Lung Ventilation and Perfusion in Prone and Supine Postures with Reference to Anesthetized and Mechanically Ventilated Healthy Volunteers

Sven Nyrén, M.D.,* Peter Radell, M.D., Ph.D.,† Sten G. E. Lindahl, M.D., Ph.D.,‡
Margareta Mure, M.D., Ph.D.,§ Johan Petersson, M.D., Ph.D.,‖ Stig A. Larsson, Ph.D.,#
Hans Jacobsson, M.D., Ph.D.,** Alejandro Sánchez-Crespo, M.Sc., Ph.D.††

CME This article has been selected for the ANESTHESIOLOGY CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

ABSTRACT

Background: The literature on ventilation (V) and lung perfusion (Q) distributions during general anesthesia and controlled mechanical ventilation in supine and prone position is contradictory. The authors aimed to investigate whether V, Q, and ventilation to perfusion ratio (V/Q ratio) matching in anesthetized and mechanically ventilated volunteers are gravity dependent irrespective of posture.

Methods: Seven healthy volunteers were studied at two different occasions during general anesthesia and controlled mechanical ventilation. One occasion studied ventral to dorsal V and Q distributions in the supine posture and the other in the prone posture. Imaging was performed in supine posture at both occasions. A dual radiotracer technique and single photon emission computed tomography were used. V and Q were simultaneously tagged with ^{99m}Tc-Technegas (Tetley Manufacturing Ltd., Sydney, Australia) and ^{113m}In-labeled macroaggregates of human albumin (TechneScan LyoMAA, Mallinckrodt Medica, Petten, The Netherlands), respectively.

Results: No differences in V between postures were observed. Q differed between postures, being more uniform over different lung regions in prone posture and dependent in supine posture. The contribution of the vertical direction to the total V/Q ratio heterogeneity was larger in supine (31.4%) than in prone (16.4%) ($P = 0.0639$, two-tailed, paired t test) posture.

Conclusions: During mechanical ventilation, prone posture favors a more evenly distributed Q between lung regions. V distribution is independent of posture. This results in a tendency toward lower V/Q gradients in the ventral to dorsal direction in prone compared with supine posture.

What We Already Know about This Topic

❖ Oxygenation improves in some patients with acute lung insufficiency on prone positioning
❖ The effect of prone *versus* supine positioning on lung ventilation and perfusion is controversial

What This Article Tells Us That Is New

❖ In anesthetized and mechanically ventilated healthy volunteers, regional lung ventilation did not differ with position, whereas perfusion was more uniform in the prone position

* Clinical Research Fellow, Department of Molecular Medicine and Surgery, Karolinska Institute, and Department of Radiology, Karolinska University Hospital. † Associate Professor and Head, Department of Pediatric Anesthesia and Intensive Care, ‡ Professor of Anesthesiology and Director of Research, § Associate Professor and Head of Section, ‖ Anesthesiologist, Department Anesthesiology and Intensive Care, # Professor and Head, †† Physicist, Department of Nuclear Medicine, ** Professor, Departments of Nuclear Medicine and Radiology, Karolinska University Hospital.

Address correspondence to Dr. Nyrén: Department of Molecular Medicine and Surgery, Karolinska Institute, Solna, SE 171 76 Stockholm, Sweden. sven.nyren@karolinska.se. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

IN 1991, Glenny *et al.*[1] stated that gravity is a minor determinant of pulmonary blood flow distribution. This publication challenged the existing dogma of gravity-dependent lung perfusion.[2] At about the same time, the question of positioning patients supine or prone while treating for acute lung insufficiency was revitalized.[3–8] A complete understanding of the complex interactions between lung perfusion and ventilation has not been reached, although a recent publication discovered a higher expression of nitric oxide synthase in dorsal parts of human lung compared with ventral parts, indicating a role of nitric oxide in directing lung blood flow.[9]

In 1978, Rehder *et al.*[10] stated that gas distribution, considered an indicator for local ventilation, during general anesthesia and mechanical ventilation, is preferentially dorsal in supine and ventral in the prone position. Thus, that it is dependent at both postures. In contrast with this, Tokics *et al.*[11] reported, in 1996, that ventilation is predominantly ventral and nondependent in the supine, anesthetized, and mechanically ventilated man. They also reported, in agreement with several other studies,[12–19] that lung perfusion is predominantly dorsal and dependent in the supine position. Many investigators have found lung perfusion to be more uniform in prone than in supine postures.[14–21]

Improved blood oxygenation in patients with acute lung insufficiency when turned to prone position has been observed.[4–8] The underlying mechanisms are still unclear. We hypothesized that the perfusion (Q) distribution along the ventral to dorsal direction in prone posture is less affected by gravity than in supine posture, resulting in a better ventilation (V)/perfusion (Q) matching distribution. Furthermore, it is of interest to study V and Q in humans during general anesthesia and mechanical ventilation to contribute to the discussion of earlier conflicting results. A dual radioisotope technique, previously developed in our group, which enabled simultaneous relative regional measurements of V and Q,[22,23] was used.

Materials and Methods

Subjects
Seven nonsmoking healthy volunteers (mean age, 31 yr; range, 26–39 yr; three men and four women) were included. They were of normal height (mean, 172 cm; range, 163–178 cm) and weight (mean, 70 kg; range, 57–91 kg). The local ethical and radiation safety committees (Stockholm, Sweden) approved the study, and written informed consent was obtained from all participants.

Radiopharmaceuticals
Approximately 50 MBq of [^{99m}Tc]-Technegas (Tetley Manufacturing Ltd., Sydney, Australia) was used as tracer for V. Simultaneously, 50 MBq of ^{113m}In-labeled macroaggregates of human albumin (TechneScan LyoMAA, Mallinckrodt Medica, Petten, The Netherlands) was used as tracer for Q.

Anesthesia
An intravenous catheter was inserted into a peripheral vein. Monitoring equipment for electrocardiogram and pulse oximetry was applied. During anesthesia, inhaled and exhaled gases were analyzed using a DATEX AS/3 monitoring equipment (Datex Division of Instrumentarium Corp., Helsinki, Finland). Fractions of inhaled oxygen, end-tidal concentrations of carbon dioxide, minute ventilation, respiratory rate, and peripheral arterial oxygen saturation were all recorded. The levels of applied positive end-expiratory pressure were recorded continuously.

Anesthesia was induced by intravenous injection of 200 mg propofol, followed by an continuous infusion of propofol at a rate of $8 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. Tracheal intubation was performed after establishing muscle relaxation by intravenous injection of 0.6 mg/kg rocuronium bromide. Alfentanil was used for analgesia. The subjects were then connected to a Servo 900C ventilator (Siemens-Elema, Stockholm, Sweden) set in a volume-controlled mode. A tidal volume of 8–10 ml/kg, a breathing frequency of 8–12/min, and a positive end-expiratory pressure of 3–4 cm H_2O were used. Fraction of inhaled oxygen was set at 0.3, and both respiratory rate and tidal volume were continuously adjusted to obtain a constant end-tidal concentration of carbon dioxide. Before administration of the radiopharmaceuticals, an inspiratory recruitment maneuver was sustained for 30 s at an airway pressure of 30 cm H_2O. The Technegas was then mixed with normal air and inhaled at a constant flow into the endotracheal tube between the Y-piece and the subject.[24] Simultaneously, the ^{113m}In-labeled albumin macroaggregates were administered intravenously. After examination, muscle relaxation was reversed, trachea was extubated, and the subject was transferred to the recovery room.

Study Design
The volunteers were fasted for 6 h before examinations. Each subject was examined at two different occasions with single photon emission computed tomography (SPECT) technique (one for isotope administration in prone position and one for isotope administration in supine position), at least 2 days apart and in random order. The study aimed at comparing distribution of radiopharmaceuticals after administration in prone and supine postures, whereas all registrations were performed with the subjects in supine position. Thus, at registration, anatomical conditions are identical. Differences in distribution will therefore be attributed to physiologic conditions at the time of radiopharmaceutical administration.

The study design is shown in figure 1. Induction of anesthesia and muscle relaxation followed by intubation of the trachea was always made in the supine position. When studying V and Q in prone position (fig. 1A), subjects were turned to prone position and a lung recruitment maneuver was performed to minimize atelectasis. Ten minutes after reaching a stable and comfortable prone position, radiopharmaceuticals were simultaneously administered. The subjects were then turned to supine position, and 10 min later, another recruitment maneuver was performed followed by a transmission and a tomography examination.

In part of the investigation, when supine posture was maintained throughout (fig. 1B), recruitment maneuvers were performed 15 min after intubation of the trachea. Ten minutes later, radiopharmaceuticals were administered, and SPECT examinations were performed.

SPECT Examination
A three-headed Triad XLT gamma camera (Trionix, Twinsburg, OH) with medium energy collimators was used. Examinations were performed using a four-energy window SPECT
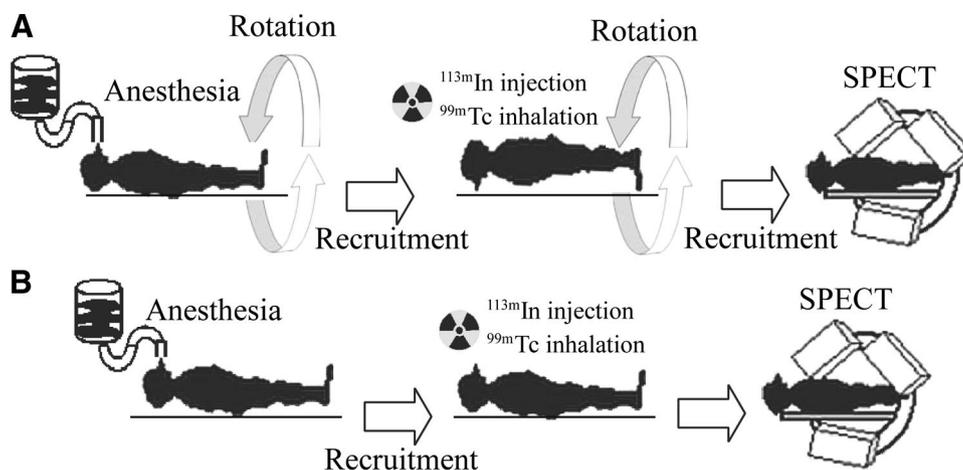
Fig. 1. Study design. Each subject was examined with single photon emission computed tomography technique at two different occasions, (*A*) radiopharmaceuticals administered in prone position and (*B*) radiopharmaceuticals administered in supine position. In both occasions, image registration was performed in supine position.

technique.[22] One primary energy window was centered at 140 keV (^{99m}Tc) representing V and another window at 392 keV (^{113m}In) representing Q. The remaining two windows were placed just below each of the primary energy windows to allow scatter and spill-down corrections. Acquisition was performed with 72 projections covering 360° and an acquisition time of 25 min. A 128 × 128-image matrix with a pixel size of 3.56 mm^2 was used. A 15-min transmission scan with a ^{99m}Tc-filled line source was made directly before or after the SPECT study for adequate attenuation correction and to delineate the lungs in the images. Reconstruction was made in the three planes using filtered back projection. Spatial resolution of the reconstructed data, after filter back projection and correction for scatter and attenuation, estimated as the full width half maximum of a point source is 18 mm for ^{99m}Tc and 25 mm for ^{113m}In.[25]

Data Analysis

After reconstruction and correction for photon scattering, attenuation, activity decay, and organ outline,[22] the SPECT data were pixel-wise normalized to the total activity administered. Thus, each pixel counts represents the relative blood flow or ventilation at that specific position in the lung. The relative ventilation or perfusion distributions were expressed as a percent of the total ventilation or perfusion in each individual.

The lungs of every individual were divided into 21 volumes of interest of equal distance along the ventral to dorsal axis, and the values for V, Q, and ventilation to perfusion (V/Q) ratio were plotted along the ventral to dorsal axis (fig. 2).

To enable intersubject comparison, the coronal projections (3.56-mm thick) were then pixel-wise added into three compartments of equal volume in the anterioposterior direction. The total ventilation, perfusion, and average V/Q ratio in each of these lung compartments were pixel-wise calculated (fig. 3). A two-tailed, paired Student *t* test with Bonferroni correction was used for significance testing between the three equal volumes (Excel, Microsoft Corporation, Redmond, WA). A *P* value less than 0.016 was considered statistically significant.

The contribution of the vertical direction to the total heterogeneity of the regional distribution of the ventilation, perfusion, and V/Q ratios, in prone and supine positions, was estimated using a variance analysis of the data set. To ensure that random image noise does not influence the analysis, the root mean square noise component for each SPECT data set was first calculated and then subtracted from the image. Each pixel in the noise-free image was then normalized to the total lung mean pixel value and the total variance (SS$_{total}$) obtained as the sums of squares of the pixel-wise deviations from this mean. In a second step, the mean pixel value for each isogravitational plane was also
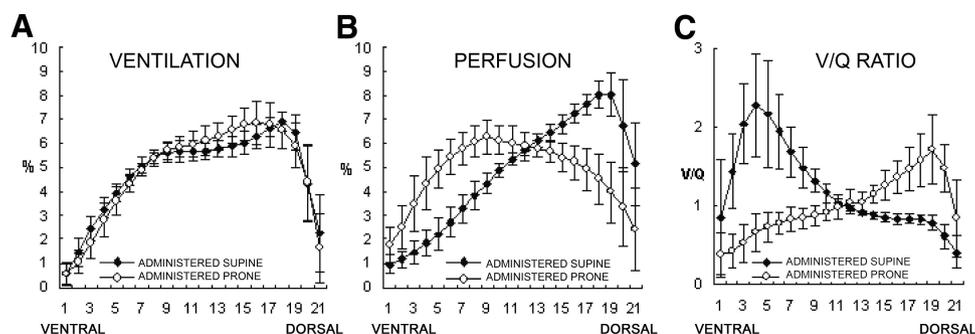

Fig. 2. Regional distributions of (*A*) ventilation, (*B*) perfusion, and (*C*) ventilation-perfusion ratios (V/Q) in the ventral to dorsal direction at supine and prone positions. Data are based on the equally spaced 21 volumes of interest. Data points represent mean ± 1 SD.
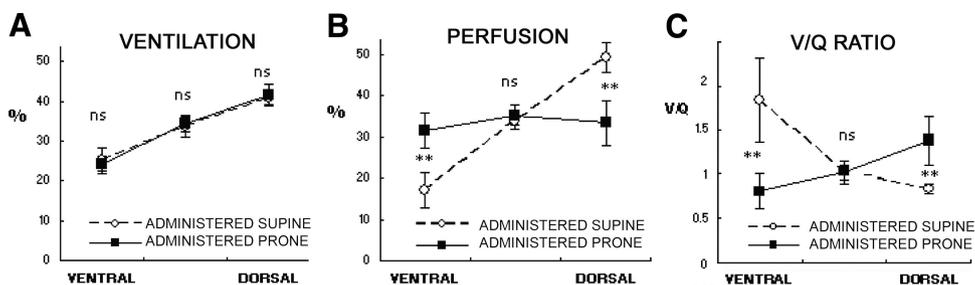
Fig. 3. Relative distributions within the three equal volumes presented in ventral to dorsal direction for the ventilation (*A*), perfusion (*B*), and ventilation-perfusion ratios (V/Q) (*C*). Data points represent mean ± 1 SD. ** *P* < 0.01, for comparisons between supine and prone positions. ns = not significant.

obtained and subtracted from every pixel within that plane. The variance of all these new pixel values for the entire lung was then calculated and considered to represent the residual heterogeneity without the influence from the vertical direction ($SS_{residual}$). Finally, the variance due to the vertical direction was calculated as the difference between the total and the residual variance.

$$SS_{vertical} = SS_{total} - SS_{residal} \quad (1)$$

The contribution to the total heterogeneity explained by the vertical direction was then obtained as:

$$SS_{vertical}(\%) = 100 \frac{SS_{vertical}}{SS_{total}} \quad (2)$$

A two-tailed Student *t* test was used to compare the $SS_{vertical}(\%)$ in prone and supine positions (Excel, Microsoft Corporation). A *P* value less than 0.05 was considered statistically significant.

Results

Recorded routine monitoring variables at the different postures are shown in table 1.

Table 1. Subjects Vital Parameters at Radiopharmaceutical Administration

	Supine	Prone	*P* Value
Heart rate (per min)	62 ± 12	69 ± 9	0.067
Fraction of inhaled oxygen (%)	0.31 ± 0.01	0.29 ± 0.02	0.063
End-tidal oxygen (%)	26 ± 1	25 ± 2	0.269
End-tidal carbon dioxide (%)	3.9 ± 0.2	3.9 ± 0.2	0.911
Oxygen saturation of peripheral blood (%)	98 ± 1	98 ± 1	0.457
Positive-end expiratory pressure (cm H$_2$O)	4 ± 0	5 ± 1	0.200
Tidal volume (ml)	612 ± 68	594 ± 190	0.743
Respiratory rate (per min)	10 ± 2	11 ± 4	0.515
Minute volume (l)	6.1 ± 1.3	6.1 ± 1.3	0.955
Mean airway pressure (cm H$_2$O)	7.9 ± 2.8	9.4 ± 3.9	0.183

Values are expressed as mean ± SD.

Regional Distributions of V, Q, and V/Q

There were no statistically significant differences in V distribution between prone and supine positions (table 2; figs. 2 and 3). Conversely, the Q distribution differed between prone and supine postures. Table 2 and figures 2 and 3 show a uniform Q distribution over different lung regions in the prone posture, whereas a more dependent distribution in the supine posture.

In ventral and dorsal lung regions, V/Q ratios were different in prone and supine positions, whereas mid-lung portions were similar in both postures (table 2).

Variance Analysis of the Regional Distribution of V, Q, and V/Q

The contribution to the total heterogeneity explained by the vertical direction is presented in table 3. The variation of V in the vertical direction (ventral to dorsal) was nearly identical in prone and supine postures (*P* = 0.589). For Q, however, large variations in the regional distribution along the vertical direction were found between supine and prone postures (*P* = 0.0006). The fraction of the total variance in the spatial distribution of Q, attributable to the vertical direction, is reduced from 45.8% in supine posture to 20.0% in prone posture (table 3). The fraction of the total variance attributable to the vertical component in the V/Q distribution was reduced from 31.4 ± 14.1% in supine posture to 16.4 ± 14.2% in prone posture (*P* = 0.0639; table 3). Hence, a

Table 2. Regional Distribution of Lung Ventilation and Perfusion within the Lung

	Ventral 1/3	Mid 1/3	Dorsal 1/3
Ventilation in supine (%)	25 ± 3	34 ± 3	41 ± 2
Ventilation in prone (%)	24 ± 2	34 ± 2	42 ± 3
P value	0.28	0.54	0.62
Perfusion in supine (%)	17 ± 4	34 ± 2	49 ± 4
Perfusion in prone (%)	31 ± 4	35 ± 3	33 ± 5
P value	0.0007	0.15	0.0008
V/Q ratio in supine	1.8 ± 0.5	1.0 ± 0.1	0.8 ± 0.1
V/Q ratio in prone	0.8 ± 0.2	1.0 ± 0.1	1.4 ± 0.3
P value	0.003	0.98	0.002

Values are expressed as mean ± SD.
V/Q = ventilation to perfusion ratio.

Table 3. The Contribution to the Total Heterogeneity Explained by the Vertical Direction (%)

	Vertical Component, $SS_{vertical}$, of the Total Variance (%)
Ventilation in supine	18.0 ± 6.7
Ventilation in prone	19.6 ± 9.8
P value	0.589
Perfusion in supine	45.8 ± 7.9
Perfusion in prone	20.0 ± 10.3
P value	0.0006
V/Q in supine	31.4 ± 14.1
V/Q in prone	16.4 ± 14.2
P value	0.0639

Values are expressed as mean ± SD.
V/Q = ventilation to perfusion ratio.

tendency toward a smaller contribution of the vertical component to the V/Q spatial distribution was observed in prone compared with supine posture.

Discussion

The main findings of this study in healthy individuals during anesthesia and mechanical ventilation are as follows:

i.   V is not affected by administration posture.
ii. Q is dorsally distributed in supine position and is more uniform between different lung regions in prone position.
iii. There is a tendency toward a more homogenous V/Q distribution along the vertical direction in prone compared with supine posture.

In contrast to Tokics *et al.*,[11] we found that ventilation seems dependent in supine position in anesthetized mechanically ventilated healthy volunteers. However, Tockis *et al.* reported the observation of dependent lung atelectasis, which may have been prevented in our study by the use of recruitment maneuvers not described by Tokics *et al.* Another important difference is the quantification of the activity distribution. Although, in our study, we perform a scatter and attenuation correction routine based on transmission scans,[22] Tockics *et al.* report that no correction routines were applied, which results in a false quantification of the activity distribution.

Our results regarding regional distribution of V and Q follow the same pattern as described in previously published investigations in animals (dogs,[1,13,15,17,26] lambs,[16] baboons,[19] pigs,[20] and sloths[26]) and in humans.[19,10,11,21,22] In particular, the values reported in the literature for the variation in ventilation explained by positioning in the vertical direction range from 12 to 33% in supine position and from 5 to 25% in prone position.[10,11,17,21] Corresponding values for lung perfusion are between 7 and 73% in supine position and between 5 and 26% in prone position.[1,17,18,21]

The observed lower variation in Q distribution along the vertical direction while in prone position is consistent with previous publications.[12,14,19] This effect could, to a large extent, be explained by the higher expression of nitric oxide synthase in human dorsal lung regions compared with ventral regions.[9] The variation in V/Q ratio distribution along the vertical direction was somewhat lower in prone than in supine position ($P = 0.0639$). Hence, the current series shows no obvious functional advantage in pulmonary circulation in prone compared with supine posture. This could be explained by the low power of the sample (n = 7) and the use of healthy volunteers. In the presence of lung disease, such as acute lung insufficiency, the more uniform lung perfusion in prone position is most likely the main explanation for the improved gas exchange when turned to prone position.[4–8]

Nuclear medicine techniques are well suited for the study of pulmonary ventilation and blood perfusion. The current technique, developed and evaluated in our group, provides simultaneous relative quantification of V and Q distributions.[22,23] It also involves individually tailored correction for photon attenuation and scattering, which is necessary for adequate quantification of data in the complex anatomy of the chest. However, SPECT images suffer from a limited spatial resolution that results in partial volume effects, which hampers image quantification in regions near the edge of the object. In our study, we performed edge detention based on anatomical images from the transmission scan. This gives us an accurate definition of the anatomical extensions of the lung, reducing the impact of partial volume in the calculations of the variance. In fact, the variance calculated in the lungs defined by the edge detection algorithm did not differ from the variance calculated by excluding the most outer 5-pixel thick layer of the lung tissue (data not shown). Another important assumption is that the radiopharmaceuticals are trapped in the alveoli and in the capillary bed in direct proportion to ventilation and perfusion, respectively, and that the activity remains stable throughout the examination. Previous studies have confirmed this.[27–29] Both tracers are currently used in routine clinical lung scintigraphy.

Based on these results in anesthetized and mechanically ventilated healthy individuals, it is concluded that V is not affected by posture and Q is gravity dependent in supine posture and uniformly distributed between different lung regions in prone posture. From a functional gas exchange standpoint, the tendency for a more evenly distributed V/Q matching along the vertical direction while in prone position, observed in these healthy volunteers, could be more pronounced in patients with acute lung insufficiency.

References

1. Glenny RW, Lamm WJ, Albert RK, Robertson HT: Gravity is a minor determinant of pulmonary blood flow distribution. J Appl Physiol 1991; 71:620–9
2. West JB, Dollery CT, Naimark A: Distribution of blood flow in isolated lung: Ration to vascular and alveolar pressures. J Appl Physiol 1964; 19:713–24

3. Gattinoni L, Tognoni G, Pesenti A, Taccone P, Mascheroni D, Labarta V, Malacrida R, Di Giulio P, Fumagalli R, Pelosi P, Brazzi L, Latini R: Prone-supine study group: Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med 2001; 345:568–73

4. Mure M, Martling CR, Lindahl SG: Dramatic effect on oxygenation in patients with severe acute lung insufficiency treated in the prone position. Crit Care Med 1997; 25:1539–44

5. Langer M, Mascheroni D, Marcolin R, Gattinoni L: The prone position in ARDS patients. A clinical study. Chest 1988; 94:103–7

6. Douglas WW, Rehder K, Beynen FM, Sessler AD, Mars HM: Improved oxygenation in patients with acute respiratory failure: Prone position. Am Rev Respir Dis 1977; 115: 559–66

7. Pelosi P, Brazzi L, Gattinoni L: Prone position in acute respiratory distress syndrome. Eur Respir J 2002; 20:1017–28

8. Albert RK, Leasa D, Sanderson M, Robertson HT, Hlastala MP: The prone position improves arterial oxygenation and reduces shunt in oleic-acid-induced acute lung injury. Am Rev Respir Dis 1987; 135:628–33

9. Rimeika D, Nyrén S, Wiklund NP, Renström-Koskela L, Tørring A, Gustafsson LE, Larsson SA, Jacobsson H, Lindahl SGE, Wiklund CU: Regulation of regional lung perfusion by nitric oxide. Am J Respir Crit Care Med 2004; 170:450–5

10. Rehder K, Knopp TJ, Sessler AD: Regional intrapulmonary gas distribution in awake and anesthetized-paralyzed prone man. J Appl Physiol 1978; 45:528–35

11. Tokics L, Hedenstierna G, Svensson L, Brismar B, Cederlund T, Lundquist H, Strandberg A: V/Q distribution and correlation to atelectasis in anesthetized paralyzed humans. J Appl Physiol 1996; 81:1822–33

12. Reed JH Jr, Wood EH: Effect of body position on vertical distribution of pulmonary blood flow. J Appl Physiol 1970; 28:303–11

13. Beck KC, Rehder K: Differences in regional vascular conductances in isolated dog lungs. J Appl Physiol 1986; 61:530–8

14. Wiener CM, Kirk W, Albert RK: Prone position reverses gravitational distribution of perfusion in dog lungs with oleic acid-induced injury. J Appl Physiol 1990; 68:1386–92

15. Beck KC, Vettermann J, Rehder K: Gas exchange in dogs in the prone and supine positions. J Appl Physiol 1992; 72:2292–7

16. Walther SM, Domino KB, Glenny RW, Polissar NL, Hlastala MP: Pulmonary blood flow distribution has a hilar-to-peripheral gradient in awake, prone sheep. J Appl Physiol 1997; 82:678–85

17. Treppo S, Mijailovich SM, Venegas JG: Contributions of pulmonary perfusion and ventilation to heterogeneity in V(A)/Q measured by PET. J Appl Physiol 1997; 82:1163–76

18. Glenny RW, Bernard S, Robertson HT, Hlastala MP: Gravity is an important but secondary determinant of regional pulmonary blood flow in upright primates. J Appl Physiol 1999; 86:623–32

19. Mure M, Domino KB, Lindahl SG, Hlastala MP, Altneier WA, Glenny RW: Regional ventilation-perfusion distribution is more uniform in the prone position. J Appl Physiol 2000; 88:1076–83

20. Prisk GK, Yamada K, Henderson AC, Arai TJ, Levin DL, Buxton RB, Hopkins SR: Pulmonary perfusion in the prone and supine postures in the normal human lung. J Appl Physiol 2007; 103:883–94

21. Musch G, Layfield JD, Harris RS, Melo MF, Winkler T, Callahan RJ, Fischman AJ, Venegas JG: Topographical distribution of pulmonary perfusion and ventilation, assessed by PET in supine and prone humans. J Appl Physiol 2002; 93:1841–51

22. Sánchez-Crespo A, Petersson J, Nyrén S, Mure M, Glenny RW, Thorell J-O, Jacobsson H, Lindahl SGE, Larsson SA: A novel quantitative dual-isotope method for simultaneous ventilation and perfusion lung SPET. Eur J Nucl Med 2002; 29:863–75

23. Petersson J, Sánchez-Crespo A, Rohdin M, Montmerle S, Nyrén S, Jacobsson H, Larsson SA, Lindahl SG, Linnarsson D, Glenny RW, Mure M: Physiological evaluation of a new quantitative SPECT method measuring regional ventilation and perfusion. J Appl Physiol 2004; 96:1127–36

24. Sánchez-Cresp A, Rohdin M, Carlsson C, Bergstrom SE, Larsson SA, Jacobsson H, Lindahl S, Jonsson B: A technique for lung ventilation-perfusion SPECT in neonates and infants. Nucl Med Commun 2008; 29:173–7

25. Sanchez Crespo Alejandro (2005): Novel computational methods for image analysis and quantification using position sensitive radiation detectors. Thesis, Faculty of Science, Medical Radiation Physics, Stockholm University, Stockholm, Sweden

26. Hoffman EA, Ritman EL: Effect of body orientation on regional lung expansion in dog and sloth. J Appl Physiol 1985; 59:481–91

27. Amis TC, Crawford AB, Davison A, Engel LA: Distribution of inhaled 99mtechnetium labelled ultrafine carbon particleaerosol (Technegas) in human lungs. Eur Respir J 1990; 3:679–85

28. Tapling GV, MacDonald NS: Radiochemistry of macroaggregated albumin and newer lung scanning agents. Semin Nucl Med 1971; 1:132–52

29. Wagner HN Jr: Regional ventilation and perfusion, Principles of Nuclear Medicine. Edited by Wagner HN Jr, Szabo Z, Buchanan JW. Philadelphia, Saunders, 1995, pp 881–95