THE RADIOISOTOPIC ESTIMATION OF REGIONAL BLOOD FLOW, BLOOD VOLUME, AND HEMATOCRIT IN THE DOG LUNG

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The use of radionuclides has allowed the measurement of regional pulmonary blood flow (rPBF) by several techniques since the introduction of the use of $^{133}$Xe by Knipping in 1957 (1). The work of West (2) with $^{18}$O labeled CO$_2$ and Ball (3) with $^{133}$Xe has demonstrated the gradient of pulmonary perfusion in the upright position and alterations caused by exercise, drugs, and disease states. This work has been confirmed by Wagner and others (4) using particles of $^{131}$I-iodinated human serum albumin (HSA) and $^{113m}$In.

Regional pulmonary blood volume (rPBV), however, has received little attention. “Central blood volume” can be measured by the Fick principle and dye-dilution techniques. These methods have shown increased central blood volume in patients with mitral stenosis, in left ventricular failure (5), and in the supine position (6), and diminished volume in the upright position, in decreased cardiac output (7), and with positive pressure breathing (8). Weissler (9) has shown the same effects of posture using $^{131}$I-HSA and a single probe over the right upper lobe.

Knowledge of the distribution of blood volume as well as blood flow within the lung is important to the understanding of pulmonary physiology. In this project we have used isotopic methods to confirm previous reports on rPBF and to observe the distribution of rPBV.

MATERIALS AND METHODS

Tracers.
1. Indium-$^{113m}$-iron hydroxide particles were used to measure blood flow. The particles were obtained from a routine lung scan preparation (10). They range in size from 15 to 90 microns. The nuclide emits a 390-keV gamma ray with a half-life of 1.7 hr. About 1,000 $\mu$Ci were injected intravenously.
2. Red-cell volume was measured by intravenous injection of 5 ml of red blood cells labeled with 75 $\mu$Ci of $^{51}$Cr-sodium chromate (Mallinckrodt/Nuclear) by standard techniques.
3. Plasma volume was measured by intravenous injection of 75 $\mu$Ci of $^{125}$I-radiiodinated serum albumin (Mallinckrodt/Nuclear).

Standard solutions of each tracer were prepared by adding a known weight of each solution to 100 cc volumetric flasks.

Procedure. Six mongrel dogs, weighing 20–27 kg were anesthetized with 20 mg/kg of sodium pentothal. Each dog was placed on a Harvard respirator and ventilated through an endotracheal tube at a rate of 20 breaths/min and a tidal volume of 500 cc. Maximum airway pressures were above 20 cm H$_2$O. A sternal splitting thoracotomy was then performed with special care to achieve maximum hemostasis.

Three dogs were placed in the upright position and secured to their operating board while the other three remained supine. The three isotope preparations were injected through a femoral vein cannula. Peripheral blood samples were drawn from the femoral artery 2, 4, and 6 min later. Ten to 15 min after injection of the isotopes, the pulmonary hila were isolated and clamped simultaneously at maximum inspiration, and liquid nitrogen was poured into the chest to harden the lungs in situ. Both lungs were then removed and placed in a container of liquid nitrogen.

The frozen lungs were cut on a band saw into 2-cm-thick sections from apex to base. Each section was dissected equally into anterior, lateral, and posterior divisions, and samples of each division were placed into vials. The lung samples, blood samples, and duplicate aliquots of each standard were placed in a Picker Liquimat counter, and the $^{113m}$In activity was counted immediately. After 24 hr the $^{113m}$In activity was negligible, and the $^{51}$Cr and $^{125}$I activity was counted by a double-window method.

Regional blood flow was expressed as a percent of the total injected $^{113m}$In activity per gram wet...
results from the two isotopes were similar, and the $^{125}$I curves are shown in Fig. 2. Again there were no significant variations among the three divisions in most of the lungs.

In the supine dogs five of the six lungs were shown to have a nearly horizontal plot, indicating uniform distribution of blood volume. Two lungs had shown a slightly increasing gradient from apex to base in the $^{125}$I data in Table 2. The $^{51}$Cr data in Table 3 was similar, with four lungs showing uniform volume, one significantly increasing and one decreasing gradient.

Five of the six upright lungs had significant positive gradients of volume using the $^{125}$I label. Three showed positive gradients with the $^{51}$Cr label. One and three lungs, respectively, showed essentially uniform volume distribution.

**Regional hematocrit.** From the red-cell and plasma volumes, the regional hematocrit in each sample could be calculated. Plots of the regional hematocrit against the level of lung demonstrated that the hematocrit remained relatively constant throughout the lung and that posture had no effect on the regional hematocrit.

**DISCUSSION**

Particles of $^{113}$mIn-iron hydroxide act as microemboli, essentially all of which are retained in the precapillary arterioles of the pulmonary circulation after one passage through the lungs. Peripheral blood measurements showed that 92–95% of the radioactivity was retained in the lungs of our dogs. Essentially no particles reach the lungs through bronchial circulation. Therefore the $^{113}$mIn activity in an area

![Figure 1](image1.png)

**FIG. 1.** Regional blood flow. $^{113}$mIn activity per gram lung tissue for each section is plotted against distance of that section from lung apex. Lungs from supine dogs are shown as dashed lines and lungs from upright dogs as continuous lines.

![Figure 2](image2.png)

**FIG. 2.** Regional blood volume. $^{125}$I activity per gram lung tissue for each section is plotted against distance of that section from lung apex. Lungs from supine dogs are shown as dashed lines and lungs from upright dogs as continuous lines.
of lung is a measure of its relative perfusion from the pulmonary artery (10).

Chromium-51-labeled red cells and HSA are commonly used to measure red-cell and plasma volume since they remain in the intravascular space. However, albumin does leak slowly out of this space, tending to give falsely high estimates of blood volume. To minimize this error we injected the radio-isotope no more than 25 min before clamping the hila of each lung.

Several statements can be made from our observations. The rPBF was uniform throughout the supine lungs, and no significant gradient was apparent. In the upright dogs rPBF was negligible in the upper one third of the lungs, and in the lower two thirds flow steadily increases. The pattern of the blood-flow distribution in these lungs is in agreement with that found by West (11) in isolated dog lungs using $^{133}$Xe and an external scanner.

The apices correspond to West's Zone 1. In this zone the alveolar pressure exceeds pulmonary arterial pressure, collapsing the small alveolar vessels and reducing the flow to zero.

The lower two thirds of our dog lungs correspond to West's Zone 2. Here pulmonary artery pressure has risen above alveolar pressure, while pulmonary venous pressure is still below alveolar. The microvasculature functions as a Starling resistor, allowing intermittent flow which varies with the difference between arterial and alveolar pressure.

West also describes a third zone in which both arterial and venous pressures have risen above alveolar pressure in the lower part of the lungs, giving continuous flow. This zone is not present in this
MILDER, LISBERG, EVENS, AND POTCHEN study. This is attributable to the relatively high maximum alveolar pressure which was greater than venous pressure, even at the bases.

The blood-volume distribution in the supine dogs was uniform as would be expected since flow and pressure are uniform. In the upright dogs there was a positive gradient in the same direction as the flow gradient. It should be noted, however, that the volume gradient has only one zone while the flow curve has two zones. The increasing blood volume at the apices could be explained by the redistribution of blood volume into the apex when the lungs were laid down for freezing. Another possibility is that this volume is from bronchial artery blood which may perfuse the apices through enlarged bronchopulmonary collaterals when there is no pulmonary artery flow.

We are not able to make a quantitative comparison of the rPBF and rPBV in these lungs because they were determined in different situations. The flow measurements were fixed at the time the isotope first passed through the lungs in the living dog. The flow was not determined until the lungs were frozen and in a static state.

SUMMARY

Relative regional pulmonary blood flow and regional pulmonary blood volume were measured by injecting $^{113m}$In particles, $^{51}$Cr-labeled red cells, and $^{125}$I-labeled IHSA into open-chest ventilated dogs and counting the activity in sections of the lungs.

Supine dogs showed uniform distribution of rPBF and rPBV. In upright dogs there was a linear gradient of rPBF and rPBV from apex to base. The flow distribution was characteristic of West's Zones 1 and 2. The volume distribution was the result of static conditions imposed by freezing the lungs.

Regional hematocrit was found to be uniform in all dogs, regardless of posture.

ACKNOWLEDGMENT

This project was in part supported by NIH Training Grant Number 1 T01 GM01747-01 and the USAEC Grant Number AT(11-1)-1653 under which this document becomes AEC Number C0-1653-98.

Ronald G. Evens is a James Picker Advanced Academic Fellow in Radiology, National Research Council, National Science Foundation.

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