Measurement of Regional Pulmonary Function
by the Use of Isotopes

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ABSTRACT

The study of radioisotopes to measure regional lung function, using radioactive gas, is presented.

Introduction

Radioisotopes used in the measurement of lung function have made possible the regionalization of measurements of perfusion and ventilation that heretofore have been dependent on measurements of split function, minute ventilation, tidal volume, vital capacity and oxygen uptake measured by differential bronchospirometry or estimates of ventilation and perfusion based on function fluoroscopy and inspiration and expiration chest X-rays. Beginning with the studies of Knipping, there has been increasing use of radioisotopes to measure regional lung function, at first of larger regions of the lung, but more recently as newer methods of instrumentation have been developed, to measure smaller regions. This method will deal only with the use of radioactive gas because radioactive tagged microemboli measure perfusion and not function.

Radioactive gases such as $^{133}$Xenon or $^{15}$O$_2$ are used to measure both perfusion and ventilation. Although $^{16}$O$_2$ has been used in the measurement of regional lung function, it has the disadvantage of a half life of two minutes. $^{133}$Xenon, with a half life of 5.24 days, has been a more practical isotope for clinical use. The material may be either injected as a solution or inhaled as a gas. The use of a gas, rather than particulate matter, should provide a closer approximation to the gas exchange for CO$_2$ and O$_2$ than tagged microspheres or macroaggregate.

The half life of $^{15}$O$_2$ is so short that it is impossible to use unless the laboratory is adjacent to a nuclear reactor. The most commonly used gas isotope is $^{133}$Xenon. This gas is a low energy gamma emitter and is available commercially either in a sterile pyrogen-free solution in normal saline or as a gas. A crucible is also available for use in which an ampoule of one Ci of $^{133}$Xenon gas can be placed and then crushed so that the gas goes into solution in saline. The material is handled easily with proper isotope precaution.

Method

Two commonly used techniques are available for the measurement of radioactivity. The earliest and, until recently, the most...
commonly used equipment for the measurement of radioactivity is the multiprobe system in which either stationary or movable single probes (three to four in a bank over left and right chest) are used to measure radioactivity. Several manufacturers are marketing multiprobe units (four on each side) which are adjustable according to patient size. The output of these units is usually by multichannel strip chart giving counting rates for each probe.

The scintillation camera is becoming more widely used for clinical studies because of its ready availability in most hospital isotope units. This unit enables one to measure radioactivity levels throughout most of the lung at the same time. The camera consists of a large (10.5 to 11 in) crystal with a number of photo multiplier tubes located behind the crystal in such a way that the location of a radioactive particle can be recorded on the X-Y axis and either can be displayed on an oscilloscope or can be stored in a memory unit for transfer to digital tape.

The activity levels shown in figure 1 indicate the outline of 10 percent of maximal activity and show that most of both lungs is included in the matrix when breath is held at resting lung volumes (Functional Residual Capacity plus Tidal Volume). There is ample room at the bottom of the lung for expansion to Total Lung Capacity. A variety of recording and processing systems are available for data handling. A block diagram of the system used is shown in figure 2.

The distribution of blood flow in the lung is affected by gravity with greater perfusion going to dependent parts of the lung. In order to evaluate the effect of gravity change on perfusion, patients are studied in both upright and supine positions. A ten minute period is allowed between change in position for equilibration. Detectors are positioned against the back. In the case of the scintillation camera, the top of the camera is positioned at the dorsal process of the seventh cervical vertebra; the patient is centered over the camera. Many studies of lung function with radioisotopes have involved injections at Total Lung Capacity (TLC). Our patients have been studied at Functional Residual Capacity (FRC) and at TLC for both perfusion and inhalation studies.
Perfusion Studies

A plastic catheter is inserted into a vein directed toward the superior vena cava and is taped in place. A slow drip of 5 percent Dextrose in water is attached to the catheter. When the subject is to be injected, the radioactive Xenon (3 cm) in saline solution (measured in a dosimeter) usually is less than 1 cc in volume and is in a tuberculin syringe attached to a 3-way stopcock. A second syringe filled with 5 cc sterile saline is also attached to the 3-way stopcock. The stopcock is connected to the catheter tube and the patient is instructed in open glottis breathholding. Approximately four or five seconds after injection and flush, which are done rapidly, the patient is instructed to stop breathing for approximately 10 seconds. A strip chart, recording total radioactivity from the camera, shows a plateau as maximum radioactivity is measured. After this is accomplished, normal breathing is resumed. The same procedure is repeated in the supine position at resting lung volumes and at Total Lung Capacity with the patient holding his breath with open glottis at a maximum inspiration of three to four seconds after injection of the bolus. During the perfusion study, the patient has a nose clip on and breathes room air through a one-way valve that either conducts the expired air through an activated charcoal absorber or vents it to the outside.

Inhalation Ventilation

A properly shielded 13 liter Collins spirometer is used. Room air in the spirometer is tagged with 1 mc per liter of 133Xenon. The subject is turned into the circuit which includes a CO₂ absorber at end tidal expiration. After three normal tidal breaths, the subject has a 10 second breathhold and then inspires to TLC for another 10 second breathhold. The subject then breathes to equilibrium over a two minute period or until equilibrium is reached, as measured by the strip chart monitoring the counting rate from the camera.

After the first injection of radioactivity, it is important that measurements of background be made following each individual study in order that these values may be subtracted from each subsequent study.

Calculation

By the authors' method, values for perfusion, clearance, and ventilation are calculated for each of 1,600 sites in a 40 × 40 matrix (figure 1) and data are presented in a digital form on a 1,600 site matrix as well as a computer drawn 3-dimensional model where the z-axis represents level of radioactivity or slope of the clearance curve (figure 3). Relatively low levels of radioactivity are used in this study, thus a smoothing program is required for greater statistical reliability. Perfusion levels are calculated from clearance slopes of radioactivity dur-

![Figure 2. Block diagram of system used in this method.](image-url)
Figure 3. A 3-dimensional computer drawn model illustrating perfusion in the lower model, clearance rate with the z-axis related to rate of clearance in the middle model, and gas exchange (product of perfusion and clearance) in the upper model. The models are illustrated with their respective 1,600 site matrices.

Slopes differ from site to site, dependent both on body position and disease. In the normal lung, for example, the rate of clearance of radioactive gas differs among upper, middle and lower zones of the lung (figure 4). In the diseased lung, the difference in clearance rates may be seen in adjacent sites in a 1,600 site matrix.

Gas exchange potential is estimated by multiplying the slope of the clearance during quiet breathing by the amount of radioactivity deposited following injection. This
states that: gas exchange = ht (perfusion) \times \text{slope (ventilation)} \ (\text{figure 5}). When perfusion is great and clearance is rapid, there will be more gas exchange. When either clearance or perfusion is reduced, gas exchange will be proportionately reduced.

**Discussion**

Measurement of regional lung function at resting levels of ventilation avoids the changes in perfusion and ventilation that occur at other lung volumes.\(^3\) The use of clearance rate following perfusion as a measure of ventilation and as a factor in the calculation of gas exchange assumes that ventilation measured in this manner is limited to perfused air containing alveoli and is closer to true alveolar ventilation than ventilation measured by inhalation of \(^{133}\text{Xenon}\) containing air from a spirometer. There is no way to differentiate by external counting rates whether or not radioactivity is in conducting airways or in alveoli. The use of clearance rate as a measure of ventilation offers advantages over single or multiple breath methods because radioactive gas starts in perfused air containing alveoli; therefore, the rate of clearance is a reflection of alveolar ventilation. Further, variations in regional time constants in diseased lungs may be better identified by clearance techniques than by single breath methods using inhalation from a spirometer.

When ventilation is measured by inhalation of a single breath, it may appear that more ventilation is present than is truly ventilation of perfused alveoli because radioactive gas in conducting airways is
counted just as is radioactive gas in alveoli. Several breathholds are important in the pathological state because regions of lung that are underfused or unventilated at resting lung volumes may be perfused and/or ventilated at TLC. Care should be exercised in the interpretation of ventilation as the amount of radioactivity that can be washed into the lung after repeated breaths. Ventilation and perfusion are time related and therefore measurements of flow/unit time rather than simple volumes. Ventilation measured by equilibrium counts include all but totally obstructed lung regions.

The limit of resolution of the system and of the radioactive gas is approximately 0.75 in so that areas smaller than this may be missed. It should also be remembered that these studies are two-dimensional and that regions of high activity and regions of low activity at different depths in the same area may cancel each other out and appear as normal.

$^{133}$Xenon is highly soluble in rubber or plastic. An assay of radioactivity in a syringe that has been exposed to Xenon may give an erroneously high counting rate. Syringes should be checked for background before reuse.

Clinical Interpretations

The practical application of these techniques has been of clinical value. The measurement of regional gas exchange (perfusion x clearance) has provided a means of evaluating regional lung function as a measure of the efficacy of treatment or as a means of preoperative evaluation in lieu of differential bronchospirometry. Measurement of regional gas exchange has proved to be a more effective approach to the clinical evaluation of such disease as cystic fibrosis than measurement of ventilation-perfusion ratios. The difficulty of arriving at true equilibrium in the diseased lung by rebreathing methods seriously hampers the usefulness of the V/Q indices as described by Ball, West and others in the practical clinical situation.

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References


Academic criteria in need of resurrection: "Structured curricula instead of the 'cafeteria' style of education that is so often confused with intellectual freedom; objective standards and criteria of evaluation instead of the currently fashionable chaos of subjectivity; respect for hard intellectual labor instead of the cult of self-expression and 'creativity'; an understanding of the values of specialization instead of an orgy of 'interdisciplinary' chitchat."

Peter L. Berger