Can Dynamic Krypton-81m Imaging Separate Regional Ventilation and Volume?

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This study explores the assumption that ^{81m}Kr static images represent regional ventilation. Dynamic acquisition of ^{81m}Kr ventilation images permits creation of time-activity curves and the possible separation of the confounding influences of ventilation and volume. By using a two-compartment gas mixing lung phantom, the results demonstrate that both total and tidal ^{81m}Kr are closely related to regional ventilation. In 61 children and 15 adult volunteers, there was good agreement between fractional ventilation assessed by total and tidal ^{81m}Kr. The dynamic steady-state ventilation image can be analyzed to separate tidally exchanged and resident ^{81m}Kr. This may allow regional ventilation to be distinguished from regional volume.

J Nucl Med 1992; 33:1935–1939

In routine ventilation lung scanning, regional lung function is assessed by inspection of four krypton-81m (^{81m}Kr) ventilation images (posterior, right posterior oblique, left posterior oblique and anterior) and a chest radiograph. These steady-state ventilation images are recorded during tidal breathing until a predetermined number of counts has been acquired. The technique has the advantages of speed, simplicity and provides an image of regional ventilation whose value has been established in both adults (*1*) and pediatrics (*2,3*).

Fazio and Jones (*1*) argued that ^{81m}Kr activity would only reflect regional ventilation if inspired and alveolar ^{81m}Kr did not reach equilibrium. When ventilatory turnover is high (greater than 3 liters/liters/min) and equilibrium has been reached, they predicted that regional activity would reflect lung volume rather than ventilation. This would have important implications in pediatric practice where specific ventilation is typically much higher in infants (5–10 liters/liter/min), declining to normal adult values in the second decade of life (*4*). Davies (*5*) has recently refuted this argument and shown that ^{81m}Kr images can be used in small infants to map regional ventilation. He argues that steady-state ^{81m}Kr images are not a pure ventilation signal even in adults, but rather a composite of regional lung ventilation and regional lung volume.

Activity of a gaseous radiotracer within the lungs can be seen to fluctuate with respiration, rising during inspiration as fresh radionuclide is inhaled and falling during expiration. Dynamic acquisition of ^{81m}Kr in short timed frames, allows construction of such time-activity profiles and the possible separation of the confounding influences of ventilation and volume.

Analysis of these profiles identifies that total ^{81m}Kr activity (the classical steady-state image) is the area under the curve and as such is a composite of activity above an "end expiratory plateau" (tidal ^{81m}Kr) and that below (resident ^{81m}Kr).

This work reports an evaluation of dynamic ^{81m}Kr imaging in a two-compartment lung model in children who were seen for routine respiratory investigations and in a group of adult volunteers.

MATERIALS AND METHODS

Lung Model

A simple, ventilated two-compartment lung model was constructed, in which each lung was represented by a 500 ml anesthetic rubber bag inside an airtight perspex box. The mouths of the bags were attached to ports in the side of the box, connected outside to differential pressure pneumotachographs and a "Y" connector. A continuous suction pump provided a constant vacuum within the box to maintain the bags at a constant level of inflation, while ventilation of the bags was achieved using a sine wave pump. The distribution of ventilation to each bag could be altered using fine wire mesh resistance. Flow signals from the two pneumotachographs were electronically integrated to provide a tidal volume tracing recorded on a 4 channel tape recorder (RACAL STO 4). Flow linearity was confirmed for each pneumotachograph and volume calibrations were performed with a 50-ml syringe prior to each run. Tidal volume and ^{81m}Kr traces were synchronized by a digital electronic signal which was simultaneously recorded. Once the end expiratory volumes of the compartments were stable, ^{81m}Kr was bled into the model and after 10–20 sec a dynamic ventilation image of 100 frames was acquired at 5 frames per second. Ventilation was stopped at end expiration and resident volume determined by allowing the bags to deflate and recording the volume of air flowing through the pneumotachographs. A small positive pressure was applied to ensure complete emptying. The pneumotachograph signal was

Received Dec. 18, 1991; revision accepted May 28, 1992.
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TABLE 1
Fractional Tidal Volume (TV), Total ^{81m}Kr and Tidal ^{81m}Kr with Parameters from Individual Bags of Minute Ventilation (MV) and Tidal Volume (ITV)

Run	TV	Total ^{81m}Kr	Tidal ^{81m}Kr	MV Bag 1	MV Bag 2	ITV Bag 1	ITV Bag 2
1	0.4	0.27	0.36	1008	1536	21	32
2	0.48	0.40	0.49	3564	3906	198	217
3	0.37	0.38	0.39	1026	3906	57	96
4	0.44	0.48	0.49	5874	7627	196	254
5	0.40	0.49	0.40	3510	5160	117	172
6	0.14	0.27	0.17	2730	17323	91	577
7	0.33	0.41	0.30	3625	7525	120	250
8	0.30	0.36	0.23	6552	15561	218	518
9	0.48	0.46	0.47	4400	4757	209	226
10	0.75	0.57	0.75	6898	2260	328	107
11	0.50	0.48	0.50	10061	9957	218	215
12	0.47	0.45	0.50	7780	8599	172	191
13	0.49	0.53	0.52	4334	4495	197	204
14	0.46	0.47	0.47	3653	4219	166	191
15	0.51	0.51	0.54	4404	4154	200	188
16	0.45	0.50	0.47	7200	8804	327	400

	TV	Total ^{81m}Kr	Tidal ^{81m}Kr
Median	0.46	0.47	0.47
Range	0.14–0.75	0.27–0.57	0.18–0.75

replayed on a Gould 6000 6 channel pen recorder and the tidal volume to each bag was read directly from this. Sixteen different runs with varying resistances were made using the model (Table 1).

Ventilation distribution was expressed as:

$$\frac{\text{Tidal volume (Bag 1)}}{\text{Tidal volume (Bag 1 + Bag 2)}} \text{ or TV.}$$

The individual frames were summated to produce a single image, which was used to define regions of interest (ROIs) corresponding to the two compartments. Time-activity curves were then generated for each ROI. Total ^{81m}Kr activity in each compartment was displayed and its distribution described as:

$$\frac{\text{Total } ^{81m}\text{Kr activity (Bag 1)}}{\text{Total } ^{81m}\text{Kr activity (Bag 1 + Bag 2)}} \text{ or Total } ^{81m}\text{Kr.}$$

Distribution of tidally exchanged ^{81m}Kr was calculated by subtracting resident from total ^{81m}Kr activity (Fig. 1) within each compartment and the distribution is described as:

$$\frac{\text{Tidal } ^{81m}\text{Kr activity (Bag 1)}}{\text{Tidal } ^{81m}\text{Kr activity (Bag 1 + Bag 2)}} \text{ or Tidal } ^{81m}\text{Kr.}$$

Children and Adults

Sixty-one children in attendance for $\dot{V}/\dot{Q}$ scans as part of their routine respiratory investigations underwent dynamic posterior ^{81m}Kr ventilation scans (240 frames at 0.2 sec/frame) and ^{99m}Tc-macroaggregate perfusion imaging using an adult dose of 80 MBq, which was scaled down according to the weight of the child. Dynamic posterior ^{81m}Kr ventilation scans were performed on 15 adult volunteers during tidal breathing. The age range of subjects was 3 wk to 39 yr (Table 2). All studies were acquired in the supine position. All children had a chest radiograph; the first 22 children had this radiograph assessed by one author (IG) who did not view the ventilation image. The lung fields were scored as

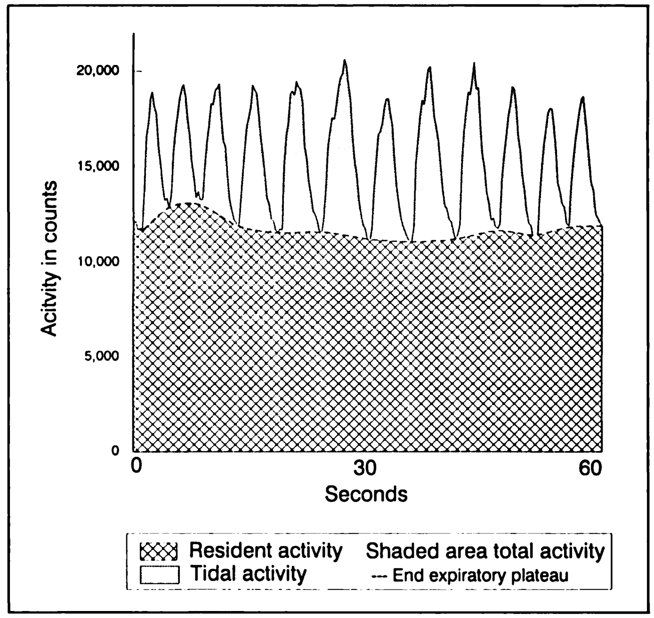

FIGURE 1. Time-activity curve of the right lung from a dynamic ^{81m}Kr lung scan of one child from the study.

either showing unilateral or bilateral changes or no changes. Krypton-81m data were analyzed as described in the "lung model" section using ROIs drawn around the right and left lungs.

Statistical Analysis

Simple linear regression analysis was applied using the least squares principle to the model and patient data. A p value of 0.05 or less was considered significant.

RESULTS

Lung Model

The summated ^{81m}Kr images (i.e., total ^{81m}Kr activity) provided an accurate picture of the distribution of tidal volume to the two compartments (Table 1). The ratio of total ^{81m}Kr activity recorded over each bag (total ^{81m}Kr) was related to ventilation distribution within the model (TV) (Fig. 2) ($r^2 = 0.63$). However, tidally exchanged ^{81m}Kr (tidal ^{81m}Kr) agreed more closely with ventilation distribution ($r^2 = 0.95$), as indicated by a stronger positive correlation (Fig. 3). Resident ^{81m}Kr activity showed no correlation with resident volume (Fig. 4) ($r^2 = 0.1$) and total ^{81m}Kr activity was found not to correlate with resident volume (Fig. 5) ($r^2 = 0.02$).

Children and Adults

The relationship between total and tidal ^{81m}Kr activity was examined using distribution of this tracer to the right

TABLE 2
Fractional Ventilation to Right Lung

Patient	Age (yr)	Calculated from total ^{81m}Kr	Calculated from tidal ^{81m}Kr	Ratio
Median	8.2	53	52	1.02
Range	0.03–39	34–91	32–88	0.77–1.13

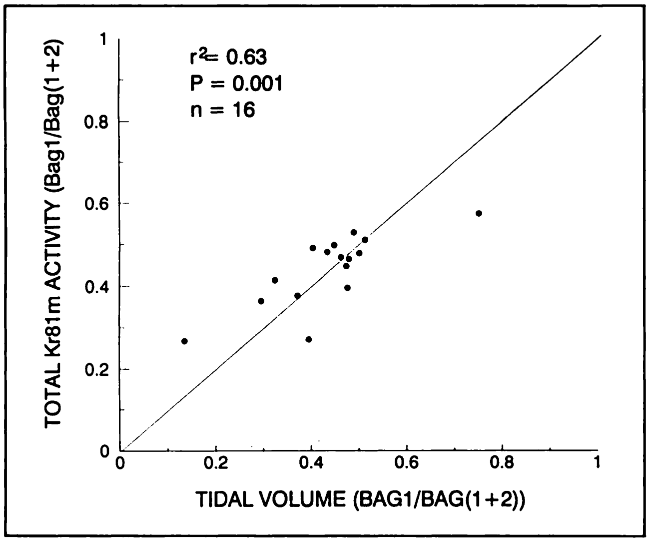

FIGURE 2. Lung model. Relationship between fractional total ^{81m}Kr activity and fractional tidal ventilation within the model.

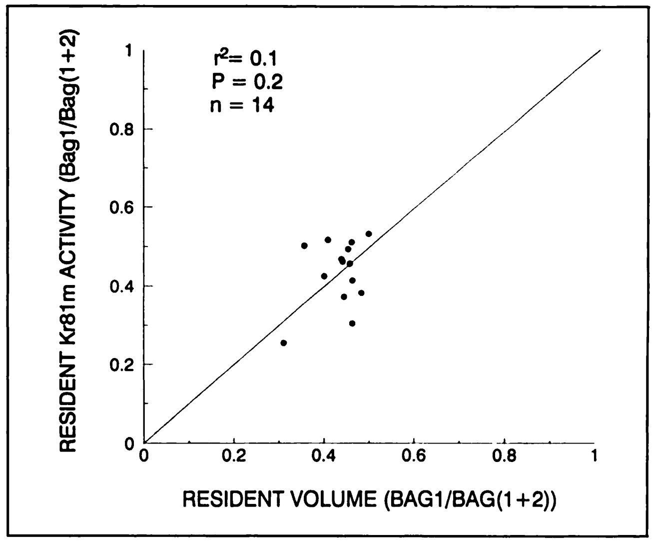

FIGURE 4. Lung model. Relationship between fractional resident ^{81m}Kr activity and fractional resident volume.

lung as a marker of fractional ventilation. Values for fractional ventilation to the right lung (Vf R) calculated with either total or tidally exchanged ^{81m}Kr were similar (Table 2). This can be demonstrated by comparing Vf R calculated with total and tidal ^{81m}Kr activity (Fig. 6). The mean value of this ratio is:

$$\frac{\mathrm{Vf\,R\,(Total\,^{81m}Kr)}}{\mathrm{Vf\,R\,(Tidal\,^{81m}Kr)}} = 1.003\ (95\%\ \text{confidence limits}\ 0.88\text{–}1.20).$$

Tidally exchanged ^{81m}Kr activity in the right lung was slightly lower than total ^{81m}Kr. Mean difference between Vf R (Total ^{81m}Kr) and VfR (Tidal ^{81m}Kr) was 2.54 (−12.1 to +6.3), probably accountable in all but one patient (see below) by normal variability of radioactive decay. When these results were analyzed according to the results of the chest radiograph, no difference was observed between those with normal right lungs (Vf R >45%) and children with unilateral changes (Vf R <45%). No effect of age was apparent.

The discrepancy between the two techniques in one child requires further discussion. T.D., a 20-day-old neonate, was referred for the investigation of persistent respiratory symptoms. Chest radiography showed hyperlucency of the left upper lobe and a diagnosis of congenital lobar emphysema of the left upper lobe was made. Whole-body plethysmography demonstrated hyperinflation. FRC (pleth) was 320 ml (predicted normal range 110–210) and airway resistance was increased compatible with the diagnosis. However, when investigated further, the ^{81m}Kr steady-state ventilation image showed equal activity in the right and left upper zones and the perfusion image showed decreased activity to the left upper zone, which is uncharacteristic of congenital lobar emphysema.

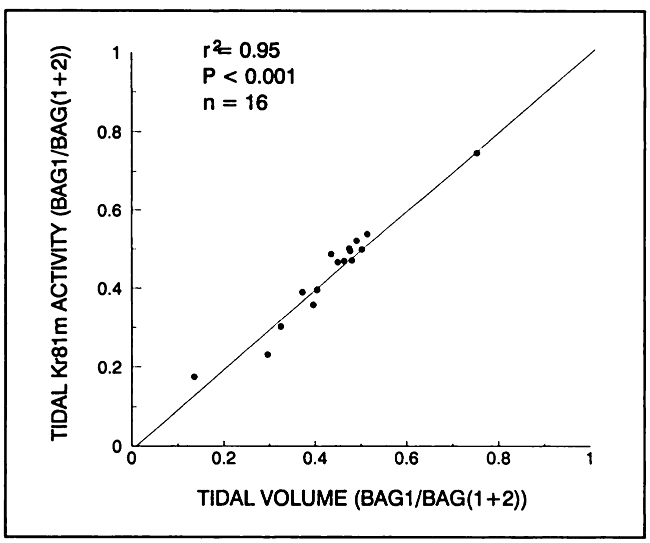

FIGURE 3. Lung model. Relationship between fractional tidal ^{81m}Kr activity and fractional tidal ventilation within the model.

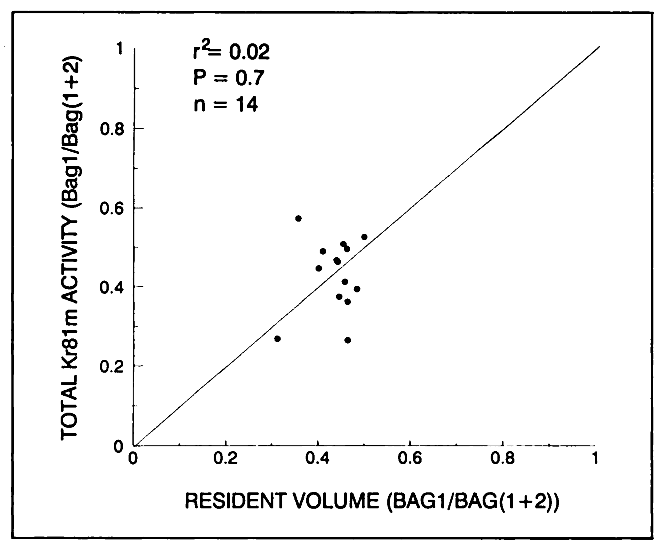

FIGURE 5. Lung model. Relationship between fractional total ^{81m}Kr activity and fractional resident volume.

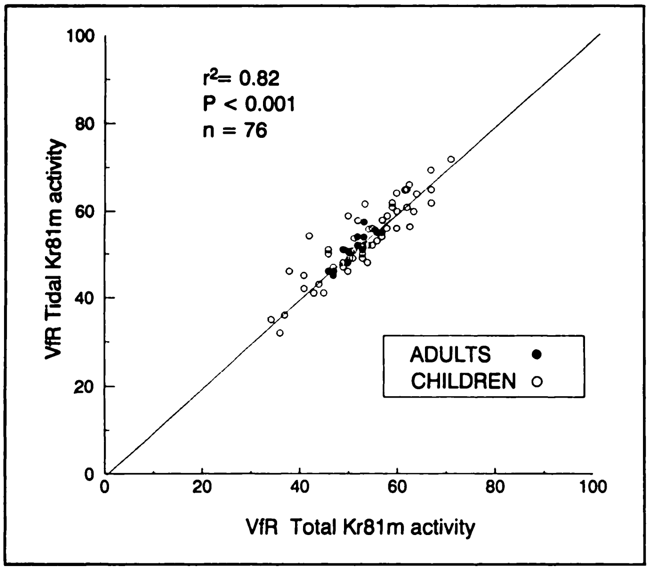

FIGURE 6. Patients. Relationship between fractional ventilation to the right lung calculated from tidal ^{81m}Kr activity and total ^{81m}Kr activity.

Analysis of the dynamic ventilation image demonstrated a discrepancy between the ventilation distribution calculated using total and tidally exchanged ^{81m}Kr. Fifty-eight percent of total ^{81m}Kr activity was distributed to the hyperinflated left lung, whereas only 46% of tidally exchanged activity was recorded over the left lung. The $\dot{V}/\dot{Q}$ lung scan was repeated 1 mo later with similar results: (Vf(L)) calculated from total ^{81m}Kr was 55.8% compared with 44.2% using tidally exchanged activity. In this infant, the increased activity of the abnormal left lung seen on the steady-state image was a reflection of the increased volume of that lung rather than ventilation. It is obviously much more difficult to prove this in vivo, but the distribution of ventilation calculated from the dynamic scan would seem more in keeping with clinical and radiographic findings in this patient.

DISCUSSION

Krypton-81m, with a half-life of 13 sec, is an ideal radiotracer for ventilation lung scanning. Few investigators have used dynamic acquisition to augment the information gained (*6*). The technique of dynamic lung scanning requires no additional time, yet may provide additional physiological and pathological data that are unavailable with static ^{81m}Kr imaging. Krypton-81m has been used to understand pulmonary physiology to better advantage in children (*5,7*). These works suggest that ventilation in children of any age responded differently to a change in posture when compared to adults. The assumption being that the ^{81m}Kr static image represented regional ventilation; the current work explores that assumption.

In the simple lung model used, the results demonstrate that both total and tidal ^{81m}Kr are related to regional ventilation, although the tidally exchanged ^{81m}Kr activity is the more accurate. The lung model is not a true representation of the human lung. The bags are a perfect gas mixing model in which ^{81m}Kr is distributed evenly in the end expiratory volume and consequently inspired and compartmental ^{81m}Kr will be in equilibrium. Yet, this model demonstrates quite clearly that distribution of tidal ^{81m}Kr activity gave a more accurate assessment of ventilation (Fig. 3) than total ^{81m}Kr activity (Fig. 2), as shown by the stronger positive correlation. Further analysis of the resident component of the static image (Fig. 4) was found not to correlate with resident volume, which accounts for the more accurate assessment by tidal ^{81m}Kr than total ^{81m}Kr. In the lung model, this shows the limitations of the static image when used as an indication of ventilation or volume.

The invasive procedures necessary for direct comparison of ^{81m}Kr distribution and ventilation in patients make it ethically difficult to conduct such studies. There was, however, good agreement between fractional ventilation assessed by total and tidal ^{81m}Kr in all but one patient. Although this result alone cannot prove the accuracy of the technique when examining smaller lung volumes, when taken with the results of Gordon et al. (*2*) and Li et al. (*8*), it is strongly suggestive that both tidal and total ^{81m}Kr activity provide an accurate reflection of regional ventilation. The persistent and marked discrepancy between the two techniques in one child highlights a problem when looking at children with large differences between ventilation and volume. The previous experience in children with lobar emphysema would suggest that the lobe with air trapping may take part in tidal breathing when the child is in certain postures (*9,10*).

This work illustrates the limitations of using total ^{81m}Kr activity to determine regional ventilation. When there is gross disparity between resident volume and ventilation, i.e., a hyperinflated yet relatively under ventilated region of lung, total ^{81m}Kr (the steady-state image) may give a false impression of regional ventilation because it includes the distribution volume of ^{81m}Kr as well as the tidally exchanged ^{81m}Kr. Our model demonstrated that tidally exchanged ^{81m}Kr activity gave a more accurate picture of ventilation distribution.

CONCLUSION

Krypton-81m dynamic ventilation imaging is feasible in pediatric practice. This is of particular importance in younger children in whom faster frame rates are needed to capture the pattern of ventilation.

The dynamic steady-state ventilation image can be analyzed to separate tidally exchanged and resident ^{81m}Kr. This may allow "regional ventilation" to be distinguished from "regional volume."

In the simple lung model, the results demonstrate that both total and tidal ^{81m}Kr activity are closely related to regional ventilation, although tidally exchanged ^{81m}Kr activity is a more accurate guide.

In one child, in whom there was a gross disparity between volume and ventilation, tidal ^{81m}Kr activity may give a more accurate guide to regional ventilation.

The contribution of resident ^{81m}Kr to total activity is similar in all age groups. Steady-state ^{81m}Kr images can therefore be used throughout childhood to monitor the progress of pediatric respiratory disease as long as there is no gross disparity of lung volumes on chest radiography.

ACKNOWLEDGMENTS

The authors would like to thank Barbara MacDonald for her valuable technical assistance. Mark F. Lythgoe is supported by the Welton Foundation.

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EDITORIAL

Go with the Flow—But How Far?

There is well-established logic behind the use of ^{81m}Kr in evaluating lung disease (*1–7*). Its energy allows ^{81m}Kr ventilation studies to follow ^{99m}Tc-MAA perfusion scans. Its short 13.4-sec half-life allows it to be administered intermittently, so that ventilation images can be alternated with perfusion images. Krypton-81m studies can be easily performed on infants, children and on patients being mechanically ventilated. The gas does not require expensive delivery systems, room monitors, ventilation ducts, fans or charcoal traps. Its low dosimetry and absence of radioactive waste disposal problems make it a very attractive alternative to ^{133}Xe or ^{127}Xe. Perhaps most important, the static distribution of ^{81m}Kr reflects the pattern of lung ventilation ($\dot{V}$). It is therefore directly comparable to ^{99m}Tc-MAA perfusion ($\dot{Q}$) studies obtained to screen for pulmonary emboli. The tidally ventilated gas volume ($\dot{V}$) is also an important element of the ventilation-perfusion ratio ($\dot{V}/\dot{Q}$), a parameter describing the lung's primary function of gas exchange (*5,8,9*).

Static ^{81m}Kr images reflect ventilation because of the nature of bulk air flow in the lung. When ^{81m}Kr enters the oropharynx, it is swept along the inhaled air, moving down the branching labyrinth of narrowing bronchi, past 19 to 21 divisions of airways. At about the 20th generation of bronchiole, the transporting motion of the tidal air has diminished to the extent that any farther progress toward the alveolar membrane is by diffusion alone. Although the remaining journey is but a small fraction of the total distance, the last few millimeters are the longest in the trip, consuming minutes of time. This paradox of travel is due to the ever increasing arborization of the airway. The pyramid of volume comprising the lung airspace is arranged such that of the 3.5 liters of resting lung gas only 220 ml occupy the space in the first 17 generations of conducting airway. The cross-sectional area expands from 2.5 cm^2 in the trachea to over 180 cm^2 by the beginning of the pulmonary respiratory zone. It continues to expand to a surface area of over 70 square meters at the pyramid's base, the alveolar membrane. The resting tidal volume of 550 cc is partially expended in the conducting airway such that about 300 cc enters the respiratory zone of the lung. Thus, about 10% of the alveolar air is exchanged with each resting tidal breath. This respiratory tidal flow acts to maintain a diffusion gradient of gas tensions in the alveolus such that transfer of CO_2 and O_2 takes place efficiently. Beyond the gases in the dead space, a significant fraction of the molecules inhaled into the alveoli with each breath are also exhaled. What importance does this have? It means that the radioactive species of a short-lived isotope is primarily concentrated in the dead space, in the terminal conducting airways and in the proximal respiratory zone. The molecules that occupy the more distal alveolar regions (90% of lung volume) have had a much longer residence and a correspondingly lower specific activity. This consequence of the short ^{81m}Kr half-life means that the remaining radioactive gas resides primarily in the tidal space of the lung. Hence, count rates from the chest increase dramatically with inspiration. The faster the tidal volume is refreshed, the higher its mean activity,

Received Jul. 27, 1992; accepted Jul. 27, 1992.
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