Gravity effects on regional lung ventilation determined by functional EIT during parabolic flights

INÉZ FRERICHS, TARAS DUDYKEVYCH, JOSÉ HINZ, MARC BODENSTEIN, GÜNTER HAHN, AND GERHARD HELLIGE

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Frerichs, Inéz, Taras Dudykevych, José Hinz, Marc Bodenstein, Günter Hahn, and Gerhard Hellige. Gravity effects on regional lung ventilation determined by functional EIT during parabolic flights. J Appl Physiol 91: 39–50, 2001.—Gravity-dependent changes of regional lung function were studied during normogravity, hypergravity, and microgravity induced by parabolic flights. Seven healthy subjects were followed in the right lateral and supine postures during tidal breathing, forced vital capacity, and slow expiratory vital capacity maneuvers. Regional 1) lung ventilation, 2) lung volumes, and 3) lung emptying behavior were studied in a transverse thoracic plane by functional electrical impedance tomography (EIT). The results showed gravity-dependent changes of regional lung ventilation parameters. A significant effect of gravity on regional functional residual capacity with a rapid lung volume redistribution during the gravity transition phases was established. The most homogeneous functional residual capacity distribution was found at microgravity. During vital capacity and forced vital capacity in the right lateral posture, the decrease in lung volume on expiration was larger in the right lung region at all gravity phases. During tidal breathing, the differences in ventilation magnitudes between the right and left lung regions were not significant in either posture or gravity phase. A significant nonlinearity of lung emptying was determined at normogravity and hypergravity. The pattern of lung emptying was homogeneous during microgravity.

ventilation distribution; weightlessness; noninvasive monitoring; electrical impedance tomography

However, the use of radioactive gases (e.g., $^{133}$Xe) is not suitable in studies performed during short-term and sustained microgravity. Therefore, other tracer gases (e.g., $N_2$, He, $SF_6$, Ar) have been used under these circumstances. Single- and multiple-breadth washin and washout of nonradioactive test gases have effectively been applied to follow the distribution of lung ventilation in a few studies during parabolic flights (11, 28) and spaceflights (19, 33, 36). These methods exhibit good sensitivity to ventilatory inhomogeneities, yet the disadvantage is their inability to locate the inhomogeneities within the lung. To study lung function during short-term and sustained weightlessness on the regional level, a noninvasive radiation-free method satisfying the safety criteria and the methodological limitations imposed by experimentation under microgravity conditions is needed.

In the present study, performed during parabolic flights, we have for the first time followed the effects of gravity on regional lung function in a transverse thoracic plane. We have studied subjects lying in the right lateral and supine postures, i.e., in body positions not examined so far. The information on regional lung ventilation was obtained by the technique of electrical impedance tomography (EIT), which fulfills the stated strict criteria for application in weightlessness. This method utilizes the fact that air volume is the major determinant of electrical impedance of the lung (2, 4) and determines regional changes in lung volume in terms of regional relative changes in impedance (14). Until now, our laboratory has applied this method to follow regional lung ventilation in animals, healthy subjects, and patients in multiple ground-based studies. Functional EIT has been shown to determine the changes in lung ventilation distribution occurring in the thoracic cross section in response to, e.g., postural changes (16), variation of mechanical ventilation (15, 17), and experimental lung injury (18). A new EIT device, designed specifically for the demanding measurements during parabolic flights, has been developed in our laboratory (10) and used to study the gravity-dependent changes of regional 1) lung ventilation, 2)
lung volumes, and 3) pattern of lung emptying in subjects exposed to short periods of normogravity, hypergravity, and microgravity.

**METHODS**

Seven healthy subjects, one woman and six men, aged 26–57 yr, were studied. Physical characteristics and the results of lung function tests are given in Table 1. The experimental protocol was approved by the local university ethics committee as well as by the French Committee for Protecting Volunteers in Biomedical Research. All subjects gave their written consent. None of the subjects had previous experience of parabolic flights.

The subjects were followed on board of a specifically modified Airbus A300 aircraft operated by Novespace, a subsidiary of the French Space Agency (Centre National d’Etudes Spatiales). The parabolic flight campaign lasted 4 days. On the first 2 days, 14 and 2 parabolas were flown, and on the subsequent days the standard number of 31 parabolas was performed. The flight profile of each parabola consisted of a straight horizontal flight at normal gravity, a parabolic trajectory flight at microgravity (duration $\approx 22$ s), and a pull-out phase with descending flight at hypergravity of $\approx 1.8$ G (duration $\approx 22$ s). The parabolas, the subjects were instructed to breathe spontaneously or to perform specific ventilatory maneuvers. In case of maneuvers, either expiratory vital capacity (VC) or forced vital capacity (FVC) were carried out approximately in the middle of each gravity phase of one parabola. All subjects were trained in respiratory maneuvers. In one of the subjects, measurements could not be performed in the right lateral body position because of severe motion sickness.

**EIT.** Regional lung function was studied by EIT, a noninvasive imaging technique introduced in the mid-1980s (6). The method requires a set of surface electrodes to be equidistantly placed on the thoracic circumference in one transverse plane. In the current settings, 16 conventional self-adhesive electrocardiogram electrodes were used (Blue Sensor VL-50-K, Medicotest, Ølstykke, Denmark). The electrode plane lay at the level of the sixth intercostal space (medioclavicular line). EIT measurements were performed with the Göttingen EIT device (10).

Table 1. Physical characteristics and lung volumes of all studied subjects

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Gender</th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>TLC, liters</th>
<th>RV, liters</th>
<th>FRC, liters</th>
<th>VC, liters</th>
<th>FVC, liters</th>
<th>FEV1, liters</th>
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TLC, total lung capacity; RV, residual volume; FRC, functional residual capacity; VC, vital capacity; FVC, forced vital capacity; FEV1, forced expired volume in 1 s; M, male; F, female.

Figure 1 shows the basic principle of EIT. Small alternating electrical currents ($50$ kHz, $5$ mA$_{rms}$ (root mean square)) were injected through pairs of adjacent electrodes in a rotating mode. After each current injection, the resulting potential differences were measured between adjacent pairs of remaining electrodes. By the end of a complete cycle of current injections through all 16 electrode pairs, a set of $208$ values of surface potential differences was collected. The data were acquired at a rate of $13$ cycles/s. The individual measurements consisted of $1,500$ measuring cycles and were always initiated $30$ s before the pull-up phase.

A scheme of the complete off-line data analysis consisting of the reconstruction of simple EIT images, the generation of functional EIT images, and the calculation of quantitative EIT parameters is given in Fig. 2.

**Reconstruction of simple EIT images.** A reconstruction algorithm is needed to create an EIT image of the distribution of electrical impedance within the studied object from the values of acquired surface voltages and the excitation current. In our study, a modified version of a filtered back-projection algorithm (7) was used. The backprojection algorithm calculates the changes in impedance distribution that occur within the body with time and reconstructs tomographic images showing these local values of impedance change in a circular area within a $32 \times 32$-pixel matrix. From each set of voltages collected during a single measuring cycle, one simple EIT image is generated.

The changes in local impedance taking place in the body are determined by the backprojection algorithm with respect to reference values. This means that a simple EIT image generated in this way is an image of the distribution of

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**Table 1. Physical characteristics and lung volumes of all studied subjects**

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TLC, total lung capacity; RV, residual volume; FRC, functional residual capacity; VC, vital capacity; FVC, forced vital capacity; FEV1, forced expired volume in 1 s; M, male; F, female.

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**Figure 1. Basic principle of electrical impedance tomography (EIT).** Rotating electrical current injection (1) is performed between pairs of adjacent surface electrodes (denoted by nos. 1–16), and resulting voltages (U) are measured between pairs of remaining electrode pairs.
relative impedance change within the body, e.g., in the chest. In the present study, the reference values were calculated from a sequence of data sets obtained from several consecutive measuring cycles during tidal breathing at 1 G. Because the subjects breathed spontaneously during this time period, the pixel reference values reflected the local lung midcapacities.

Simple EIT images show either an increase in regional impedance over lung regions at volumes larger than midcapacity or a decrease at smaller lung volumes. The values of relative impedance change in any selected pixel of a series of simple EIT images reflect the regional variation of local impedance with time. The largest variations occur over the lung regions because of gas volume changes during ventilation.

The generation of series of simple EIT images is the first step in the EIT data evaluation. In the present study, shorter series of simple EIT images representing the 1-G, 2-G, and 0-G phases were isolated at first. In case of spontaneous tidal breathing, data collected during five to nine breaths (depending on the individual respiratory rate) were used for further data evaluation. In case of maneuvers, only the data acquired during expiration from total lung capacity (TLC) to residual volume (RV) were analyzed. Additional evaluation procedures were applied to these data sets to generate functional EIT images and calculate quantitative parameters characterizing regional lung function in a concise way.

Calculation of regional quantitative parameters. Altogether, three types of functional EIT images were produced in each gravity phase. All functional EIT images were created within a circular area in a 32 × 32-pixel matrix interpolated by a factor of four to achieve better visual perception.

Functional EIT images of regional lung ventilation show the local end-inspiratory-to-end-expiratory amplitude of relative impedance change and characterize the magnitude of local tidal volume (VR) in the studied transverse plane during quiet breathing or VC and FVC during expiratory maneuvers. The higher the local ventilation, the lighter appears the corresponding area in the functional EIT image of regional lung ventilation (see Fig. 5, top).

Functional EIT images of regional shift in lung volume show the change in local end-expiratory values of relative impedance change during 2-G or 0-G phases in comparison with 1 G. During quiet breathing and expiratory maneuvers, these images show the regional shifts in FRC and RV, respectively. An increase in regional lung volume is shown in light tones and a decrease in dark ones (see Fig. 5, middle).

Functional EIT images of regional curvilinearity of lung emptying were created as follows. Regional EIT data obtained during tidal or deep expirations were fit by a polynomial function of second degree (i.e., quadratic function). Polynomial coefficients of second degree (i.e., the coefficients of the quadratic term) describe the curvature of the expiratory course of regional relative impedance change. In the case of spontaneous tidal breathing, polynomial coefficients of second degree were calculated as average values from five to nine polynomial fits to regional EIT data from consecutive tidal expirations. During VC and FVC, polynomial coefficients of second degree resulted from single fits to the EIT data. The calculated regional polynomial coefficients of second degree were then plotted at corresponding pixel positions. Regions exhibiting a slow initial fall of relative impedance change with progressively increasing rate of decline during late expiration were depicted in dark tones, and regions with opposite behavior were shown in light tones (see Fig. 5, bottom).

Calculation of quantitative EIT parameters. The quantitative parameters were calculated within two regions of interest representing the right and left lung. These regions were defined as those areas within the tomograms that exhibited high variation of relative impedance change with time characteristic of large gas volume changes occurring typically only in the lungs. This approach was used previously (16, 17), and a limit of 20% of the maximum standard deviation of relative impedance change within the image was used to define the borders of the left and right lung regions. The regions of interest were determined repetitively for each individual subject, breathing form (spontaneous, VC, and FVC), and gravity phase studied. The following quantitative parameters were calculated: 1) average amplitude of end-inspiratory-to-end-expiratory impedance change in the right and left lungs, 2) average end-expiratory impedance change in the right and left lungs, and 3) average polynomial coefficient of second degree of expiratory course of relative impedance change in the right and left lungs.

The calculation of the first two parameters is described in detail in Frerichs et al. (17). Briefly, for every image pixel within the defined lung regions, the maximum and minimum values of relative impedance change, corresponding to the end-inspiratory and end-expiratory values, were identified during several respiratory cycles in the case of tidal breathing or during one expiration with maneuvers. An average value of amplitude of end-inspiratory-to-end-expiratory impedance change and end-expiratory impedance change in the right and left lung was then calculated from all pixel values in the selected regions. The amplitude of end-inspiratory-to-end-expiratory impedance change represents the regional VR, VC, or FVC. The end-expiratory impedance change characterizes the regional FRC or RV in the right and left lungs.

The principle of calculation of the last quantitative parameter, describing regional differences in lung emptying, is...
The results of our investigation are arranged with respect to the three aspects of regional lung function studied. EIT data regarding regional 1) lung ventilation, 2) lung volumes, and 3) lung emptying behavior in two postures and three acceleration states will be presented. For better understanding, representative original tracings of relative impedance change and functional EIT images, which form the basis for quantitative evaluation, will be presented at first.

The tracings of relative impedance change in the left and right lung regions during 1 G, 2 G, and 0 G obtained in one of the studied subjects are shown in Fig. 4. The regional time courses of relative impedance change registered in the right lateral and supine postures during spontaneous tidal breathing are presented in Fig. 4, left; the tracings originating from a measurement during which the subject performed FVC maneuvers can be found in Fig. 4, right. The tracings show the typical fluctuations of the impedance signals of different amplitudes associated with tidal breathing and deep respiratory maneuvers on the background of shifts in impedance resulting from lung volume changes during the 1-G, 2-G, and 0-G phases. The tracings acquired in the right and left lung regions in the supine posture exhibit similar characteristics. In the right lateral position, the time courses of relative impedance change in the right (i.e., dependent) lung differ from those obtained in the left (i.e., nondependent) lung.

Figure 5 shows the three types of functional EIT images generated from 1-G, 2-G, and 0-G data in one of the studied subjects. During this measurement, the subject was breathing spontaneously in the right lateral body position. Functional EIT images of regional lung ventilation (top tomograms) show an uneven distribution of ventilation between the right and left lung in 1 G and 2 G: the ventilation of the dependent lung was more pronounced. In 0 G, the distribution of ventilation was symmetric. This subject breathed more deeply in 0 G than in 1 G and 2 G. Functional EIT images of regional shift in lung volume are shown in the middle tomograms of Fig. 5. Because these images visualize the shift in gas volume with respect to 1 G, the 1-G image naturally does not show any change. In 2 G, a decrease in FRC is seen in the dependent right lung, whereas an increase can be observed in the nondependent left lung. An opposite shift in regional FRC can be discerned in 0 G: a pronounced fall in lung

Fig. 3. Characterization of the regional distribution of respired air in the lungs. Plot of regional vs. overall lung volume shows the curvilinearity of lung behavior in the dependent and nondependent lung regions compared with the line of identity (dashed line) [top; modified after Milic-Emili et al. (31)]. The curvature of the plot can be characterized by the polynomial coefficient of second degree a. In EIT data evaluation, regional relative impedance change is plotted as a function of overall relative impedance change within the studied thoracic plane (bottom, circles). These data correspond with the regional vital capacity (VC r) and overall VC if they are obtained during deep expiration from total lung capacity (TLC) to residual volume. The fits of a polynomial function of second degree characterize the emptying behavior of the dependent (gray line) and nondependent (black line) lung regions. TLC r, regional TLC.

given in Fig. 3. (For better understanding, Fig. 3, top, shows the well-known diagram of regional vs. overall lung volume often used to describe the distribution of respired air in the lungs on which our evaluation is based.) To characterize regional behavior of the lungs during tidal, VC, and FVC expiration, we generated plots of regional relative impedance change vs. overall relative impedance change in the studied transverse thoracic plane. Regional and overall relative impedance changes were normalized by regional and overall tidal end-inspiratory-to-end-expiratory impedance change during quiet breathing and by TLC-to-RV impedance change during maneuvers. The plots were fit by a polynomial function of second degree. During spontaneous breathing, an average polynomial coefficient of second degree was determined from several consecutive tidal expirations; during maneuvers only one coefficient was obtained in each gravity phase. Negative values of the polynomial coefficient of second degree indicated slow initial and rapid late emptying of the corresponding lung regions compared with the average emptying behavior of the lungs in the studied cross section. Positive values of the polynomial coefficient identified lung regions that emptied more rapidly at the beginning of expiration and experienced a decrease in their rate of emptying toward the end of expiration (Fig. 3, bottom; see also Fig. 8 with original data).

Statistical analysis. Paired Student’s t-test was used to test the significance of differences between the parameters obtained in the right and left lung regions. One-way ANOVA was applied to check the effect of acceleration on the calculated parameters. P < 0.05 was considered significant.
Regional lung ventilation during parabolic flights.

Volume took place in the left and an increase in the right lung. Functional EIT images of regional curvilinearity of lung emptying (bottom tomograms) identified an asymmetric behavior of the dependent right and nondependent left lung during deflation in 1 G. The right lung emptied preferentially at the beginning and left lung at the end of expiration. This behavior was even more pronounced in 2 G and almost abolished in 0 G.

The mean breathing rates determined in both postures and all gravity phases during spontaneous tidal ventilation are given in Table 2. No significant effect of gravity on breathing rate was found in either posture.

Table 3 shows the mean areas of the regions of interest determined for all postures, breathing forms, and gravity phases studied that were used during the calculation of quantitative parameters. The size of the areas of the regions of interest was not significantly influenced by the breathing form and the gravity phase. The area of the right lung region of interest was significantly larger than the left one in the supine but not in the right lateral body position.

Regional lung ventilation. Figure 6 shows the end-inspiratory-to-end-expiratory amplitude of impedance change of all studied subjects and the corresponding mean values obtained during spontaneous tidal breathing (left) and VC (right) in 1 G, 2 G, and 0 G. For

Table 2. Spontaneous breathing rates in the studied subjects

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<th>Posture</th>
<th>1 G</th>
<th>2 G</th>
<th>0 G</th>
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<td>Right lateral</td>
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<tr>
<td>Supine</td>
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<td>21.3 ± 5.4</td>
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Values are means ± SD given in breaths/min. Data were obtained with the subjects in 2 body positions during phases of different gravity. 1 G, normogravity; 2 G, hypergravity; 0 G, microgravity.
comparison, the mean tidal values that were significantly smaller than the VC data and the FVC mean values that were not significantly different from the VC data were included in Fig. 6, right.

During spontaneous breathing in the right lateral posture, the mean end-inspiratory-to-end-expiratory amplitude of impedance change did not significantly differ from the nondependent left lung in either acceleration phase. During VC and FVC, the differences between the lungs were significant during 1G and 2G. The differences were reduced, but still significant, during 0G. Acceleration did not exhibit any effect on the amplitude of impedance change during either tidal breathing or expiratory maneuvers.

In the supine posture, no significant differences between the right and left lungs were determined during either spontaneous breathing or VC and FVC. Acceleration had no significant effect on the amplitude of impedance change in either ventilation form studied.

Regional lung volumes. Figure 7 summarizes the results on lung volume changes occurring in both studied postures during different acceleration phases. Figure 7, left and right, shows the results obtained during spontaneous breathing and VC, respectively.

A significant effect of gravity on the end-expiratory impedance change was detected in the right lateral posture during spontaneous breathing. Both in 2G and 0G, the end-expiratory impedance change in the right and left lung differed significantly from each other. The end-expiratory lung volume (i.e., FRC) in the nondependent left lung rose in 2G and fell in 0G. An increase in the end-expiratory lung volume was observed in the dependent right lung in 0G. During deep expiratory maneuvers, the end-expiratory impedance change values in the dependent right lung were similar to the data obtained during tidal breathing; i.e., regional RV after deep expiration resembled FRC during tidal ventilation. In the nondependent left lung, significantly lower values were obtained during VC and FVC when compared with tidal breathing, reflecting lower regional lung volume at RV than FRC.

The end-expiratory impedance change values determined in the right and left lungs in the supine posture were similar during spontaneous breathing and deep expiration, respectively. The values tended to be higher during 0G than in 1G and 2G; however, the effect of acceleration was found significant only during tidal breathing.

### Table 3. Area of the regions of interest

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<td></td>
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<td>2 G</td>
<td>0 G</td>
</tr>
<tr>
<td>Right lateral</td>
<td>23.1 ± 4.7</td>
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<tr>
<td>Supine</td>
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<th>Posture</th>
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Values are means ± SD given in percentage of the total electrical impedance tomography image area. Data were obtained with the subjects in 2 body positions during phases of different gravity. ROI, region of interest.

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Fig. 6. End-inspiratory-to-end-expiratory and TLC-to-residual volume amplitude of impedance (imp) change obtained in all subjects (denoted by nos. 1–7) in the right and left lung regions during spontaneous tidal breathing (left) and VC maneuvers (right), respectively. The individual 1-G, 2-G, and 0-G points are connected by dotted lines for visualization of the trend. ● And thick solid lines represent the mean values. Gray solid lines in the diagrams at right show the mean values obtained during spontaneous breathing (SB); thin solid lines represent the mean data during FVC. ns, Nonsignificant effect of acceleration. *Significantly different from the right lung, P < 0.05. **Significantly different from the right lung, P < 0.01.
Regional lung emptying. Figure 8 shows the plots of normalized regional vs. overall impedance change obtained in one of the studied subjects in both body positions and all acceleration phases during a VC maneuver together with the corresponding fits of a polynomial function of second degree. The right and left lung exhibited a dissimilar course of lung emptying in the right lateral posture during 1 G and 2 G, whereas in 0 G and in the supine posture, the curvature of the plots was minimal.

Figure 9 summarizes the quantitative results on regional lung emptying obtained in both postures in all subjects studied. In the right lateral body position, significant curvilinearity of lung emptying was established in the dependent and nondependent lung in 1 G and 2 G. The polynomial coefficient of second degree

Fig. 7. End-expiratory impedance change obtained in all subjects (denoted by nos. 1–7) in the right and left lung regions, representing regional FRC during spontaneous tidal breathing (left) and residual volume during VC maneuvers, respectively (right). The individual 1-G, 2-G, and 0-G points are connected by dotted lines to visualize the trend. And thick solid lines represent the mean values. Gray dotted lines in the diagrams at right show the mean values obtained during SB; thin solid lines represent the mean data during FVC. s, Significant effect of acceleration. *Significantly different from the right lung, \( P < 0.05 \). **Significantly different from right the lung, \( P < 0.01 \).

Fig. 8. Fits of polynomial function of second degree to plots of regional right (r) or left (l) lung relative impedance change vs. overall relative impedance change. Original 1-G, 2-G, and 0-G data obtained in subject 4 in the right lateral and supine postures during a VC maneuver are presented.
was positive in the dependent right lung and negative in the nondependent left one. This reflects faster initial emptying in the dependent lung and slower in the nondependent one, whereby the behavior of the lungs was reversed during late expiration. During VC, the curvilinearity of lung emptying was more pronounced. However, during FVC, the curvature of normalized plots of regional vs. overall impedance change was smaller and comparable with the curvature of normalized plots during spontaneous tidal breathing.

In the supine body position, acceleration did not result in such differences in lung emptying behavior between the right and left lung. The curvatures of the normalized plots of regional vs. overall impedance change were minimum during tidal, as well as deep, expirations.

The individual correlation coefficients ($R^2$) of polynomial fits of second degree to the plots of regional vs. overall relative impedance change calculated for both lung regions in both postures were in the range 0.897–0.997 during tidal breathing, 0.991–0.999 during FVC maneuvers, and 0.931–0.999 during VC maneuvers.

**DISCUSSION**

Parabolic flights offer the unique possibility of studying the lung function repetitively during short periods of normal gravity, hypergravity, and microgravity. Until now, global aspects of the lung function were mostly focused on. Changes in global lung volumes, expiratory flow, thoracic and airway dimensions, and lung and chest wall mechanics occurring in response to different levels of acceleration have been described (8, 12, 13, 20, 32). The only information addressing the effect of gravity on lung ventilation distribution was obtained in two studies that utilized the single-breath washout of test gases in sitting healthy subjects (11, 28). This means that, so far, regional aspects of the lung function were followed only in one body position using a method that is not able to locate the ventilatory inhomogeneities within the lung.

In the present study, we have characterized the gravity-related changes of regional lung function in two horizontal body positions. Regional lung ventilation, lung volumes, and lung-emptying behavior were determined in different gravity phases in a thoracic cross section. During spontaneous breathing, no significant differences between the ventilation of the dependent and nondependent lung regions were determined in either gravity phase, whereas during deep expirations the differences were significant and persisted also during 0 G. Significant effect of gravity on local lung volume was found, resulting in rapid shifts in regional FRC level. Significant inhomogeneity of lung emptying between dependent and nondependent lung regions was established during spontaneous breathing as well as during deep expirations in 1 G and 2 G. This inhomogeneity was abolished in 0 G.

The distribution of regional lung function in different gravity phases was studied by EIT for the first time. EIT is a noninvasive, nonhazardous imaging method that, at present, can be regarded as experimental and not ready for routine clinical use yet. In our study, we were able to collect stable data from all studied subjects as a result of the use of a newly developed high-performance EIT device that exhibits a high signal-to-noise ratio (10) and guarantees undis-
turbed measurements even in methodologically dem-
demanding conditions on board of an aircraft flying par-
abatic trajectories where experiments of a total of 13
different research groups were performed in parallel.

The results of several experimental and clinical stud-
ies have shown that EIT is a promising technique for
continuously studying regional lung ventilation with
good time resolution over long periods of time (14). Gas
volume in the lungs is the main determinant of lung
impedance (2, 4), and a linear relationship between the
lung volume change and the measured relative imped-
ance change determined by EIT has been documented
by measurements performed during active or passive
stepwise inflation of the lung (e.g., Refs. 22, 23), as well
as during continuous ventilation (17). The ability of
EIT to correctly detect regional lung ventilation has
been checked by a morphological staining technique
(22) and single photon emission computed tomography
(24). (Until now, the results of the latter study have
only been published in an abstract form.) Further vali-
dation experiments using fast-electron-beam com-
puted tomography as a reference technique are being
currently performed by our research group.

EIT uses electrical excitation currents for imaging
biological tissues. Because electrical current flows also
outside the plane defined by the attached array of
surface electrodes, EIT quantifies regional lung venti-
lation in a three-dimensional slice of lung tissue rather
than in a pure two-dimensional cross section. This is a
major difference between EIT and other established
imaging techniques using, e.g., straight ionizing radi-
ation beams, which enable true two-dimensional image
generation. The effect of the third dimension on the
EIT image generation has been studied previously by
moving vertically quasi-point (21) or extended (34)
conducting or insulating objects in cylindrical tanks
filled with saline. In the former study, using a tank
with dimensions comparable with a human torso and a
centrally located 6-cm large test object, it was con-
cluded that the maximum impedance change was mea-
sured when the object lay within the studied trans-
verse plane and that the object contributed to the
registered impedance change by 50% of its in-plane
signal at a vertical distance of ∼6 cm above and below
the plane.

The dimensions of the chest change with breathing
movements, and they are affected by gravity as well.
These effects are not expected to have played a signif-
ificant role in the measurements of the present study
and in all EIT measurements based on the determina-
tion of relative impedance changes in general. This is
the consequence of the known low sensitivity of EIT
systems measuring relative impedance changes to con-
figurational changes and noncircularity of the studied
subjects (5). The fact that the effect of changing chest
wall dimensions on EIT measurements can be ne-
glected in measurements of relative impedance change
was also confirmed by Adler et al. (1).

The quality of pulmonary EIT imaging has been
enhanced by adopting a functional approach in EIT
data evaluation as used in the present investigation.

Functional EIT is based on the implementation of
novel evaluation procedures and extraction of physi-
ologically relevant data from EIT measurements. Func-
tional evaluation tools eliminate the problem of inter-
preting a time series of several hundreds of simple EIT
images. They also enable the generation of new types of
tomograms and calculation of quantitative parameters
providing concise physiologically relevant information
on different aspects of local lung function. In the
present study, information on the distribution of re-
gional lung ventilation, lung volumes, and lung emp-
ty ing behavior was derived from three types of EIT
images and parameters obtained by functional evalua-
tion of the same EIT data sets.

The quantitative parameters were calculated within
two regions of interest representing the right and left
lung areas. Large relative impedance change with time
occurring typically only in the lung tissue due to air
volume fluctuations associated with tidal breathing or
deep expirations was used as a criterion for identifying
the regions of interest during individual runs of data
evaluation. The chosen procedure provides a stable and
reproducible tool for identifying lung regions because
the size of the EIT images is not affected by the chang-
ing dimensions of the chest (e.g., due to breathing
movements) as the EIT electrodes are fixed on the
thoracic surface. Therefore, the individual sizes and
forms of the right and left lung regions in a given
posture do not exhibit large variation. This was con-
firmed by the finding that the gravity phase and
breathing form did not significantly influence the size
of the areas of selected regions of interest. Conse-
quently, the quantitative EIT parameters calculated
within these regions were not biased by the procedure
for identifying the regions of interest.

Interpretation of EIT data in terms of lung ventila-
tion and volume distributions has been validated and
used in our laboratory’s previous experimental and
clinical studies. The amplitude of end-inspiratory-to-
end-expiratory impedance change and the end-expira-
tory impedance change reflect the local VR and FRC, as
shown in an experimental study on pigs ventilated
mechanically with different ventilatory patterns (17).
A redistribution of lung ventilation and volumes re-
sulting from unilateral lung injury, postural changes,
variation of ventilatory parameters, and lung pathol-
gy was determined by functional EIT in experimental
(16, 18) and clinical (15) studies as well.

The characterization of regional lung emptying be-
havior by fitting the regional vs. overall expiratory
course of relative impedance change by a polynomial
function was used for the first time. The generation of
plots of regional vs. overall relative impedance change
was inspired by the established way of characterizing
regional inhomogeneity in the distribution of respired
air in the lungs introduced by Milic-Emili et al. (31):
the heterogeneity of lung emptying (or filling) is iden-
tified by simultaneous measurement of local and over-
all lung volume changes determined by the 133Xe tech-
tique. Regional lung volume, expressed as percentage
of regional TLC or VC, is plotted as a function of overall
lung volume, expressed as percentage of global TLC or VC (see Fig. 3). Were the lung volume changes uniform in all lung units, then a linear relationship between regional and overall lung volumes would be found in this type of diagram. In the case of inhomogeneous lung behavior, a nonlinear relationship is determined. The interpretation of plots of regional vs. overall relative impedance change, used in the evaluation of EIT data, was similar. The nonlinearity of lung emptying was characterized by fitting the data by a polynomial function of second degree, whereby the polynomial coefficient of second degree described the curvature of the plot. This approach using a polynomial fit to describe regional vs. global lung volume changes was used previously, e.g., in an animal experimental study using pulmonary parenchymal markers (37).

The results on the distribution of regional lung ventilation, lung volumes, and lung emptying behavior in 1 G, 2 G, and 0 G are discussed below.

Regional lung ventilation. The analysis of regional lung ventilation did not reveal significant differences in the magnitude of ventilation between the dependent and nondependent lung in the right lateral posture during tidal breathing. As far as the 1-G phase is concerned, this was an unexpected result because significantly higher ventilation of the dependent lung was found in this posture in our previous study on healthy spontaneously breathing subjects followed during normal gravity (16). The explanation of the present finding is probably the large age inhomogeneity of the studied group of subjects, with the youngest subject being 26 and the eldest 57 yr old. In contrast with the present study, the subjects studied previously were all in their twenties. It is known that the distribution of lung ventilation is age dependent (25). In young subjects, the dependent lung receives a larger portion of inspired air than the nondependent one. The distribution of ventilation becomes more homogeneous and is even inverted with increasing age due to a loss of lung elastic recoil. In fact, the functional EIT images of regional lung ventilation obtained in the eldest subject studied (Fig. 10) revealed higher ventilation of the nondependent lung in 1 G and 2 G and a rather homogeneous ventilation distribution during 0 G. Nevertheless, although the P value was reduced from 0.19 to 0.14 in 1 G and from 0.22 to 0.13 in 2 G, if the data of the eldest subject were excluded from statistical analysis, the differences in ventilation magnitudes between the dependent and nondependent lung regions remained statistically insignificant. Thus the effect of age on the ventilation distribution could not be clearly established from the present results because a higher number of elderly and young subjects would be needed.

During VC and FVC maneuvers in the lateral posture, the dependent lung experienced a higher gas volume change on deflation in 1 G and 2 G. This was an anticipated result because it is known that the upper lung regions are more extended after a full expiration than are the lower ones (30). However, the persistence of this difference in 0 G was not expected. This may be related to the short duration of the weightlessness period and the fact that some of the subjects performed the maneuver early in 0 G when the gas distribution was affected by the preceding 2-G phase.

In the supine posture, the distribution of ventilation between the right and left lung was always similar, revealing no significant differences during either tidal breathing or expiratory maneuvers. This is consistent with the identical position of both lungs in the gravity field in this body position.

The effect of acceleration on the right and left lung VR, VC, and FVC was not significant in either lying posture studied. This may be explained by the fact that the breathing pattern was not significantly influenced by gravity during parabolic flights. In our study, only the breathing rates that did not exhibit any significant gravity-dependent variation were determined. Previous studies performed with subjects in a different (i.e., upright) posture, and, therefore, not quite comparable with our experiments with the subjects in the horizontal body position, did not find any systematic effect of gravity on the global VR (12, 32) and FVC (13) during parabolic flights.

Regional lung volumes. Gravity exerted a significant effect on the regional FRC in the right and left lungs in the right lateral body position during tidal breathing. The determined shifts in FRC occurring in the dependent and nondependent lungs in 2-G and 0-G phases were of opposite nature. The end-expiratory impedance change determined in the right and left lung did not exhibit any significant differences during 1 G (see Fig. 7, top left). This does not mean that regional FRC values in the dependent and nondependent lungs were identical in 1 G. In fact, it is well known that the nondependent regions have a higher resting volume than the dependent ones (31). However, because EIT determines relative impedance values and end-expiratory impedance change is given in relation to regional midcapcity, the above-mentioned 1-G finding of similar end-expiratory impedance change in the dependent and nondependent lungs reflects only the fact that the gas volume change between the midcapacity and the end-expiratory volume was also similar in both lungs. When compared with 1 G, FRC significantly increased in the nondependent lung during 2 G. This means that nondependent lung regions were even more expanded at the end of normal tidal expiration in 2 G. During

Fig. 10. Functional EIT images of regional lung ventilation obtained in subject 1 in the right lateral body position during SB in phases of different acceleration (1 G, 2 G, and 0 G). Light regions show the regional lung ventilation. The image orientation is the following: ventral is at the bottom and the right side of the body is on the left of the image.
0 G, regional FRC fell below the 1-G level in the formerly nondependent lung, and it rose above it in the formerly dependent lung. This finding indicates that regional FRC became more homogeneously distributed because the right lung was compressed less and the left one expanded less in 0 G.

Gravity did not affect regional RV obtained in the right lateral posture during expiratory maneuvers. In the dependent right lung, the end-expiratory impedance change values determined during expiratory maneuvers were comparable with those during tidal breathing. This means that the right lung, lying lower in the gravity field, was already so much compressed at the end of tidal expiration that it did not deflate significantly more during full expiration; i.e., regional FRC was similar to regional RV. In the nondependent lung, regional RV was lower than regional FRC in all gravity phases, indicating that these initially more expanded lung regions always experienced a gas volume decrease during deep deflation.

In the supine posture, gravity significantly influenced regional FRC during tidal breathing. An increase in FRC was observed in both lungs during 0 G, probably due to gravitational unloading of the abdomen. As expected, RV was not affected by acceleration. No significant differences between end-expiratory lung volumes in the right and left lungs were detected in either acceleration phase during spontaneous breathing and expiratory maneuvers because of the identical orientation of the lungs with respect to the gravity vector.

**Regional lung emptying.** Significant effect of gravity on the pattern of lung emptying in the dependent and nondependent lung was detected in the right lateral body posture both during tidal breathing as well as during VC and FVC. During 1 G and 2 G, the dependent lung emptied preferentially early in expiration, whereas its contribution to the expiratory volume was diminished late in expiration. Opposite emptying sequence was observed in the nondependent lung. The emptying of the right lung did not differ from that of the left lung in 0 G. The pattern of lung emptying found at 1 G resembles the previously described behavior of the lungs, which is markedly sequential in the lateral posture (3, 35). In our study, a significant curvilinearity of lung emptying was found in the studied thoracic orientation of the lungs with respect to the gravity vector.

The curvilinearity of regional vs. overall lung emptying in 1 G and 2 G was significantly higher during VC than spontaneous breathing. This finding can be explained by the dissimilar behavior of the dependent and nondependent lung regions at small and large lung volumes, respectively (31). During deep expiration from TLC to RV, this effect naturally increases the curvature of the normalized regional vs. overall impedance change compared with tidal breathing. During FVC, the curvilinearity of the plots of regional vs. overall impedance change in the dependent and nondependent lungs was smaller than during VC, signifying that the lung emptying became more linear. Thus the present findings show a more even contribution of the dependent and nondependent lung to gas emptying during forced than slow VC maneuver. This is in agreement with the results of several test gas washout studies that revealed a more uniform distribution of respired air in the lungs at higher flow rates (26, 29).

In the supine posture, gravity did not affect the average regional lung emptying behavior of the right and left lung during spontaneous tidal breathing. A small difference between the pattern of the right and left lung emptying was found in 2 G. The explanation of this finding is unclear; a slight change in body posture in the pull-up phase affecting the mechanical behavior of the lungs can be considered as a potential cause of this phenomenon. During VC and FVC, no differences between the lungs were determined, and the emptying behavior was similar in all acceleration phases, as expected, on the background of the identical effect of gravity on both lungs in this posture.

**Conclusions.** The effect of gravity on local lung function regarding 1) regional lung ventilation, 2) regional lung volumes, and 3) regional pattern of lung emptying was studied in two horizontal postures during short periods of normogravity, hypergravity, and microgravity. The use of functional EIT enabled the location and visualization of pulmonary gravity-dependent phenomena in a transverse plane. A rapid redistribution of regional lung ventilation (VT, VC, FVC), lung volumes (FRC), and lung emptying behavior in response to increased and decreased acceleration was revealed. The obtained results demonstrate the ability of high-performance EIT devices to provide physiologically relevant information on lung ventilation during weightlessness.

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