INSTRUMENTATION

In Vivo Regional Quantitation of Intrathoracic Tc-99m using SPECT: Concise Communication

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A whole-body single-photon emission computed tomographic system (SPECT) was used to quantitate the activities of a series of Tc-99m point sources in the dog's thorax and to evaluate attenuation of a uniform esophageal line source containing a known concentration of Tc-99m.

A first-order attenuation correction and an empirically derived attenuation coefficient of 0.09 cm^{-1} were used in the SPECT analyses of the intrathoracic point sources. The relationship between SPECT measurements of multiple point-source activities and the same sources measured in air was linear over a range of 100 to 1000 μCi (slope 1.08; R^2 coefficient of determination 0.97). These data are sufficiently accurate to allow an estimate of the regional activity of radiopharmaceutical in the dog's thorax and justify their use in experimental quantitation of regional pulmonary perfusion.

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The three-dimensional imaging properties of multislice imaging systems using single-photon emission computed tomography (SPECT) improve the spatial portrayal of a radionuclide when compared with conventional studies of large organs, especially the liver and the lung (*1*,*2*). Desirable characteristics of camera-based SPECT systems include total volume imaging, elimination of overlying and underlying radionuclide activities, increased contrast for centrally located lesions, and a potential for quantitative measurements of regional tracer concentrations and volumes. There are many factors affecting quantitation using the SPECT system. The most significant include:

1. Gamma camera/collimator performance characteristics (system sensitivity and calibration, spatial and energy resolution, regional sensitivity variations, and spatial distortions).

2. Physical aspects of the measuring process (attenuation, Compton scattering, and total number of detected photons).

3. Factors relating to the reconstruction process (spatial filter, interpolation, linear and angular sampling, and the accuracy of the algorithms used to compensate for attenuation, Compton scattering, and imperfect spatial resolution).

4. Effects of patient or organ motion and temporal changes in the tracer distribution (*3*).

We have previously shown that our dual SPECT system using a large-field-of-view scintillation camera can determine accurately the regional radiopharmaceutical concentration of a distributed source in a uniformly attenuating cylinder 22 cm in diameter (Fig. 1) (*4*). In this study we have first established that our system can determine accurately the radioactivities of widely separated point sources in air and in a water-filled phantom. We have then used the system to determine the accuracy of measurement of the radioactivities of widely separated Tc-99m intrabronchial point sources and an esophageal Tc-99m line source in the dog's thorax.

Accurate quantitation of regional tracer concentration in the dog's thorax offers considerable promise in the study of regional pulmonary and cardiac perfusion, regional pulmonary ventilation, distribution of inhalant droplets, and pulmonary and cardiac metabolic activity.

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METHOD

Separated Tc-99m point sources of known activity, ranging from 10 to 800 μCi, were scanned in air with a tomographic unit.* The SPECT unit used in the animal and phantom studies consisted of a rotating gantry on which were mounted two large-field-of-view scintillation cameras (equipped with low-energy all-purpose collimators) rotating through 360°. The system operated with a 8/32 minicomputer† with 256 kbyte of memory and a microprocessor control display system with image memory. A 360° cycle time of 26 min was chosen for the study (*1*). The activities of the sources were measured using the SPECT system (*4*) and compared with the true activities as determined by well counting to establish the accuracy of the SPECT measurements over a wide range of field positions between the camera heads. Regions of interest (ROIs) encompassing the images of the point sources were used to obtain SPECT counts from the reconstructed transaxial images. A voxel was included in the ROI if it were located within approximately three resolution distances (3 × 1.3 cm) from the centroid of the image of the isolated radionuclide source.

The total activity A of an isolated radiating source can be estimated from a set of contiguous SPECT sectional images by summing the SPECT measured count rate N_{ijk} per voxel over a three-dimensional region of interest containing the image of the source:

$$A = C \sum_i \sum_j \sum_k N_{ijk}, \quad (1)$$

where C is a calibration factor related to the detection efficiency of the camera/collimator system (scintillator efficiency, collimator sensitivity, energy window) and the normalization of the reconstruction process (*4*). This nearly time-invariant "constant" factor can be determined by using a calibrated standard source, or by using an independent measurement of a test source (e.g., with a well counter) to compute a value for C. For this investigation the calibration constant C was determined by comparing SPECT scan data of a point source in air with measurements of that source made in a well counter.

Ten mongrel dogs weighing between 25 and 32 kg were then studied. The dogs were anesthetized and intubated. Three widely separated fine catheters (0.05 mm i.d.), each containing a pertechnetate (Tc-99m) source of known activity (length 1.0–2.0 cm) molded into the catheter tip, were introduced into the peripheral bronchial tree of each dog. The pertechnetate activity in the catheter tips ranged from 100 to 1000 μCi. The positions of the catheters were confirmed fluoroscopically and radiographically. Body-contour measurements were acquired simultaneously with primary photopeak projection data either using a Xe-133 line transmission source or, alternatively, gamma radiation that had undergone Compton scattering. These body-contour data are required by the multiplicative attenuation compensation technique used in determining tracer distribution (*1*). At the completion of the study the intrabronchial point sources were then removed and scanned in air by the tomographic unit. Count rates were again determined using ROIs that completely encompassed the images of the point sources. An empirically derived attenuation coefficient value $\mu = 0.09$ cm^{-1} was applied to the in vivo data in the algorithm for first-order attenuation compensation, and a comparison was made with the decay-corrected SPECT evaluation of the point sources in air. This average value for the attenuation coefficient was determined by reconstructing the same point-source data using a range of values (from $\mu = 0.07$ to 0.14 cm^{-1}) and comparing the in vivo count rates with those measured in air. A similar experiment was also performed using the esophageal line source (see below). An analysis of these data indicated that values ranging from 0.08 to 0.10 cm^{-1} provided reasonable compensation for the complete set of 32 transverse sections. In this paper we adopted a constant value of 0.09 cm^{-1}.

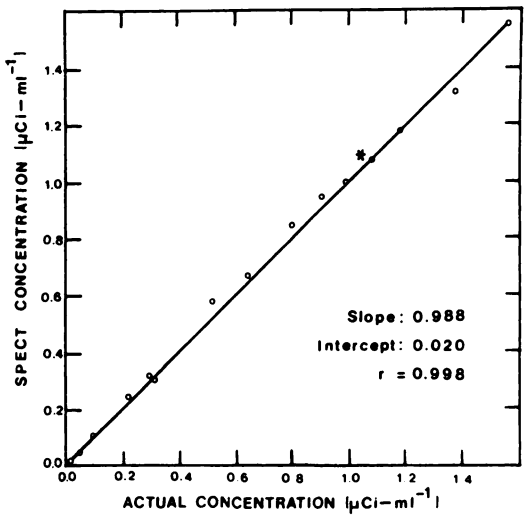

FIG. 1. Relationship between calculated SPECT concentration (μCi/ml) and actual concentration of distributed extended source in a cylinder 22 cm in diameter. A constant calibration factor was determined using the Tc-99m 1.08 μCi/ml source.

An esophageal line source containing pertechnetate, 90 μCi/cm, was introduced into each dog's esophagus and a SPECT scan performed. Body-contour measurements were again acquired simultaneously using the above-described methods. The line source was then removed and scanned by the tomographic unit in air. The data from these two SPECT examinations consisted of 32 contiguous transaxial slices, each 6.4 mm thick. In the in vivo study the 32 slices extended from distal to proximal esophagus. Decay-corrected SPECT count rates obtained from ROI data with and without the application of the first-order attenuation compensation were compared with the SPECT line-source data in air.

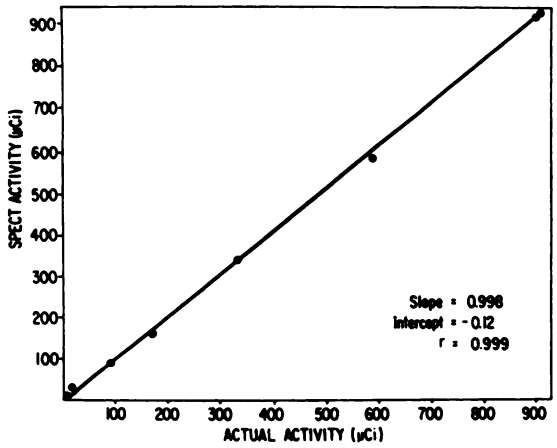

FIG. 2. Relationship between calculated SPECT-measured activity of point sources in air and actual activity (μCi).

RESULTS

Figure 2 relates the SPECT estimates of the various Tc-99m point activities (in air) to the actual activities. The data show that the system's linearity is maintained over a wide range of activity.

The intrathoracic point-source data are shown in Fig. 3. The results show that the SPECT determination of radioactivity in isolated point sources in a dog's thorax is also linear over a wide range. Furthermore, the empirically derived attenuation coefficient of 0.09 cm^{-1} and the first-order compensation allow an accurate determination of regional point-source radioactivity.

The esophageal line-source study demonstrates the nonuniformity of attenuation in a dog's thorax (Figs. 4A and 4B). These studies, two of which are illustrated, show some of the limits involved in using the average μ of 0.09 cm^{-1}. In the distal esophagus the average attenuation of gamma photons for the 360° angular range used for

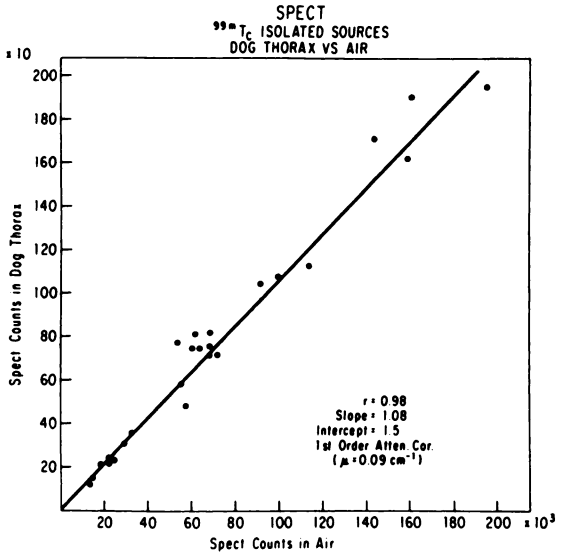

FIG. 3. Relationship between SPECT counts from isolated point sources distributed widely in dog's thorax and same sources in air ($p < 0.01$).

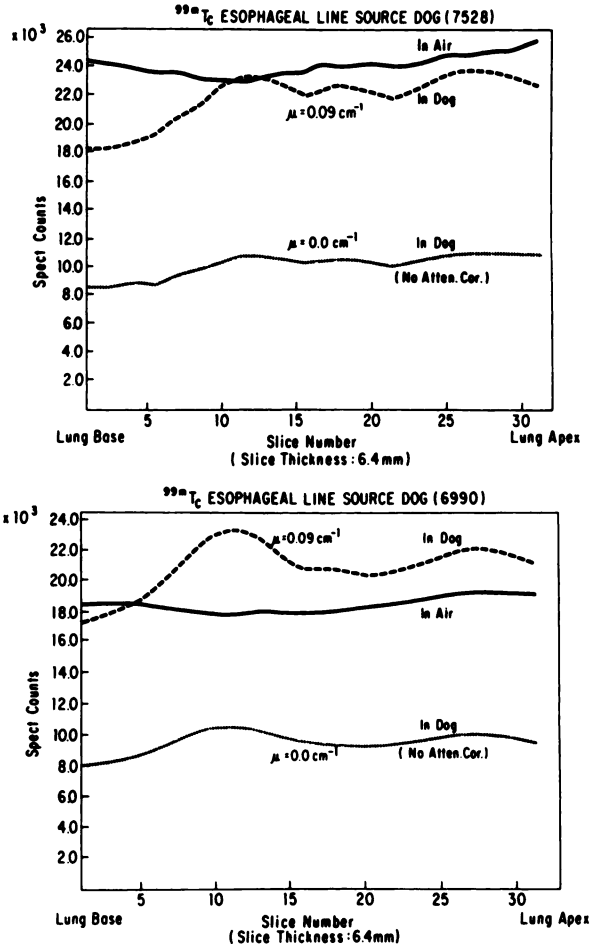

FIG. 4A, 4B. Line-source evaluations in dog esophagus and in air. SPECT counts obtained from ROI data are shown for each of 32 contiguous transaxial images. First and last slices correspond to lung base and apex. Value of μ = 0.09/cm was used for attenuation coefficient with the first-order algorithm. Data indicated by μ = 0.00/cm has not been compensated for attenuation. Note increased attenuation at lung base due to effects of heart and liver.

the collection of projection data is greater than at the mid and upper esophageal levels. The slight variation seen in the measurement made in air probably results from residual sensitivity variations in the intrinsic camera response, although a flood compensation algorithm is routinely used. We are currently upgrading our SPECT system by replacing the present Anger detectors with others having correction circuitry for sensitivity and distortion. We anticipate an improvement in SPECT quantitation with the use of these sophisticated cameras.

DISCUSSION

Despite the fact that the thorax attenuates gamma activity nonuniformly, a first-order multiplicative attenuation compensation technique and an empirically derived attenuation constant of 0.09 cm^{-1} allow an accurate estimation of the activity of widely separated point

sources in the dog's thorax. The average attenuation coefficient for each SPECT section could be determined by performing a transmission CT scan and boundary detection techniques to compute more accurate regional values for the attenuation coefficient. Similar methods have been proposed for positron ECT systems (*5*). Linearity is maintained over the range investigated (100–1000 μCi). We chose to evaluate point sources in our study to minimize the effects of Compton scattering and finite spatial resolution. Although spatial resolution degrades significantly with distance from the surface of parallel-hole collimators, the spatial resolution in the reconstructed SPECT image plane is reasonably uniform (13 ± 1 mm) (*4*). Furthermore, as a result of relatively fine sampling (6.4 mm) along the long axis of the patient, our SPECT system exhibits longitudinal resolution that is comparable to the resolution within the reconstructed plane (*4*).

We have shown that the SPECT-measured image contrast of spherical sources placed in a uniform background is degraded more for small-diameter spherical sources than for larger-diameter sources, this being a result of the finite resolution of the SPECT system (*4*). The image contrast C_{image} is defined as

$$C_{image} = \frac{[\text{Counts/pixel}]_{sphere} - [\text{Counts/pixel}]_{background}}{[\text{Counts/pixel}]_{background}}. \quad (2)$$

The image contrast is also degraded by the inclusion of Compton scattered photons (*4*). The actual object contrast, $C_{obj} = Q_s - Q_b$, where Q_s and Q_b are the radionuclide concentrations in the sphere and background, respectively, is related to the SPECT-measured C_{image} as follows:

$$C_{obj} = C_{image}(CF_{avg})^{-1}(1 + SF_{avg})^{-1}, \quad (3)$$

where SF_{avg} is the average scatter fraction (~0.4) of the system for the particular source geometry (*4*). CF_{avg} is an average contrast factor that compensates for the finite spatial resolution of the SPECT system. The contrast factor can be computed numerically if the system's spatial resolution and the diameter of the sphere are known or can be measured. Published, tabulated values for contrast factor (CF) (*6*) result in accurate SPECT-measured concentration ratios (provided a compensation algorithm is also applied for Compton-scattered events) over a wide range of values (*4*). The contrast factor approaches unity for diameters greater than two or three times the SPECT spatial resolution (FWHM). This implies that larger objects can be quantitated directly, but, careful compensation techniques are required for smaller sources. It is often possible to measure the size of the source directly from the multislice SPECT data. Alternatively, complementary imaging modalities such as TCT or ultrasound can be used. If the source dimensions cannot be readily determined, there remain three options: (a) recognize and accept the inherent error of the measurement as we have described above; (b) for isolated structures surrounded by little or no background activity, it is possible to measure the total radioactivity contained in the structure; or (c) perform relative rather than absolute measurements by utilizing an internal standard that, for example, might be a known normal structure of the same size symmetrically located within the field of view.

Additional work is required to determine the effect of Compton "crosstalk" resulting from extended sources. However, we have found (to be published) that regional quantitation is possible in the animal thorax model (using Tc-99m microspheres) by setting the SPECT count rate for the total lung region equal to the total injected dose (in μCi). The calibration factor determined in this manner can then be used to measure radionuclide concentrations (μCi/ml) using relative regional count-rate measurement limited by the crosstalk resulting from respiratory motions and the system's finite spatial resolution.

The nonuniform attenuation of the thorax is nicely demonstrated in the esophageal line study. From the distal esophagus, attenuation of radiation is greater than at the mid and upper levels. This is probably due to the presence of the heart and liver in the lower third of the thorax and upper abdomen. For specific studies in the lower third of the thorax it seems likely that an attenuation factor greater than 0.09 cm^{-1} should be used. Respiratory motion has undoubtedly degraded the data but its effect is averaged during the 26-min acquisition time used in our studies and does not affect the count rates determined using ROIs that completely encompass the point-source images. Inaccuracies in the measured body contour may also contribute to the observed errors. The current body-contour algorithm results in only a single body contour located near the central reconstructed transverse slice. This same contour is then used for the remaining transverse slices.

The technique for attenuation compensation used in these studies was a multiplicative correction (*7*). The correction matrix value $C_{att}(X,Y)$ for a point (X,Y) is computed and is inversely proportional to the average attenuation observed by that point for all angular samples. An improvement in attenuation compensation can be made by reprojecting the first-order corrected image to generate a set of projections that are then compared with the original projections to obtain a set of error projections. The resulting error image multiplied by C_{att} is added to the first-order-corrected image to obtain the final image. This second-order attenuation compensation significantly increases the processing time and also increases noise in the reconstructed image. The first-order correction provides an adequate compensation for most

evaluations and was used in this investigation.

In practical terms, this study has shown that isolated regional radiopharmaceutical activities can be determined accurately in vivo in the dog thorax, but before an accurate evaluation of the regional radionuclide concentrations in a Tc-99m perfusion lung scan is possible, additional work will be required to determine the significance of the increased Compton "crosstalk" in an extended source. Other potential sources of error in the estimation of regional radionuclide concentrations include changes in lung volume between inspiration and expiration. This affects the concentration of activity per milliliter of lung tissue, which is seen by the cameras to vary during each respiratory cycle. Its effect has not been determined but it could be minimized by gating so that projection data are collected from only a selected segment of the respiratory cycle, at the cost of more time.

This study was a first step in determining the accuracy of our SPECT system in measuring intrathoracic regional radionuclide activities in vivo. Accurate measurements of regional radionuclide activity potentially have many applications in medicine, including the quantitation of regional pulmonary perfusion, which can be performed with a slight modification of standard radiolabeled microsphere techniques (*8–10*). Accurate in vivo noninvasive measurements of regional perfusion will appreciably enhance our understanding of pulmonary physiology and pathology.

SPECT scanning can readily be performed in man and offers the same potential as in the experimental animal model. We are undertaking further work to develop the resolution, attenuation, and scatter compensation methods appropriate to human subjects so that SPECT scanning can be utilized to determine quantitatively the concentrations of intrathoracic tracers.

FOOTNOTES

* Siemens Gammasonics, Inc., 2000 Nuclear Drive, Des Plaines, IL 60018.

† Perkin-Elmer, Inc., 2 Crescent Pl., Oceanport, NJ 07757.

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