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A Clinical Comparison of Xe-127 and Xe-133 for Ventilation Studies

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Xenon-133 and xenon-127 were compared by performing ventilation studies with both radionuclides in 19 patients with a variety of lung diseases. Assessment of the counting rate over the chest, relative to the radioactivity in the lungs, permitted the evaluation of each isotope in terms of usable photons detected by a scintillation camera with a large field of view and appropriate collimation. A greater photon yield was obtained with Xe-127. Markedly improved resolution was shown by measurement of a line phantom, but was not apparent on subjective appraisal of scintiphotos except in the washout phase. Xenon-127 appears to be preferable to Xe-133 because of the higher counting rates, lower patient radiation dose, and longer shelf life. In addition, a prior perfusion study using a Tc-99m radiopharmaceutical does not affect the quality of a Xe-127 ventilation study. The use of Xe-127 therefore permits the selection for ventilation studies of only those patients with suspected pulmonary embolism, and eliminates unnecessary radiation exposure. A further improvement in image quality obtained with Xe-127 should be possible with certain modifications of the scintillation camera that would permit use of the 375-keV photopeak along with the 172- and 203-keV gamma energies. Charcoal traps designed for Xe-133 will require additional shielding and longer storage time when used for Xe-127. Xenon-127, however, might be used again after appropriate processing.

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The use of Xenon-127 in preference to Xenon-133 was initially pointed out by Arnot et al. in 1971 (*1*). Application of Xe-127 to ventilation studies was examined by Hoffer et al. (*2*), but only preliminary evaluation could be carried out because of the limited quantities of the nuclide available at that time. Since then substantial quantities of Xe-127 have been produced by the Brookhaven Linac Isotope Producer (BLIP) and distributed to a number of users. Accordingly, it was decided to carry out a clinical comparison of Xe-127 and Xe-133 in a series of patients in order to evaluate whether or not the theoretical advantages secondary to the physical decay properties of Xe-127 could be realized in a clinical situation.

Xenon-127 decays by electron capture with a 36.4-d half-life. The principal gamma emissions and abundances are: 172 keV (25%); 203 keV (68%); and 375 keV (18%).

These photons provide better intrinsic spatial resolution than is possible with the less abundant (37%) 81-keV gamma photons of 5.3-d Xe-133. Accordingly, one would expect higher counting rates, and better spatial resolution when using Xe-127. Other advantages are better penetration through the chest wall by the gamma photons, a longer shelf life, and the possibility of performing a ventilation study immediately following a perfusion study with a Tc-99m radiopharmaceutical.

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MATERIALS AND METHODS

Radiopharmaceuticals. Xenon-127 was prepared on the BLIP by the following reaction:

$$^{133}Cs(p,2p5n)^{127}Xe.$$

Approximately 10 mCi of Xe-133 gas and 5 mCi of Xe-127 were administered to each patient.

For perfusion imaging Tc-99m from a generator system was used to label macroaggregated human serum albumin or albumin microspheres.

Instrumentation. A camera* with a large field of view was used in all studies. Initially, a medium-resolution, 280-keV collimator was used for both radionuclides. Shortly after the study was initiated, a medium-sensitivity, 140-keV collimator was obtained and used for the Xe-133 studies. For Tc-99m this collimator has a sensitivity 2.3 times that of the higher-energy collimator (*3*). A 25% window centered over the 81-keV photopeak was used for Xe-133, and for Xe-127 a 35% window to include the 172- and 203-keV peaks.

A semi-automated gas delivery system was used.† Data were acquired on a dedicated small-computer system.

Methods. Nineteen male patients, with a variety of pulmonary problems, were referred from the Veterans Administration Hospital, Northport, New York, for this study (Table 1). All patients had chest roentgenograms and spirometry before the radioactive gas measurements. Spirometry was used to measure lung volumes, 1-sec forced expiratory volume, closing volume, flow-volume loops, and maximum mid-expiratory flow rate. The order of the procedures was: spirometry, a Xe-133 ventilation study, a Xe-127 ventilation study, and a perfusion study with Tc-99m macroaggregated albumin. Late images of the head, chest, and abdomen were also obtained in most patients following the Xe-127 washout but before the perfusion study. These images were obtained as part of a separate study of the whole-body retention of Xe-127 (*4*). Accordingly we did not perform the Tc-99m perfusion study before the ventilation study, although this is possible and ordinarily preferable.

TABLE 1. PATIENTS STUDIED IN COMPARING XE-133 AND XE-127

Patient No.	Age (yr)	Diagnosis
1	53	Emphysema
2	58	Emphysema, lung cancer
3	55	Bronchial asthma
4	48	Fibrosis
5	55	Fibrosis, emphysema
6	59	Metastatic cancer
7	62	Fibrosis, COPD
8	60	Tuberculosis, inactive
9	66	Tuberculosis, inactive
10	67	Emphysema, mass lesion left lung
11	56	COPD, bullous emphysema
12	24	Suspected chronic bronchitis
13	65	Chronic bronchitis, right middle lobe pneumonia
14	19	Normal
15	43	Bilateral apical emphysema
16	64	Fibrosis, emphysema
17	52	Emphysema
18	58	COPD
19	52	Tuberculosis, inactive

With the patient seated in front of the scintillation camera (with posterior chest against the collimator face), a mouthpiece connected to the gas delivery system was inserted and the nasal passages closed by an external clamp. After a suitable time for patient adjustment and background counts, the radioxenon was injected as a bolus directly into the mouthpiece at functional residual capacity as the patient was inhaling slowly to total lung capacity. The first breath in was held for 20–30 sec and then the patient resumed normal breathing to equilibrate the concentration of radioactive xenon in the lungs and spirometer. A second total lung capacity was obtained at about 6 min, just before washout, which was then carried out for 5–10 min. The gas was vented through an exhaust system. During the equilibrium phase, a sample of gas was obtained from the mouthpiece in a calibrated glass ampule and was used to relate the radioactivity in the lungs to counting rate as measured over the chest. The samples were counted with a Ge(Li) detector calibrated against standards.

Scintiphotos were obtained of total lung capacity during the first breath in, at equilibrium, and sequentially at 1-min intervals during washout of radioxenon. Computer acquisition was carried out during the entire study.

For comparison with the ventilation studies, injection of the Tc-99m macroaggregated albumin was performed with the patient seated. Perfusion images were obtained in the anterior, posterior, and both lateral projections.

The two xenon studies were compared by determining the ratio of externally detected counts over the chest to the radioactivity, in millicuries, in the lungs during the first breath-hold and during equilibrium. A profile of count rate over the lungs from apex to base was determined in five patients with both radioxenons at equilibrium.

Three matching pairs of scintiphotos from each patient were evaluated independently by three physicians experienced in nuclear medicine in order to

TABLE 2. CLINICAL DIAGNOSIS AND COUNTING RATE RATIO

Patient No.	Defect: Ventilation		Defect: Perfusion		Ratio: Xe-127/Xe-133 counts per millicurie	
	R	L	R	L	1st breath-hold	Equilibrium
1	Multiple	Multiple	Multiple	Mid, base	0.97*	1.34*
2	Mid	Mid	Apex	Apex	—	1.09*
3	—	Multiple	—	—	1.04*	1.27*
4	—	—	—	Multiple	—	1.15*
5	Apex, base	Base	Mid, base	—	—	1.18*
6	Mid	Apex	Multiple	Multiple	—	0.98
7	Multiple	Multiple	—	Mid, apex	—	1.15
8	Apex	—	Apex	—	1.69	1.61
9	Apex	Multiple	Multiple	Multiple	1.25	1.19
10	Base	Base	—	Base	—	1.57
11	Multiple	Multiple	Multiple	Multiple	1.11	—
12	—	—	—	—	1.52	1.12
13	Apex	Apex	Mid	—	1.55	1.33
14	—	—	—	—	1.65	1.08
15	Apex	Apex	—	—	1.75	1.21
16	Multiple	Multiple	Multiple	Multiple	1.20	1.18
17	Apex	Base	—	—	1.36	1.13
18	Apex	Apex	Apex	Apex	1.59	1.23
19	Multiple	Multiple	Multiple	Multiple	1.41	1.18
				Mean ± s.d.	1.39 ± 0.26	1.22 ± 0.16

* Xe-133 study performed with 280-keV collimator and correction factor of 2.3 applied for decreased sensitivity compared to 140-keV collimator.

determine whether they preferred one isotope over the other. The scintiphotos were arranged in random fashion with respect to patients and radiotracers. The three views selected for each patient showed lung images at total lung capacity for the initial inspiration, at equilibrium, and during the second minute of washout. They were evaluated on the basis of three criteria: image clarity and definition, detectability of defects, and image-to-background activity. The results were evaluated statistically by analysis of variance using Snedecor's F test.

Following the perfusion study, the spectrometer was reset for Xe-133. Using the posterior perfusion images of 5 patients, the counting rates above room background were then measured in order to determine the "breakthrough" of Tc-99m counts into the Xe-133 channel. Similarly, the "breakthrough" of Tc-99m counts into the Xe-127 channel was measured after reinstalling the 280-keV collimator and resetting the spectrometer for Xe-127.

A line phantom containing radioactive gas was imaged with and without scattering material (5-cm paraffin) to simulate the chest wall. For both radioxenons, a full width at half-maximum (FWHM) was determined for the line spread functions. In addition, a line spread function was determined on an older model camera‡ using a low-energy collimator and Xe-133, and a medium-energy collimator and Xe-127.

RESULTS

From the measurements of the gas radioactivity in samples obtained at equilibrium, the concentration in the lungs at functional residual capacity could be estimated for each patient. The ratio Xe-127/Xe-133, in terms of counts over the chest per millicurie of lung radioactivity was 1.22. The ratio was consistent and unrelated to clinical diagnosis (Table 2). A similar ratio was determined as a function of counts at the first breath in and found to be 1.39.

Assessment of scintiphoto image quality in the studies performed with the two radioxenons showed no statistically significant differences between them for two of the three criteria. In analyzing the scintiphotos for image-to-background activity at total lung capacity for the initial inspiration, and at equilibrium, the Xe-133 images were superior to those of Xe-127 ($p < 0.01$), whereas the Xe-127 image after 2 min of washout was superior to that of Xe-133 ($p < 0.01$). Scintiphotos from a normal ventilation study are shown in Fig. 1. Occasionally the two isotopes exhibited differences that seemed to be primarily due to a change in various parameters, such as rate of inspiration, lung volume, or the level

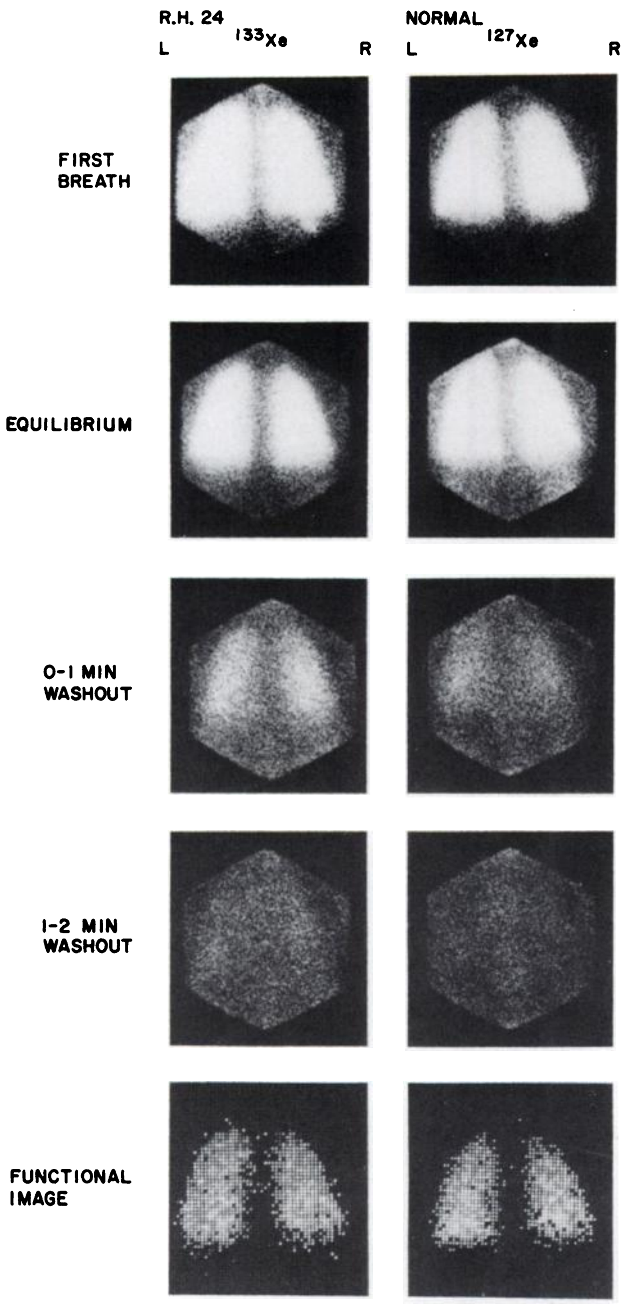

FIG. 1. Scintiphotos of patient with suspected chronic bronchitis secondary to tear-gas inhalation. Ventilation is normal and washout rapid. Xe-133 and Xe-127 images were similar. Functional image is obtained by dividing image from 1 min of washout into equilibrium image by means of a dedicated small computer.

of airway resistance, possibly due to patient fatigue and other indeterminate factors (Figs. 2 and 3).

No significant difference was seen in profile counts of the lungs as obtained with the two nuclides. There was essentially the same relative distribution of detected activity from apex to base with Xe-133 and Xe-127.

The Tc-99m counts observed in the Xe-127 channel with the 280-keV collimator were 1.11% ± 0.85 of the counts observed for the Tc-99m setting with the 140-keV collimator. The range was 0.11%–2.40%. The activity was not diffusely distributed across the field of view but was higher toward one edge. This was due to a slight nonuniformity of response of the photomultiplier tubes. In contrast, the Tc-99m counts observed in the Xe-133 channel, with the 140-keV collimator used for both, were 56.5% ± 5.8 (range of 46.7%–61.5%) of the counts observed for the Tc-99m. The activity was distributed over the entire lung field.

The studies performed with the line phantom are presented in Table 3. These show a significant difference in the resolution between Xe-133 and Xe-127, FWHM being greater for the former. This reflects the poorer inherent resolution at 81 keV. Particularly noteworthy is the markedly poorer resolution obtained with the older, 19-photomultiplier Searle camera. The image degradation with Xe-133 is so marked that the line phantom could not be resolved to any degree when scattering material was interposed between phantom and detector. Spectral measurements obtained with and without interposed scattering material indicate that the scatter spectrum constitutes a major fraction of detected counts in the Xe-133 window, and is less marked with Xe-127 (Fig. 4).

DISCUSSION

The theoretical advantages of Xe-127 over Xe-133 are due to their comparative physical characteristics

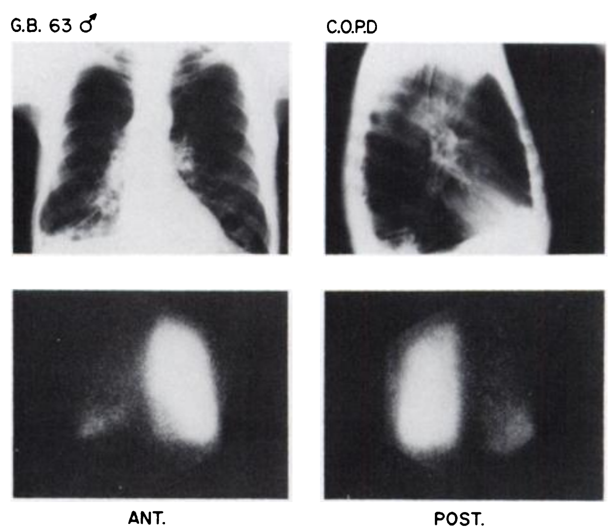

FIG. 2A. Chest roentgenograms in this patient show flattening of the diaphragm and chronic inflammatory disease in the right lower lobe, posteriorly, with a clinical diagnosis of chronic obstructive pulmonary disease. Perfusion images, obtained with Tc-99m macroaggregated albumin, show severe perfusion deficit in almost entire right lung.

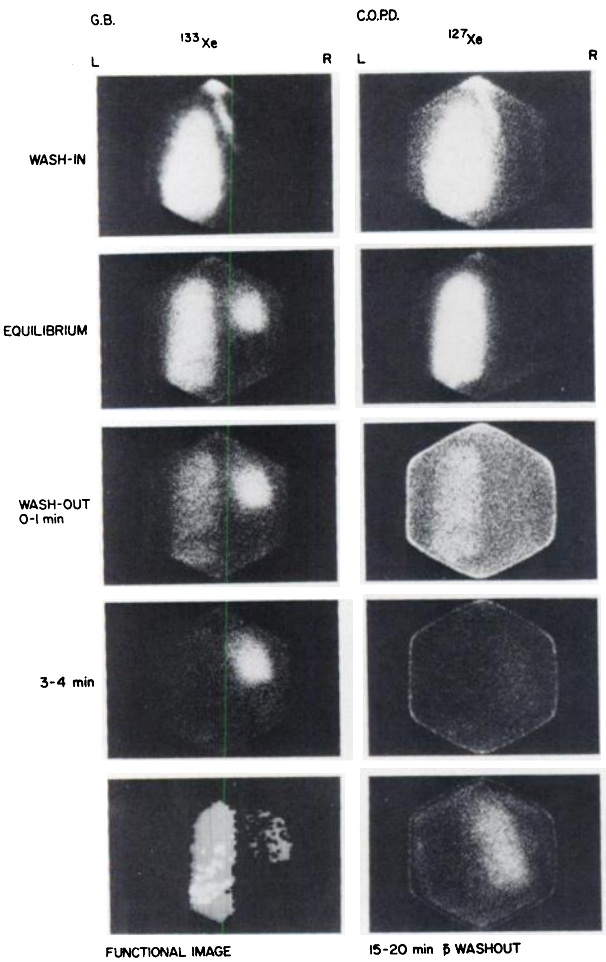

FIG. 2B. Comparative ventilation studies in same patient show a marked difference between the two studies. In Xe-133 study some accumulation of radioactivity is seen in right upper lobe at equilibrium; it washes out very slowly. No accumulation is seen at equilibrium in right lung with Xe-127, but a 5-min accumulated image at 15–20 min after start of washout shows radioactivity, though only in right lung. This may be result of diffusion from plasma as well as of small amounts trapped during respiration.

and have been partially demonstrated in this study. Certainly there should be no difference in physiological behavior between the two. The various parameters of comparison will be considered in turn.

1. Higher photon flux per millicurie administered activity is evident from our data. We obtained an advantage factor of 1.22–1.39 in this series of 19 patients. Hoffer et al. (*2*) demonstrated an advantage of 3.7 in favor of Xe-127 using a medium-energy diverging collimator for both nuclides. The degree to which the count rate is improved depends on the instrumentation and collimation used. The use of a camera with a large field of view obviates the need for the less efficient diverging collimators. The highest-sensitivity collimators available from the manufacturer were not used in these studies. With Tc-99m radiation, the ratio of sensitivity of the available highest-sensitivity collimators to those used in this study is 1.43 for the 140-keV collimator and 2.6 for the 280-keV collimator. Use of the highest-sensitivity collimators would result in a further gain by a factor of 1.8 for Xe-127 over Xe-133, thereby increasing the ratio of detected counts per millicurie (Xe-127/Xe-133) to 2.20–2.50.

A modification of our present equipment could permit the inclusion of all three major photopeaks (172, 203, and 375 keV). This option might be advantageous in that more penetrating high-energy photons, for which the intrinsic resolution of the gamma camera is somewhat improved, would be

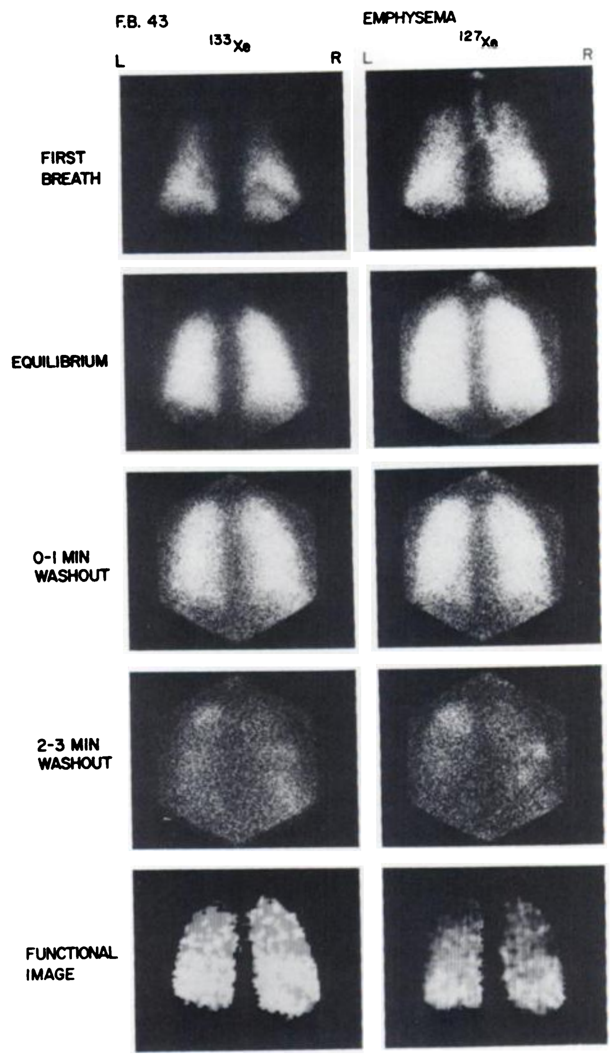

FIG. 3. Linear region of diminished radioactivity is present in right lower lung field of this patient in the scintiphoto, obtained while holding first breath containing Xe-133. It is not noted in Xe-127 first-breath scintiphoto. Washout images show scattered regions of delayed washout with both radionuclides, perhaps more clearly seen with Xe-127. Functional images again show some differences between the two studies.

TABLE 3. LINE SPREAD RESOLUTION MEASUREMENT

	FWHM (mm)			
	Ohio-Nuclear Series 110 Large-field-of-view camera		Searle Radiographics Pho/Gamma III H.P. camera	
Source-detector distance	Xe-127*	Xe-133†	Xe-127‡	Xe-133‖
0	7.59	9.64	9.34	12.9
6.35 cm	9.76	12.17	12.5	~20
6.35 cm with 5 cm paraffin	11.80	13.29	~20	Not resolvable

* 280-keV medium-resolution collimator, 35% window.
† 140-keV medium-sensitivity collimator, 25% window.
‡ 410-keV medium-energy collimator, 35% window.
‖ 140-keV high-sensitivity collimator, 25% window.

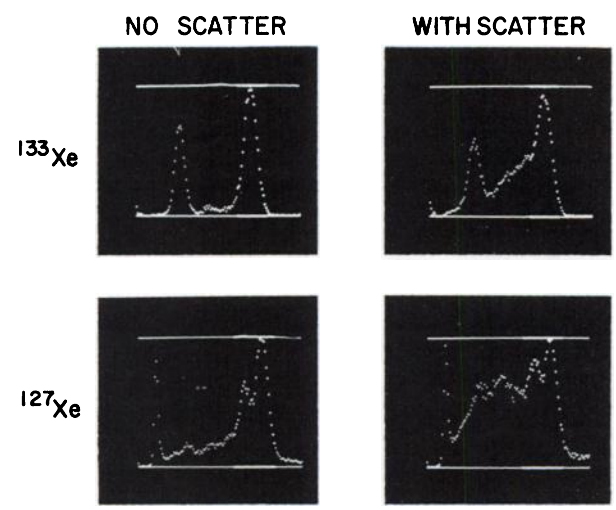

FIG. 4. Spectra of Xe-133 and Xe-127 obtained with large-field-of-view camera, with and without scatter. Xe-133 spectrum shows 81-keV photopeak at right and cesium x-rays (~31 keV) at left. With 5 cm of scattering material interposed between source and detector, scatter spectrum is seen which becomes part of 81-keV photopeak. In Xe-127 spectrum the 172- and 203-keV photopeaks are at right and iodine x-rays (~28.5 keV) are at left. The 375-keV photopeak is off scale. Scatter spectrum is mostly below 172-keV peak but does enter into it to some extent.

included. Scattered radiation then becomes a smaller proportion of the detected radioactivity. However, a less efficient collimator must be used at the higher energy, at which the detection efficiency of the crystal is also less.

We note that a somewhat larger advantage factor for Xe-127 was obtained with the first breath-hold than at equilibrium. This may be because a significant proportion of counts at equilibrium are from chest-wall activity, whereas during the first breath-hold the greater chest-wall penetration of Xe-127 photons outweighs the weakly penetrating 81-keV photons of Xe-133.

Hines et al. (*5*) made a theoretical comparison of the various radioisotopes of xenon. Their analysis indicated that Xe-127 had the highest useful photon flux per millicurie, taking into consideration tissue penetration and detector and collimator efficiency. In their study Xe-127 was calculated to give a photon flux 2.7 times that from Xe-133. These findings are consistent with the data of Hoffer et al. (*2*) and with the results of our study.

2. Intrinsic resolution at the photon energies of Xe-127 is better in most imaging systems than at the 81-keV energy of Xe-133 due to the statistics of light gathering. We measured resolution with appropriate collimation for both Xe-133 and Xe-127 and the results confirmed improved resolution with the higher-energy photons. Note that the camera used for these studies is of the latest type, delivering superior performance at lower energies compared with the older cameras. The difference between the two nuclides is more pronounced with the earlier instrumentation, accounting for generally poorer images with Xe-133.

Other factors that affect resolution are scattered radiation and information density. It is not possible to separate scattered radiation from the photopeak at 81-keV. With Xe-127 the scattered radiation from the 375-keV photons enters into the 172-keV peak to some extent but constitutes a minor contribution to detected counts (Fig. 4). It is likely that some septal penetration of the 280-keV collimator by the 375-keV photons contributes to background in the scintiphotos. This may account for a slight preference expressed by the observers for the Xe-133 images with regard to the image-to-background ratio. With the possible modifications that would permit the inclusion of the 375-keV photons, together with a high-energy collimator, scattered radiation will be even less a factor than in this study.

Because of the short time increments of acquisition in ventilation studies, information density can be a limiting factor in resolution unless adequate amounts of activity are administered. With Xe-127 the increased photon flux permits either the use of substantially less administered activity for the same counting rates, or higher counting rates for the same level of activity.

3. The higher photon energies of Xe-127 permit imaging to be performed immediately following a Tc-99m lung perfusion study. Although it has been suggested that Xe-133 can be used in such circumstances (*6*), there can be difficulty in following this sequence for the diagnosis of pulmonary embolism, particularly when chronic pulmonary disease is pres-

ent. The ability to select patients before the ventilation study can result in substantial savings in money and time as well as in a reduction of radiation dose. In this study we have seen only minimal evidence of Tc-99m counts in the Xe-127 window, in contrast to the substantial Tc-99m counts in the Xe-133 window. Care must be taken to have the camera properly tuned, however, in order to avoid stray counts in the Xe-127 window.

4. A more accurate reflection of ventilation volumes is theoretically possible with Xe-127 in comparison with Xe-133. Our studies failed to show any quantitative difference in detected ventilation volume. Inclusion of the 375-keV photopeak, however, might permit demonstration of such a difference.

The lower-energy photons of Xe-133 are more readily absorbed by the chest wall. Therefore, more of the detected counts originate from superficial radioactivity. At late washout times the chest-wall activity can be a major proportion of detected activity. The clearer washout images with Xe-127 are probably due to better penetration through the chest wall, with an improved lung-to-background ratio.

5. The radiation dose from Xe-127 is considerably lower than that from Xe-133 because of the electron-capture mode of decay of Xe-127. The "S" value (rads/μCi-h) for radiation to the lung from the lung as a source organ is 1.1×10^{-4} for Xe-127 and 3.0×10^{-4} for Xe-133 (7). Therefore the lung radiation dose for Xe-127 will be $\sim$1/6 of the dose from Xe-133 for equal information densities.

6. The shelf life of Xe-127 is such that it can be kept readily available in any nuclear-medicine laboratory. The 36.4-day half-life is no detriment as far as radiation dose is concerned because the major determinant of dose is the short biologic half-life.

Xenon-127 could be shipped monthly without severe losses due to decay, either en route or on the shelf. Xenon-125 requires essentially daily shipments, as does the ^{81}Rb–^{81m}Kr generator. Xenon-133 must be supplied at approximately weekly or biweekly intervals.

7. The economics of the use of Xe-127 compared with Xe-133 depend to a great extent on manner of use. Bulk quantities of Xe-133 are relatively inexpensive in cost per millicurie, but if there is considerable loss because of decay, the cost per patient study will be much higher than when initially considered. When Xe-133 is purchased in less-than-curie lots, the cost is comparable with the present cost of Xe-127, based on the required activity per patient study and decay losses.

8. The higher energy and long half-life of Xe-127 may complicate disposal after use. Some manufacturers of equipment are beginning to supply modifications to permit the use of Xe-127. The question of the trapping or venting of the gas following a study can be resolved only through assessment of projected levels of use and knowledge of local regulatory requirements. There is a possibility of recycling of Xe-127 by appropriate reprocessing. This may or may not result in appreciable savings, and should be evaluated.

ADDENDUM

In a recent in vitro study with lung models (*J Nucl Med* 18: 221–225, 1977), Coates and Nahmias also found that the resolution with Xe-127 was much better than with Xe-133, and that the scatter of Tc-99m into the Xe-133 window was considerable, but did not occur with Xe-127.

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FOOTNOTES

* Series 110, Ohio-Nuclear, Inc., Solon, Ohio.

† RADX Corp., Houston, Texas.

‡ Pho/Gamma III, H.P., Searle Radiographics Inc., Des Plaines, Ill.

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