
Aerosol Penetration Ratio: A New Index of Ventilation

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Superimposition of nuclear medicine scintigrams and standard radiographs provides a unique opportunity for merging functional information intrinsic to nuclear medicine images with the high resolution anatomic detail of radiographs. A newly developed image processing system allows the merging of two separate films of greatly varying sizes to form a single composite image. Subsequent quantitative analysis of the composite image may be performed. Using the superimposition technique, [^{99m}Tc]DTPA aerosol ventilation scans (4.5 × 4.5 cm) were superimposed upon chest radiographs (35.6 × 43.2 cm) in 17 cystic fibrosis (CF) patients. Subsequent quantification of the area of nuclear scan ventilation and the radiographic lung area was then performed. A new quantitative radiologic index of ventilation, the aerosol penetration ratio (APR), was defined. Linear correlation of aerosol penetration ratio with residual volume (RV) as percent of total lung capacity (TLC) measured by body plethysmography was good. We conclude that the APR has validity as a physiologic parameter which localized regional excessive residual volume and correlates well with RV/TLC, the "gold standard" pulmonary function index of obstructive airway disease.

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Traditionally, nuclear medicine imaging provides a measure of dynamic function, while standard radiography displays high resolution anatomic detail. By superimposing radiographs and nuclear medicine scans, a precise anatomic distribution and quantification of functional abnormality can be portrayed with great clarity. Several investigators have demonstrated that in chronic obstructive lung disease, there is good correlation among numerous measurements on standard PA and lateral chest radiographs with corresponding pulmonary function tests (1-6). Using cystic fibrosis as a prototype of chronic obstructive lung disease, we have studied the superimposition of technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) aerosol ventilation scans with standard radiographs to determine its possible clinical applicability.

MATERIALS AND METHODS

Seventeen patients with CF (13 male, four female) ranging in age from 13 to 25 yr underwent ventilation imaging using

a [^{99m}Tc]DTPA aerosol. The diagnosis of CF was established by the Gibson-Cook titration method (8). Seven of these patients had more than one aerosol study performed. Standard PA and lateral chest radiographs (10-ft tube film distance, 120 kV) were obtained within 1 wk of the ventilation study. All patients had body plethysmography performed on the same day or within several days of the aerosol study.

The aerosol studies were performed using a commercially available system* which delivers particles with an average diameter of 0.5 μ. For each study, 40-60 mCi of [^{99m}Tc]DTPA in a volume of 2.0 ml of sterile water containing 10% ethanol by volume was placed into the nebulizer. The ethanol was added prior to the commencement of the ventilation study in order to increase the efficiency of aerosol delivery (9). The flow rate of oxygen through the nebulizer was 10 l/min. The patients were placed supine with a nose clip in position. They were instructed to take slow, deep breaths through a mouthpiece attached to the aerosol device. At least 3 min of nebulized breathing was necessary to obtain a count rate of 5,000-8,000 cps. A wide field-of-view gamma camera with a LEAP collimator acquired 500k count images in the anterior, posterior, right and left lateral LPO and RPO projections.

Images from [^{99m}Tc]DTPA aerosol ventilation scans measuring 4.5 × 4.5 cm were superimposed with chest radiographs measuring 35.6 × 43.2 cm using a newly developed video imaging system† (Fig. 1). This imaging system is comprised of two independently operated video cameras and a rear-illuminated viewing station. A device for mixing the video signals

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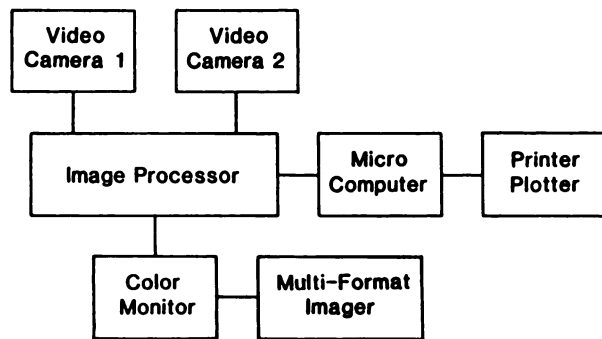


FIGURE 1
Schematic block diagram of video imaging system. Video camera 1 and 2 are independently operated. Signals from both cameras are merged and digitized within image processor. Color monitor, printer-plotter, and multi-format imager are available for image storage

from both cameras creates a composite analog image on the display monitor. Differential zoom lenses (15–150 mm) and an image “stretch” control allow for proper registration of the smaller nuclear scan upon the chest radiographs. The composite analog image can then be digitized (512 × 512 pixels) to permit various quantitative analyses, including area measurement on a pixel by pixel basis. The system resolution is approximately three line pairs per millimeter in the normal mode and five line pairs per millimeter when magnification is used (7).

The process of superimposing ventilation scans upon the chest radiographs with subsequent measurement of aerosol penetration ratio (APR) is performed in several stages. These stages are:

1. Creation of the radiographic mask.
2. Registration of the ventilation scan upon the chest radiograph with subsequent background subtraction of the ventilation scan.
3. Determination of the number of pixels comprising both the radiographic mask and the ventilation image with subsequent calculation of APR (see below).

The radiographic mask is created in the following manner. Using standard PA and left lateral chest radiographs in full inspiration, four separate radiographic masks were drawn (right lateral, left lateral, anterior, and posterior). A hand held light pen traced the lung area of the chest radiograph. The lung boundaries on PA chest radiograph consisted of the diaphragm inferiorly, lateral margins of the vertebral column medially and pleural margins laterally and superiorly. The PA chest radiograph is used to create both anterior and posterior radiographic masks which differ only in the inclusion of the heart shadow within the area of posterior radiographic mask. The left lateral radiograph is used to produce both the right and left lateral radiographic masks which are identical. The right and left lateral radiographic masks are bound by the diaphragm inferiorly and pleural margins posteriorly, superiorly, and anteriorly.

Creation of ventilation images of proper size for optimum superimposition with the chest radiography is a subjective procedure. Structures such as diaphragm, hypopharynx, trachea, and soft tissues of the chest wall are used to align and size the ventilation image upon the radiographic mask.

Registration of the ventilation scan upon the chest radiograph is performed in the following manner. In similar projection (e.g., left lateral ventilation scan upon lateral chest radiograph), the ventilation scan is imaged by camera 2 and the chest radiograph by camera 1. Differential zoom control and image stretch controls on camera 2 are manually adjusted so that various nuclear imaged structures (hypopharynx, diaphragm, heart, trachea, and soft tissues of the chest wall) are in proper registration with the identical structures imaged by the chest radiograph. Once proper registration of the lung ventilation scan upon chest radiograph is achieved, a 10% background subtraction of the nuclear scan is performed. The background subtracted ventilation image is then stored within computer memory and the total number of pixels comprising the area of nonzero pixels is measured. Typically, 8,000–15,000 nonzero pixel elements comprise a single ventilation image. The corresponding radiographic mask is recalled from computer memory and a similar calculation of number of pixels comprising the radiographic mask area is performed.

Figures 2A and 2B illustrate an example of the radiographic mask and the properly registered and background subtracted ventilation scan. The process of superimposition of ventilation scan with the radiographic mask is repeated in the right lateral, left lateral, anterior, and posterior positions. Ratios of number of pixel elements in ventilation image/number of pixel elements in radiographic mask in each of the four projections (anterior, posterior, right lateral, left lateral) are calculated. The arithmetic average of these ratios provides for identification of a new radiologic index of ventilation, the aerosol penetration ratio:

$$APR = \frac{1}{4} \sum_{i=1}^4 R_i \text{ where}$$

$$R_i = \frac{\# \text{ pixels in the ventilation scan}}{\# \text{ pixels in the radiographic mask}}$$

in the *i*th projection.

In order to assess “goodness of fit” of the superimposition technique in normal controls, three healthy volunteers had both [^{99m}Tc]DTPA aerosol scans and standard chest radiographs with two lead-backed cobalt-57 (⁵⁷Co) markers placed over the eleventh ribs at midaxillary position. Superimposition of hypopharynx, heart, diaphragm, and the bilateral lead-backed ⁵⁷Co markers was performed and the APR was subsequently measured.

We also investigated possible variation of APR caused by superimposing aerosol scans, (which are time-integrated during tidal volume breathing) with chest radiographs taken both in deep inspiration and during stopped tidal volume breathing of three CF patients. Lead-backed ⁵⁷Co markers were positioned over the lateral eleventh ribs for both aerosol scans and chest radiographs.

RESULTS

Correlation of the APR with the residual volume expressed as a percent of total lung capacity is demonstrated in Fig. 3. The linear correlation of APR with RV/TLC is good ($r = 0.747$, $p < 0.001$); the APR measured in the normal control population is $98.5 \pm 0.6\%$.

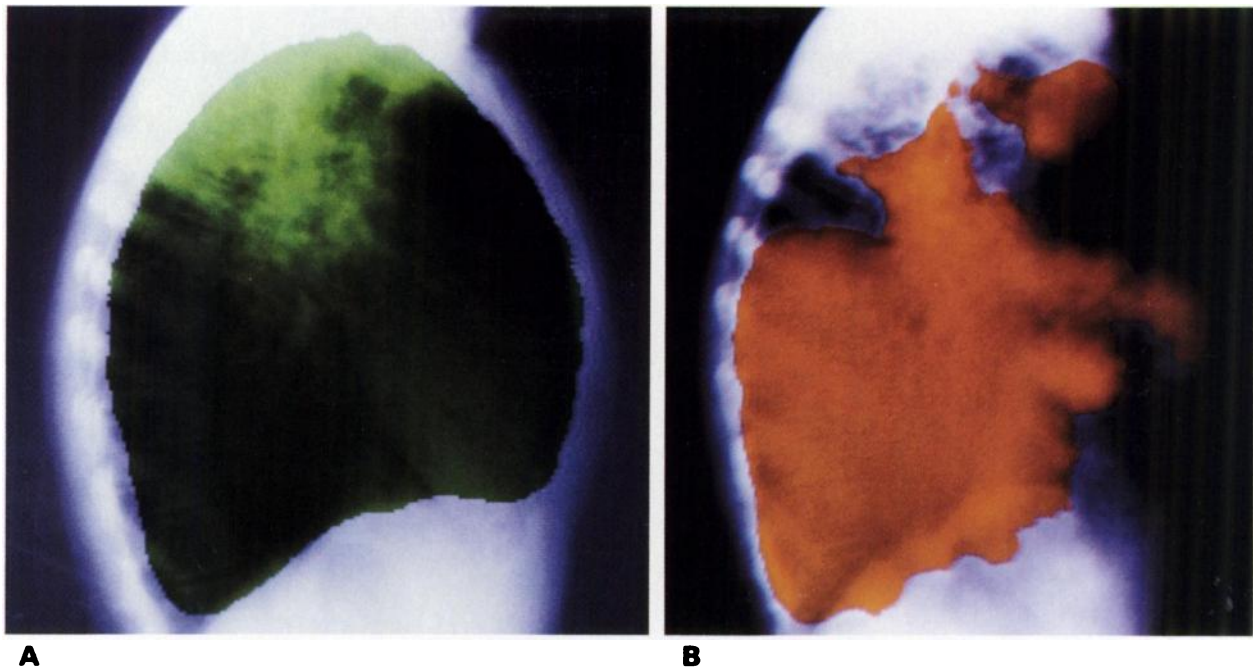


FIGURE 2

A: Example of lateral radiographic mask (in green). B: Superimposition of corresponding right lateral [^{99m}Tc]DTPA aerosol ventilation (properly registered and 10% background corrected) scan upon lateral chest radiograph

Percent variation of APR measured with superimposition of [^{99m}Tc]DTPA aerosol scans upon chest radiographs taken in deep inspiration and stopped tidal volume breathing is $2.2 \pm 0.7\%$.

Measurement of intraobserver and interobserver variability was made by selecting six matched ventilation scans and chest radiographs from randomly selected CF patients. Twenty four ratios R_i , were measured in right and left lateral, anterior, and posterior projections on two separate occasions separated by 6 wk by Observer A(S.S) and Observer B(P.J). Neither observer had any prior knowledge of the previous results. Results of intraobserver variability for Observer A and Observer B demonstrate excellent reproducibility of measurements ($r = 0.951$ and $r = 0.978$, respectively). Interobserver variability measured by average percent variability is $5.3 \pm 4.8\%$.

DISCUSSION

Cystic fibrosis (CF) is the most common lethal genetic disease of Caucasians. It is a progressive disease in which tenacious mucous secretions obstruct the small airways. As the lung disease progresses, the volume of trapped air distal to obstructions increases, causing an increased total lung capacity. Therefore, the residual volume, expressed as percentage of total lung capacity, increases as CF lung disease progresses (10,11).

Several investigators have applied measurements of chest radiographs to estimate pulmonary function tests in chronic obstructive lung disease (1-6). Salem and Warwick have described the use of planimetric techniques using plain chest radiographs in CF for the determination of TLC (1). We have shown that the degree of aerosol penetration measured by superimpo-

sition technique of [^{99m}Tc]DTPA with chest radiographs with subsequent measurement of APR has an excellent linear correlation with the quantity RV/TLC, a clinical useful "gold standard" in assessing severity of airway obstruction.

A potential problem in the measurement of the APR, that of "shine-through" from contralateral lung does exist with our superimposition technique which utilizes four orthogonal projections. However, we feel that the effect from "shine-through" is minimized for two reasons. First, the APR is comprised of ratios in four projections, only two of which, the right and left lateral projections, are subjected to overlap of contralateral lung. Therefore, "shine-through" only effects two of the four terms in calculations of APR. Second, those instances in which one lung is essentially nonventilated are apparent on the anterior and posterior projections permitting exclusion of that lateral projection from the determination of APR. In this manner, the effect of "shine-through" is minimized.

A second potential problem of the superimposition technique is misregistration of the aerosol ventilation scan with the chest radiograph. With careful attention to proper superimposition of the diaphragm, pleural margins, heart, and trachea, error from misregistration is minimized. Independent measurements of APR by two observers show the APR to be highly reproducible. Moreover, comparison measurements of APR with and without lead-backed ^{57}Co markers show no significant differences. Also, no significant differences of APR were measured when superimposing aerosol scans with chest radiographs taken in deep inspiration and chest radi-

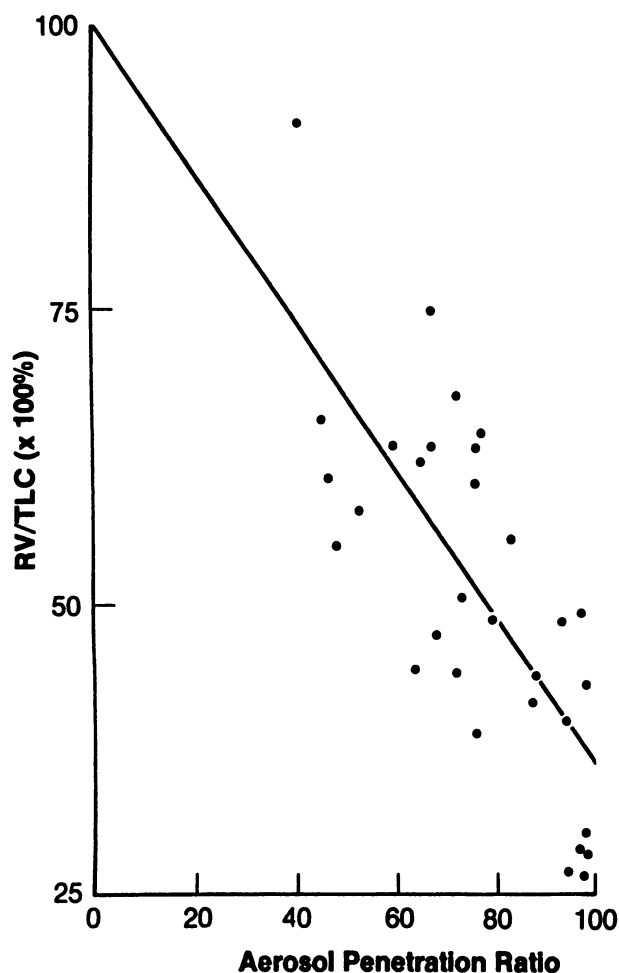


FIGURE 3
Correlation between aerosol penetration ratio and RV/TLC in 17 CF patients. Seven patients had repeat examinations. Solid line is linear regression ($r = 0.747$, $p < 0.001$)

ographs taken in stopped tidal volume breathing. We believe that although superimposition of ventilation scan with the radiograph is a subjective procedure, meticulous attention to technique will result in accurate and reproducible measurements of APR.

Further investigation of the clinical utility of APR in CF, currently in progress, suggests that changes in APR will be useful in assessing efficacy of therapy in hospitalized CF patients. The radionuclide ventilation image shows the exact regional localization of the excessive residual volume, a result not obtainable with total-body plethysmography. The measurement of APR provides for quantification of the excessive residual volume. For these reasons, the radionuclide technique described here is of value for the anatomic demonstration of regional

excessive residual volume and will be useful in the assessment of therapy in chronic obstructive pulmonary disease.

FOOTNOTES

* Ultra Vent, Diagnostic Products Div., Mallinckrodt Inc., St. Louis, MO.

† Measuronic, Inc., Great Falls, MT.

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