Pulmonary blood flow redistribution by increased gravitational force

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Departments of Physiology and Biophysics, 2Medicine, and 3Anesthesiology, University of Washington, Seattle 98195; 4The Mountain-Whisper-Light Statistical Consulting, Seattle, Washington 98122; and 5Crew Technology Division, Armstrong Laboratory, Air Force Medical Center, Brooks Air Force Base, Texas 78235

Hlastala, Michael P., Myron A. Chornuk, David A. Self, Harry J. Kallas, John W. Burns, Susan Bernard, Nayak L. Polissar, and Robb W. Glenny. Pulmonary blood flow redistribution by increased gravitational force. J. Appl. Physiol. 84(4): 1278-1288, 1998.—This study was undertaken to assess the influence of gravity on the distribution of pulmonary blood flow (PBF) using increased inertial force as a perturbation. PBF was studied in unanesthetized swine exposed to −Gx (dorsal-to-ventral direction, prone position), where G is the magnitude of the force of gravity at the surface of the Earth, on the Armstrong Laboratory Centrifuge at Brooks Air Force Base. PBF was measured using 15-µm fluorescent microspheres, a method with markedly enhanced spatial resolution. Each animal was exposed randomly to −1, −2, and −3 Gx. Pulmonary vascular pressures, cardiac output, heart rate, arterial blood gases, and PBF distribution were measured at each G level. Heterogeneity of PBF distribution as measured by the coefficient of variation of PBF distribution increased from 0.38 ± 0.05 to 0.55 ± 0.11 to 0.72 ± 0.16 at −1, −2, and −3 Gx, respectively. At −1 Gx, PBF was greatest in the ventral and cranial and lowest in the dorsal and caudal regions of the lung. With increased −Gx, this gradient was augmented in both directions. Extrapolation of these values to 0 G predicts a slight dorsal (nondependent) region dominance of PBF and a coefficient of variation of 0.22 in microgravity. Analysis of variance revealed that a fixed component (vascular structure) accounted for 81% and nonstructure components (including gravity) accounted for the remaining 19% of the PBF variance across the entire experiment (all 3 gravitational levels). The results are inconsistent with the predictions of the zone model.

The distribution of ventilation and perfusion and, accordingly, the gas exchange function of the lung are governed by a number of gravitational and local (nongravitational) factors. The gravitational model of pulmonary perfusion states that regional perfusion is determined by local alveolar and hydrostatic pressures. The zone model (19) postulates that gravity is the principal determinant of regional perfusion, explaining the observation that perfusion increases from nondependent to dependent lung regions. The zone framework postulates that the blood flow at any isogravitational plane is determined by the balance between alveolar pressure, arterial blood pressure, and venous blood pressure. Because gravity has a greater vertical effect on vascular pressures, the relative zone-pressure relationships, and hence pulmonary vascular flow, vary with vertical height. The gravitational model of pulmonary blood flow (PBF) distribution was developed from studies that measured blood flow to relatively large regions of lung (19, 30). Supporting evidence was provided by Greenleaf et al. (12) and Kaneko et al. (20). More recently, similar gravitational dependence has been seen in humans by use of radioactive 81mKr with an external gamma camera (1, 2), again with limited horizontal resolution. As the spatial resolution of blood flow measurements has improved, experimental observations show less influence of gravity on PBF distribution.

Several investigators have demonstrated isogravitational perfusion heterogeneity. These observations include regional perfusion variability within horizontal planes (25); a radial distribution of flow with the greatest perfusion located centrally in lung lobes (13, 14); and isogravitational perfusion that is increased in dorsal regions regardless of posture, implying an anatomic component (3, 4) to perfusion distribution. Glenny et al. (11) used microspheres to mark perfusion to 1.9-cm³ voxels of lung and concluded that gravity accounts for only 4% of the blood flow distribution in the anesthetized mechanically ventilated dog in the prone or supine posture. This conclusion results from the enhanced spatial resolution offered by the animal experiments in contrast to earlier human experiments with external counters (19). Thus the vast majority of the influences on ventilation and perfusion distribution comes from the local, nongravitational factors.

Previous studies in a high-gravity (inertial force) environment using methods with poor spatial resolution have been interpreted in the context of the zone model. That model suggests that at the level down the lung where venous pressure exceeds alveolar pressure, the waterfall effect will cease to operate and blood flow will be proportional to the arteriovenous pressure difference. This level then would define the functional transition between zones 2 and 3. Previous work using methods with poor spatial resolution (7) demonstrated that as +Gz (head-to-foot inertial load, where G is the magnitude of the force of gravity at the surface of the Earth)1 increased, the effective waterfall zones (1) were progressively extended downward to regions of higher

1 In keeping with the standard notation in acceleration research, we use the three vectors of G force as follows: x (ventral to dorsal), −x (dorsal to ventral), y (right to left), −y (left to right), z (cranial to caudal), and −z (caudal to cranial).
venous pressure. The zone model also predicts uniform blood flow within isogravitational planes. Furthermore, the effects of increasing alveolar pressure through positive-pressure breathing may enhance this trend, causing the apparent zone 2–3 transition to move even more caudally. West and Dollery (29) obtained data consistent with the interpretation that positive-pressure breathing enlarged zone 2 at the expense of zone 3 and enlarged zone 1 at the expense of zone 2.

We undertook this study to determine the quantitative effect of gravity on PBF distribution by increasing the magnitude of the gravity vector in the dorsal-to-ventral direction (–Gx) in unanesthetized prone pigs using the fluorescent microsphere method with enhanced spatial resolution. The goal was to quantify the changes in regional PBF distribution in response to increased –Gx and test the zone model hypothesis.

**MATERIALS AND METHODS**

This study was approved by the Animal Care Committee of the University of Washington. Animals were managed according to National Institutes of Health regulations and the “Guiding Principles in the Care and Use of Animals” of the American Physiological Society. Four female miniature swine (45.8 ± 3.0 kg) were chemically restrained with ketamine (22–34 mg/kg), intubated, and placed in positive-pressure ventilation (tidal volume 15 ml/kg, frequency adjusted to maintain arterial Pco2 between 35 and 40 Torr) with ~1% isoflurane (to effect). A surgical plane of anesthesia was maintained at all times while the catheters were being placed. Two Swan-Ganz catheters (5- and 7-Fr in 2 animals and two 7-Fr in 2 animals) were introduced into each jugular vein and advanced under fluoroscopy into the pulmonary artery. The pulmonary arterial catheters were used for determination of cardiac output (thermal dilution) and core body temperature, withdrawal of a reference pulmonary arterial blood sample, and measurement of pulmonary arterial pressure and central venous pressure. The proximal port of one of the Swan-Ganz catheters was used for microsphere injection. A catheter was placed into the right carotid artery for measurement of arterial blood pressure and determination of arterial blood gases. An esophageal balloon was introduced to monitor respiration in intrathoracic pressure. Surgical sites were infiltrated with 2% bupivacaine, animals were given 5,000 IU of heparin, and electrocardiogram leads were attached. The animals were fitted with a swine antigravity suit (Armstrong Laboratory Centrifuge). The animal and couch were transported to the centrifuge facility, and the couch was attached to the animal arm of the centrifuge. Lateral thoracic X rays were taken for lung position. Once fully awake, the animals were exposed randomly to –1, –2, and –3 Gx while prone (with head toward the center of the centrifuge) (Table 1). An exposure of one of the G levels was repeated, but the repeated data are not analyzed here. The animals were placed in the horizontal contoured platform (prone position) with the head toward the center of rotation. The platform was allowed to pivot, with the center of mass of the platform directly below the pivot axis of the platform. As the centrifuge began to rotate, a radial component of force, coupled with the fact that the center of mass of the pig and the platform were below the center of rotation of the platform, resulted in a pivoting of the animal platform, with the head of the pig rotating downward to the floor and the tail of the pig rotating in the upward (skyward) direction (Fig. 1). The net force (gravity and the radial centrifugal force) and the pivoting of the animal result in a net force in the –Gx direction (dorsal-to-ventral; same direction as in the resting prone position). For each G exposure, once the centrifuge reached a stable G plateau and the animal reached a quasi-steady state in terms of arterial pressure and breathing patterns, simultaneous withdrawal of 5 ml of arterial blood for blood-gas determination from the carotid catheter and injection of iced saline through the Swan-Ganz catheter for thermal-dilution cardiac output measurement were performed by remote control. Outputs from the Swan-Ganz temperature probe were connected to a cardiac output computer (Baxter Healthcare). After these measurements, the microspheres were injected at a rate of ~4 ml/min (~30 s) via the proximal port of the Swan-Ganz catheter. Reference blood samples (10 ml) were withdrawn from the distal port of the Swan-Ganz catheter at a rate of 4.94 ml/min. Between each G exposure, the centrifuge arm was stopped, the next set of microspheres was injected at a rate of 4.94 ml/min (~30 s) via the proximal port of the Swan-Ganz catheter. Reference blood samples (10 ml) were withdrawn from the distal port of the Swan-Ganz catheter at a rate of 4.94 ml/min. Between each G exposure, the centrifuge arm was stopped, the next set of microspheres was

![Fig. 1. Schematic diagram of centrifuge in operation. Initially, animal is oriented in prone position with head toward center of rotation. As centrifuge rotates, weighted sling assembly rotates in head-down direction, resulting in an increase in inertial force in –Gx direction.](image-url)

**Table 1. G exposure sequence**

<table>
<thead>
<tr>
<th>Pig</th>
<th>Run 1</th>
<th>Run 2</th>
<th>Run 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>–3 Gx</td>
<td>–1 Gx</td>
<td>–2 Gx</td>
</tr>
<tr>
<td>2</td>
<td>–2 Gx</td>
<td>–3 Gx</td>
<td>–1 Gx</td>
</tr>
<tr>
<td>3</td>
<td>–1 Gx</td>
<td>–3 Gx</td>
<td>–2 Gx</td>
</tr>
<tr>
<td>4</td>
<td>–1 Gx</td>
<td>–2 Gx</td>
<td>–3 Gx</td>
</tr>
</tbody>
</table>
After the experiment the animals were deeply anesthe-
tized, intubated, ventilated, and given 10,000 IU of heparin
and 350 mg of papaverine intravenously. The animals were
exsanguinated via the arterial catheters, and intravascular
volume was replaced with normal saline containing heparin.

Data processing. Relative blood flow to each piece was
measured with a Corning model 158 blood-gas electrode
system.

Relative blood flow to each piece was
determined as the weighted mean of
cardiac output (reference blood), l/min

Table 2. Physiological variables by G level

<table>
<thead>
<tr>
<th>Test</th>
<th>Temp, ºC</th>
<th>PaO2, Torr</th>
<th>PaCO2, Torr</th>
<th>pH</th>
<th>Heart rate, beats/min</th>
<th>MAP, mmHg</th>
<th>PAP, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>3</td>
<td>94.9 ± 5.2</td>
<td>37.7 ± 2.3</td>
<td>t</td>
<td>A</td>
<td>128.0 ± 14.0</td>
<td>351.5 ± 35.7</td>
</tr>
</tbody>
</table>

Values are means ± SD; omitted SD values indicate that only 1 animal was available at 3 G; n, no. of animals used for hypothesis test. PaO2 and PaCO2, arterial Po2 and PCO2; MAP, mean arterial pressure; PAP, pulmonary arterial pressure; CVP, central venous pressure; Pes, esophageal pressure; A, repeated-measures ANOVA comparing 1, 2, and 3 G; t, paired t-test comparing 1 and 2 G. *P < 0.05; †P < 0.01; ‡P < 0.001.

The x, y, and z directions for lung spatial locations are identical to the G vector directions in this report. In previous reports from our laboratory, we switch the x and y coordinates. Care should be taken when spatial distributions are compared with our previous articles.
where $F_{ij}$ is the observed relative flow for piece $i$ and G level $j$, $F_i$ is the mean relative flow for piece $i$ across the different G levels considered, $n$ is the number of states, and $m$ is the number of pieces. The variance component due to pieces was estimated by

$$
\hat{\sigma}_{\text{pieces}}^2 = \frac{\sum_{i=1}^{m} (F_i - \bar{F})^2}{m - 1}
$$

The grand mean across all pieces and states $\bar{F}$ has a value of 1.0 because of normalization of flow, as described earlier.

Because the variation across pieces and the variation across gravitational states (including time and methodological noise) are the only sources of variation in flow, their relative contributions to the total variance can be calculated as percentages. The percentage of variation across pieces is as follows:

$$P_{\text{pieces}} = 100 \cdot \frac{\hat{\sigma}_{\text{pieces}}^2}{\hat{\sigma}_{\text{pieces}}^2 + \hat{\sigma}_{G}^2}.$$ 

The negligible methodological noise contributes primarily to $\hat{\sigma}_{G}^2$ and slightly to $\hat{\sigma}_{\text{pieces}}^2$.

**RESULTS**

Physiological data. Basic physiological data for the animals are shown in Table 2. With increasing $-G_x$, gas exchange worsened, as indicated by a decrease in arterial $P_{O_2}$ from 94.9 to 43 Torr. Hypoventilation was indicated by the increased arterial $P_{CO_2}$ (48.7 Torr) at $-3 \ \text{G}_x$. At $-3 \ \text{G}_x$, an acceptable arterial blood sample was obtained in only one animal because of problems with the automatic blood sampler. Cardiac output was determined from the fluorescent microspheres using a reference withdrawal pump (see Ref. 11 for details) and from thermodilution. The thermodilution method did not work well at higher $G$ levels, because the temperature did not return to baseline, disabling the cardiac output calculation. We relied on the microsphere cardiac output, which increased at $-3 \ \text{G}_x$, in a manner that paralleled the increase in heart rate.

Heterogeneity. The histograms shown in Fig. 2 demonstrate the distribution of WNRF. For pig 2 at $-1 \ \text{G}_x$, the distribution is centered on a normalized flow of 1.0. As the $-G_x$ level increases (Fig. 2, B and C), the overall heterogeneity increases, as indicated by the broader histograms and larger CVs of flow, and become more skewed, as indicated by the asymmetry. At $-3 \ \text{G}_x$, ~10% of lung pieces had a near-zero WNRF. These pieces tended to be in the most dorsal regions of the lung.

Perfusion heterogeneity is indicated by the CV, which averaged $38 \pm 5$, $55 \pm 13$, and $72 \pm 0.16\%$ (SD) for $-1$, $-2$, and $-3 \ \text{G}_x$, respectively. The increase in heterogeneity with increased $-G_x$ is shown in Fig. 3. The increase in CV with gravitational force was well fit in each animal with a linear model with $R^2$ ranging from 0.90 to 1.0. Extrapolation of the linear regression model for each animal allows estimation of the magnitude of heterogeneity of PBF that might be expected at 0 G (mean CV = 22 ± 3%). The CV increases by 17 ± 6% per unit increase in G.

To examine the vertical (dorsal-to-ventral) dependence of PBF, the normalized blood flow to each piece was plotted (Fig. 4) as a function of vertical height within the lung. One animal is shown for $-1 \ \text{G}_x$ (A), $-2 \ \text{G}_x$ (B), and $-3 \ \text{G}_x$ (C). CV, coefficient of variation.
and Table 3. Each point in Fig. 5 represents the slope (gradient) of normalized flow with vertical distance for a specified pig at a specified G force. The x gradient of the regression line for flow vs. vertical distance up the lung becomes more negative (net shift ventrally) with increasing $G_x$. Extrapolation of the linear fit line to 0 G reveals no net vertical dependence of blood flow (intercept of $0.010 \pm 0.017$) in the absence of gravitational inertial force. The vertical gradient steepens by $0.035 \pm 0.008$ relative flow unit per centimeter for every G unit.

A small negative flow gradient from the hilum of each lung out to the periphery was found at $-1G_x$ (Fig. 6A). The mean gradient for all animals was $-0.037$ relative flow unit per centimeter. This radial gradient increased in magnitude substantially as the G force increased (Fig. 6, B and C).

The slopes of the radial gradients (Fig. 6) are plotted against G level for all four animals in Fig. 7. Extrapolation of the linear regression line to 0 G for each animal reveals an intercept of $-0.013 \pm 0.019$ and a change per unit G level of $-0.029 \pm 0.008$, showing no significant radial gradient of PBF after elimination of $-G_x$ load.

A simple linear regression model of flow gradient for each spatial dimension ($x$, $y$, $z$, and $D_H$) vs. gravity was carried out, and the slopes are presented in Table 4. Table 4 shows the change in a given gradient per unit change in G. $R^2$ for the 16 regressions presented here was a minimum of 0.83, and in 12 of the 16 regressions $R^2$ was $\geq 0.95$, indicating a good fit by the linear models for gradient vs. G. Table 4 shows large changes in gradients as G increases. The ventral-dorsal, caudal-cranial, and hilar gradients change significantly with G ($P < 0.05$, t-test), and the change in the left-right gradient is small and nonsignificant. The largest change with G occurs for the ventral-dorsal gradient, where a one-unit increase in G, e.g., from 1 to 2, would increase the gradient by 0.035 relative flow unit per centimeter. Thus a lung region that was 10 cm more ventral than a comparable dorsal region would have a flow that increased by 0.35 more than the dorsal regions for the 1-G change. Given a mean flow of 1.0, the regional contrast is substantial.

The similarity of flow among G levels is demonstrated by partitioning the variation in flow into its components (Table 5). A mean of 81% of the variance of flow across gravitational states is explained by structure. This structural dominance is strikingly consistent across the animals in this study (78–86%). Although gravity results in a considerable shift in blood flow
distribution, the primary determinant of distribution is piece location.

**DISCUSSION**

The important findings of this study are as follows: 1) regional PBF becomes more heterogeneous with increasing $-G_x$ force; 2) extrapolation of observations to 0 G indicates persistent perfusion heterogeneity in microgravity; and 3) a fixed structural component is the major determinant of regional perfusion across all $G_x$ levels.

Methodological issues. To estimate regional PBF reliably, the fluorescent microsphere method must fulfill several criteria. First, the microspheres must have a distribution in the microcirculation similar to whole blood. These 15-µm microspheres have a density (1.04 g/dl) very close to blood and have recently been validated for measurement of regional PBF in dogs (10). In addition, Laughlin et al. (22) showed that radiolabeled microspheres of even greater density (1.23 g/ml) are suitable for use at high acceleration levels. Second, the number of microspheres have to be large enough to limit the effect of method error on the statistics. We injected $2 \times 10^6$ microspheres per injection, which provided >400 microspheres per tissue sample when blood flow was $\approx 25\%$ of average flow.

Flow to each lung piece was normalized by the weight of the sample. This provided blood flow per alveolar volume, since alveoli are uniform in size at total lung capacity. This process allowed for correction for variations in sample size. In addition, samples with >25% airway tissue were excluded from the analysis because

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**Table 3. Slopes of flow vs. x, y, z, and $D_h$ dimensions by gravitational level**

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>$D_h$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$-1 , G_x$</td>
<td>$-0.020 \pm 0.019$</td>
<td>$-0.007 \pm 0.015$</td>
<td>$0.019 \pm 0.016$</td>
<td>$-0.042 \pm 0.023$</td>
</tr>
<tr>
<td>$-2 , G_x$</td>
<td>$-0.069 \pm 0.028$</td>
<td>$-0.002 \pm 0.022$</td>
<td>$0.036 \pm 0.016$</td>
<td>$-0.071 \pm 0.020$</td>
</tr>
<tr>
<td>$-3 , G_x$</td>
<td>$-0.091 \pm 0.032$</td>
<td>$0.011 \pm 0.022$</td>
<td>$0.055 \pm 0.019$</td>
<td>$-0.100 \pm 0.031$</td>
</tr>
</tbody>
</table>

Values are means ± SD expressed as weight-normalized relative blood flow per centimeter; $n = 4$. x, Ventral-dorsal direction; y, right-left direction; z, cranial-caudal direction; $D_h$, distance from hilum.
of the disproportionate weight and volume of airway cartilage on weight normalization.

Alveolar volumes were uniformly distended throughout the lung during drying at high lung volume (25–30 cmH₂O). This volume was chosen to reproduce the alveolar volume distribution in the prone animal. Although there is evidence that alveolar volumes decrease down the lung near functional residual capacity in the erect human (29) and the head-up dog (9), there is no vertical gradient in alveolar size when animals are in the prone posture. Different methodologies have confirmed these findings, including intraparenchymal metallic markers (18), high-resolution computed tomographic scanning (17), and the dynamic spatial reconstructor (16). A uniform distribution of alveolar volumes in the prone posture is supported by studies showing that the vertical gradient in pleural pressure in supine animals is abolished when the animals are turned prone. These studies have been performed in a variety of animals, including rabbits (21), pigs (24), dogs (3), and ponies (26). Because alveolar volume is determined by the local transpulmonary pressure, PA – Ppl, where PA is alveolar pressure and Ppl is pleural pressure, the absence of a pleural gradient in the prone position confirms that alveolar volumes are uniformly distributed down the lung in a prone pig (at –1 Gₚ).

The configuration of the lung after it is dried may be slightly different from that in vivo. Lung drying occurs during suspension from the trachea with a pressure of 25–30 cmH₂O; therefore, lung volume will be slightly greater than in the intact lung. This will increase linear dimensions slightly. Because lungs dry during suspension from the trachea, the orientation of gravity is different, possibly resulting in a slight distortion relative to the intact lung. The shape of the lung will be slightly different from that of an in vivo lung because of the lack of physical constraints of the chest wall and diaphragm. It is also possible that in the chest the weight of the heart may result in some compression of any lung below it. The volume of this ventral lung is quite small and would have little influence, if any, on the regressions. Even though these factors are difficult to quantitate, they are expected to be quite unimportant with respect to the major findings of this study.

The average CV of PBF for the four pigs at –1Gₚ was 38% (1.9-cm³ piece). This is within the range of other studies of PBF heterogeneity. Melsom et al. (23) examined distribution of PBF in horizontal lung slices in awake goats and found a mean heterogeneity of 38% (1.5-cm³ piece) without considering the effect of vertical differences, which likely would have slightly increased apparent heterogeneity. Parker et al. (27) observed a mean heterogeneity of 47% (1.0-cm³ piece) in awake chronically catheterized dogs, and Glenny et al. (11) found a mean heterogeneity of 45% in the supine position and 41% in the prone position (1.9-cm³ piece) in halothane-anesthetized prone dogs. We found a CV of 31% (1.9-cm³ piece) in Thoroughbred horses (5, 15) and 30% (1.7-cm³ piece) in lambs (28). In this study, heterogeneity increased substantially with increasing inertial force in pigs.

The distribution of PBF vs. height up the lung (Fig. 4) is only slightly dependent on vertical position (vertical slope = –0.20 WFRL/cm, Table 3). This is consistent with the zone model in direction but not in magnitude. The apparent gravity dependence (as shown by the mean PBF in each isogravitational plane) increases with increasing –Gₚ (Table 3). This change in mean flow is consistent with predictions of the zone model.

The pigs in this study demonstrated a large degree of isogravitational heterogeneity at all three –Gₚ levels (prone position; Fig. 4A). This observation is not consistent with the zone model. The magnitude of isogravitational heterogeneity increased with increasing –Gₚ to a maximum at –3 Gₚ (Fig. 4C) in all animals. It is this isogravitational heterogeneity that argues most strongly against the relevance of the zone model. If gravity and the “hydrostatic column” in the arterial and venous blood vessels are the dominant features in determining PBF distribution, then this very large heterogeneity in isogravitational planes is impossible.

Another curious feature of the vertical PBF distribution (Fig. 4) is the nonlinear shape at each –Gₚ level. This shape is accentuated with increasing –Gₚ, with a

![Graph](image)

**Fig. 7.** Radial flow gradient (distance from hilum) vs. –Gₚ. Individual regression lines are shown for each animal. Heavy line, regression for all animals and G levels combined.

### Table 4. Spatial gradients vs. Gₚ

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Dₓ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>–0.044</td>
<td>–0.011</td>
<td>0.025</td>
<td>–0.037</td>
</tr>
<tr>
<td>2</td>
<td>–0.032</td>
<td>0.021</td>
<td>0.012</td>
<td>–0.027</td>
</tr>
<tr>
<td>3</td>
<td>–0.039</td>
<td>0.008</td>
<td>0.020</td>
<td>–0.032</td>
</tr>
<tr>
<td>4</td>
<td>–0.026</td>
<td>0.018</td>
<td>0.017</td>
<td>–0.020</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>–0.035 ± 0.008</td>
<td>0.009 ± 0.014</td>
<td>0.019 ± 0.005</td>
<td>–0.029 ± 0.007</td>
</tr>
</tbody>
</table>

Values are expressed as weight-normalized relative blood flow per centimeter per Gₚ.
decrease in flow in the dorsal and ventral regions. The decrease in flow in the ventral regions is surprising, with the prediction of an increased hydrostatic pressure with increased acceleration. The large decrease in flow in the ventral regions may be due to alveolar collapse and related increase in vascular resistance. Another potential explanation is that alveolar collapse may cause venous closure, causing vascular trapping of blood in capillaries and/or venules. With the decrease in flow in the dorsal and ventral regions, PBF is shifted toward the vertically middle regions. The mean flow and the range of variation of WNRF increase with increased \( G \times \) in the middle regions.

The PBF distribution demonstrates a significant radial component (Fig. 6) that steepens with increasing \( G \times \). The PBF in peripheral (most distant from the hilum) regions is decreased relative to the mean PBF. In these prone pigs the most distant regions are largely within the dorsal-caudal regions of the lungs. The increased force of acceleration may cause physical distortion of the most dorsal alveoli, resulting in increased vascular resistance and decreased PBF.

The mean flow in isogravitational planes is similar to that shown in human subjects by Bryan et al. (6). Figure 8 shows data from human subjects with perfusion measured using macroaggregated albumin labeled with \( ^{131} \text{I} \). The percent flow (representing counts) is shown for injections performed in the seated position at \(+1\), \(+2\), \(+3\), and \(+4\) \( G \times \) (cranial-to-caudal inertial force). An external scintillation scanner was used to measure total blood flow across the chest in a given region. As in our study, the distribution of blood flow was determined after return to 1 G. Each curve represents one injection in a different subject. These authors demonstrated an apparent downward (in the direction of the G vector) shift of the horizontally averaged blood flow, with a decrease in flow in the upper regions and an increase in flow in the lower regions. However, the downward shift of peak flow is surprisingly small for increased \( G \times \) level.

For comparison, our data are plotted in a comparable manner in Fig. 9. Total flow to a given isogravitational plane is plotted against vertical height up the lung in pig 2. Plots were similar for all individual animals. In our case the G vector is in the dorsal-to-ventral direction. Data are shown for \(-1\), \(-2\), and \(-3\) \( G \times \), with the upper and lower regions oriented similar to the orientation in the data of Bryan et al. (6) (Fig. 8). The general shapes of the curves are similar. There is a shift of the average blood flow in the direction of the G vector. If totaled across the lung in isogravitational planes (Fig. 9), our data would appear consistent with the zone model, as was interpreted by Bryan et al. in seated human subjects. However, the individual piece flow distribution (Fig. 4A) demonstrates a heterogeneity in the isogravitational planes. This isogravitational heterogeneity cannot be explained by the zone model.

Glaister (8) demonstrated that the linear gradient of mean flow and distance down the lung in humans exposed to \(+G \times \) increased as inertial force increased. The vertical gradient, calculated from Glaister’s Fig. 7–6, was 0.09, 0.19, and 0.32 per centimeter for \(+1\), \(+2\), and \(+3\) \( G \times \), respectively. The vertical gradient increased

Table 5. Variation in flow

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Variance</th>
<th>%Variance</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
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<td></td>
<td>Structural</td>
<td>Nonstructural</td>
<td>Total</td>
<td>Structural</td>
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<td>0.100</td>
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<td>0.057</td>
<td>0.411</td>
<td>86.1</td>
</tr>
<tr>
<td>4</td>
<td>0.147</td>
<td>0.033</td>
<td>0.180</td>
<td>81.7</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>0.270 ± 0.101</td>
<td>0.062 ± 0.028</td>
<td>0.332 ± 0.124</td>
<td>81.4 ± 3.5</td>
</tr>
</tbody>
</table>
by $-0.115$ relative blood flow unit per centimeter per $G_x$ unit. Our data have a similar pattern, with the vertical gradient increase of $0.035$ relative blood flow unit per centimeter per $-G_x$ unit. Although the pattern of change is similar, the magnitude is smaller in the pigs, even though the height of the lung in the prone pig is comparable to that in the seated human. This magnitude difference may be due to the difference in species or the different orientation of the $G$ vector relative to the lung orientation: $-G_x$ in our pig studies and $+G_z$ in Glaister's study. Another potential factor consists of the smoothing and edge effects of the scintillation counter methodology, causing distortion of the human data.

An example of the change in WNRF from $-3$ to $+1$ $G_x$ is shown in Fig. 10. Figure 10A shows a shift from the left to the right sides. Figure 10B plots the change in flow vs. height up the lung in the vertical direction. WNRF decreased near the ventral and dorsal surfaces, whereas flow increased in the central regions. Figure 10C shows more of the decreased flow in the caudal regions. Thus the regions with decreased flow tended to be in the dorsal and caudal regions and more distant from hila in the radial direction (Fig. 10D).

As the $-G_x$ level increased, the dorsal, caudal, and ventral peripheral regions of the lung likely became distorted. The dorsal caudal regions are stretched and the ventral regions collapsed, likely resulting in an increase of regional pulmonary vascular resistance in both regions. As shown in Fig. 10, the more dorsal regions had a reduced PBF with $-3$ $G_x$. The central regions had an increased PBF with $-3$ $G_x$. Because total PBF increased slightly with $-G_y$, the PBF shifted toward the lower-resistance hilar regions of the lung. This results in an increase in the radial gradient of PBF distribution, as shown in Fig. 6.

The center of flow is calculated as a spatial average of the flow determined for the $x$, $y$, and $z$ coordinates with an arbitrary origin in centimeter units. With increased inertial force, the center of flow shifts in the direction of the inertial force as modified by parenchyma-dependent distortions. Table 6 lists the mean shift in center of flow.

<table>
<thead>
<tr>
<th>Table 6. Change in center of flow</th>
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</table>

<table>
<thead>
<tr>
<th>Direct distance</th>
<th>$3G_x$-1$G_x$</th>
<th>$3G_x$-2$G_x$</th>
<th>$2G_x$-1$G_x$</th>
</tr>
</thead>
<tbody>
<tr>
<td>x (dorsal to ventral)</td>
<td>$1.78 \pm 0.54$</td>
<td>$0.58 \pm 0.43$</td>
<td>$1.20 \pm 0.28$</td>
</tr>
<tr>
<td>y (left to right)</td>
<td>$0.74 \pm 0.74$</td>
<td>$0.33 \pm 0.57$</td>
<td>$0.14 \pm 0.36$</td>
</tr>
<tr>
<td>z (caudal to cranial)</td>
<td>$1.24 \pm 0.28$</td>
<td>$0.64 \pm 0.29$</td>
<td>$0.60 \pm 0.27$</td>
</tr>
<tr>
<td>Values are means $\pm$ SD in cm.</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
flow in each of the three axes for the four pigs. The overall shift in center of flow with increasing inertial force is in the right, ventral, and cranial directions.

The zone model was developed in the 1960s on the basis of data obtained with external radiation counters. This methodology, by necessity, determines an average value of flow for specific isogravitational planes. The vertical distribution of PBF in the present pig data, when averaged across isogravitational planes, is similar to the earlier data. The complete spatial variation, as measured by the small 1.9-cm³ pieces, is much greater than the variation across means of isogravitational planes. This observation is not predicted using the zone model. It is informative that the variation in flow within individual pieces is quite small: <20% of the total variation across all the pieces and the three -G₁ levels. If the zone model were to dominate flow, it would be expected that the variation in flow within each volume would be much larger than the variation among specific regions.

Despite the observation that pulmonary blood shifts markedly with increasing inertial force when external scintillation counters are used, the data from finer spatial resolution show a remarkable similarity of flow within each region. When the inertial force is increased threefold, the PBF distribution changes minimally. Less than 19% of the flow variance results from the increased gravitational force.

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