuations).

Statistical analysis

Cardiorespiratory parameters measured in ZEEP conditions among the patients with lobar, patchy, and diffuse CT attenuations were compared using a one-way analysis of variance. Correlations between reopening of collapsed lung regions measured on a single, three, and all CT sections were performed by means of a simple linear regression analysis and agreement between the three methods was tested using the method proposed by Bland and Altman [21]. The statistical analyses were performed using Statview 5.0 (SAS Institute, Cary, N. C., USA). All data are expressed as mean ± SD and statistical significance level was fixed at 0.05.

Results

Clinical characteristics and cardiorespiratory status

Thirty-nine patients with ALI (nine females and 30 males, mean age 53 ± 18 years) were studied. ALI was related to postoperative pulmonary infection (*n* = 20), bronchopulmonary aspiration in the postoperative period (*n* = 8), lung contusion (*n* = 7), and septic shock from extra-pulmonary origin (*n* = 4). According to CT lung morphology, 14 patients were classified as having lobar CT attenuations, 16 patients as having patchy CT attenuations, and nine as having diffuse CT attenuations (Fig. 1). As shown in Table 1, the patients with diffuse CT attenuations had the highest LISS, ARDS-SS, peak inspiratory pressure (Pmax), end-inspiratory plateau pressure (Pplateau), mean pulmonary arterial pressure (Ppa) and true pulmonary shunt (Qs/QT), and the lowest quasi-static respiratory compliance (Cqs) suggesting that the respiratory function was more impaired than in the two other groups.

Reopening of collapsed lung regions measured on a single, three, and all CT sections in the three groups of patients

As a mean, reopening of collapsed lung regions was overestimated when measured on a single (6 %) or three CT sections (11 %, Fig. 2). However, the limits of agreement characterizing the single juxtadiaphragmatic CT section were wide, ranging between –37 % and +25 %, indicating that in many patients, reopening of collapsed lung regions was either underestimated or overestimated. The limits of agreement were narrower when PEEP-induced reopening of collapsed lung regions was measured on three CT sections, ranging between –29 % and +7 %, indicating that in the majority of patients, PEEP-induced reopening of collapsed lung regions was overestimated. The bias and the limits of agreement were not influenced by the lung morphology pattern.

Discussion

In patients with ALI, PEEP-induced reopening of collapsed lung regions measured on a single juxtadiaphragmatic CT section overestimates or underestimates the overall reopening of collapsed lung regions. When three CT sections are used to quantify reopening of collapsed lung regions, systematic overestimation is made. The lung morphology pattern does not seem to influence the error made.

Table 1 Clinical characteristics and cardiorespiratory parameters in the three groups of patients with acute lung injury (ZEEP, $FiO_2 = 1.0$). (*Delay* mean delay between the onset of Acute Lung Injury and inclusion in the study, *LISS* lung injury severity score, *ARDS-SS* ARDS severity score, *Cqs* quasi-static respiratory compliance, V_T tidal volume, *RR* respiratory rate, *Pmax* peak inspiratory pressure, *Pplateau* end-inspiratory plateau pressure, *PEEP* positive end-expiratory pressure, *Qs/QT* true pulmonary shunt, *Ppa* mean pulmonary arterial pressure, *Ppcw* pulmonary capillary wedge pressure, *PVRI* pulmonary vascular resistance index, *group LA* lobar CT attenuations, *group PA* patchy CT attenuations, *group DA* diffuse CT attenuations)

	LA (*n* = 14)	PA (*n* = 16)	DA (*n* = 9)	*P* values
Age (years)	60 ± 16	51 ± 19	44 ± 18	NS
Delay (days)	5 ± 2	5 ± 4	7 ± 4	NS
LISS	1.8 ± 0.6	2.5 ± 0.6	2.7 ± 0.8	0.005
ARDS-SS	3.2 ± 2.2	11.6 ± 2.2	16.5 ± 2.3	< 0.0001
Shock	50 (7)	56 (9)	78 (7)	NS
Mortality	36 (5)	38 (6)	44 (4)	NS
Cqs (ml/cmH_2O)	61 ± 17	49 ± 12	37 ± 8	< 0.001
V_T (ml)	662 ± 117	735 ± 206	651 ± 136	NS
RR (b/min)	19 ± 3	22 ± 6	23 ± 2	NS
Pmax (cmH_2O)	20 ± 5	27 ± 8	30 ± 5	0.003
Pplateau (cmH_2O)	14 ± 3	20 ± 6	22 ± 3	< 0.001
PEEP (cmH_2O)	13.6 ± 2.5	13.3 ± 2.7	13.8 ± 2.9	NS
PaO_2 (mmHg)	175 ± 51	126 ± 73	134 ± 107	NS
Qs/QT (%)	36 ± 3	40 ± 7	47 ± 12	0.008
Ppa (mmHg)	22 ± 7	27 ± 5	28 ± 8	0,03
Ppcw (mmHg)	9 ± 3	10 ± 3	12 ± 4	NS
PVRI (dynes · sec^{-1} · cm^{-5} · m2)	294 ± 124	362 ± 131	281 ± 156	NS

Correlations and agreements

In five patients with ARDS, Tagliabue et al. found a good correlation between the mean CT number characterizing three CT sections taken at the apex, hilum, and base and the mean CT number characterizing the overall lung [22] and concluded that three CT sections were representative of the entire lung. In the present study, statistical correlations were found between PEEP-induced reopening of collapsed lung regions measured on a single, three, and all CT sections in a series of patients with ALI. However, a high statistical correlation between two methods does not mean that the two methods are equivalent. In the present study, PEEP-induced reopening of collapsed lung regions was measured as the decrease in nonaerated lung volume assessed on contiguous CT sections performed from the apex to the diaphragm. The hypothesis tested was that measurements made on a single juxtadiaphragmatic CT section or on three CT sections (apex, hilum, base) were representa-

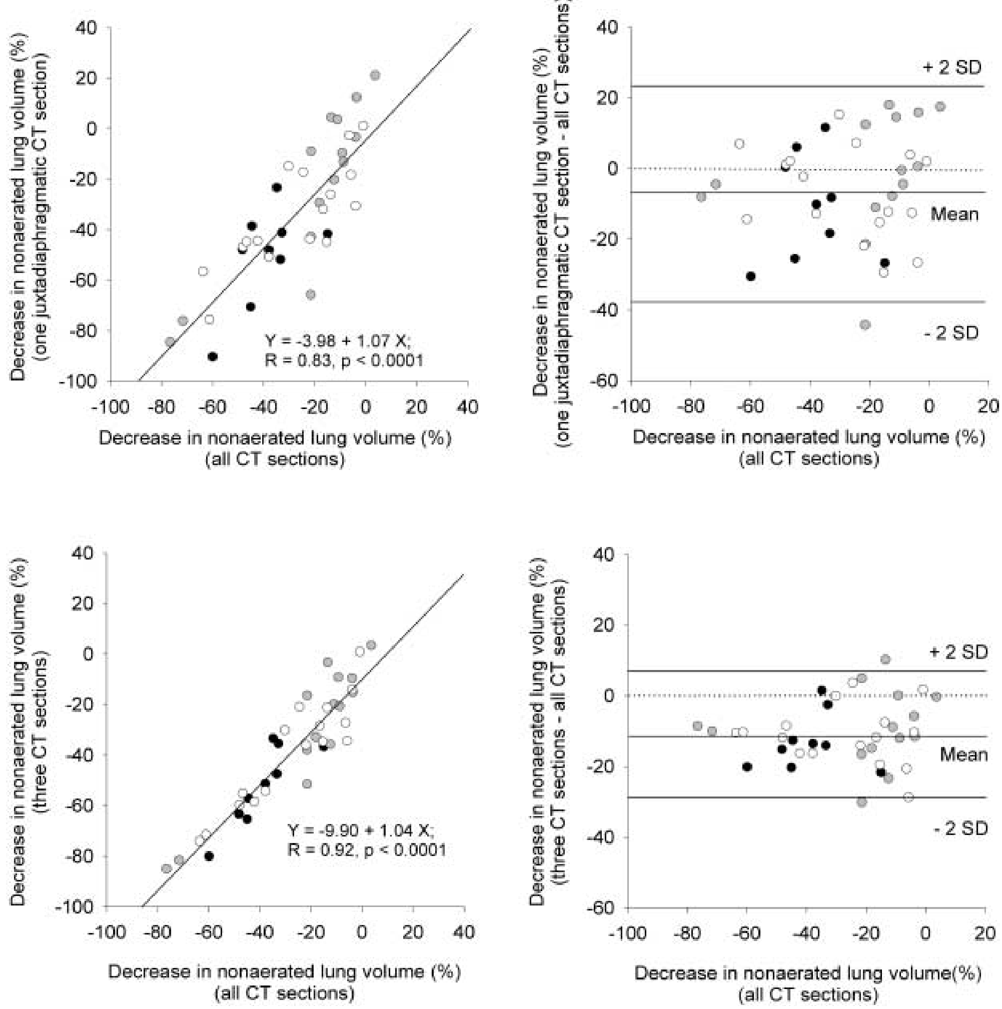

Fig. 2 Linear regression analysis and Bland and Altman representation of PEEP-induced reopening of collapsed lung regions measured on a single juxtadiaphragmatic CT section vs all CT sections *(upper panels)*, and on three CT sections vs all CT sections *(lower panels)* in 39 patients with ALI. Patients with diffuse CT attenuations are represented as *black circles*; patients with patchy CT attenuations as *gray circles,* and patients with lobar CT attenuations as *white circles*

tive of measurements performed on the entire lung. The statistical analysis according to Bland and Altman [21] shows that the measurements performed on a single juxtadiaphragmatic CT section overestimate or underestimate the overall reopening of collapsed lung regions. If performed on three CT sections, measurements systematically overestimate the overall reopening of collapsed lung regions.

Factors influencing the intrapulmonary distribution of PEEP-induced reopening of collapsed lung regions

At least three factors may have an impact on the measurement of reopening of collapsed lung regions performed on a limited number of CT sections.

The first is lung anatomy. When using three CT sections – apical, hilar, and juxtadiaphragmatic – the exact anatomical level of the "hilar" section is critical for obtaining a representative sample of the entire lung. Upper lobes – including the middle lobe on the right side and the lingula on the left side – have a volume equivalent to lower lobes in healthy volunteers [7, 13]. A "hilar" CT section obtained 1 cm below the carina level as previously recommended [1, 23], contains 75 % of upper lobe and 25 % of lower lobe (segment 6) [24]. Therefore, for anatomical reasons, the three CT sections will be mainly representative of the reopening of collapsed lung regions occurring in the upper lobes. An accurate representation of what PEEP does in upper and lower lobes would require a "hilar" CT section located 3–4 cm below the carina where upper and lower lobes occupy 50 % of the lung area [24].

The second factor that may bias the measurements performed on a limited number of CT sections is the cephalocaudal distribution of PEEP-induced alveolar recruitment. We recently demonstrated that the reopening of collapsed lung areas decreases from the apex to the diaphragm in a majority of patients with ARDS [9]. The reason for that is that the lower part of the rib cage is submitted to mechanical forces such as cardiac weight [11] and increase in abdominal pressure [13] that act as counterforces to PEEP. Therefore it is not surprising that measuring reopening of collapsed lung regions on three CT sections that are more representative of upper than lower lobes results in a systematic overestimation of the reopening of collapsed lung regions occurring in the overall lung.

A third confounding factor that may act in the opposite direction is the loss of lung volume at the lower lobe level. We recently demonstrated that PEEP-induced reopening of collapsed lung areas of lower lobes is inversely correlated with the overall volume of lower lobes [13]. The more atelectatic are the lower lobes, the lower the PEEP-induced reopening of collapsed lung areas. Therefore in patients with atelectatic lower lobes, the juxtadiaphragmatic CT section may underestimate PEEP-induced reopening of collapsed lung regions occurring in more cephalic parts of the lung.

For a given individual patient, the error made when measuring reopening of collapsed lung regions on a single or three CT sections will depend on the relative importance of these different confounding factors.

Appendix A: Members of the ARDS CT Scan Study Group

The following members of the ARDS CT Scan Study Group participated in the study:

- L. Puybasset
- Neurosurgical ICU, Department of Anesthesiology, Hôpital de la Pitié-Salpêtrière, Paris, France
- J. Richecoeur
- General ICU, Hôpital de Pontoise, Pontoise, France
- S. Vieira
- Hospital De Clinicas de Porto Allegre, UFRGS, Brazil
- J.M. Constantin
- Department of Anesthesiology, Hôpital Gabriel Montpied, Clermont Ferrand, France
- P. Grenier, P. Cluzel
- Department of Radiology, Hôpital de la Pitié-Salpêtrière, Paris, France
- F. Préteux, C. Fetita
- Institut National des Télécommunications, Evry, France

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