MEASUREMENT OF REGIONAL AREA GAS EXCHANGE BY PERFUSION AND CLEARANCE OF ^{133}XE FROM THE LUNG

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Measurement of regional area gas exchange in the lung has been carried out with ^{133}Xe by intravenous injection and measurement of perfusion distribution and clearance curves at 1,600 nonindependent sites. Data have been collected with an Anger camera, 1,600-word memory unit with digital tape recorder, and processed by an IBM 360/40 computer. Multiplying intensity of postinjection radioactivity (perfusion) by clearance rates during normal breathing (ventilation) provides information as to regional gas exchange. The inclusion of both perfusion and ventilation in a single measurement offers a more fundamental approach to gas exchange than either one taken singly. Good correlation with differential bronchospirometry exists in those patients studied in this manner so far. The use of a three-dimensional model to depict lung function offers a practical approach to the problem of evaluation of the regional lung function.

The lung's performance as a gas-exchange organ has been measured by carbon monoxide and oxygen transfer methods, by arterial partial pressures for oxygen and carbon dioxide, and A-a gradients for these gases. Regionalization of these functions has been possible by differential bronchospirometry for the left and right lungs. This study deals with an approach to regionalization of gas exchange using ^{133}Xe at 1,600 nonindependent sites.

The qualities of short half-life, inert character, and low solubility make xenon almost ideal for the study of both ventilation and perfusion. Following intravenous injection and breathhold, xenon passes into the pulmonary capillary bed and 95% is diffused into air-containing alveoli (*1*). After the first pass through the pulmonary capillary when breathing is resumed, it is cleared from the lung by ventilation. Since the use of ^{133}Xe for pulmonary studies was first introduced by Knipping (*2*), regional perfusion and clearance has been measured using as many as 16 detectors simultaneously. More recently, the scintillation camera has permitted the simultaneous recording of gamma radiation from the whole lung (*3*). This technique has been used to measure static distribution of both ventilation and perfusion as well as washin and washout times by recording oscilloscope displays either photographically or with a video tape. Regional studies have also been processed by computer for 80 sites in the lung (*4*).

This report deals with the use of clearance rates from multiple sites and the calculation of regional area gas exchange (RAGE) as a clinically useful tool in the appraisal of lung function.

Details of data handling in our method have been reported elsewhere (*5*). The patient is positioned upright with a Nuclear-Chicago Anger camera facing the back. The collimator used has 1,000 holes and is 1½-in. thick. The field of view encompasses approximately 90% of the lung field (*6*). The camera is connected to a RIDL 1,600-word memory unit leading to an Ampex 9-channel digital tape recorder. The 1,600-word memory unit permits a 40 × 40 matrix to be recorded with each matrix element representing about ¼ in. This dimension is, of course, considerably smaller than the resolution of the system. However, as with most display systems, we have found that sampling at several times the rate of the maximum spatial frequency component improves the visual integration of the distribution. Accumulated counts are transferred to tape every 2.4 sec with 0.4 sec for transfer, and the information is processed by an IBM 360/40 digital computer.

After implantation of a plastic catheter in the

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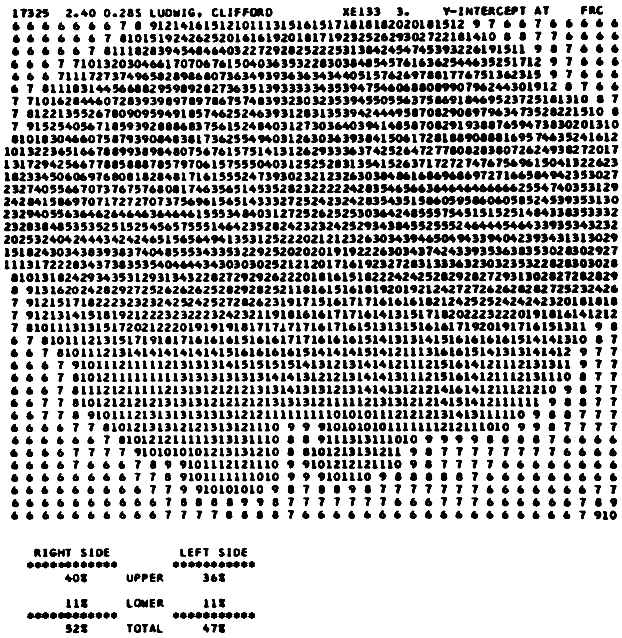

FIG. 1. Numerical representation or matrix of perfusion activity at 1,600 sites. Values in left lower corner represent percent distribution to four quadrants of lung.

antecubital vein, 3 mCi of ^{133}Xe are injected rapidly followed by a bolus of 5 cc of normal saline. The patient hyperventilates briefly before injection and following injection maintains a 10–15-sec open-glottis breathhold at functional residual capacity + tidal volume (FRC + TV) and then resumes breathing at a normal rate after the xenon level in the lung has plateaued as measured by a rate monitor.

Perfusion distribution is calculated from the extrapolation of the disappearance slopes with the ordinate at zero time. This level is referred to as the Y-intercept and is calculated for each site in the 40×40 matrix. Zero time is defined as the time of maximum total counts from the lung before breathing is resumed. Disappearance slopes for each site are calculated by the method of least squares, and standard deviation of the slopes over lung region are less than 15%. After computer processing, each of the 1,600 regional sites is given a numerical value from 1 to 99 (Fig. 1) related to the level of activity at each site. Levels of radioactivity at each site are displayed in a three-dimensional model with the highest levels of activity being given the highest elevation in the model and the lowest level of activity the lowest elevation (Fig. 2). The right and left lungs are displayed in four separate views, two from the apex and two from the base. The mediastinum is seen as the valley between the right and left lungs. The right and left oblique views from the apex and base permit better identification of regions that might otherwise be hidden from view by proximal sites. The models are drawn by a computer-driven plotter.

Clearance of xenon from perfused regions of the lung is displayed in a similar manner. The disappearance slope for each site is given a value of from 1 to 99. Sites of rapid clearance are given high values and those of slow clearance are given lower values on the three-dimensional model. Figure 3 shows two different clearance rates. Clearance plotted semilogarithmically is a straight line. On the 40×40 matrix, the faster clearance is given the taller bar and the slower clearance the lower bar. When clearance rates have been identified for each of the 1,600 sites, a three-dimensional model depicting clearance rates for both left and right lungs can be viewed as a single presentation.

Values for regional area gas exchange are obtained by multiplying height by slope (Fig. 4) in which height is equivalent to perfusion and the disappearance rate is equivalent to ventilation of the perfused regions. The product is then assigned a relative value between 1 and 99, and a three-dimensional model is constructed similarly to that used for depicting perfusion and clearance rates.

DISCUSSION

For purposes of this paper, we have chosen the upright position with breathhold at FRC + TV. This position and breathhold were chosen because most physical activity and most measurements of other parameters of lung function are carried out in the upright position.

Breathhold at FRC + TV followed by normal

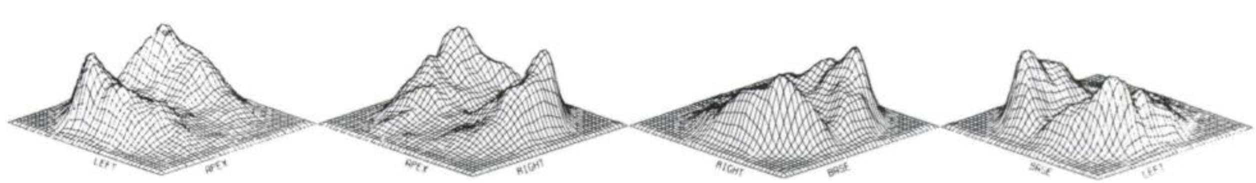

FIG. 2. Three-dimensional model of perfusion in upright position displays lungs with mediastinum represented as valley between right and left lungs. Two models at left show perspective from apex looking over left and right shoulders. Two models on right basalar views from right and left base. Height of each site is related to intensity of radiation at that site. This is normal subject.

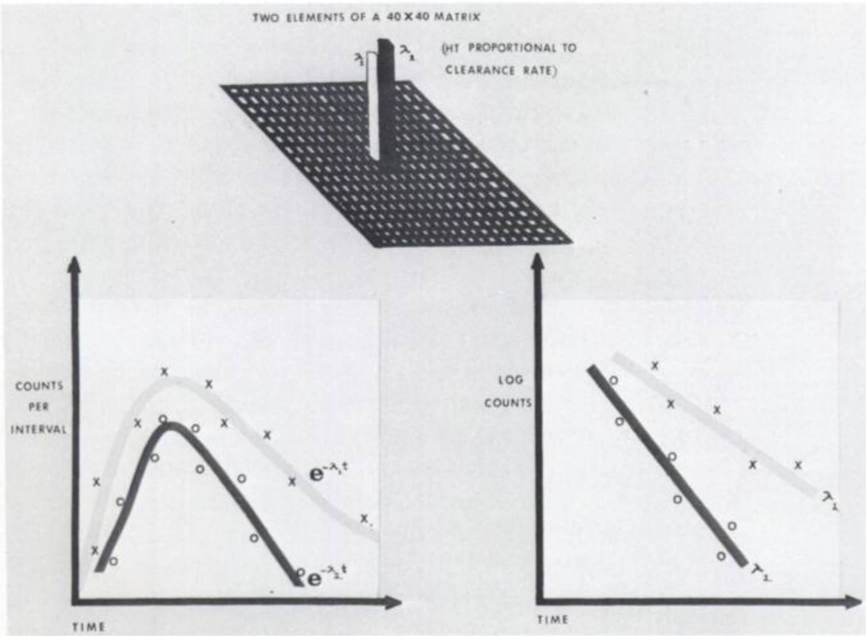

FIG. 3. Two different clearance rates are illustrated in diagram with height of bar at two different sites being related to clearance of ^{133}Xe from lung as seen in washout curves. After clearance rates have been constructed for each site, three-dimensional model depicting dynamic lung function is drawn by computer-driven plotter.

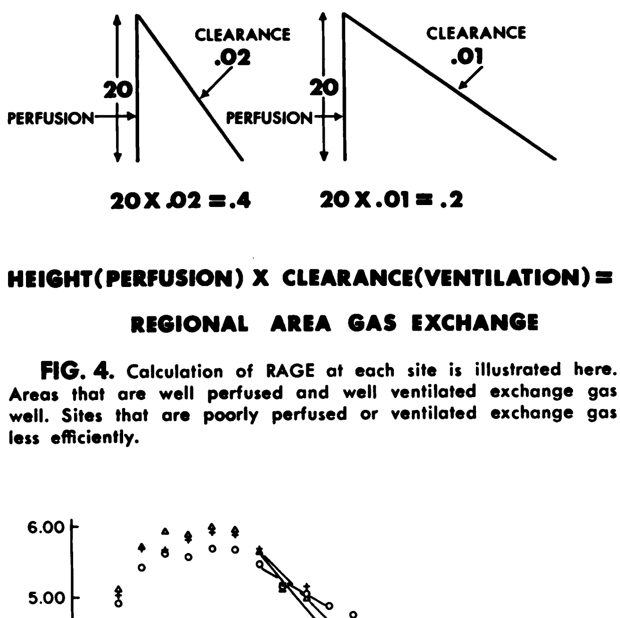

FIG. 4. Calculation of RAGE at each site is illustrated here. Areas that are well perfused and well ventilated exchange gas well. Sites that are poorly perfused or ventilated exchange gas less efficiently.

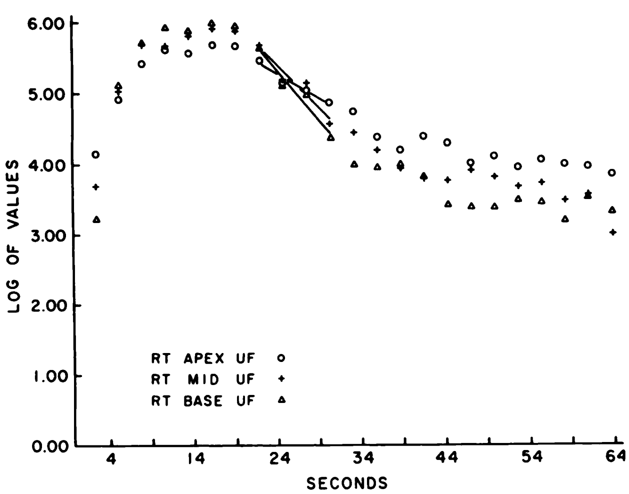

FIG. 5. Clearance rates for three lung zones are illustrated here in upright position, breathing quietly after breathhold at FRC + TV. Rates of clearance are seen to increase from apex to base when log of counts is plotted against time.

breathing compares best with resting cardiac output insofar as matching normal resting sites of ventilation and perfusion.

Multiple sites. The use of multiple small sites is based on the premise that there are significant regional variations in both perfusion and ventilation. This opinion is supported by the regional differences that are known to exist between the upper, middle, and lower lungs (*7,8*) as seen in Fig. 5. These findings in normal subjects are in agreement with the findings of West, et al (*7*) who have shown the regional variation in perfusion between apex and base and Milic-Emili, et al (*9*) who have shown regional variation in percent volume change of apical and basalar regions of the lung during breathing.

The importance of multiple small sites to measure postperfusion regional ventilation has been emphasized by Anthonisen, et al (*10*). They pointed out that in the nonhomogeneous lung, regions with varying clearance rates and perfusion levels may provide misleading information when taken as a large unit, that, in essence, one sees an "averaged-out" value for postperfusion washout, which is a mixture of many different levels of perfusion and clearance. The regional differences in clearance of contiguous sites in a patient with severe obstructive disease are illustrated in Fig. 6. The smaller the site, therefore, the better one can evaluate regional differences. Ideally, one would measure the site of a single alveolus; however, such resolution is impossible. The use of multiple sites permits measurement of variation in very small regional areas with significant size of lesions, perhaps as small as ¾ in. Limitation as to size depends on the limitation of camera and data

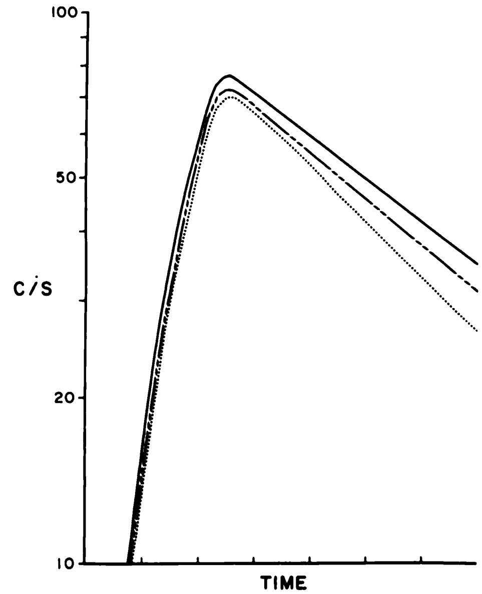

FIG. 6. Clearance curves of three adjacent sites with log of counts/second plotted against time are seen to show significant variation. Each site is drawn from square array of nine elements measuring approximately ¾ in. on side.

collection resolution as well as the safety of the dose of radioisotope administered.

Regional area gas exchange. The use of the word "area" in the description of regional gas exchange is intended to emphasize the two-dimensional quality of the information obtained by a single camera collecting data from the posterior chest wall. The variation of resolution with depth as well as considerations of absorption of gamma radiation and scattering (resulting from the nonhomogeneous tissue mass that constitutes a diseased lung) precludes obtaining a completely accurate portrayal of perfusion and ventilation in a three-dimensional lung. Area then implies the limitation of such a collecting system. The concept of regional area gas exchange is based on the premise that well perfused and well ventilated regions of the lung offer the best possibility for gas exchange. Those regions that are well perfused and poorly ventilated or poorly perfused and well ventilated are less capable of efficient function in the transfer of oxygen and carbon dioxide. Two sites of identical perfusion and different clearance rates (Fig. 6) would have significantly different values for regional gas exchange. As reported by Miorner (*11*), the correlation of differential bronchospirometry with percent perfusion and percent ventilation to the right or left lungs was excellent. These findings are to a large degree related to the homeostatic reflexes in the lung that adjust ventilation and perfusion reciprocally (*12*). However, abnormalities of ventilation-perfusion relationship in which the non- or poorly ventilated lung continues to be perfused (pneumonia, bronchitis, etc.), or the perfused areas are poorly ventilated (airway obstruction), are sufficiently common so that the combination of regional perfusion and clearance offers a practical clinical approach to the measurement of regional lung function.

An illustration of this is seen in Fig. 7 showing a perfused left lung, but the xenon was trapped and showed essentially no clearance over the normal period of study. The gas exchange ability of this lung in the upper model is seen to be totally ineffective in spite of the fact that it was well perfused. Zonal clearance curves in Fig. 8 illustrate the complete lack of clearance from the left lung. The most important measure of the reliability of this approach is to compare regional area gas exchange meas-

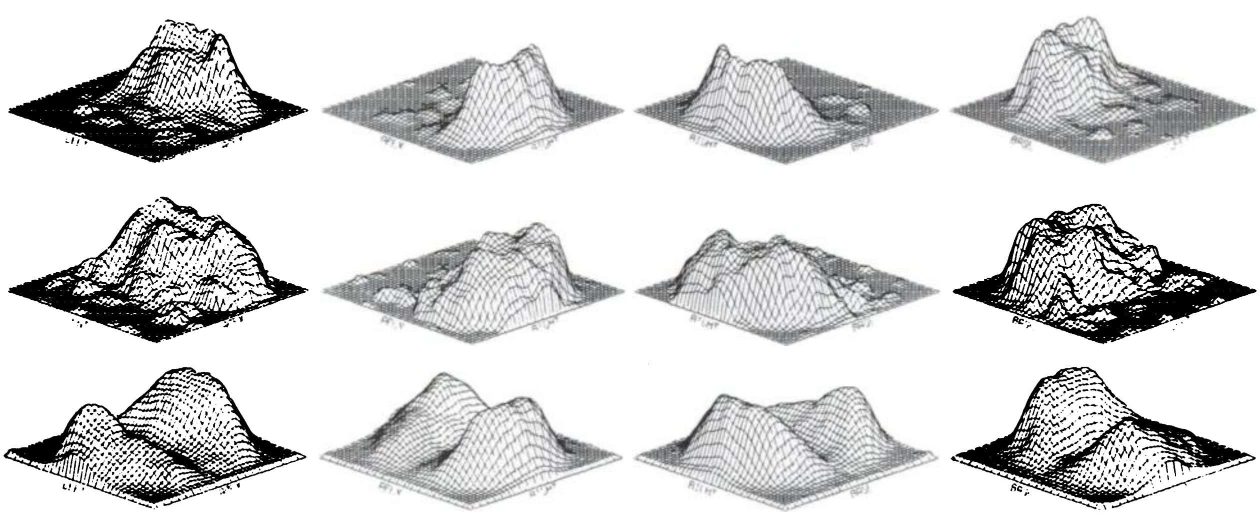

FIG. 7. Perfusion (lower set) is seen to be almost equal in both lungs whereas clearance (middle set) shows very poor washout for left lung. RAGE (upper set) is seen to be essentially zero for left lung in spite of adequate perfusion.

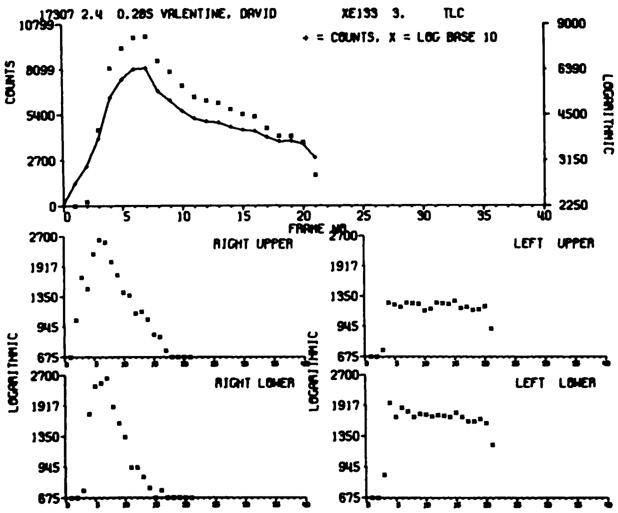

FIG. 8. Clearance rates for whole lung and for upper and lower halves of right and left lung are shown for patient illustrated in Fig. 7. Clearance of ^{133}Xe from both upper and lower regions of left lung is seen to be essentially zero. Significant amount of ^{133}Xe remains in lung after 22 frames (62 sec).

ured by taking the sum of counts in the regional gas exchange matrix and calculating the percent division between the right and left lungs. These values were then compared to percent oxygen uptake by differential bronchospirometry.

Three patients with severe bullous disease have been studied in this manner, one patient pre- and postbullectomy, and one in the sitting and recumbent position. As seen in Table 1, the values agree within a few percent. Although problems of depth in the lung exist—because of the poor resolution of the relatively low energy of ^{133}Xe (80 keV)—a reasonably reliable regionalization appears to exist even in the badly diseased lung. Of particular interest is the switch in function from right to left after surgery. This approach to dynamic scanning offers an approach to evaluation of regional function that makes possible appraisal of relative function of the lung in small regions.

Although such an approach does not identify deadspace ventilation, which contains radioactive gas during inhalation of ^{133}Xe from a spirometer, it does identify those areas that are perfused and in which gas exchange can occur. It has been reported by a number of workers, and has certainly been our experience, that the clearance times after inhalation of ^{133}Xe are much shorter in certain disease states such as cystic fibrosis than are postperfusion clearance times. Measurement of postperfusion washout times would seem to offer a more realistic evaluation of true alveolar ventilation than washin or washout times after ventilation. This is because perfused xenon starts out in alveoli and inhaled xenon may be in either alveoli or conducting airways.

The application of regional area gas exchange to clinical situations can be seen in Fig. 9. This patient developed sarcoidosis with considerable loss of ventilatory function and subsequently an aspergillus infection similar to those reported by Israel (*13*). Surgical intervention was considered because of recurrent hemoptysis from the left upper lobe. Xenon studies, including the three-dimensional model and regional clearance rates (Fig. 9), show very little

TABLE 1. REGIONAL AREA GAS EXCHANGE COMPARED TO DIFFERENTIAL BRONCHOSPIROMETRY*

		^{133}Xe Regional area gas exchange			Differential bronchospirometry percent oxygen uptake
			slope	perfusion	
Patient AP					
	Right lung	62%	48	54	58%
	Left lung	38%	51	46	42%
Patient BG preop					
	Right lung	58%			56%
	Left lung	42%			44%
3 months postop					
	Right lung	39%			37%
	Left lung	61%			63%
Patient AF upright					
	Right lung	50%	45	49	47%
	Left lung	50%	55	51	53%
Recumbent					
	Right lung	44%	39	51	39%
	Left lung	56%	61	49	61%

* This table shows a comparison of % oxygen uptake by differential bronchospirometry compared to the calculated uptake between the right and left lungs using RAGE. Patient BG was studied pre- and 3 months postoperative for a bullectomy. Patient AF, a man with bullous disease, was studied in the upright and recumbent position.

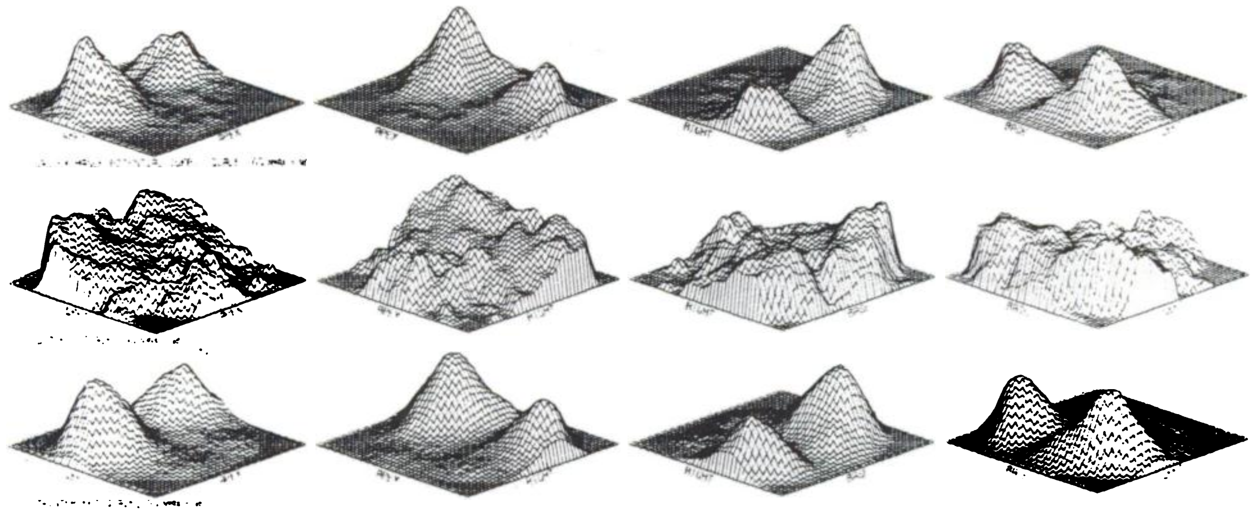

FIG. 9. Three-dimensional models of patient with sarcoid, cystic lung disease, and aspergillosis. Perfusion is seen in lower set, clearance rate in middle set, and RAGE in upper set. Height at each of 1,600 sites is related to regional perfusion, clearance, or gas exchange. Perfusion, clearance, and RAGE are shown to be markedly decreased in both upper lung fields.

function in either the right or left upper lobe. Ventilation of these areas, however, is significantly better than perfusion.

Appraisal of regional function in the lung of a patient whose overall function is compromised may provide vital information concerning the possible loss of regional function following surgery. It is possible to assign a value equivalent to the percent of total lung gas exchange contributed by small regions so that a more definitive statement of loss following removal may be made. The use of this technique to portray regional perfusion, ventilation, and clearance may offer valuable aid in the preoperative assessment of regional lung function.

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