VENTILATION-PERFUSION RELATIONSHIP IN HUMANS MEASURED BY SCINTILLATION SCANNING

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The use of ^{131}I-labeled macroaggregated human albumin (MAA ^{131}I) for estimating regional pulmonary arterial flow appears well established and in wide usage (*1–3*). Lopez-Majano *et al* (*4*) and Rogers and co-workers (*5*) have shown that the distribution of the deposition of labeled albumin in the two lungs correlates well with bronchospirometric division of oxygen uptake. De Nardo *et al* have addressed themselves to the possibility that the macroaggregates might behave differently than a soluble agent, but their studies indicate no difference in the distribution of MAA ^{131}I and an injected solution of ^{133}Xe (*6*). Regional ventilation has presented a more difficult parameter to measure. Most attempts have involved the "spot checking" of three to eight areas of each lung field by placing radiation detectors in fixed locations over the chest wall and/or the use of unphysiologic maneuvers such as breath-holding, which changes the diameter of the airways and therefore can not fail to produce a change in the ventilatory distribution pattern. These techniques, which are based on the method of Ball *et al* (*7*), have yielded much useful information relative to the distribution of ventilation and perfusion in the normal, especially the effects of postural alterations, but are much less suited to the examination of the patient with localized pulmonary disease. This paper presents a technique for obtaining quantitative regional information relative to ventilation and perfusion from all areas of the lung during the "steady state."

METHODS

Patients are studied in the supine position. Data are accumulated with a Picker Dynapix, a 10-crystal rectilinear scanner (*8*). The counts from each radiation detector are fed into an electronic interface which assigns x and y coordinates, locates anatomic landmarks and records the count information directly in computer-compatible format on ½-in. magnetic tape. The details of the interface construction and function have been previously reported (*9*).

Ventilatory distribution is determined by having the subject breathe into a "closed-system" spirometer containing ^{133}Xe. We have found that 1–3 mc of the gas provides ample activity to allow the scanner to operate at a speed of 2 cm/sec and still furnish sufficient information for a statistically significant study. The low activity required for the measurement has the additional advantage of economy of ^{133}Xe, because a single 200 mc vial of the test gas will provide 8–10 studies even if spaced over an interval of a week or more.

Operation of the scanner is begun simultaneously with ^{133}Xe breathing. Two successive 8-line/in. washin scans are obtained. These can be accomplished in less than 6 min. At the beginning of the 8th minute of ^{133}Xe breathing, a 16-line/in. "equilibration" scan is obtained for the determination of the ventilated space. During the xenon breathing, the volume of the system is kept constant by adding oxygen. On completion of this study the patient is switched into an "open-circuit" oxygen-breathing system and two successive 8-line/in. washout scans are recorded. Thus in approximately 15 min, two washin, an equilibrium and two washout studies are performed. Following the last washout and with the patient's position unchanged, 200 μc ^{131}I-labeled MAA are injected intravenously and a 16-line/in. perfusion scan is recorded.

The data from the above studies are recorded on magnetic tape and are then processed on the IBM 7040-1401 computing system at the University of Miami Computer Center. Details of the data manipulations and computer programs are presented elsewhere (*10*). Seven-level analog maps of the equilibration ventilation and perfusion data are obtained (Fig. 1). These serve several purposes. First, they supply visual reference of the quality of the study as well as the definition of any gross areas of abnormality. Second, they are useful in the delineation

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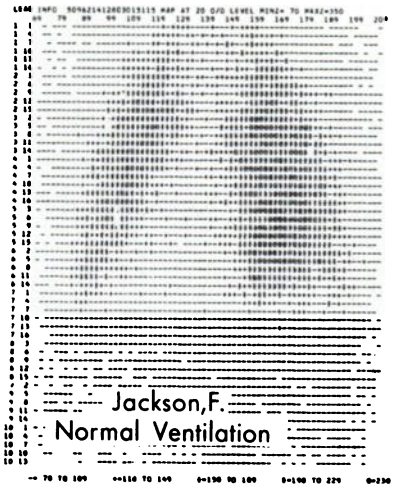

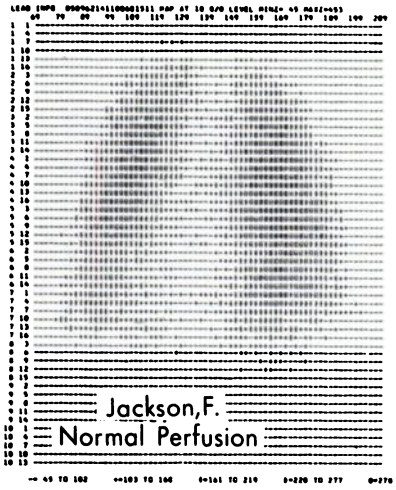

FIG. 1. Seven-level analog maps of ventilation (equilibrium) and of perfusion for a normal subject, F.J., are shown. Levels of increasing degrees of activity are denoted by symbols of increasing complexity. Background has been suppressed to allow clearer visualization of lung fields. In this and all subsequent illustrations, left lung is on the viewer's left.

of the margins of the lungs for use with the digital data printouts.

The "equilibrated" ventilation and perfusion scans are processed to give corrected numerical values for the collected counts. The counts for each 1.20 × 1.35-cm area are summed and printed in the correct anatomic position. These data are then "normalized" by assigning a value of 1.00 (× 1,000) for the block of the lung field with the greatest activity. All other areas are then presented as a fraction of this highest value (Fig. 2). The "normalization" of the data is performed to accomplish two objectives. First, it allows direct comparison of the regional data although the absolute levels of radioactivity might be different; for example, direct comparison of ventilation with perfusion information or repeated studies in the same individual. Second, it makes the precise definition of the lung's margins less critical. If regional percentages were dependent on the sum of the values within the lung fields, then a crucial consideration would be the exact definition of the margins of the mediastinum, diaphragm and thoracic cage.

The "normalized" equilibration ventilation data is compared to the perfusion values and a "ventilation"-perfusion ratio is printed for each of the anatomic areas (Fig. 3). Although this is actually a comparison of the ventilated and perfused spaces rather than a true ventilation-perfusion ratio as defined physiologically, its usefulness in certain clinical situations will be made apparent later. It should be noted that a value of 1.00 (× 1,000) for the V/P ratio as defined above indicates a similar degree of activity in the designated area at the equilibrium for ventilation and for perfusion whether or not the degree of activity for the area is "normal" in relation to other areas.

One of the most critical areas in the use of steady-

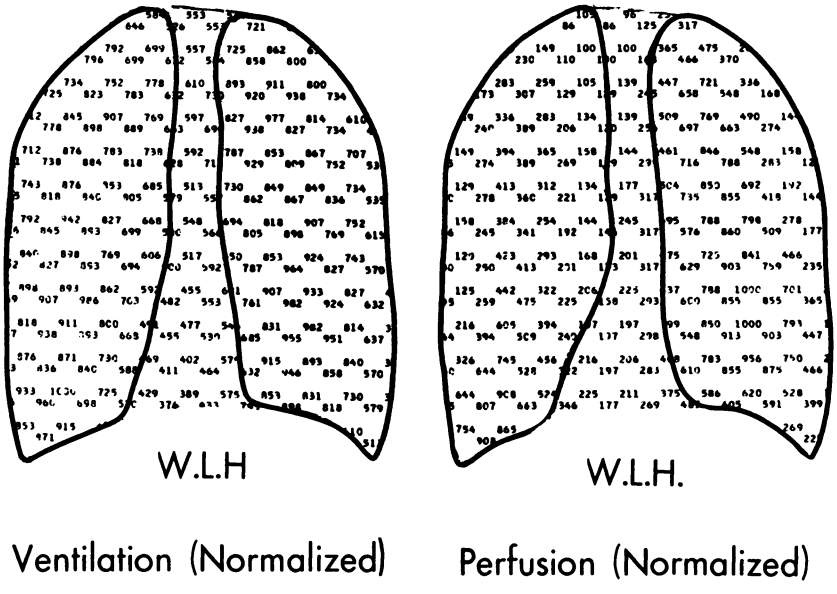

FIG. 2. "Normalized" ventilation (equilibrium) and perfusion in subject F.J. Each value represents relative performance of area 1.20 × 1.35 cm (see text). Relatively low values at the lung bases is thought to be reflection of diaphragmatic movement during measurements.

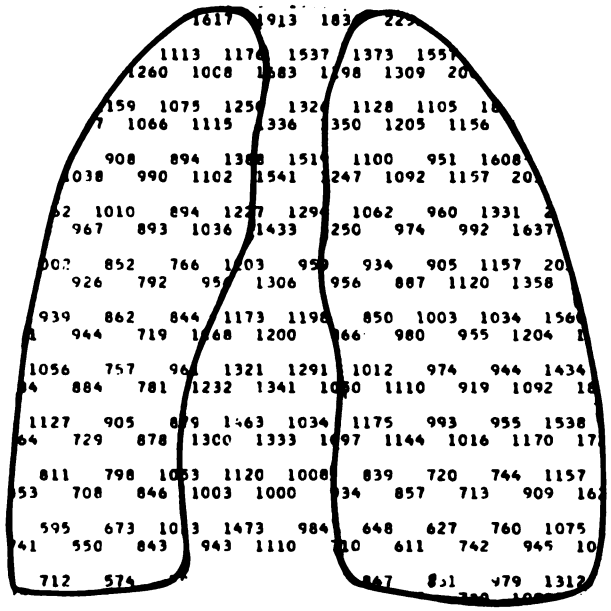

FIG. 3. Ratios of relative ventilated space to perfusion in subject F.J. Value of 1.00 (× 1,000) is indicative of similar proportion of ventilation to perfusion in each of depicted areas of scan.

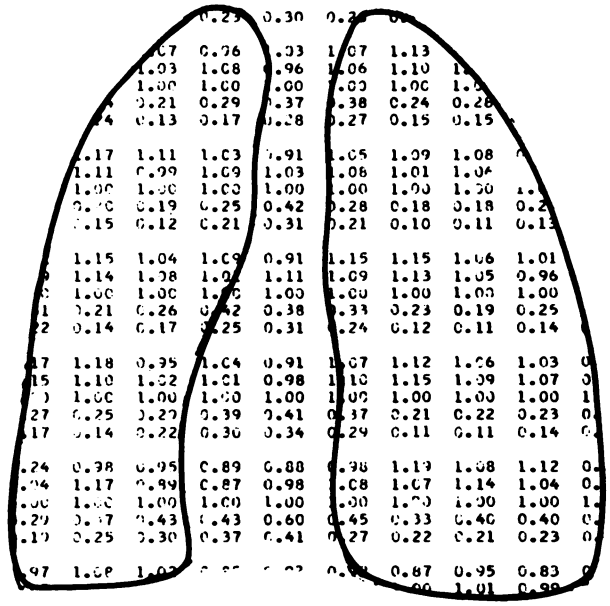

FIG. 4. Regional ventilation in subject F.J. as determined by rate of entrance and egress of ^{133}Xe. Each five-membered set of values denote washin-equilibrium-washout dynamics of 2.40 × 2.70-cm area portrayed (see text).

state scanning techniques lies in the ability to quantitate regional ventilation. Ideally we would like to assign a numerical value for regional ventilation as a fraction of the gas exchange per unit time, and our program is being constantly altered to attain this goal. At the moment we are relying on the washin-washout relationship to define regional gas distribution. For ease of computer display the dimensions of the regional areas measured have been doubled (2.40 × 2.70 cm). Each area contains five members (Fig. 4). The third value in each block is always 1.00, representing the ^{133}Xe activity at equilibrium. The first and second members represent the washin and the fourth and fifth washout, all presented as fractions of the equilibrium value. At this time, six separate readouts (two analog and four digital) are required to derive the essential information in each patient study. These are: the analog maps of "equilibrated ventilation" and perfusion (*2*); the "normalized" digital values for equilibration ventilation and perfusion (*2*); the "ventilation"-perfusion ratio table (*1*); and the washin-washout ratio graph (*1*). It is hoped that as our experience grows, the improvement in techniques and programming may allow simplification of the data display without loss of information content.

RESULTS

To demonstrate the technique described above in the abnormal lung, we have chosen a patient with bullous emphysema. This condition lends itself well to study by nuclear-medical techniques for several reasons. First, the area of involvement can usually be easily identified by simple radiographic techniques (Fig. 5). Second, from the extensive background of previous physiologic investigations, it is expected that there would be abnormalities in both ventilation and perfusion. These would be characterized by a delay in achieving ventilatory equilibrium coupled with a reduction in the rate of rinsing the ^{133}Xe from the involved areas as well as an associated reduction or absence of perfusion to the bullae. Figures 6–9 give the scan data on the subject whose chest roentgenogram was presented as Fig. 5. The analog maps demonstrate that at equilibrium, ventilation appears reasonably uniform but the perfusion study indicates the sharp delineation of the bullous areas (Fig. 6). These visual impressions are confirmed by the "normalized" data (Fig. 7), and the discrepancy between the ventilated and perfused spaces in the areas of bullous disease is well demonstrated in the ventilation/perfusion ratio map (Fig. 8). The

delayed ventilation in the diseased regions can be seen on the washin-washout ratio display (Fig. 9).

DISCUSSION

Many of the pulmonary diseases of major physiologic interest are sharply localized or have great regional variability. The lack of adequate techniques for the assessment of these geographic differences has furnished the incentive to investigate the radioisotopic methods. However, to those investigators demanding quantitative evaluation, the visual scans alone have not sufficed. Obviously both phases, ventilation and circulation, must be studied either simultaneously or as close to that ideal as possible. The information obtained must be available in numerical form and all areas of both lungs should be examined. In view of the sophisticated electronic systems currently available, the attempts to quantitate visual scans by the amount of light transmission through the photographic film rather than directly from count information seems archaic and the use of spot checks of six, 10 or even 12 areas does not appear compatible with the goals sought.

The objections to breath-holding itself as a technique for the study of patients with regional disease have already been mentioned. The recent attempts to use nebulized labeled particles to delineate ventilation are so fraught with artifact and error that even the advocates now consider it more in the nature of a bronchographic demonstration than a measure of air flow (*11*). Since the measurement desired is one of gas flow, it would seem most logical to use a gas for this purpose. ^{133}Xe appears to serve this role adequately. Its short half-life and poor solubility in tissue make it a safe agent. Based on calculations using the spirometer concentration at the beginning and end of the study, and the subjects' previously determined functional residual volume, the amount of gas absorbed is less than 20% and essentially all of this is rapidly excreted in the expired air when the patient is switched into the oxygen-breathing circuit. The relatively small amounts absorbed and the speed and completeness of excretion also appear to negate the possibility that the presentation of the radioactivity could represent other than ventilatory distribution. The often voiced criticism that absorbed material may recirculate by systemic circulation and either by deposition in tissue fat or by tissue capillary flow may erroneously appear as ventilation can be easily disproved. Figure 10 presents the analog ventilatory map in a 67-year-

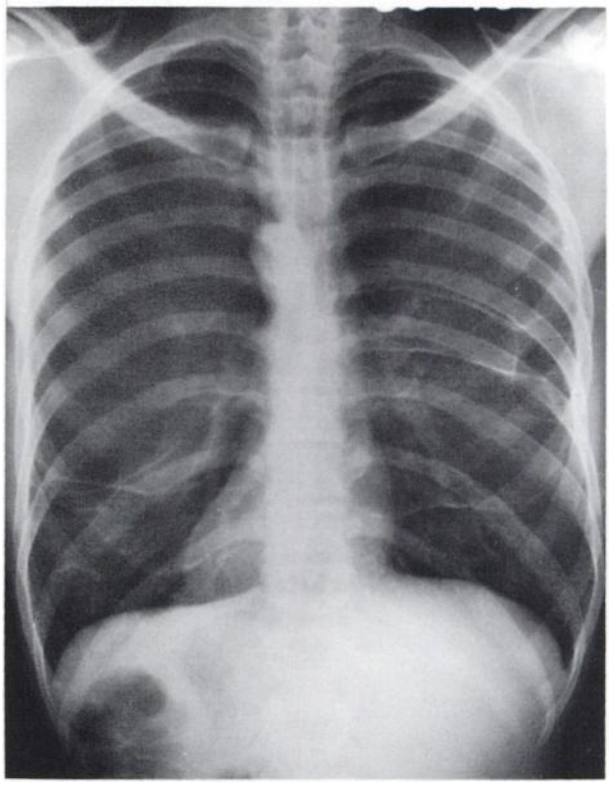

FIG. 5. Chest roentgenogram on patient W.L.H. with bullous emphysema. Left lung is on the viewer's left to correspond with scanning data.

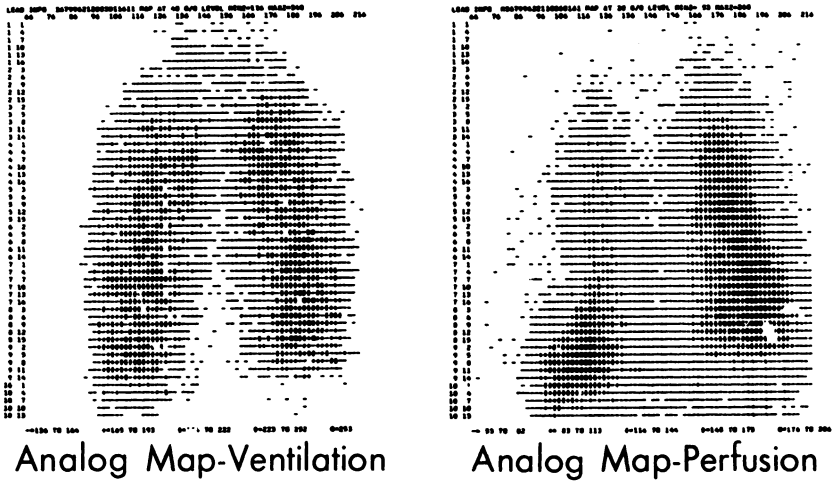

FIG. 6. Seven-level analog maps for ventilation (equilibrium) and for perfusion in patient W.L.H. Markedly reduced perfusion in diseased regions is readily seen.

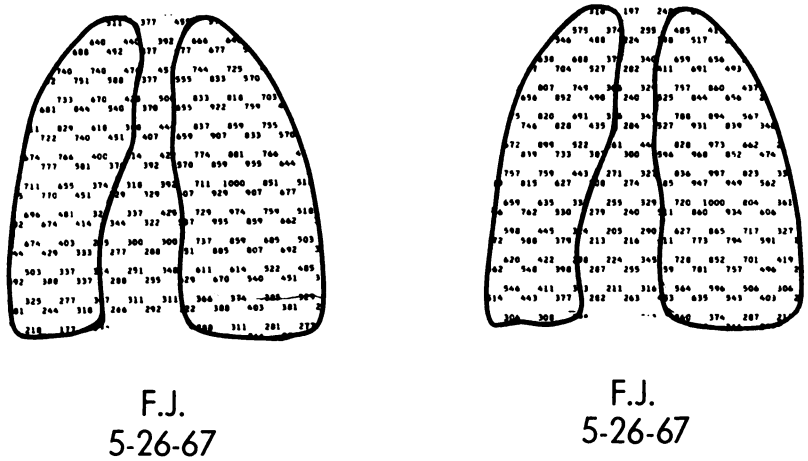

FIG. 7. Normalized ventilation (equilibrium) and perfusion data in patient W.L.H.

old male with a left chronic pneumothorax. The absence of detectible radiation over the *nonlung* containing thoracic cage is immediately apparent.

The major problem in the ventilation scans, as the authors see it, is in the collection of sufficient repetitive data from the same areas over sufficiently short intervals to allow accurate measurement of the rate of accumulation. Work is currently in progress which will allow collection of data accumulated from the areas described at 15–20-sec intervals and will hopefully elucidate this problem. The extensive experience developed with the use of labeled macro-

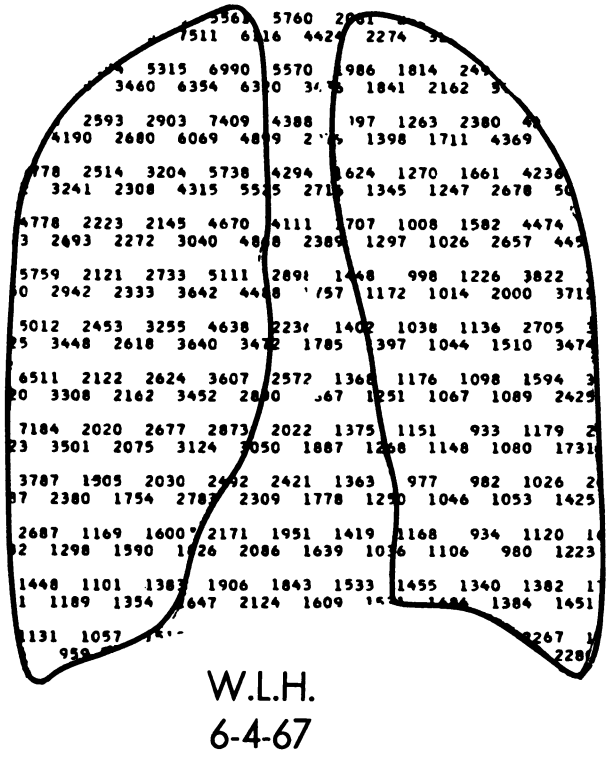

FIG. 8. "Ventilation"-perfusion ratios (× 1,000) in patient W.L.H. Note that in noninvolved areas, relationship of ventilated-to-perfused spaces is close to unity whereas in areas of bullous disease equilibrium ventilation ranges from 2 to 7 times perfusion.

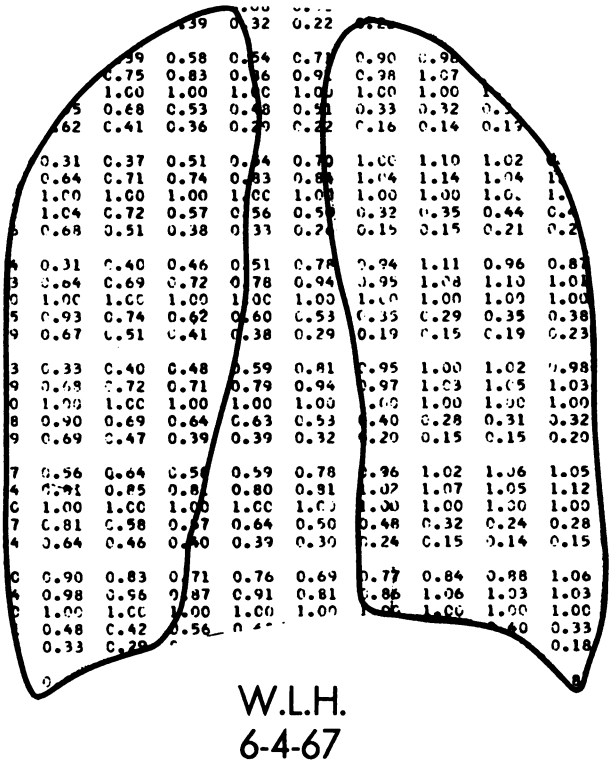

FIG. 9. Washin-washout ratios for patient W.L.H. Ventilation is normal only in area of right lung free of bullae and although greatest abnormality is in diseased portion of left lung, there is evidence of impaired ventilation in compressed areas at left base.

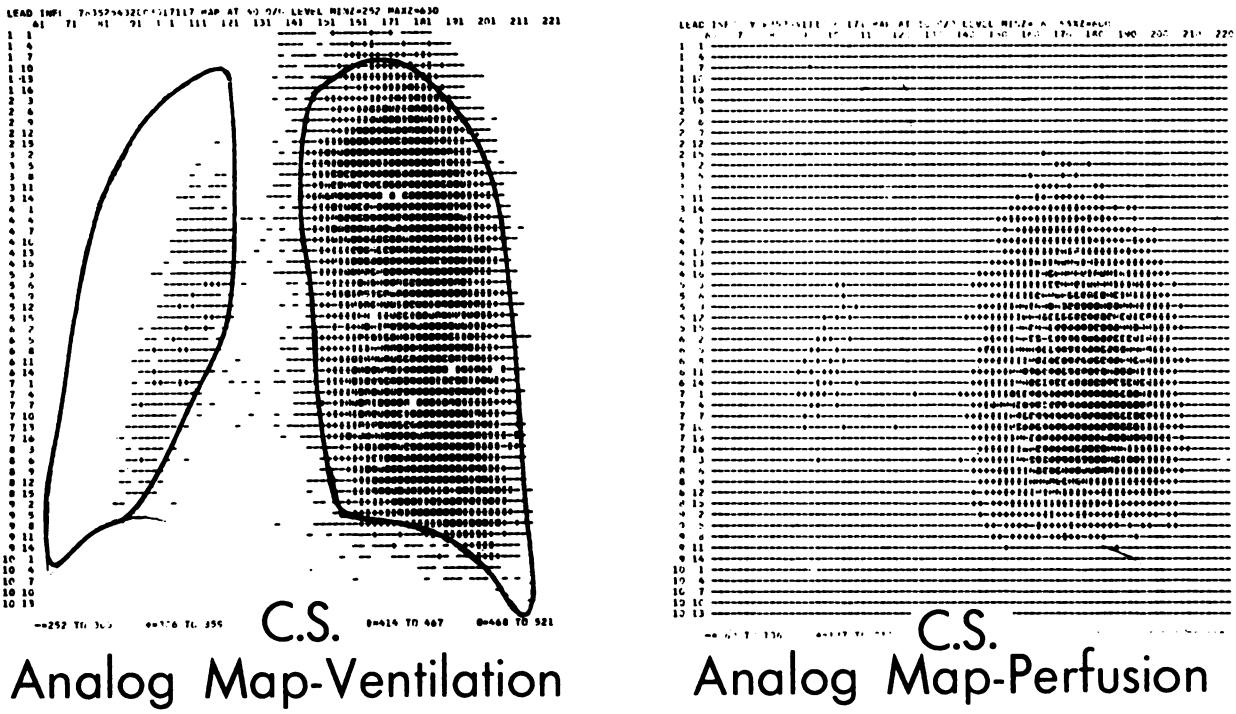

FIG. 10. Analog ventilation and perfusion maps on patient G.S. with large bullous lesion in right apex and chronic left pneumothorax. Absence of radioactivity over nonlung containing left thorax in ventilation scan disproves possibility of nonventilatory representation.

aggregated human albumin indicates that this material is entirely adequate for the purpose desired. When used as recommended, it is a safe agent and the single reported fatality appears to represent an overdosage of the aggregated albumin in this patient with a markedly limited vascular bed secondary to carcinoma (*12*).

Several workers have reported no measurable influence on the diffusing capacity of the lungs for carbon monoxide after MAA injection, further attesting to the safety of the material (*13,14*).

The major disadvantage with the currently available material for physiologic use is its prolonged presence in the pulmonary vasculature. This precludes rapidly repeated studies which might be of value in, for example, the acute effects of therapeutic agents on pulmonary circulation. The possibility of obtaining this type of information from repeated injections of smaller amounts of MAA-^{131}I has been considered and is under investigation in this laboratory.

The theoretical possibility that the macroaggregates do not accurately portray blood flow in the diseased lung does exist. One might postulate that localized areas of reduced circulation might appear as totally devoid of pulmonary arterial flow with the single bolus of macroaggregates, whereas soluble agents in recirculation techniques might detect the presence of the reduced flow. Reference to the study of the comparison of the soluble agent with MAA has been previously made, but it should be noted that this study involved only normal subjects (*6*). The study of Lopez-Majano *et al* (*4*) and Rogers *et al* (*5*) which did compare MAA ^{131}I and bronchospirometry in patients with lung disease did show excellent correlations but this still does not preclude the possibility that small areas of reduced blood flow appeared by scanning as totally ischemic. Comparison of the circulated space determined by tagged MAA with that of a recirculating agent or, for example, labeled erythrocytes should answer the question.

SUMMARY

A method for determining regional pulmonary ventilation-perfusion relationships during the "steady state" by quantitative scintillation scanning is presented using a 10-crystal rectilinear scanner. Regional air distribution is measured by the rates of washin and washout of ^{133}Xe and perfusion is determined immediately thereafter using ^{131}I-labeled macroaggregated human albumin. Data are accumulated and recorded on magnetic tape for computer analysis to obtain numerical presentation.

The method has proven valuable in the assessment of regional pulmonary function in normal subjects and patients with a variety of pulmonary diseases.

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