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Atelectasis and Chest Wall Shape during Halothane Anesthesia

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Background: **Anesthesia produces atelectasis in the dependent areas of the lungs by mechanisms that remain unknown. It has been proposed that anesthesia produces a cephalad shift in the end-expiratory position of the diaphragm, which compresses the lungs and produces atelectasis. This study tested the hypothesis that the extent of atelectasis is correlated with the cephalad displacement of the dependent portion of the diaphragm produced by halothane anesthesia in healthy young human subjects.**

Methods: **Twelve volunteers (mean age 34 yr) were studied while awake and during approximately 1.2 minimum alveolar concentration halothane anesthesia. Chest wall configuration was determined using images of the thorax obtained by three-dimensional fast computed tomography. Functional residual capacity was measured by a nitrogen dilution technique. Measurements were performed during quiet breathing in all subjects and after paralysis with 0.1 mg/kg vecuronium and mechanical ventilation in six subjects. Atelectasis was assumed to be present in regions of the lung that showed radiographic attenuation values similar to solid organs such as the liver.**

Results: **Atelectasis in dependent lung regions was not apparent in scans performed while the subjects were awake. Anesthesia with spontaneous breathing increased the volume of atelectasis measured at end-expiration by more than 1 ml in 9 of 12 subjects. For all subjects, the volume of atelectasis was 29 ± 10 ml (M ± SE), representing 0.67 ± 0.23% of the total thoracic volume. The distribution of atelectasis varied along the cephalocaudal axis, with less atelectasis in more cephalad transverse sections. Paralysis and mechanical ventilation significantly decreased the volume of atelectasis present at end-expiration. There was no correlation between the average amount of cephalad displacement of the most dependent region of the diaphragm and the amount of atelectasis, nor was there any correlation between the amount of atelectasis and anesthesia-induced changes in the end-expiratory position of any chest wall structure.**

Conclusions: **The dependent lung atelectasis produced by halothane anesthesia does not appear to be related to changes in the position of any single chest wall structure in these healthy young subjects, but rather to an interaction of several factors that remain to be identified. (Key words: Anesthetics, volatile: halothane. Lung: breathing pattern; diaphragm; functional residual capacity; gas exchange; intrathoracic blood volume; rib cage; shunt. Measurement techniques: dynamic spatial reconstructor; fast computed tomography.)**

ANESTHESIA impairs gas exchange in the lungs. An important series of investigations from Hedenstierna and colleagues has revealed one source of this impairment.[1–13] They found that anesthesia consistently produces densities in the dependent regions of the lung as imaged by computed tomography. The extent of these densities, thought to represent areas of atelectasis, is correlated with the magnitude of shunt produced by anesthesia. The densities are observed in patients anesthetized with both volatile and intravenous anesthetic agents (with the exception of ketamine[3]) during both spontaneous breathing and mechanical ventilation, and can be reduced by continuous positive pressure applied to the airway. These atelectatic areas may represent a significant source of postoperative pulmonary morbidity in some patients, because they may persist for some time after surgery.[4,11]

Significant questions about these densities remain, some related to technical limitations of conventional computed tomography scanners. In the studies to date, only two transverse sections of the thorax were obtained. Thus, the distribution and extent of densities is not fully known, nor is the fraction of total lung volume they may represent. The temporal resolution of conventional scanners is such that it has not been possible to determine if the extent of atelectasis varies over the course of a breath as expansile forces applied to the lung increase with inspiration.

Important questions also remain about the mechanism responsible for the formation of atelectasis. It has

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been suggested that atelectasis forms when lung tissue is compressed by the surrounding chest wall.[9] Specifically, it has been hypothesized that a loss of end-expiratory tone in the diaphragm allows the vertical gradient of abdominal pressure to be transmitted to the thorax, causing cephalad diaphragm displacement and compression of the dependent regions of the lung.[13] Studies employing three-dimensional computed tomography to provide images of the entire thorax have shown that the dependent regions of the diaphragm move cephalad with the induction of anesthesia, which could promote atelectasis.[14–16] However, anesthesia does not consistently produce a net cephalad displacement of the diaphragm; rather, the most consistent finding is an inward motion of the rib cage. Lung expansion is determined by a complex interaction between lung and chest wall, and it may not be possible to simply predict regional changes in lung volume based on local changes in the surrounding chest wall.

The overall goal of this study was to use fast three-dimensional computed tomographic scanning to provide new descriptive information about the phenomenon of dependent lung atelectasis and to explore questions related to mechanism in healthy young volunteers. We reasoned that if compression of lung tissue by the diaphragm caused atelectasis then the amount of dependent lung atelectasis should be correlated with the cephalad motion of the most dependent portion of the diaphragm.

Materials and Methods

This study was approved by the Institutional Review Board. Scanning data for this analysis were obtained from two prior studies of anesthetized subjects.[15,16] Details of the experimental procedures are given in these reports; we concentrate here on features germane to the current analysis.

A total of 12 subjects (9 men and 3 women) were studied while in the supine position. The subject characteristic were as follows: median age, 32 yr (range, 27–48); median height, 176 cm (range, 164–195); median weight 70 kg (range, 56–87), and body mass index, (weight/height^2), 22 kg $\cdot$ m^{-2} (range, 20–27). A radial arterial catheter was inserted for arterial blood gas analysis (Instrumentation Laboratories 1302, Lexington, MA). Each subject was placed in the dynamic spatial reconstructor, a high-speed radiographic scanner that uses the computed tomography principle to provide three-dimensional images of the thorax. This technique has been described in detail elsewhere.[14,15,17] The dynamic spatial reconstructor has sufficient temporal resolution to image thoracic structures during quiet breathing and sufficient volume resolution to determine a known volume to within 2%.[18]

Dynamic spatial reconstructor images were obtained while the awake subject quietly breathed a gas mixture of 30% oxygen, balance nitrogen. The subjects breathed through a mouthpiece and noseclip with the arms raised until the humeri were vertical to permit scanning. We have shown that neither the breathing apparatus nor the arm position significantly affects the pattern of breathing.[15] Scans of 300 ms duration were triggered manually at end-expiration during three consecutive breaths and gated together during later analysis.[15] Because the cephalocaudal height of the imaging field was not sufficient to include the entire thorax, these initial scans included only the superior half of the thorax. The subject was then shifted cephalad, and a similar sequence of scans was obtained to image the inferior portion of the thorax.[15] During subsequent analysis, the superior and inferior images were joined to produce end-expiratory images of the entire thorax. In six subjects (group 1, subjects 1–6), scans were also performed at end-inspiration while awake.

Immediately after scanning, the functional residual capacity (FRC) was measured in duplicate using a nitrogen dilution technique.[15,19,20] Each subject performed six vital capacity maneuvers into a 4-l bag initially filled with 100% O_2 after the bag was connected to the mouthpiece at end-expiration. Nitrogen concentrations in the bag were determined before and after this maneuver by a mass spectrometer (Perkin-Elmer MGA 1100, Buffalo Grove, IL).

Anesthesia was induced with inhalational halothane using balance oxygen. The trachea was intubated with a 9.0-mm ID endotracheal tube during deep halothane anesthesia, then the inspired halothane concentration was adjusted to maintain approximately 1.2 minimum alveolar concentration end-tidal concentration in a 30% O_2, balance nitrogen inspired gas mixture. After the pattern of breathing had stabilized, dynamic spatial reconstructor scans at end-expiration during quiet breathing were performed in all subjects (groups 1 and 2). In six subjects (group 2, subjects 7–12), 0.1 mg/kg vecuronium was then administered, and complete neuromuscular blockade was confirmed by the absence of response to peripheral ulnar nerve stimulation. The lungs were mechanically ventilated using a tidal volume and breathing frequency matched to that observed

while awake and breathing quietly, without extrinsic positive end-expiratory pressure (breathing frequency of 10 ± 1 min^{-1}, tidal volume of 735 ± 18 ml, inspiratory-expiratory ratio of 1:2, peak airway pressure of 12 ± 2 cm H_2O). The thorax was then scanned at end-expiration and end-inspiration. In both groups, measurements of FRC were performed after scanning, using passive inflation of the lungs.[15]

After these measurements, the neuromuscular blockade was reversed (if required) and the subject was allowed to emerge from anesthesia. No untoward effects were observed.

Data Analysis

Details of image processing to define chest wall boundaries and validation of the dynamic spatial reconstructor in measuring chest wall motion have been described previously.[14,15,17,21] Each scan produced a three-dimensional volume image of the thorax composed of cubic volume elements (voxels) with edge lengths of 1.5 mm; thus, each milliliter of image volume was composed of approximately 300 voxels. Radiographic attenuation values in these images ranged from 0 to 255, in which 0 was air and blood in the cardiac chambers was approximately 200.[22] This system differs from conventional computed tomographic scanners, which use an attenuation range from −1,000 to 1,000 Hounsfield units. Images were processed using the ANALYZE system (Mayo Foundation, Rochester, MN) to define each voxel in the image as being in the thoracic cavity, the abdominal cavity, or the background. The total thoracic volume was determined by counting the number of voxels in the thoracic cavity above the diaphragm. Changes in the end-expiratory positions of chest wall structures were determined as described previously.[15,17] To summarize, changes in the boundaries of the thorax measured at end expiration were quantified as (1) a change in the average cephalocaudal position of the diaphragm as a function of vertical distance, (2) the volume swept by diaphragm with changes in position, and (3) the volume swept by the rib cage with changes in position (fig. 1). Changes were analyzed during the transitions from awake to anesthetized and breathing spontaneously (group 1) or from awake to anesthetized, paralyzed, and mechanically ventilated (group 2).

Areas of atelectasis were defined as follows. First, the binary image of voxels distinguished as being in the thoracic cavity was multiplied by the original image to yield an image of only the thoracic contents (fig. 2,

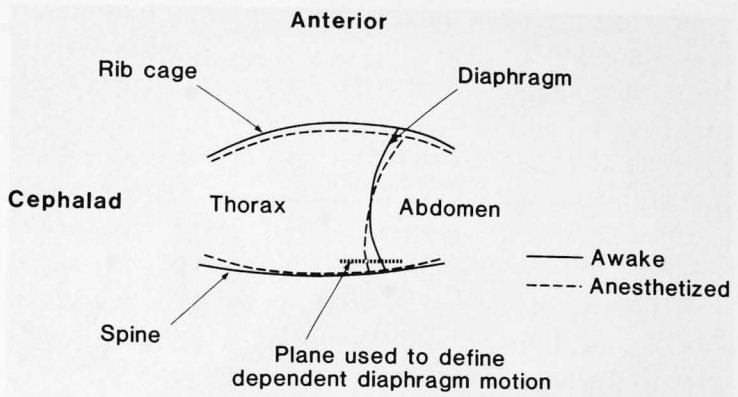

Fig. 1. Diagram of a midsagittal section of the thorax while awake (solid lines) and while anesthesized (dashed lines). Stippled area denotes the plane used to calculate the change in the average end-expiratory position of the diaphragm with the induction of anesthesia.

top). The heart and other major mediastinal structures were then removed from the image using a combination of computer thresholding and operator interaction as described previously. This left an image of predominantly the lung, including the smaller pulmonary vessels, but excluding the chest wall and major mediastinal structures (fig. 2, *middle*). We reasoned that the radiographic attenuation of atelectatic areas would be similar to the attenuation of other solid structures with similar tissue densities such as the abdominal contents. For each scan, a portion of the abdominal contents that excluded any bowel gas was sampled, and a histogram of radiographic attenuations within this volume was plotted (fig. 3). The mean (M) and standard deviation (SD) of this distribution was determined. In preliminary work, a histogram of the lung image also was obtained for scans obtained while awake. No areas of high density (corresponding to lung atelectasis) were observed in these images. There was little overlap between the distributions of lung and abdominal radiographic attenuation values while awake (fig. 3). A threshold value to include most areas of approximately solid tissue density and exclude most areas of density approximating aerated lung was computed as $M - (2 \cdot SD)$ of the abdominal histogram. This threshold was applied to the lung image and used to generate an image coding all voxels with values greater than this threshold (fig. 2, *bottom*). This method, which does not depend on subjective operator interaction, yielded areas that corresponded closely to areas of increased lung tissue density observed in scans (fig. 2, *bottom*). The volume of atelectasis measured was relatively insensitive to the exact threshold chosen, varying by less than 10% as

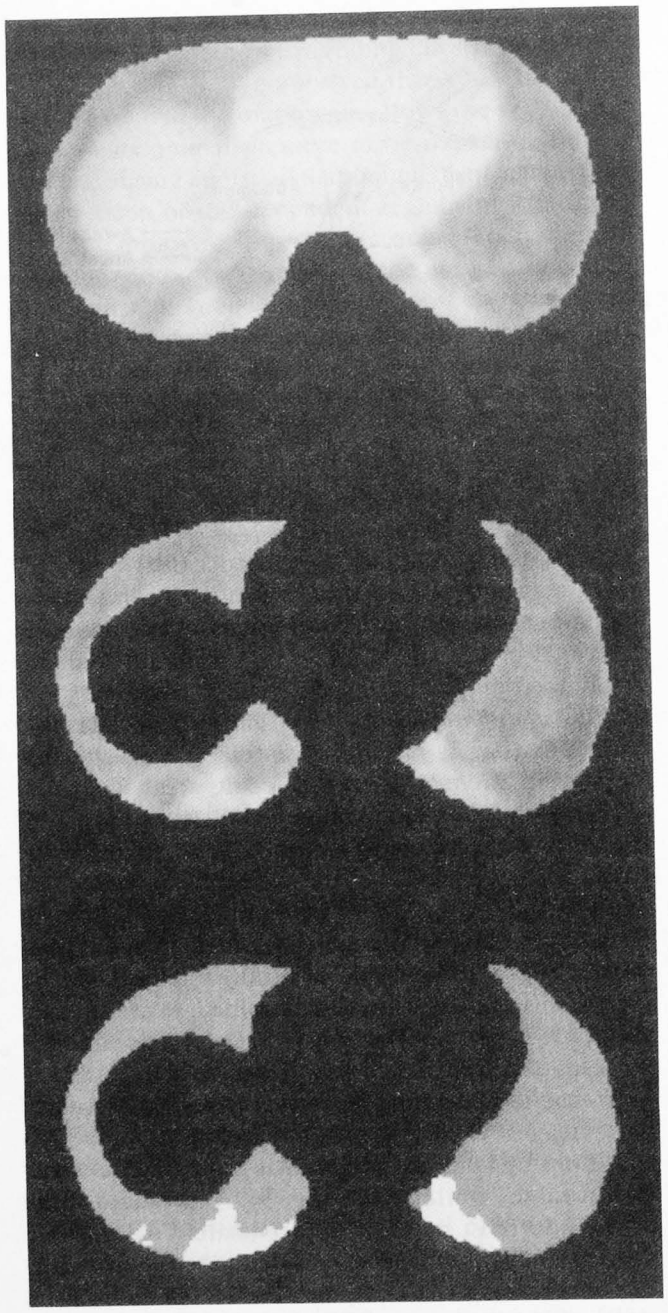

Fig. 2. Example of image processing. A transverse section of the thorax in an anesthetized subject breathing spontaneously (#4), with the surrounding rib cage removed through processing (*top*). The heart and right hemidiaphragm are clearly visible. The section after the heart and abdominal contents have been removed, leaving an image of predominantly the lung (*middle*). The outline of the lung in gray, with areas of atelectasis defined by application of a density threshold (see text for details) shown in white (*bottom*).

the threshold varied between M − (1 · SD) and M − (3 · SD).

As an estimate of the efficiency of gas exchange, the alveolar to arterial gradient for the partial pressure of oxygen was calculated from arterial blood gasses and the inspiratory fraction of oxygen by using standard formulas.[23]

Analysis revealed that most datasets were not normally distributed. Thus, paired comparisons were performed using the Wilcoxon signed rank test. The relationship between two variables was determined using the Spearman rank correlation, which is relatively insensitive to outlying values.[24] When appropriate, variables were scaled to account for differences in subject size using the awake total thoracic volume for volume measurements and the cube root of the awake total thoracic volume for linear measurements. A P value of less than 0.05 was considered to be significant.

Results

Areas of increased lung radiographic attenuation (*i.e.*, image density), suggestive of atelectasis, in dependent lung regions were not apparent in scans performed while the subjects were awake. This impression was confirmed by quantitative analysis, which yielded a low volume of atelectatic areas (table 1).

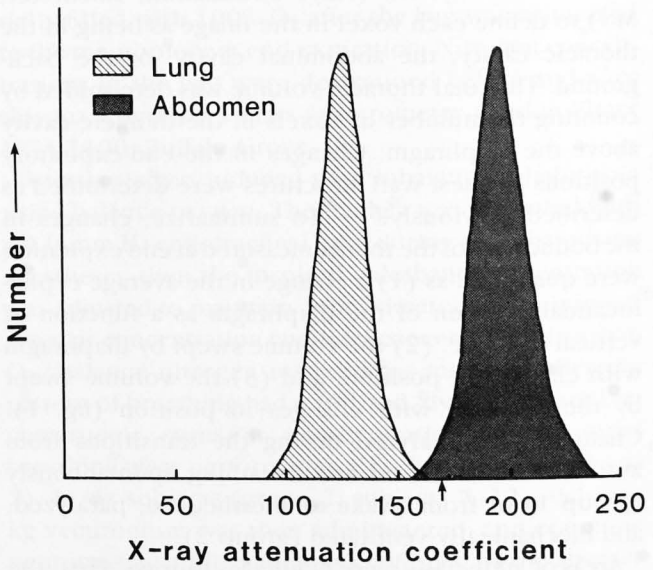

Fig. 3. Example of a histogram generated by sampling volumes corresponding to the lungs and abdomen. Arrow shows threshold for definition of tissue density in this image (see text for details).

Table 1. Volume of Atelectasis

Subject No.	Awake Volume (ml) Total Thorax
1	3
2	5
3	5
4	8
5	1
6	3
7	1
8	0
9	0
10	0
11	2
12	1
Mean	2
SE	1

Total lung volume (ml) was calculated as
from thoracic images.
* Significantly different from awake, Wilc
2,259 ± 136 ml, respectively.

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ration (group 2; table 2).

Table 1. Volume of Atelectasis

Subject No.	Awake Volume (ml) Total Thorax	Anesthetized, Spontaneous Breathing				
		Volume (ml)				
		Right Hemithorax	Left Hemithorax	Total Thorax	% Total Thoracic Volume	% Total Lung Volume
1	3	32	24	57	0.85	1.26
2	5	20	10	30	0.77	1.24
3	5	17	9	26	0.72	1.30
4	8	23	0	23	0.52	0.83
5	1	0	0	0	0.00	0.00
6	3	9	9	18	0.40	0.63
7	1	0	2	2	0.04	0.06
8	0	5	2	7	0.14	0.22
9	0	0	0	1	0.02	0.03
10	0	71	52	123	2.92	4.65
11	2	11	14	25	0.67	0.94
12	1	18	18	36	1.02	1.57
Mean	2	17	12	29*	0.67	1.06
SE	1	6	4	10	0.23	0.36

Total lung volume (ml) was calculated as the difference between the total thoracic volume and the volume of the heart and mediastinal structures, both obtained from thoracic images.

* Significantly different from awake, Wilcoxin signed rank test, $P < 0.05$. Mean values for the volumes of the right and left hemithoraces were 2,120 ± 129 and 2,259 ± 136 ml, respectively.

Anesthesia with spontaneous breathing increased the volume of atelectasis measured at end-expiration by more than 1 ml in 9 of 12 subjects, an increase that was statistically significant (table 1). The areas of atelectasis were consistently distributed in the most dependent areas of the lungs (figs. 2 and 4). For all subjects, the volume of atelectasis was 29 ± 10 ml. This represented 0.67 ± 0.23% of the total thoracic volume and 1.06 ± 0.36% of the total lung volume. There was no significant difference in the volume of atelectasis that developed in the right and left hemithoraces (fig. 4 and table 1). However, the distribution of atelectasis varied along the cephalocaudal axis, with less atelectasis in more cephalad transverse sections (fig. 5).

During spontaneous breathing while anesthetized, the amount of atelectasis at end-inspiration did not significantly differ from the amount of atelectasis at end-expiration (26 ± 8 and 22 ± 8 ml, respectively, group 1, n = 6). This finding was also true in subjects who were paralyzed and mechanically ventilated (end-expiratory and end-inspiratory atelectatic volumes of 14 ± 8 and 13 ± 5 ml, respectively, group 2, n = 6). Paralysis and mechanical ventilation significantly decreased the volume of atelectasis present at end-expiration (group 2; table 2).

Data were analyzed attempting to correlate the amount of atelectasis with changes in the configuration of chest wall structures produced by anesthesia. The FRC was significantly decreased during anesthesia as compared with awake values, both with spontaneous breathing (by 297 ± 53 ml, n = 12) and with paralysis and mechanical ventilation (by 348 ± 67 ml, n = 6). There was no correlation between the relative change in FRC and the relative amount of atelectasis ($r_s = -0.28$, $P = 0.26$, n = 18; fig. 6). As reported previously,[15] anesthesia changed the end-expiratory shape of the diaphragm, with a cephalad displacement of the most dependent regions of the diaphragm and a caudad displacement of the nondependent regions. There was no correlation between the average amount of cephalad displacement of the most dependent region of the diaphragm and the amount of atelectasis ($r_s = 0.24$, P = 0.33, n = 18; fig. 7). Similar results were obtained when the motion of the diaphragm was scaled according to thoracic volume ($r_s = 0.23$, $P = 0.35$, n = 18). Furthermore, there was no correlation between the amount of atelectasis and anesthesia-induced changes in the end-expiratory position of any chest wall structure (table 3).

Anesthesia with spontaneous breathing significantly increased the alveolar to arterial gradient for the partial

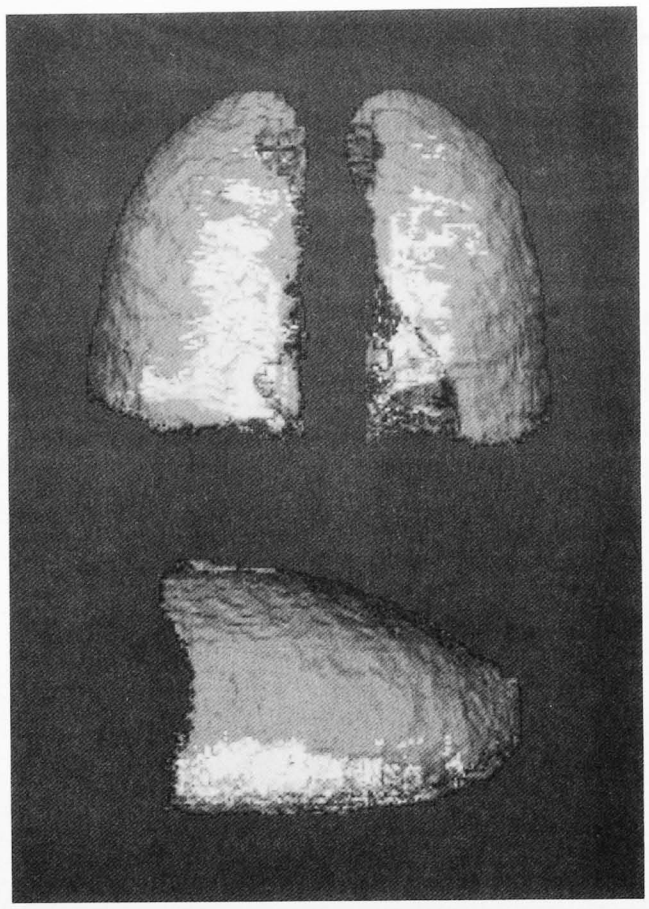

Fig. 4. Two-dimensional representation of a volume image from an anesthetized subject (#4) in which the surface of the lung is shown in shades of gray and areas of atelectasis are shown in white. Conceptually, this represents the view of a gray transparent three-dimensional model of lung shape, with a superimposed opaque white model of atelectasis. This anteroposterior view (*top*) clearly shows the right and left lungs, with a visible cardiac shadow. The lateral view (*bottom*) demonstrates that the atelectatic areas are located in the most dependent lung regions. In this view, down is posterior, and left is caudad.

pressure of oxygen (from 10 ± 1 to 25 ± 4 mmHg; n = 12). There was a significant correlation between the relative volume of atelectasis produced by anesthesia and the increase in the alveolar to arterial gradient for the partial pressure of oxygen ($r_s = 0.76$, $P = 0.003$; fig. 8). Anesthesia and paralysis with mechanical ventilation also increased the alveolar to arterial gradient for the partial pressure of oxygen compared with the awake state (to 35 ± 7 mmHg), an increase that was also significantly correlated with the development of atelectasis ($r_s = 0.89$, $P = 0.03$, n = 6, data not shown).

Discussion

All previous studies of lung atelectasis produced by anesthesia, except for one initial report,[25] are from Hedenstierna's group. In their studies, transverse computed tomographic scans of the chest were generally obtained at two levels: just cephalad to the right hemidiaphragm while awake (hereafter referred to as scan 1), and 5 cm cephalad to this first scan (scan 2). Data were analyzed by expressing the atelectatic area, determined either by manual tracing or computer thresholding, as a percentage of the total intrathoracic area measured in transverse section. The mean atelectatic area in scan 1 reported over a series of several studies ranges from 1.0% to 6.1% of the intrathoracic area.[1,2,4,5,7,8,9,11] In a summary of their experience with 45 patients anesthetized with halothane or enflurane and in whom the lungs were mechanically ventilated,[10] the atelectatic areas represented 1.9 ± 0.3 and 1.4 ± 0.3% of intrathoracic areas for scans 1 and 2, respectively. Of these 45 subjects, atelectasis developed in 39 (87%). When analyzed in a similar manner, comparable values in our study are 1.2 ± 0.3% and 0.5 ± 0.2% for regions corresponding to scans 1 and 2 during anesthetized spontaneous breathing (n = 12), and 0.39

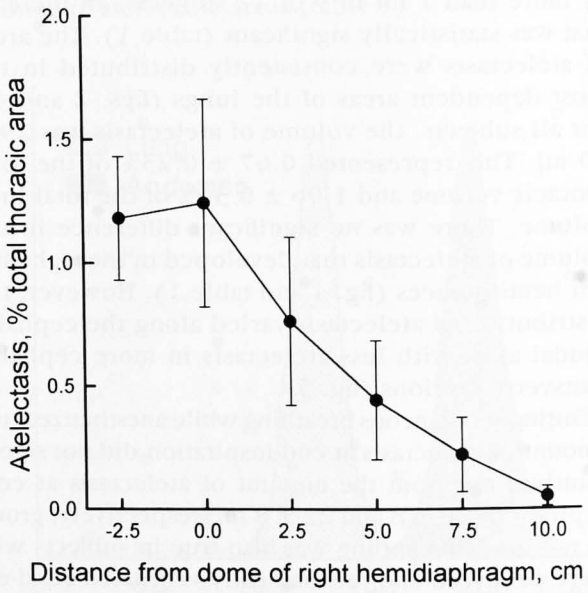

Fig. 5. Relation between the area of atelectasis in serial transverse sections during halothane anesthesia with spontaneous breathing, expressed as a percentage of the total thoracic area, and the cephalad distance from the dome of the right hemidiaphragm (positive numbers denote the cephalad direction). Values are mean ± SE, n = 12.

Table 2. Effects of Ventilation Mode on the Volume of Atelectasis at End-expiration in Anesthetized Subjects (Group II)

	Spontaneous Breathing			Paralysis and Mechanical Ventilation		
Subject No.	ml	% Total Thoracic Volume	% Total Lung Volume	ml	% Total Thoracic Volume	% Total Lung Volume
7	2	0.04	0.06	1	0.02	0.03
8	7	0.14	0.22	5	0.10	0.15
9	1	0.02	0.03	0	0.00	0.00
10	123	2.92	4.65	53	1.21	1.83
11	25	0.67	0.94	9	0.24	0.33
12	36	1.02	1.57	17	0.49	0.73
Mean	32	0.80	1.24	14*	0.34*	0.51*
SE	19	0.45	0.72	8	0.19	0.29

Total lung volume was calculated as the difference between the total thoracic volume and the volume of the heart and mediastinal structures, both obtained from thoracic images. Subject numbering convention is consistent with table 1.

* Significant difference from spontaneous breathing, $P < 0.05$, Wilcoxin signed rank test.

± 0.19 and 0.17 ± 0.09% during paralysis and mechanical ventilation (n = 6). Of our 12 subjects, atelectasis developed in 9 (75%). Thus, the incidence and extent of atelectasis found in the current study appears to be generally consistent with that found in previous work, although the amount of atelectasis may be less extensive in the current study. Strict comparisons are not possible because of differences in scanning and analysis techniques and, possibly, because of differences in subject characteristics. We studied young volunteers (mean age 34 yr) with no smoking history, whereas Hedenstierna's subjects were older (mean ages ranging from 41 to 68 yr) patients about to undergo surgery that included smokers. Because these factors may affect lung and chest wall properties, the tendency to form atelectasis may differ. However, Gunnarson *et al.*[10] found that neither smoking history nor age was correlated with the extent of atelectasis in a summary of several studies, so the significance of these differences remains unclear.

Previous work has shown that the extent of atelectasis is consistently less in the more cephalad scan (scan 2)

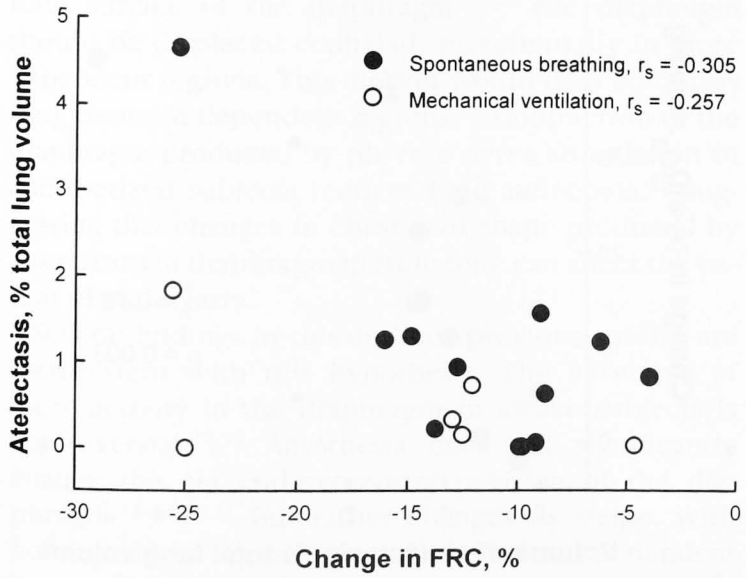

Fig. 6. Relation between the volume of atelectasis, expressed as a percentage of the total lung volume, and the decrease in functional residual capacity produced by halothane anesthesia, expressed as a percentage change from the awake functional residual capacity. Also shown are the Spearman correlation coefficients (r_s) for these relationships.

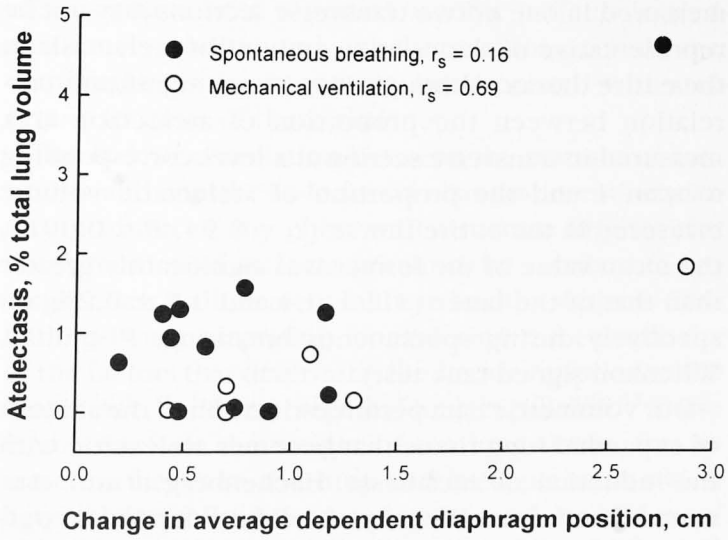

Fig. 7. Relation between the volume of atelectasis, expressed as a percentage of the total lung volume, and the change in the average position of the dependent diaphragm with the induction of anesthesia (see fig. 1). Positive values denote that the average position moved cephalad. Also shown are the Spearman correlation coefficients (r_s) for these relationships.

Table 3. Correlation between Volume of Atelectasis and Changes in the End-expiratory Position of Chest Wall Structures

	Spontaneous Breathing (n = 12)		Paralysis, Mechanical Ventilation (n = 6)	
	r_s	*P*	r_s	*P*
FRC	−0.31	0.32	−0.26	0.66
Thoracic volume	−0.25	0.42	−0.02	0.99
Volume displaced by rib cage	−0.13	0.67	−0.31	0.56
Volume displaced by diaphragm	−0.20	0.51	0.14	0.80
Dependent diaphragm motion	0.13	0.67	0.60	0.24

Values are Spearman rank correlation coefficients (r_s) and *P* values for correlation between the volume of atelectasis, expressed as a fraction of lung volume, and the change in a variable caused by the transition from awake to the specified condition, scaled for variations in thoracic volume among subjects.

FRC = functional residual capacity.

compared with the more caudal scan (scan 1),[1,2,4,5,7–9,11] a finding that we confirm. Only one subject (#4) exhibited atelectasis that extended more than 10 cm cephalad of the diaphragm. Atelectasis also extended caudad to the dome of the diaphragm. Thus, the distribution of atelectasis is heterogeneous both in gravity-dependent (anteroposterior in supine subjects) and nongravity-dependent (cephalocaudal) axes. This finding implies that the relative amount of atelectasis measured in one or two transverse sections may not be representative of the relative amount of atelectasis in the entire thorax. Although there was a significant correlation between the proportion of atelectatic area measured in transverse section at a level corresponding to scan 1 and the proportion of atelectatic volume measured in the entire thorax ($r_s = 0.94$, $P < 0.001$), the mean value of the former was significantly greater than that of the latter (1.2 ± 0.4 and 0.7 ± 0.2%, respectively during spontaneous breathing, $P < 0.02$, Wilcoxon signed rank test).

Our volumetric data permit estimation of the amount of expanded lung tissue that becomes atelectatic with the induction of anesthesia. Hachenberg *et al.*[6] estimated that the mass density of the most dependent portions of the lungs of awake supine subjects was 0.40 g/ml. Using this value, the volume of expanded lung that developed atelectasis with the induction of anesthesia and spontaneous breathing was 72 ± 24 ml (range 0–306 ml), or 4 ± 1% of the FRC while awake (range of 0 to 15%). The corresponding value during paralysis and mechanical ventilation was 36 ± 20 ml (range 0–132 ml), or 2 ± 1% of the FRC while awake (range 0–7%, n = 6). Thus, it appears that only a small portion of the aerated lung was compromised by atelectasis in these healthy subjects. Using the same assumed value for aerated lung density in dependent regions, 27 ± 7% of the decrease in FRC produced by anesthesia with spontaneous breathing could be attributed to the development of atelectasis (n = 12); the corresponding value for paralysis and mechanical ventilation was 8 ± 3% (n = 6). Thus, the majority of the decrease in FRC produced by anesthesia must be attributed to other mechanisms, such as increases in thoracic blood volume[15,18] and decreased volume of aerated lung regions without the development of atelectasis.

Inspiration should not affect the volume of true atelectasis during spontaneous or mechanical ventilation, an expectation that we confirmed. This finding also argues for the reproducibility of the measurements of atelectasis within subjects. This result is consistent with those of Rothen *et al.*,[8] who found that sustained airway pressures of greater than 20 cmH_2O were necessary to significantly decrease the amount of atelectasis in anesthetized, paralyzed subjects. The volume of atelectasis

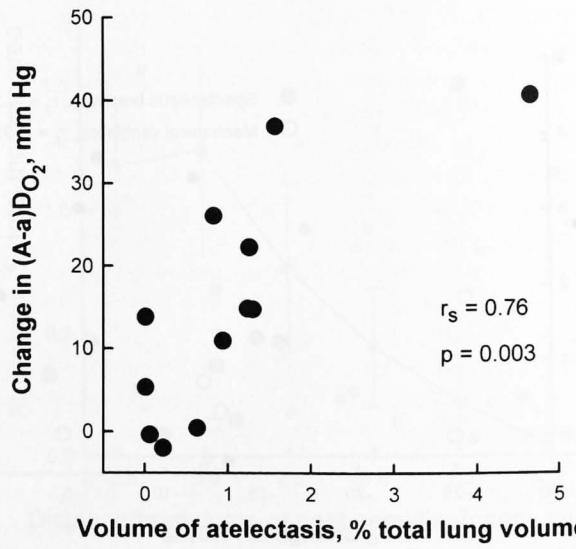

Fig. 8. Relation between the change in the alveolar to arterial gradient for the partial pressure of oxygen and the volume of atelectasis produced by halothane anesthesia with spontaneous breathing, expressed as a percentage of the total lung volume. Also shown is the Spearman correlation coefficient (r_s) for this relationship.

was significantly decreased by paralysis and mechanical ventilation in these subjects. In contrast, previous studies have shown that paralysis and mechanical ventilation either does not change[4] or increases[2] the area of atelectasis. These studies differed somewhat in protocol from ours; anesthesia was induced with thiopental in one study, the end-tidal concentration of halothane during spontaneous breathing was unspecified, and scans during spontaneous breathing were performed before endotracheal intubation. However, it is not immediately apparent how these factors could account for the different pattern of results. The transition from spontaneous breathing to mechanical ventilation increased the tidal volume (from 288 ± 15 to 735 ± 18 ml) and changed the motion of the chest wall, which must have affected the expansile forces applied to the lung (see discussion later).

The mechanisms responsible for atelectasis formation remain unknown. The rapid development of atelectasis with anesthetic induction shown in previous work suggests that the primary mechanism is related to changes in chest wall shape rather than resorption of gas from poorly ventilated but perfused regions, although gas absorption may accelerate and accentuate atelectasis formation.[1,12] It has been hypothesized that the induction of anesthesia abolishes tonic activity in the diaphragm present in awake supine subjects.[26] Because the vertical gradient of hydrostatic pressure on the abdominal surface of the diaphragm exceeds that on the lung surface of the diaphragm,[27,28] the diaphragm should be displaced cephalad, preferentially in more dependent regions. This motion would then compress lung tissue in dependent regions.[29] Contraction of the diaphragm produced by phrenic nerve stimulation in anesthetized subjects reduces lung atelectasis,[13] suggesting that changes in chest wall shape produced by alterations in diaphragm muscle tone can affect the extent of atelectasis.

Several findings in this and our previous studies are inconsistent with this hypothesis. The existence of tonic activity in the diaphragm in awake subjects is controversial.[15,30] Anesthesia does not significantly change the net end-expiratory position of the diaphragm,[14–16,25,31] but rather changes its shape, with nondependent regions moving caudad and dependent regions moving cephalad. These changes in position may be related to anesthesia-induced changes in the other chest wall structures to which the diaphragm attaches.[15] The cephalad motion of the dependent diaphragm could still compress lung tissue and produce atelectasis, and indeed the subject with the greatest motion also had the greatest amount of atelectasis (fig. 7). However, for all subjects, there was no correlation between cephalad motion of the dependent diaphragm and the amount of atelectasis, as would be expected if this was the primary mechanism responsible for atelectasis. Furthermore, in anesthetized subjects, paralysis and mechanical ventilation produced a small cephalad shift in end-expiratory diaphragm position as compared with its position during spontaneous breathing,[16] while the amount of atelectasis decreased. The tidal excursion of the most dependent portion of the diaphragm, which could also affect the formation of atelectasis, was not significantly different between spontaneous breathing and mechanical ventilation (1.0 ± 0.1 and 1.1 ± 0.1 cm, respectively). These results do not support a primary role for diaphragm displacement in the genesis of atelectasis in these healthy subjects.

It is possible that no correlation was seen between the amount of atelectasis and diaphragm displacement because of the relatively modest amount of atelectasis that developed in most of these healthy volunteers (*i.e.*, small relative to some previous observations in older surgical patients). The highly significant correlation between the volume of atelectasis and alveolar to arterial gradient for the partial pressure of oxygen demonstrates that physiologically significant correlations can be demonstrated in this group of patients with our measurement techniques over the range of atelectatic volumes measured. However, greater amounts of atelectasis have been reported in some patients in Hedenstierna's studies, and our data cannot exclude that diaphragm displacement may be associated with atelectasis in some of these patients.

The lack of correlation between the amount of atelectasis and anesthesia-induced changes in end-expiratory position of any chest wall structure implies that the formation of atelectasis cannot be ascribed to any single chest wall element in these healthy subjects. This finding is not surprising, considering the complexity of the factors that determine the stresses applied to the lung tissue, and hence regional lung expansion.[32] These factors include the weight of the lung tissue, the interaction between the lung and its container (which have intrinsically different shapes), and the effects of imbedded bronchi and blood vessels. There is sound evidence that pronounced distortion of the chest wall changes regional lung expansion in humans.[33,34] However, less pronounced changes in chest wall shape in supine humans may have little effect on regional lung

expansion.[35] Although anesthesia-induced changes in the shape of the chest wall may change the distribution of stresses applied to the lung, changes in regional lung expansion cannot be simply predicted by the local motion of the adjacent chest wall.[36,37] For example, Hubmayr *et al.*[38] found in dogs that preferential motion of the dependent portions of the diaphragm did not necessarily result in a preferential ventilation of dependent lung regions. In their study, individual lobes of the lungs slid and rotated as the chest wall changed shape, minimizing the effects of such changes on regional ventilation. The importance of such mechanisms in humans is unknown. Indeed, although promising beginnings have been made, the modeling of how changes in chest wall shape affects lung expansion has not yet reached the point where predictions can be made.[32] Currently, it can only be concluded that the interaction of several potentially significant factors, including the shape of chest wall structures (such as the thoracic spine, rib cage, diaphragm) and the volume or distribution of blood in the thorax, leads to atelectasis.

In conclusion, we have provided new quantitative information regarding the areas of increased lung density that develop with the induction of halothane anesthesia, presumably representing areas of atelectasis. Atelectasis does not appear to be related to changes in the position of any single chest wall structure in these healthy subjects, but rather to an interaction of several factors that remain to be identified.

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