Dynamic Measurement of Regional Ventilation And Perfusion Of the Lung with Xe-133

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A method for measuring regional distribution of ventilation and perfusion with Xe-133 during tidal breathing was developed with normal subjects, and compared with current breath-holding techniques in patients and in animals. Normal values for a ventilation index during washin, a perfusion index, and a washout slope index were determined in both supine and upright normal subjects. Comparisons of tidal-breathing and breath-holding measurements in patients with localized bullous disease of the lung showed roughly equal values for perfusion index by the two methods, but the tidal-breathing method was more sensitive to abnormalities in ventilation index. During occlusion of branches of the pulmonary artery in animals, the tidal-breathing and breath-holding methods were again comparable in the measurement of perfusion indices, but the tidal-breathing method provided a more sensitive assessment of ventilatory changes due to partial bronchial occlusion in animals. This technique appears superior to standard methods and is well suited to dynamic measurement of regional ventilation and perfusion in a number of experimental and clinical circumstances.

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Conventional techniques for the determination of regional ventilation or perfusion of the lung with xenon-133 require breath holding at full inspiration, or total lung capacity (TLC), after a single breath of Xe-133 or after intravenous infusion of Xe-133. It would be more desirable to assess ventilation or perfusion distribution during normal tidal breathing for several reasons: (A) breath holding may not be possible for severely ill patients or exercising subjects and is impractical during assessment of mechanical ventilation; (B) the distribution of ventilation and perfusion during a single breath to TLC may not be the same as during tidal breathing; and (C) regions with partial airway obstruction or airway closure may appear normal when Xe-133 is inhaled to a high lung volume where airways are likely to open. The purpose of this report is to describe a convenient method for assessing regional ventilation and perfusion with Xe-133 during tidal breathing and to report normal values for this technique in humans. The tidal-breathing method is also compared to the conventional breath-holding method in patients with bullous lung disease, and in animals with known occlusion of branches of the pulmonary artery or bronchi.

MATERIALS AND METHODS

Human studies. Subjects included 15 healthy, nonsmoking men, ages 23–32 years, with normal forced vital capacity (FVC), forced expired volume in 1 sec ($FEV_{1.0}$), and $FEV_{1.0}/FVC$ ratio. Each was instructed to breathe at a normal, resting tidal volume throughout the experiment. Eight subjects underwent ventilation studies in the supine position; five of these also had supine perfusion studies and upright ventilation studies. Both ventilation and perfusion studies were performed in the upright position in another seven subjects. Finally, four patients with localized bullous disease of the lungs were studied upright. Lung bullae are well suited to these experiments, since they represent well-circumscribed

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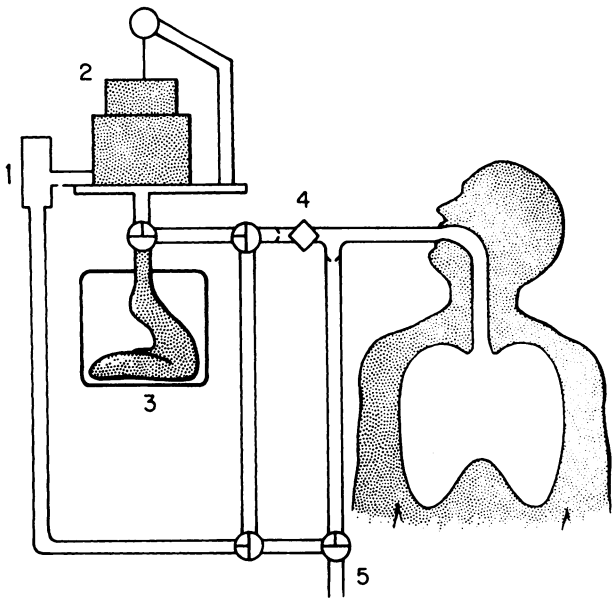

FIG. 1. Breathing circuit for Xe-133 ventilation and perfusion measurements. Apparatus is labeled as follows: 1) CO_2 absorber; 2) spirometer; 3) bag in box; 4) pneumotachograph; 5) exhaust vent. Varying position of three-way valves establishes either (A) open circuit for ventilatory washin, in which the subject inhales Xe-133 in air from bag and exhales into spirometer; or (B) closed circuit for equilibration studies, in which subject inhales from and exhales into spirometer. Spirometer, bag, and large segment of circuit are filled with xenon–air mixture initially; then patient and smaller circuit are turned into main circuit to begin ventilatory washin.

areas of ventilation and perfusion abnormalities surrounded by relatively normal lung tissue, and they are easily localized radiographically. Each patient underwent measurement of regional ventilation by the tidal-breathing method and by a breath-holding method as described by Ball et al. (*1*). One patient also had perfusion studies performed by both methods.

Equipped with a noseclip and mouthpiece, subjects breathed through an air-tight system that included a bag in a box, a soda-lime CO_2 absorber, a pneumotachograph, and a 13.5-liter spirometer. This system could be changed from open to closed circuit with three-way valves (Fig. 1). Radioactivity was measured with a multiprobe detector system for Xe-133 similar to that described by Ball et al. (*1*). Four scintillation counters were placed over each lung posteriorly, with cylindrical collimators 3 cm in diameter and 18 cm long. These counters were numbered sequentially from apex to base and designated L_1–L_4 on the left and R_1–R_4 on the right (Fig. 2). In the supine position, two additional counters were placed over each lung laterally with rectangular collimators 13 cm × 3 cm at the subject end and 18 cm long (Fig. 2). A constant position of the chest in relation to the scintillation probes was assured by periodically checking alignment of skin markers with a transparent reference grid applied to the chest posteriorly and a triple-point light beam anteriorly. Signals from each scintillation detector were directed to a pulse-height analyzer. A window width, ranging from 14 to 62 keV, centered on the 81-keV radiation of Xe-133, was adjusted so that all detectors gave the same count rate when directed toward a Xe-133 source of uniform activity. The output of each pulse-height analyzer was connected to an interface* where counts from each detector were accumulated for 1-sec intervals. These counts were transmitted on-line to a computer† under program control. Counts per second for each region were measured, and the average count rate during each breath was stored. The beginning of each breath was signaled to the computer by one of the authors operating a microswitch while observing a recording of flow from the pneumotachograph. Before calculations were performed, background radiation was measured and subtracted from values obtained during ventilation, perfusion, and equilibration studies. After each study, a sufficient pause was allowed to ensure that background counts fell to their base levels before the next measurement was begun. The

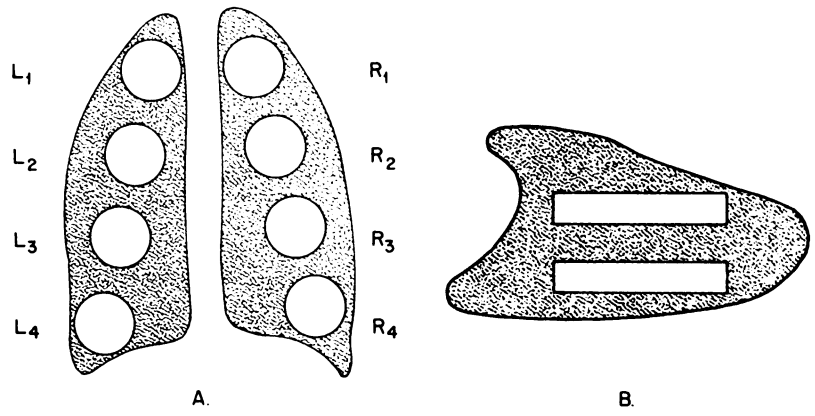

FIG. 2. Location of scintillation counters. (A) Posterior counters. (B) Lateral counters. L = left; R = right. See text for details.

problem of absorption of Xe-133 radiation in lung tissues has been dealt with in an earlier study from this laboratory (2). Scattering of radiation prior to reaching the detectors was not measured.

During open-circuit ventilatory washin, a mixture of Xe-133 in air was inhaled from the bag and exhaled into the spirometer. The bag was filled with 10–20 liters of air containing 6 mCi per liter of Xe-133. Accumulation of radioactivity in the lungs was measured during tidal breathing at functional residual capacity (FRC) without breath holding or inhalation of Xe-133 to TLC. With the apparatus in a closed circuit, the subject breathed into and out of the spirometer for 2–4 min; thereafter, when count rates from all lung regions had stabilized, measurements were made and count rates from 2 tidal breaths were stored in the computer for determination of equilibration values. Sufficient oxygen was added during equilibration to maintain a constant volume in the system. Perfusion studies were performed following a bolus injection of 3 mCi of Xe-133 dissolved in saline through an intravenous catheter advanced percutaneously to the superior vena cava; count rates were measured during tidal breathing for calculation of perfusion and washout values.

An "equilibration fraction" was obtained by expressing regional count rate from each probe as a fraction of the total counts from all probes during equilibration. This can be expressed as:

$$Fe_i = Ce_i / \sum_{i=1}^{8} Ce_i, \quad (1)$$

where Fe_i = equilibration fraction for i-th region; and Ce_i = average count rate per breath during equilibration for i-th region.

A "ventilation fraction" and a "perfusion fraction" were calculated in the same fashion during ventilatory washin and perfusion, respectively. The ventilation fraction was calculated for each breath after regional counts were above 200 per second, usually permitting calculations to begin with the second breath after the onset of washin. An average of five successive stable ventilation fractions obtained within the first minute of washin was used for ventilation calculations. The breath with the highest count rate following injection of Xe-133 was used for perfusion calculations. These fractions can be expressed as:

$$Fv_i = Cv_i / \sum_{i=1}^{8} Cv_i, \quad (2)$$

$$Fp_i = Cp_i / \sum_{i=1}^{8} Cp_i, \quad (3)$$

where Fv_i = ventilation fraction for i-th region; Fp_i = perfusion fraction for i-th region; Cv_i = average count rate per breath during ventilatory washin for i-th region; and Cp_i = average count rate per breath during perfusion for i-th region.

A "ventilation index" for the i-th region (VI_i) was derived by dividing Fv_i by Fe_i, and a "perfusion index" (PI_i) by dividing Fp_i by Fe_i. A ventilation: perfusion ratio for the region was obtained by dividing VI_i by PI_i.

The rate of ventilatory washout after perfusion was obtained by plotting the logarithm of peak counts for sequential breaths against time and calculating the slope of the exponential decay curve. The slope for each region was divided by the slope of the exponential decay for the sum of the counts from all regions to give a "washout slope index," proportional to ventilation per unit lung volume. This index was used for the numerical value of postperfusion washout (WO_i). It was anticipated that analysis of regional exponential washout after Xe-133 infusion would detect nonhomogeneity of ventilation within regions by separation of the curve into fast and slow compartments, as in the analysis of nitrogen washout curves. However, if any region had a slow compartment, it was indistinguishable from the slow washout of Xe-133 from tissues. Therefore, only the first 4–6 breaths after the beginning of washout were analyzed.

Calculation of indices was done using the eight posterior probes as a group and the four lateral probes as a separate group. The posterior counters were used for comparisons of regional ventilation and perfusion. The lateral counters were used in the supine position to detect differences in ventilation and perfusion between anterior and posterior regions.

Breath-holding studies used these same calculations for VI_i and PI_i, except that regional counts were measured during breath holding at TLC.

Animal studies. Dogs weighing 12–16 kg, and pigs weighing 42–46 kg, were studied supine with four collimated scintillation probes over each lung, placed posteriorly as previously described (2). Dogs were anesthetized with sodium pentobarbital and intubated; pigs were anesthetized with ketamine and tracheotomy was performed. All animals were ventilated with a Harvard volume ventilator.

PI_i and VI_i were calculated during tidal breathing as in the human studies. A smaller, 7-liter spirometer system was used. For PI_i a constant infusion of Xe-133 in saline was administered. For breath-holding studies the same formulas were utilized, but regional count rates were obtained during breath holding at

FRC plus 2–3 tidal volumes after a bolus injection or a single breath of Xe-133.

Vascular occlusion was performed in seven dogs with a Swan-Ganz® double-lumen balloon-tipped catheter that was floated into an appropriate branch of the pulmonary artery under fluoroscopic control. The region of the occlusion was documented after the perfusion study by injecting Xe-133 locally into the occluded segment and by selective pulmonary angiography beyond the balloon occlusion. Regional perfusion studies were performed before and during occlusion with both the tidal-breathing and the breath-holding methods. Lobar bronchi of five pigs were occluded partially or completely with a balloon-tipped catheter during visualization with a fiberoptic bronchoscope. Pigs were used to avoid the possibility of collateral ventilation (*3*). Regional ventilation studies with both the tidal-breathing and breath-holding methods were performed before and during bronchial occlusion.

In order to validate these calculations of ventilation and perfusion indices, we compared our method with a modification of the steady-state measurements described by Anthonisen et al. (*4*). In our formulas, we have made the assumption that the sum of counts from all regions

$$\left(\sum_{i=1}^{8} Cv_i \text{ or } \sum_{i=1}^{8} Cp_i\right)$$

accurately reflects inspired Xe-133 concentration (F_I) during ventilation and mixed-venous Xe-133 concentration ($C_{\bar{v}}$) during perfusion. If this is true, our method is comparable to that of Anthonisen et al. (*4*) as expressed in the following formulas:

(a) Tidal-breathing formula:

$$VI_i/PI_i = Cv_i/\sum_{i=1}^{8} Cv_i \div Cp_i/\sum_{i=1}^{8} Cp_i; \quad (4)$$

(b) Steady-state formula:

$$V_i/Q_i = Cv_i/F_I \div Cp_i/C_{\bar{v}}. \quad (5)$$

We assessed the similarity of the two methods in animal experiments. Six dogs were prepared as described above, and regional counts were measured during ventilatory washin, perfusion, and equilibration. For each of 6–8 individual regions in each dog, VI_i/PI_i was calculated according to Eq. 4. During ventilation studies, gas was withdrawn from the inspiratory line, and during perfusion studies blood was withdrawn through a catheter in the pulmonary artery. Both the inspired gas and the blood were passed through a fixed-volume tube in front of a scintillation counter. Because the volume of gas or blood was constant, the count rate measured by the detector reflected inspired Xe-133 concentration or mixed-venous Xe-133 concentration. For each region, V_i/Q_i was calculated according to Eq. 5 by substituting count rates for F_I and $C_{\bar{v}}$ as measured by the fixed-volume detector system. The time required for the gas or blood to reach the detector was measured and entered in the computer for purposes of synchronizing determination of the numerators and denominators of the equation. Both calculations were made under control conditions and during

TABLE 1. TIDAL-BREATHING METHOD

	Supine			Upright		
	VI_i	WO_i	PI_i	VI_i	WO_i	PI_i
No.	8	5	5	12	7	7
Posterior counters						
L_1	0.96 ± 0.16	1.05 ± 0.10	0.96 ± 0.12	0.80 ± 0.09	0.45 ± 0.18	0.52 ± 0.18
L_2	1.07 ± 0.07	1.07 ± 0.11	1.04 ± 0.12	0.97 ± 0.21	0.87 ± 0.21	0.96 ± 0.15
L_3	1.07 ± 0.14	0.99 ± 0.10	1.10 ± 0.16	1.00 ± 0.11	1.22 ± 0.11	1.36 ± 0.14
L_4	0.73 ± 0.22	0.72 ± 0.38	0.71 ± 0.26	1.01 ± 0.12	1.27 ± 0.27	1.09 ± 0.37
R_1	1.01 ± 0.09	0.92 ± 0.18	0.99 ± 0.17	0.84 ± 0.14	0.71 ± 0.27	0.54 ± 0.26
R_2	1.06 ± 0.07	1.06 ± 0.10	1.09 ± 0.09	1.01 ± 0.07	0.88 ± 0.13	0.94 ± 0.11
R_3	1.06 ± 0.14	1.09 ± 0.09	1.06 ± 0.15	1.13 ± 0.05	1.15 ± 0.05	1.17 ± 0.18
R_4	0.62 ± 0.25	0.84 ± 0.56	0.60 ± 0.34	1.10 ± 0.14	1.35 ± 0.13	1.27 ± 0.38
Lateral counters						
L_T	0.89 ± 0.10	0.89 ± 0.14	0.87 ± 0.15			
L_B	1.13 ± 0.11	1.09 ± 0.04	1.07 ± 0.08			
R_T	0.84 ± 0.08	0.78 ± 0.09	0.83 ± 0.15			
R_B	1.09 ± 0.11	1.10 ± 0.07	1.23 ± 0.06			

Abbreviations: VI_i = ventilation index; WO_i = washout index; PI_i = perfusion index; L = left; R = right; T = top (anterior when subject is supine); B = bottom.

Mean values ± standard deviations for ventilation, washout, and perfusion indices in normal subjects.

occlusion of lobar or segmental bronchi with a balloon-tipped catheter, and values for VI_i/PI_i and V_i/Q_i were compared for each region.

RESULTS

Human studies. Table 1 lists mean values from normal subjects for two regional indices of ventilation (VI_i and WO_i) and one of perfusion (PI_i) in four posterior regions of each lung. In upright subjects, values show a trend toward the normal apex-to-base gradient that has been described by others (*5*). Supine indices are close to 1.00 in the apical 3 regions of each lung (L_1–L_3 and R_1–R_3), lacking the gradient seen in upright measurements. Basilar counters, L_4 and R_4, have significantly lower values for all indices; this represents an impairment of basilar ventilation and perfusion related to the supine posture, as has been described in detail elsewhere (*6*).

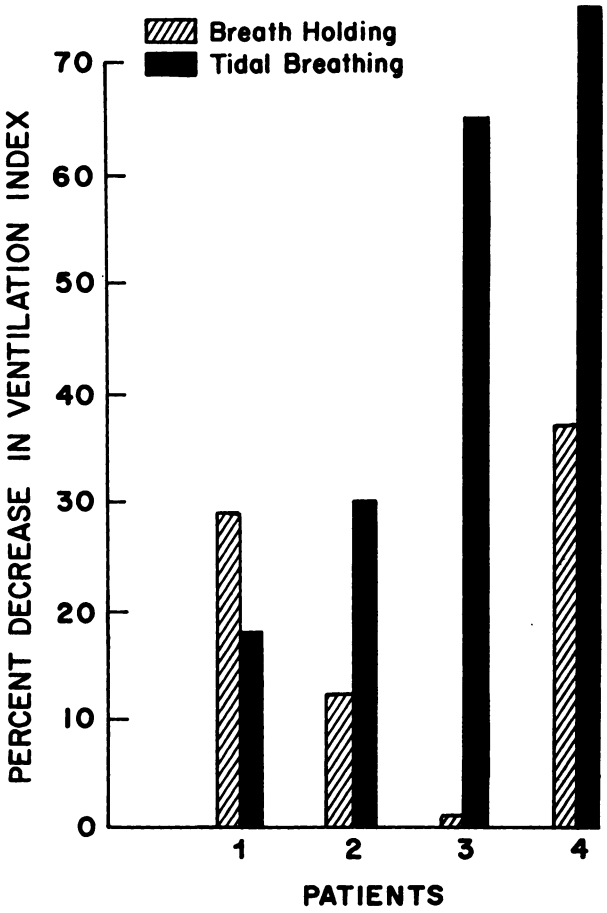

FIG. 3. Comparison of abilities of breath-holding method (hatched bars) and tidal-breathing method (solid bars) to detect decreased ventilation in region of large bulla in four patients. Vertical axis is percent decrease below a normal ventilation index of 1.00 averaged for regions corresponding to roentgenographic location of bulla. In three of four patients, the tidal-breathing method measured greater reductions in regional ventilation; in one case (Patient 3), large decrease in ventilation index was found with tidal-breathing method while almost no change was measured with breathing-holding method.

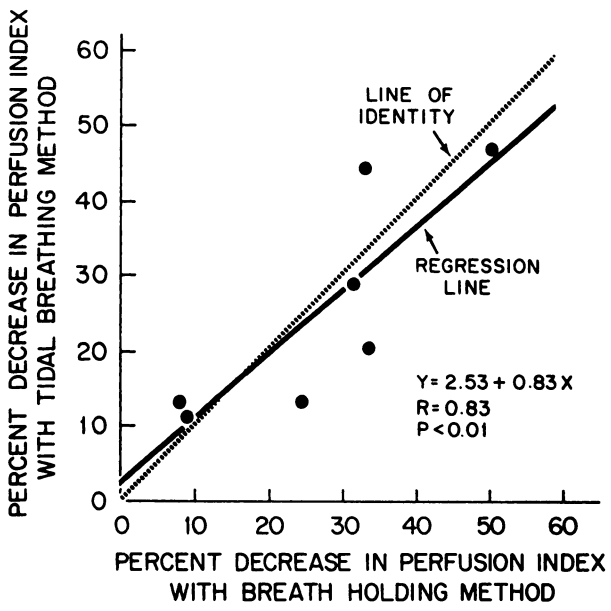

FIG. 4. Comparison of abilities of breath-holding method (horizontal axis) and tidal-breathing method (vertical axis) to detect obstruction of regional perfusion in dogs. Percent decrease in perfusion indices after balloon occlusion of branch of pulmonary artery was averaged for two probes seeing occluded region best. Two methods were equally effective in detecting perfusion obstruction, with regression line close to that of identity and correlation coefficient of 0.83 ($p < 0.01$).

Mean values recorded from lateral counters in supine subjects are also displayed in Table 1. The normal gradient of ventilation and perfusion between dependent (posterior or "bottom" counters) and nondependent (anterior or "top" counters) lung regions is evident; this gradient has also been shown by other investigators in normal, supine subjects (*7*).

In patients with bullous lung disease, the percent reductions in VI_i (below the normal value of 1.00) from all probes viewing bullae were averaged, and the results compared between the breath-holding and tidal-breathing methods. In three of the four patients, tidal-breathing indices were substantially lower than breath-holding values in the regions involved by bullae (Fig. 3). In one patient with perfusion indices recorded by both methods (Patient 4), breath-holding indices in the bullous regions averaged 77% reduction and tidal-breathing indices averaged 69% reduction.

Animal studies. *Dog perfusion studies.* For each animal, the lung region involved by the perfusion occlusion was determined by selective Xe-133 injection and angiography, and readings from the two scintillation probes that viewed this region best were used for analysis. The reduction in PI_i during occlusion below the preocclusion value was expressed as percent reduction, and values for the two counters were averaged. Comparison of percent reduction in

PI_i recorded during tidal breathing and during breath holding in all animals is displayed in Fig. 4. The points fall near the line of identity, with a correlation coefficient of 0.83 ($p < 0.01$).

Pig ventilation studies. During complete or partial bronchial occlusion, the percent reduction in VI_i was averaged from the two counters best showing the occluded region. The average percent reductions in VI_i recorded with tidal breathing and breath holding are compared in Fig. 5. During complete occlusion, both methods showed substantial reductions in ventilation, breath holding giving greater changes in both instances. With partial occlusion, the tidal-breathing method recorded greater reductions in four of five experiments; in two cases, when Xe-133 was inhaled to three tidal volumes above FRC, no change from control indices was recorded during breath holding, whereas the tidal-breathing method showed distinct decreases in VI_i in the region of the obstruction. In addition, breath-holding indices had no correlation with the degree of partial occlusion as reflected in the volume used for balloon inflation; in contrast, tidal-breathing measurements during partial occlusion showed an excellent correlation between balloon volume and the degree of reduction in ventilation index (Fig. 6).

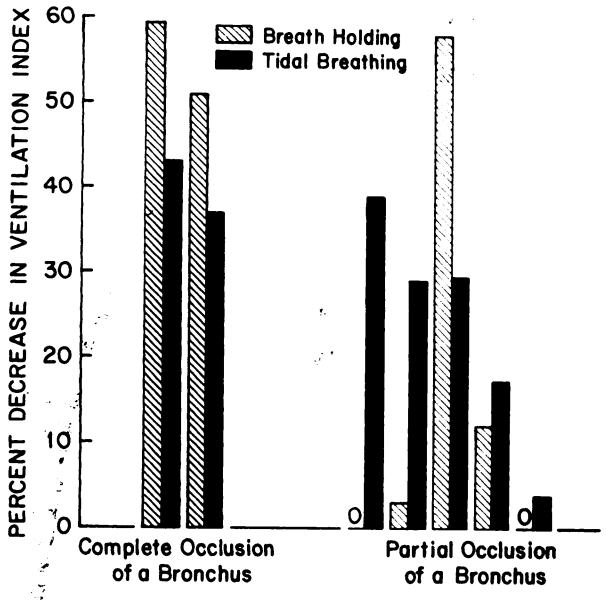

FIG. 5. Comparison of abilities of breath-holding method (hatched bars) and tidal-breathing method (solid bars) to detect regional ventilatory obstruction in pigs. Both methods detected complete obstructions well. With partial balloon occlusion of bronchi, decrease in ventilation index detected by tidal-breathing method was greater in all but one case; in 2 experiments, tidal-breathing method detected ventilatory abnormalities when breath-holding method measured no change in ventilation index.

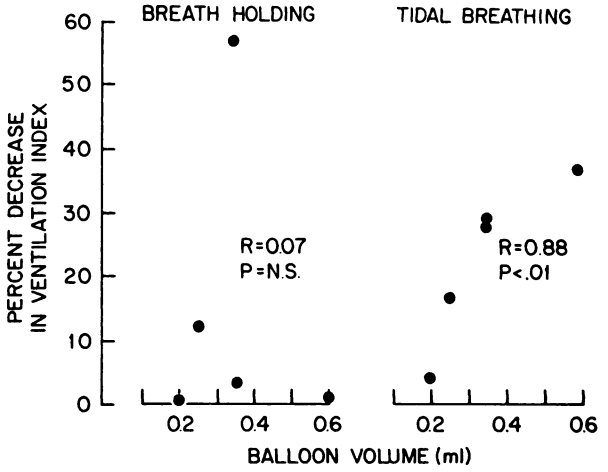

FIG. 6. Comparison of abilities of breath-holding method and tidal-breathing method to detect partial obstruction of lower-lobar bronchus of a pig. With tidal-breathing method decrease in ventilation index was linearly related to volume of saline in balloon ($r = 0.88$; $p < 0.01$), but this was not true for breath-holding method.

Dog V/Q studies. In each animal, values for VI_i/PI_i calculated from our tidal-breathing formula were compared with values for V_i/Q_i calculated by the steady-state formula of Anthonisen et al. (*4*), using measurements of inspired and mixed-venous Xe-133 concentrations with the fixed-volume scintillation-counter system. Comparisons were made during a control period and again during ventilatory occlusion caused by inflating a balloon-tipped catheter in a bronchus. Because total ventilation varied during different phases of the experiment, different degrees of ventilation:perfusion mismatch occurred. The overall ventilation:perfusion mismatch in each dog was corrected by multiplying a constant factor by the V_i/Q_i for each region from that dog. For example, results from one experiment are illustrated in Table 2. When results from all animals were compared, there were virtually no differences in values obtained by the two methods (Fig. 7).

DISCUSSION

Radioactive gas techniques have been used extensively to measure regional ventilation and perfusion, both in normal subjects (*1,5,7,8*) and in a variety of disease states (*9–11*). Most investigators, however, have used a static and relatively unphysiologic technique which involves inhalation of Xe-133 to TLC—or intravenous injection of Xe-133 at FRC with breathing holding at TLC—and subsequent external radiation counting. Because large inspired volumes have been shown to cause substantial changes in the distribution of ventilation and perfusion (*8,12*), such measurements may not accu-

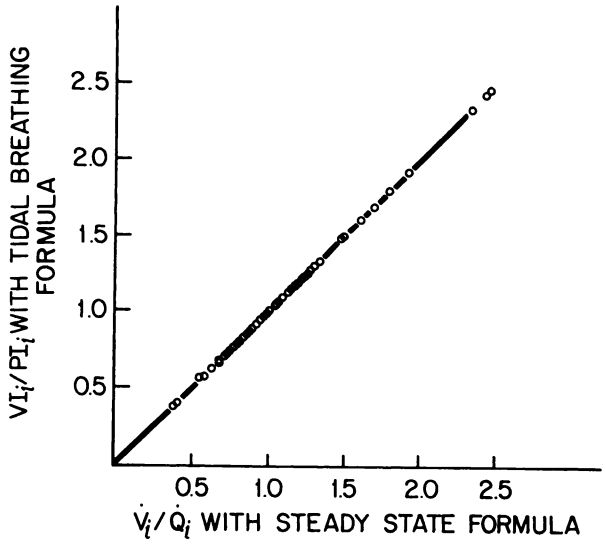

FIG. 7. Comparison of ventilation:perfusion ratios determined by tidal-breathing and steady-state methods. In dogs with balloon obstructions to bronchi, studied during tidal breathing, VI_i/PI_i calculated from tidal-breath formula (vertical axis) was same as the $\dot{V}_i/\dot{Q}_i$ calculated from steady-state formula (horizontal axis) after correction for overall $\dot{V}/\dot{Q}$ mismatching.

rately reflect the behavior of the lungs at smaller volumes where respiration usually occurs. Moreover, a static measurement of ventilation or perfusion distribution during breath holding may not describe dynamic events during normal, tidal breathing (*9*).

For these reasons, a number of authors have introduced modifications of the basic technique in an effort to record "dynamic" indices of ventilation. Several investigators (*13–16*) have measured the ventilatory washout of Xe-133 following intravenous infusion during tidal breathing. This is, indeed, a more dynamic method but is limited by the fact that the initial accumulation of Xe-133 is dependent upon perfusion distribution. Moreover, distortion of lung clearance curves may occur with this method secondary to residual Xe-133 in tissue in the chest wall and the return of Xe-133 to the lung via the circulation (*9,15*). Consequently, another method was described which employs measurement of the rate at which lung regions approach equilibrium during tidal breathing in a closed circuit (*4,9,10,16,17*). This is also a reasonable approach to the assessment of dynamic changes in ventilation. Unfortunately, the method requires rather cumbersome measurement techniques and calculations. In addition, no attempt has been made to document its accuracy or to determine its superiority over breath holding with known regional obstruction to ventilation.

The technique described in the present report is capable of providing truly dynamic determinations of ventilation and perfusion during tidal breathing. Normal values are given for supine and upright subjects (Table 1). The calculations upon which these measurements are based (Eqs. 1–4) require an important assumption: that the sum of radiation counts from all lung regions reflect inspired or mixed-venous Xe-133 concentration as the case may be. When these formulas were used for calculation of the ventilation:perfusion ratio (VI_i/PI_i), the results correlated very closely (Fig. 7) with values for V_i/Q_i obtained from a steady-state formula (Eq. 5) that uses direct measurement of inspired and mixed-venous Xe-133 concentrations. It can be seen in Table 2 that, after multiplying the V_i/Q_i from the eight regions of each individual dog by a constant (k), the products were almost identical with VI_i/PI_i as calculated with the tidal-breathing formula. This constant is capable of correcting for overall ventilation:perfusion mismatching, for the solubility of Xe-133 in blood, and for any possible failure of the probes to provide a representative sample of the lungs as a whole. This correction is necessary because VI_i/PI_i is a relative measurement and values from all eight regions will necessarily average close to one. The steady-state determination is capable of yielding an absolute V_i/Q_i for a region, but the values would be affected by overall hyperventilation or hypoventilation. Nonetheless, differences between regions would be identical with the two methods, as shown by the corrected values plotted in Fig. 7. Thus, the sum of counts from all regions is a satisfactory reflection of inspired or mixed-venous Xe-133 concentration, and the relation of regional to total count rates is an accurate way of expressing regional ventilation and perfusion.

Several features of our techniques offer important advantages over methods previously described. First, the procedure uses an open-circuit ventilatory

TABLE 2. VENTILATION:PERFUSION RATIOS CALCULATED BY A STEADY-STATE FORMULA ($\dot{V}_i/\dot{Q}_i$) AND A TIDAL-BREATHING FORMULA (VI_i/PI_i) IN A REPRESENTATIVE DOG

Region	$\dot{V}_i/\dot{Q}_i$	$\dot{V}_i/\dot{Q}_i \times k^*$	VI_i/PI_i
L_1	0.42	0.89	0.90
L_2	0.60	1.27	1.27
L_3	0.51	1.08	1.07
L_4	0.62	1.31	1.31
R_1	0.41	0.87	0.87
R_3	0.51	1.08	1.07
R_3	0.20	0.42	0.41
R_4	0.47	1.00	0.99

* k = constant used to correct for overall ventilation: perfusion mismatching. In this dog, k = 2.12. See text for details.

washin, which allows more rapid accumulation of radiation counts and does not depend upon achievement of equilibrium for determinations of regional ventilation fractions; ventilation indices can be determined from count rates during a single breath, or averaged over several breaths if desired. Second, the procedure itself and the attendant calculations are extremely simple, requiring only basic equipment and no measurements of time, volumes, gas concentration, or other parameters necessary with most previously used techniques. Third, the advantages of this method were shown in patients with bullous lung disease: perfusion changes were comparable with the two methods (see Results), but the tidal-breathing technique gave a more sensitive measurement of ventilatory impairment in most cases (Fig. 3). Similar results were obtained in animal experiments; the assessment of regional perfusion was shown to be as reliable as that obtained with established techniques (Fig. 4), and ventilation measurements were more sensitive and accurate in partial degrees of bronchial obstruction than when the breath-holding method is used (Figs. 5 and 6). Fourth, this procedure allows reliable measurements of ventilation and perfusion distribution in subjects unable to cooperate with breath holding, as during exercise or in very ill patients. Fifth, the method allows comparison of ventilation and perfusion at different levels of tidal volume, breathing rates, and other parameters. Finally, measurement of ventilation and perfusion indices are possible during mechanical ventilation, when static determinations would be inappropriate or impossible. The usefulness of the procedure under many of these circumstances has been shown (*6,18*).

The mechanisms underlying the enhanced sensitivity of the tidal-breathing method probably relate to physiologic differences in the breathing patterns used for these measurements. The large tidal volume and cessation of breathing required for breath-holding studies may disguise decrements in ventilation by opening partially obstructed airways and allowing more time for the filling of poorly ventilated lung units. Opening of obstructed airways at large lung volumes was seen with the bronchoscope during the animal experiments and has been suggested by physiologic measurements (*6,18*). Such abnormalities of ventilation are more easily detected and more accurately measured during tidal breathing at smaller volumes. Breath holding at large lung volumes is unlikely to mask perfusion abnormalities to the same degree, so that the two methods give comparable results for perfusion measurements.

Theoretically, the tidal-breathing method might underestimate regional perfusion deficits as a result of re-inspiration of common dead-space gas containing relatively large amounts of Xe-133, which would not occur with a single inspiration to TLC for breath-holding studies. The fact that the two methods showed no significant differences in perfusion measurements (Fig. 4) vitiates this theoretical objection. Thus, in regions with acute perfusion obstruction, reinspiration apparently involves regional dead-space gas to a much greater degree than common dead-space gas, and underestimation of perfusion abnormalities is unlikely.

The steady-state method of Anthonisen et al. (*4*) uses a constant infusion of Xe-133 in solution during tidal breathing. Under these circumstances, PI_i calculated separately in regions with ventilatory obstruction might be overestimated as a result of the trapping of Xe-133 entering the lungs in mixed venous blood. This problem does not occur if the steady state is reached with both ventilatory washin and perfusion washin, as described in the method of Anthonisen et al. (*4*). However, only V_i/Q_i can be calculated with this method, and Q_i alone cannot be determined. In the present study, this theoretical problem was not investigated further, for constant infusion of Xe-133 with measurement of mixed-venous Xe-133 concentration is difficult and offered no advantage over measurement of the sum of counts from all regions (Fig. 7). In human subjects, this potential problem was avoided by the use of a bolus injection of Xe-133 in solution during total breathing.

A comparison of ventilation:perfusion ratios obtained by our tidal-breathing washin method (VI_i/PI_i) with those derived from ventilatory washout (WO_i/PI_i) reveals some important differences (Table 3). The gradient from apex to base that occurs with VI_i/PI_i is not apparent in WO_i/PI_i. Ventilatory measurements with the washout method apparently reflect primarily ventilation of well-perfused alveoli,

TABLE 3. VENTILATION:PERFUSION RATIOS CALCULATED FROM VENTILATORY WASHIN (VI_i/PI_i) AND WASHOUT (WO_i/PI_i) IN UPRIGHT SUBJECTS*

	VI_i/PI_i	WO_i/PI_i
L_1	1.54	0.87
L_2	1.01	0.91
L_3	0.79	0.90
L_4	0.93	1.16
R_1	1.56	1.31
R_2	1.07	0.99
R_3	0.97	0.98
R_4	0.87	1.06

* Calculations were made using mean values for VI_i, WO_i, and PI_i from Table 1.

so that regional differences in ventilation may be masked when WO_i/PI_i is calculated. The ventilatory washin, however, yields a more direct measurement of ventilation, independent of changes in perfusion, and is thus capable of more accurate determination of the relationship between ventilation and perfusion.

In conclusion, a method for dynamic measurement of regional ventilation and perfusion during tidal breathing has been described, with features that distinguish it from currently utilized techniques. Results obtained with this method should reflect true physiologic events more closely than has been possible before, and allow study of regional lung function under circumstances in which such measurements were not previously feasible.

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FOOTNOTES

* Zen-scaler 15, Zentron, Inc., Dallas, Tex.
† Digital Equipment Corp., PDP-12, Maynard, Mass.

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