

Acoustic evidence of airway opening during recruitment in excised dog lungs

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¹Department of Medical Informatics and Engineering, and ²Institute of Surgical Research, University of Szeged, H-6720 Szeged, Hungary; and ³Center for Polymer Studies and Department of Physics, and ⁴Department of Biomedical Engineering, Boston University, Boston, Massachusetts 02215

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Hantos, Z., J. Tolnai, T. Asztalos, F. Peták, Á. Adamicza, A. M. Alencar, A. Majumdar, and B. Suki. Acoustic evidence of airway opening during recruitment in excised dog lungs. *J Appl Physiol* 97: 592–598, 2004. First published April 16, 2004; 10.1152/jappphysiol.01402.2003.—The aim of this study was to test the hypothesis that the mechanism of recruitment and the lower knee of the pressure-volume curve in the normal lung are primarily determined by airway reopenings via avalanches rather than simple alveolar recruitments. In isolated dog lung lobes, the pressure-volume loops were measured, and crackle sounds were recorded intrabronchially during both the first inflation from the collapsed state to total lobe capacity and a second inflation without prior degassing. The inflation flow contained transients that were accompanied by a series of crackles. Discrete volume increments were estimated from the flow transients, and the energy levels of the corresponding crackles were calculated from the sound recordings. Crackles were concentrated in the early phase of inflation, with the cumulative energy exceeding 90% of its final value by the lower knee of the pressure-volume curve. The values of volume increments were correlated with crackle energy during the flow transient for both the first and the second inflations ($r^2 = 0.29–0.73$ and $0.68–0.82$, respectively). Because the distribution of volume increments followed a power law, the correlation between crackle energy and discrete volume increments suggests that an avalanche-like airway opening process governs the recruitment of collapsed normal lungs.

airway closure; pressure-volume curve; avalanches

IN RECENT YEARS, it has become evident that the survival outcome of patients mechanically ventilated during acute respiratory distress syndrome (ARDS) can be significantly improved if the ventilation strategy is based on some assessment of the mechanical condition of the respiratory system (3, 17). In particular, the lower and upper knees of the pressure-volume (P-V) curve of the respiratory system have been used to optimize the positive end-expiratory pressure and tidal volume during mechanical ventilation. With the “open lung” approach (18), the positive end-expiratory pressure is set slightly above the pressure at the lower knee of the P-V curve to minimize alveolar collapse at end expiration. Animal studies also suggest that the repetitive collapse and reopening at low airway pressures can lead to injury due to the high shear stresses on the airway and alveolar walls (24), which has recently been confirmed by directly observing cell injury induced by fluid flow (\dot{V}) mimicking airway opening in a cell culture system (4). Thus understanding the mechanisms influencing recruitment and how they contribute to the formation of the lower knee of

the P-V curve is essential to minimizing the risk of injury propagation in the lung.

In the normal lung, the lower knee of the inspiratory P-V curve exists only if the inflation proceeds from the collapsed state (6, 14). However, in animal models of ARDS (6, 31) and in human subjects suffering from ARDS (7, 15), the P-V curve often exhibits a lower knee even though the lung is inflated from functional residual capacity. To relate the lower knee to recruitment, Frazer et al. (9) proposed that, during inflation, individual lung units open sequentially, and experimental data consistent with this interpretation have been presented (5). The general interpretation of the lower knee in the injured lung has been the same as for the first inflation of normal lungs from the degassed state (9, 10, 15, 28). However, the relation between recruitment and the lower knee is unclear because it has also been suggested that significant recruitment can occur in patients whose P-V curve does not exhibit a lower knee (22).

Using a computer model, Hickling (15) extended the idea of Frazer et al. (9) that alveoli open sequentially and showed that both the lower and upper knees of the P-V curve can be influenced by recruitment. More recently, Wilson et al. (37) developed a model of the P-V curve based on the mechanics of a partially or fully flooded alveolus. This model can account for the lower knee of the P-V curve without assuming sequential opening of lung units. Nevertheless, there is experimental evidence suggesting that, during mechanical ventilation of the injured lung, some alveoli expand as in the normal lung and some are overinflated, whereas some undergo cyclic collapse and sudden reopening (30). Therefore, it is likely that multiple mechanisms contribute to the lower knee of the P-V curve, including recruitment and the mechanics of fluid-filled alveoli (16). The common assumption in these studies is that all mechanisms governing the recruitment process occur at the alveolar level (5, 6, 10, 12, 36, 37).

Airway closure and reopening can also affect the process of recruitment (23). Suki et al. (35) put forth the idea that airways open in cascades or avalanches. During inflation, a collapsed airway suddenly opens at a critical opening threshold pressure (13, 19). If the threshold pressure of one or both daughter airways is also smaller than the pressure in the parent airway, then one or both segments will open simultaneously with the parent. This process continues to propagate down the airway tree, defining an avalanche of openings. Based on this concept, the P-V curve of the lung as well as its lower knee during the first inflation from the degassed state have been successfully

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modeled in symmetric (34) as well as asymmetric (20, 21) airway tree structures.

The purpose of the present study was to test the hypothesis that the mechanism of recruitment and the lower knee of the P-V curve in the normal lung are significantly influenced by the process of airway reopenings via avalanches. We reasoned that, if recruitment occurs via avalanche-like airway reopenings, then the recruited lung volume along the P-V curve should consist of a highly irregular sequence of discrete volume increments (ΔV). The distribution of these ΔV , which correspond to avalanches reaching the alveoli, should follow a power law (32, 33). Additionally, because airway opening is also associated with crackle sound generation (2, 6, 8, 23, 25, 27), we expect that the density of crackles is highest near the lower knee of the P-V curve. To test these predictions, we measured P-V loops in normal isolated dog lung lobes during inflation from the collapsed state to total lobe capacity. Recruitment in the form of discrete lung ΔV was assessed with a high-sensitivity flowmeter, and airway openings were identified as individual crackles from lung sound measurements (23). To study the effects of trapped air on recruitment, these measurements were repeated for a second inflation without degassing the lung.

METHODS

Diaphragmatic lung lobes ($n = 12$) were harvested from six mongrel dogs. The animals were anesthetized with pentobarbital sodium (30 mg/kg), heparinized (5,000 U), and exsanguinated through a femoral artery catheter. The procedure was approved by the Institutional Animal Care and Use Committees of the University of Szeged and Boston University. After thoracotomy, the lungs were removed, and the diaphragmatic lobes were separated and cannulated in the main bronchus. Preceding the inflation maneuver, the lobe was suspended in a 30-liter glass box, with the bronchial cannula led to the atmosphere through a high-resistance ($6.5 \text{ cmH}_2\text{O} \cdot \text{l}^{-1} \cdot \text{s}$) screen pneumotachograph measuring \dot{V} by means of a Validyne MP-45 ($\pm 2 \text{ cmH}_2\text{O}$) differential pressure transducer. The translobar pressure, i.e., the difference between airway opening and box pressures, was measured with another Validyne MP-45 ($\pm 30 \text{ cmH}_2\text{O}$) transducer. During the measurement, pressure was slowly increased from 0 to 30 cmH_2O in 60–120 s by decreasing the box pressure with a membrane pump (model MP 03Ez, Otto Huber, Germany). The signals of \dot{V} and pressure were low-pass filtered at 50 Hz and sampled at a rate of 256 Hz by the analog-digital board of a personal computer. A small (5-mm diameter) commercial microphone was introduced through the side-arm of the cannula in the main bronchus. The sound signal was high-pass filtered at 10 Hz and sampled at 22,050 Hz with 16-bit resolution by the sound recorder of another personal computer. After the first inflation from the collapsed state, the box was opened to atmosphere, and the lobe was kept at $P = 0$ for at least 5 min. The first inflation was followed by a second inflation of those lobes ($n = 7$), which did not leak during the first maneuver, i.e., \dot{V} approached zero at high pressure values.

An example of raw and preprocessed crackles is shown in Fig. 1. It can be seen that a crackle consists of a sharp initial negative deflection in pressure followed by some acoustic low-frequency (LF) ringing. The raw sound recordings were processed in three ways. High-pass filtering at 1 kHz accentuated the initial sharp transient of the crackle waveform and suppressed the LF after ringing. This process provided an increased temporal resolution for the identification of the successive crackles that were often superimposed and hence inseparable in the unfiltered signals. LF energy content of the crackles was obtained by digital low-pass filtering at 60 Hz and squaring the sound pressure amplitude. Finally, the time course of

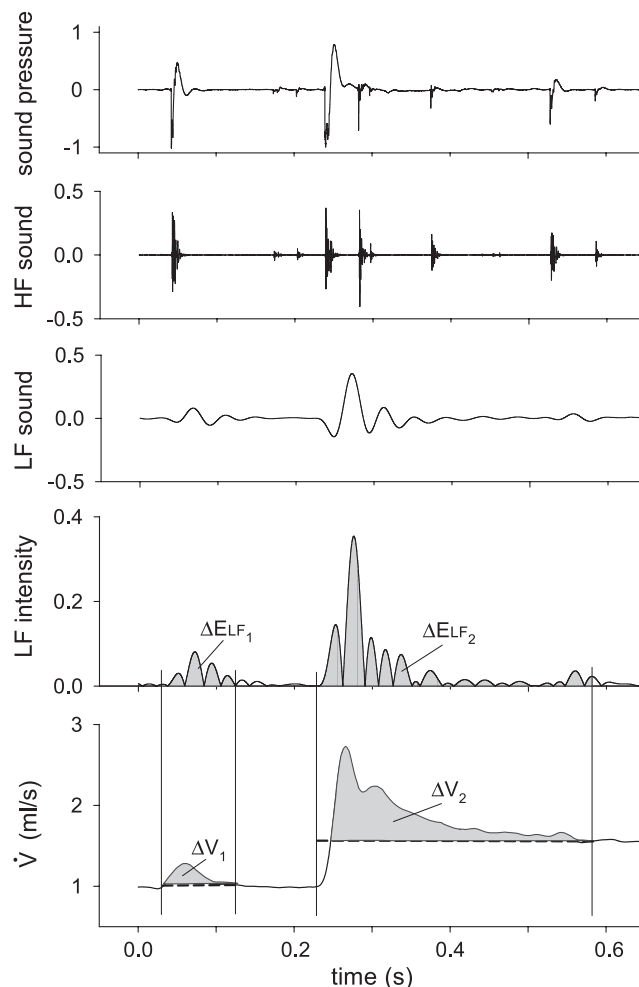


Fig. 1. A short segment of crackle sound pressure recording, its high-frequency (HF; >1 kHz) and low-frequency (LF; <60 Hz) components, and the LF sound intensity with the corresponding flow signal (\dot{V}) (top to bottom, respectively) to illustrate the calculation of discrete volume increments (ΔV) and associated crackle energy (ΔE). The beginning and end points of a \dot{V} transient (vertical lines) and the end-transient level of flow (dashed lines) were determined visually. The shaded areas between two consecutive beginning and end points indicate the cumulated LF crackle energy (ΔE_{LF}), whereas the shaded areas above the end-transient \dot{V} provide the cumulated \dot{V} (ΔV). Note that ΔE_{LF1} and ΔV_1 correspond to a single crackle, whereas ΔE_{LF2} and ΔV_2 cover several crackles whose \dot{V} transients superimpose and are difficult to separate.

sound pressure or acoustic activity during the inflation process was characterized by the total energy of the unfiltered sound (ΔE) in successive 0.25-s intervals.

The crackles were often accompanied by transients in the corresponding raw \dot{V} signal (Fig. 1), which returned to either the same or a somewhat higher level than before the transient. The signals of \dot{V} were integrated to obtain volume, and were also processed to identify the discrete ΔV corresponding to the transient spikes in \dot{V} . Wherever the successive \dot{V} transients were separable and the background noise allowed accurate identification of the beginning and end points of a \dot{V} transient (this was limited to the early and late phases of inflation), ΔV was determined. For the calculation of ΔV , the posttransient level of \dot{V} was taken as the baseline. To examine the relationship between recruitment and crackle sound, an energy package (ΔE_{LF}) for the duration of each identified \dot{V} transient was also calculated from the LF sound data and correlated with the corresponding ΔV .

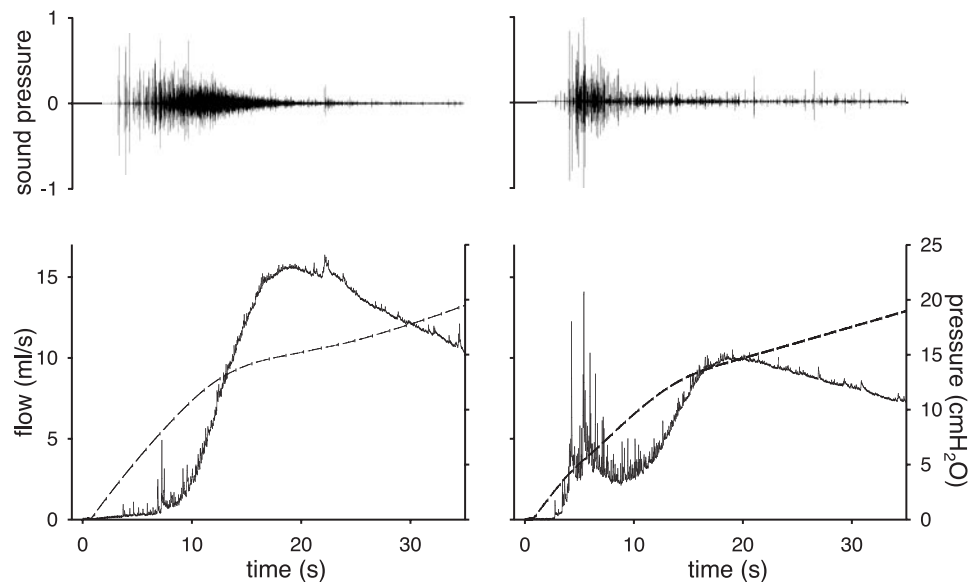


Fig. 2. Recordings of crackle sound pressure (top), inflation \dot{V} (bottom, solid lines), and translobar pressure (bottom, dashed lines) during the first 35 s of the first inflation (left) and second reinflation (right) of a lobe. Note the biphasic pattern and greater \dot{V} transients during the second maneuver.

RESULTS

Typical traces of crackle sound, translobar pressure, and central airflow during the entire recordings are shown in Fig. 2 for both the first and second inflations. In the early phase of inflation, crackles possess large amplitudes and are well separated from each other. As inflation continues, the density of acoustic events increases, which is accompanied by a decrease in crackle amplitudes. In these dense intervals, the crackles become inseparable from each other in the raw recordings. The translobar pressure steadily increased during the course of the entire inflation. The \dot{V} traces consisted of a series of spikes superimposed on a slowly varying mean level of \dot{V} . During the first inflation, the mean \dot{V} exhibited a single maximum, whereas the second inflation was characteristically biphasic with two distinct maxima: the first rise in the mean \dot{V} included massive \dot{V} transients accompanied by a significant number of crackles. The mean \dot{V} then decreased temporarily before a second rise, which was similar in character to that during the first inflation at the same lung volume.

Figure 3 illustrates the relationship between the sound energy associated with airway opening and features of the inflation P-V curves. During the first inflation, the P-V curves always exhibited a single characteristic lower knee. The corresponding acoustic activity, as characterized by the values of ΔE , increased quickly and irregularly and remained high until ~ 10 cmH₂O translobar pressure. The acoustic activity then decreased very regularly by four to five orders of magnitude, which coincided with the steep rise of volume until pressure reached the upper knee of the P-V curve. This was followed by another irregular pattern during which epochs of large values of ΔE emerged from the low acoustic activity, indicating the occurrence of sparse but still relatively large crackles. Although crackles were detected during the entire inflation process, the cumulated energy as a function of translobar pressure reached 94–98% of its final value by the lower knee. During the second inflations, the P-V curves always exhibited two distinct lower knees corresponding to the two observed maxima in the mean \dot{V} . The large values of ΔE during its fast rise occurred around the first knee of the P-V curve, and the

increase in energy was even steeper, reaching its plateau value at much lower values of pressure than during the first inflation.

To illustrate the relation between crackles and \dot{V} transients, in Fig. 4, we magnified a short segment of recording taken from an early phase of inflation where crackles were relatively rare and the transients in \dot{V} were well separated. It can be seen that every \dot{V} transient was clearly marked by a crackle or a burst of crackles, whereas not every acoustic event was accompanied by a detectable transient in \dot{V} . It is also apparent, however, that crackles of similar amplitude may correspond to either a relatively large or a much smaller \dot{V} transient. By determining the LF (<60 Hz) and high-frequency (>1 kHz) components of each crackle, it can be demonstrated that crackles with significant LF energy were always associated with detectable transients in \dot{V} , whereas those that have little LF energy were not. Another interesting feature of these data is that, after a \dot{V} transient marked by crackles with significant LF energy, the mean level of \dot{V} was usually elevated.

To quantify the observed relationship between the LF energy of crackles and the recruited volumes associated with the \dot{V} transients, we plotted the corresponding pairs of ΔE_{LF} and ΔV pooled for all lobes in Fig. 5. Because both ΔE_{LF} and ΔV spanned several orders of magnitude, linear regressions were carried out in the log-log domain, i.e., $\log \Delta E_{LF} = \delta \log \Delta V + C$. According to the unpaired *t*-test on these data, the slope δ values of the regression lines were significantly larger than unity values for both the first ($P < 0.002$) and the second ($P < 0.001$) inflation. Additionally, the slope corresponding to the second inflation ($\delta = 1.50 \pm 0.03$) was significantly larger ($P < 0.001$) than that corresponding to the first inflation ($\delta = 1.18 \pm 0.04$). The relationship $\Delta E_{LF} = C \Delta V^\delta$ was stronger for the second ($r^2 = 0.73$) than for the first inflation ($r^2 = 0.44$). In the individual lobes as well, the second inflations always resulted in higher correlation coefficients ($r^2 = 0.68$ – 0.82) than the first maneuvers ($r^2 = 0.29$ – 0.73).

To characterize the irregularities of the ΔV , we combined all data to calculate their probability density distribution (Fig. 6). The distribution probability of ΔV reached a peak between 0.02 and 0.05 ml and followed a linear decrease on the double

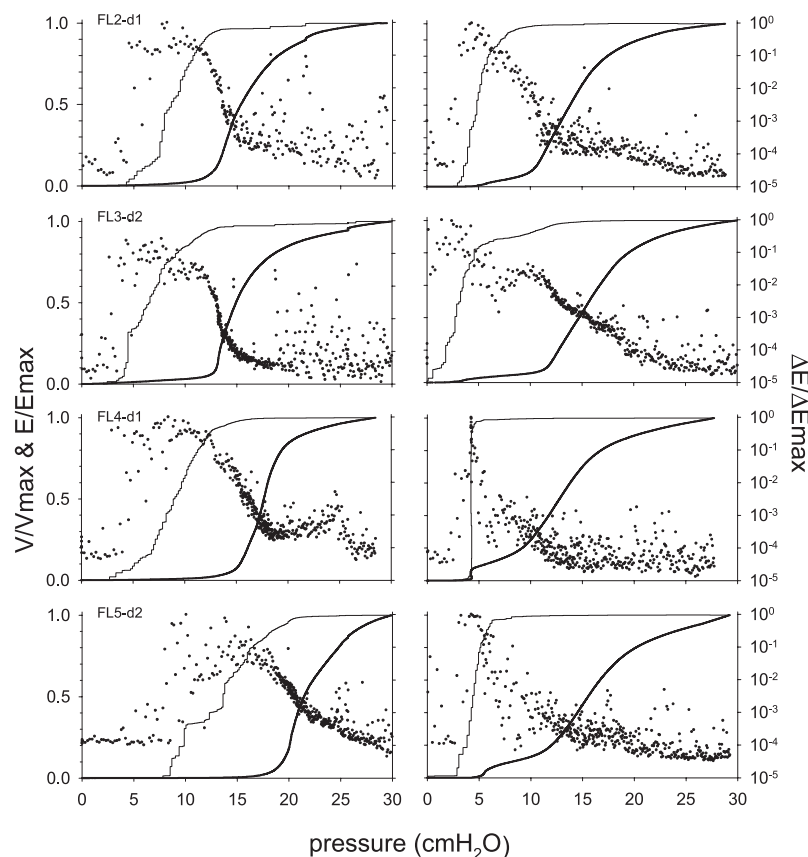


Fig. 3. Dependences of inflation volume (V ; thick lines), sound energy calculated for successive 0.25-s intervals (ΔE ; dots), and cumulated sound energy (E ; thin lines), all normalized by the corresponding maximum value (V_{\max} , ΔE_{\max} , and E_{\max} , respectively) on translobar pressure in 1 lobe of each dog during the first (*left*) and second (*right*) inflations. Note the log scale for ΔE .

logarithmic graph, indicating that the tail of the distribution follows a power law, i.e., $p(\Delta V) \sim \Delta V^{-\gamma}$. The exponents γ were 2.02 ± 0.09 and 1.88 ± 0.14 for the first and the second inflations, respectively. The exponent γ during the first inflation was not significantly different from 2. However, even though γ from the second inflation was only 6% smaller than the theoretically expected value of 2, or 7% smaller than the value of 2.02 from the first inflation, this difference was statistically significant ($P < 0.03$).

DISCUSSION

In this study, we investigated the possibility that the process of airway opening contributes to alveolar recruitment and the lower knee of the P-V curve of the lung. We employed an experimental setup in which the P-V curve and crackles, indicators of airway opening, were simultaneously recorded in isolated dog lung lobes. The main findings were that 1) recruitments occurred in discrete ΔV ; 2) the discrete ΔV were accompanied by crackles carrying LF energy; 3) in the presence of trapped air, the inflation exhibited a biphasic behavior resulting in two distinguishable lower knees of the P-V curve; and 4) the distribution of the ΔV followed a power law.

A characteristic feature of the results was that, for both the first and second inflations, the vast majority of the crackles occurred before \dot{V} reached its maximum value (Fig. 2). Because crackles are successively attenuated at every bifurcation as they propagate from the site of generation toward the trachea (2), this pattern suggests that the opening phenomena progressed from the central to the peripheral airways. The attenuation factor can be calculated from the ratio of cross-sectional

areas at bifurcations, and it has been reported to be ~ 0.65 for airway tree of the dog (2). Because every bifurcation attenuates the crackle amplitude on average by 0.65, crackles that were generated deeper in the lung became significantly attenuated once they passed >10 bifurcations. Indeed, Fig. 3 shows that the sound energy decreased by several orders of magnitude when the inflation reached the lower knee of the P-V curve, which is consistent with the decreasing envelope of the crackle time series.

During the second inflation, the cumulative sound energy reached its 95% value at a lower inflation pressure compared with the first inflation, which was accompanied by a biphasic shape of the \dot{V} (Fig. 2) and two separate lower knees along the P-V curve (Fig. 3). We explain the biphasic process in the second inflations as follows. Because the lobes were not degassed after the first inflation, increased air trapping occurred, as it was indicated by an apparently bigger lobe size before the second inflation was started. The airways leading to the trapped air regions opened first in the inflation process, and this resulted in transients in \dot{V} greater than those observed in the first inflation; because the subtended clusters of open alveoli were ready to accommodate a higher \dot{V} at the moment of the airway opening, the elevation in volume can be sudden (Fig. 3) and associated with a halt in the pressure increase, even leading to an unstable P-V relationship (1, 29). Subsequently, the reopened trapped regions became distended, causing a fall in the central \dot{V} , because the rest of the collapsed lobe was still in an early phase of recruitment. As the open regions continued to inflate, pressure increased further, which in turn resulted in a gradual opening of the remaining collapsed regions. The

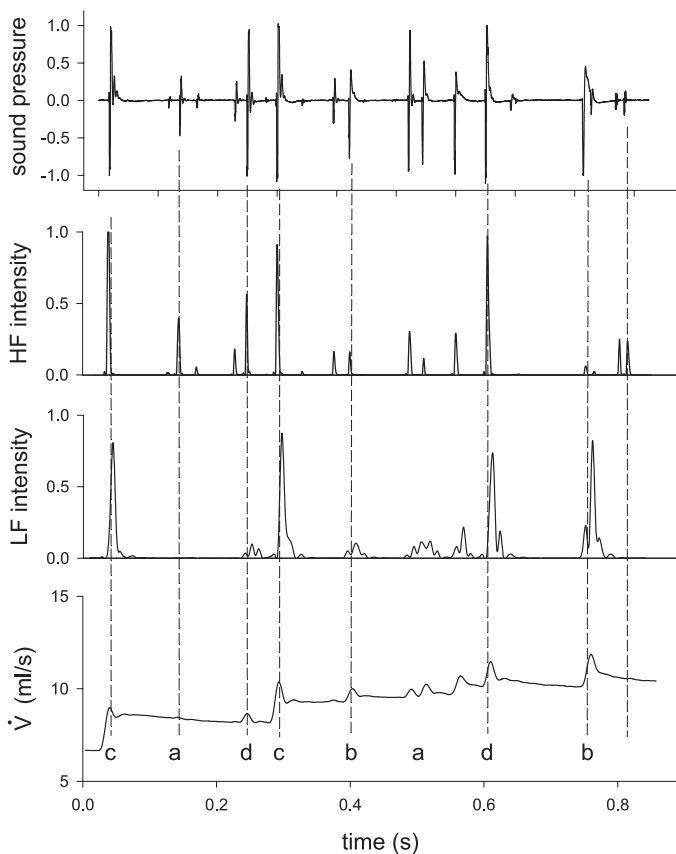


Fig. 4. A segment of crackle (*top*) and \dot{V} recording (*bottom*) during reinflation of a lobe. HF and LF sound energy data (in arbitrary units) were computed from high-pass-filtered (>1 kHz) and low-pass-filtered (<60 Hz) sound intensity, respectively. Note that the individual crackles have different HF/LF energy contents, and the size of a \dot{V} transient correlates with LF energy but not HF energy (cf. crackle types *a* and *b*). Some \dot{V} transients are followed by increased mean flow (*c*), whereas others (*d*) are not.

biphasic pattern of reopening was characteristic of any subsequent inflations performed occasionally (results not shown). We note that, although such a behavior may also occur during the inflation of *in vivo* lungs in conditions where regions of trapped air and atelectasis coexist, one should be cautious to extrapolate these results to the inflation of the ARDS lung, where the situation is further complicated by surfactant dysfunction and/or flooding of the alveoli (16).

Crackles can be viewed as direct signatures of individual airway openings, which can be considered as “microscopic”

Fig. 5. Relationships between the values of discrete ΔV and corresponding ΔE_{LF} pooled for all lobes for the first (*A*) and second (*B*) inflations.

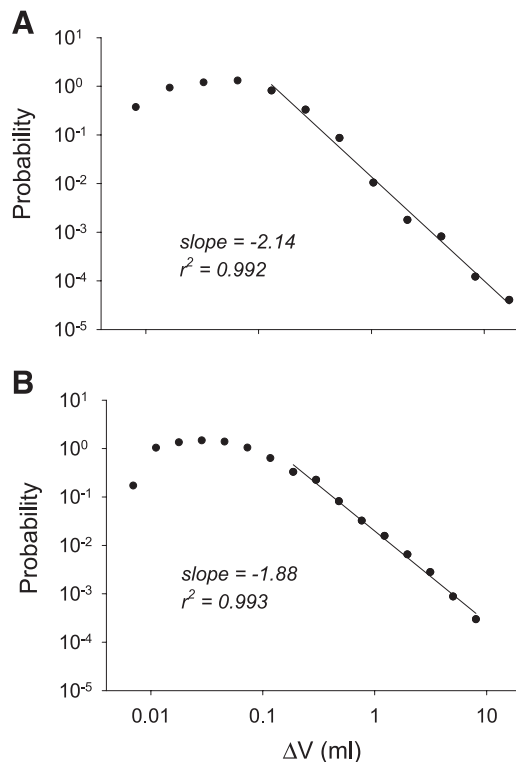
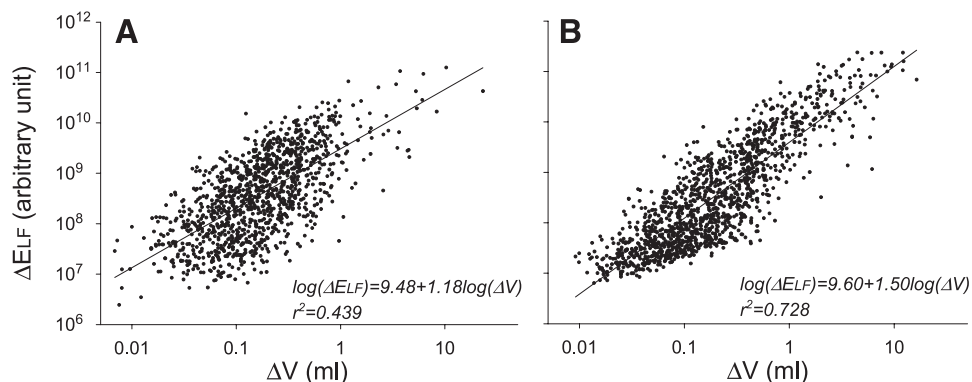


Fig. 6. Log-log plots of the probability distributions of discrete ΔV pooled from all first (*A*) and second (*B*) inflations. The lengths of the regression lines (solid lines) correspond to the ranges included in the regressions.

events contributing to the “macroscopic” P-V curve of the lung (21). The mechanism by which a crackle sound is generated is not well understood, but several concepts have been proposed (8, 10, 21). We believe that the mechanism that most likely pertains in the excised lungs that we studied is that crackles are a consequence of the rapid break-up of the fluid meniscus inside a closed airway with a small amount of air behind the closure (21). In terms of temporal properties, we argue that crackles of short duration, consisting of the initial sharp sound of the break-up of the fluid meniscus alone, may mark the opening of a single airway segment without a noticeable increase in lung volume, whereas crackles that also include an elongated ringing with a significant LF energy mark the entry of \dot{V} into a larger peripheral region. This latter crackle type indicates the sudden recruitment of lung volume, which we termed a discrete ΔV , to distinguish from the continuous

volume change corresponding to the elastic expansion of the recruited airspaces. Intuitively, for the whole lung, the sequence of opening events (at least those that trigger a change in mean \dot{V} , as illustrated by the *type c* openings in Fig. 4) can be associated with the discrete incremental component of the P-V curve as opposed to the continuous component reflecting the elastic expansion of the lung. If all \dot{V} transients could be detected and the corresponding discrete ΔV cumulated, we would be able to reconstruct that part of the P-V curve that is formed by the discrete volume recruitments. There are, however, fundamental limitations in the detection of each ΔV , imposed by both the sensitivity and the temporal resolution of the measurement of \dot{V} , especially in the middle part of the inflation where the densely overlapping \dot{V} transients cannot be separated. The number of discrete ΔV estimated by the manual determination of the time limits of the transients of \dot{V} ranged from 54 to 310 in an inflation, and this contrasts with the much larger number of crackles (ranging from 3,800 to 14,800), which were identified automatically by exploiting the finer temporal resolution and the higher signal-to-noise level in the high-pass-filtered sound recordings.

It is tempting to hypothesize that if the ΔV vs. ΔE_{LF} relationships established on the limited sets of data are sufficiently strong, they can be utilized to predict the values of ΔV from the values of ΔE_{LF} of every crackle, and, therefore, an estimate for the recruitment-related component of the inflation volume can be given. However, several factors preclude the prediction of the discrete recruited volumes from the crackles. First, as Fig. 5 demonstrates, the relationship between the ΔV and ΔE_{LF} was nonlinear because the slopes of the regression lines on the double logarithmic graphs were statistically significantly different from unity. More importantly, perhaps, the relationship was not very strong, especially for the first inflation, where the correlation coefficients ranged only between 0.29 and 0.73 in the individual lobes. The higher variability of ΔE_{LF} at any selected value of ΔV was likely due to the spatial progress of the recruitment. A slow \dot{V} transient was sensed with the flowmeter largely independently of the site of the opening, whereas the associated crackle could be subject to significantly more attenuation if the opening took place deeper in the lung and hence farther from the site of the sound recording. Thus, to be able to exploit the information in the ΔE_{LF} data for the prediction of the recruited volumes, the detailed mechanism of the spatial propagation of the reopening process should be taken into account.

The process of opening of a single airway has been studied in great detail and is known to be a complex fluid mechanical problem (13, 21, 26). The opening process within the airway tree is also a complex phenomenon and has been shown to occur in avalanches, whereby opening of a single airway can lead to the opening of many airways subtended by the airway that opens first (35). The short segment of sound and \dot{V} recordings displayed in Fig. 4 reveals various patterns of reopening. If an avalanche does not reach the alveoli, then only airways open and the recorded crackles may not be followed by a measurable \dot{V} transient because the opened volume is very small. Once an avalanche opens a path from the main bronchus to the alveoli, the corresponding recruited region is immediately available for the elastic expansion. In this case, the crackles would be followed by a \dot{V} transient, which also increases the mean level of the \dot{V} . Figure 7 illustrates sche-

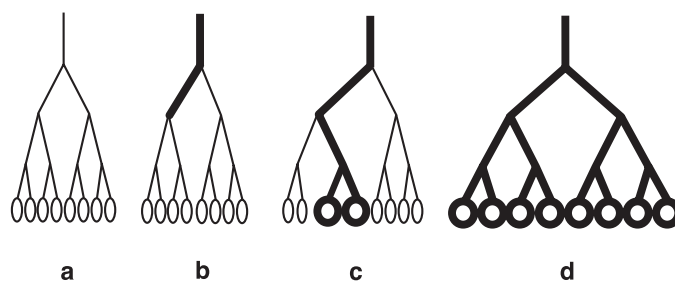


Fig. 7. Schematic illustration of the recruitment stages. *a*, Fully collapsed lung; *b*, small avalanche opening only airways; *c*, large avalanche opening to alveoli; *d*, fully recruited lung.

matically these possible patterns where an airway opening is limited to a conducting airway (*case b*) or connects a larger peripheral airspace to the root of the tree (*case c*).

The distribution of the recruited discrete ΔV has been predicted to be a power law with an exponent of 2 (32) and measured indirectly more recently (33). Our data here represent a direct assessment of the distribution of alveolar recruited volumes. During both the first and second inflations, the distribution has a plateau-like region for small ΔV followed by a region of about two decades over which the distribution linearly decreases on the log-log graph; i.e., it follows a power-law form. The plateau region is obviously due to the limitation of the measurement: although the flowmeter is able to measure very small \dot{V} corresponding to discrete volumes of 0.1 ml, below this limit the data are not reliable. It is also possible that two or more small discrete ΔV occur simultaneously, which results in a fewer number of small ΔV values. Nevertheless, for the first inflation, the data were in excellent agreement with the model prediction (32) because the theoretical value of the exponent is 2, whereas the estimated average of the exponent was 2.02. The distribution obtained from the second inflation had an exponent 1.88, which is also close to the theoretical value of 2. The reason for this small discrepancy is unclear, but it may be due to the fact that the presence of significant trapped air terminates the avalanches in larger alveolar regions than in the fully collapsed lung. As a consequence, there would be slightly larger ΔV values recorded than during the first inflation, which in turn leads to a longer tail of the distribution. Nevertheless, the power-law distribution implies that, even in the presence of trapped air, each phase of the biphasic recruitment process corresponding to the two lower knees of the P-V curve is likely to be dominated by avalanche-like airway openings.

In conclusion, we have found that, in the reinflation of isolated collapsed lungs, the elastic expansion of the alveoli is intermittently interrupted by discrete ΔV , which are accompanied by acoustic events. The majority of crackles were detected near the lower knee of the inspiratory P-V curve. Hence, in contrast to the prevailing view that recruitment occurs at the alveolar level, our data provide strong evidence that the recruitment of alveolar regions is a highly irregular process triggered by avalanche-like airway openings. We also found that the knee of the P-V curve in the presence of trapped air shifts to lower pressures, but the knee is still dominated by airway openings. Thus airway opening may also influence the recruitment process of the partially collapsed and fluid-filled lung in ARDS.

GRANTS

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