

XENON-133, ^{127}Xe , AND ^{125}Xe FOR LUNG FUNCTION

INVESTIGATIONS: A DOSIMETRIC COMPARISON

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Of the possible radionuclides of xenon, ^{127}Xe and ^{125}Xe have better physical properties for lung function measurement than ^{133}Xe . A comparison of the radiation doses for these three radionuclides has been made for a typical scintillation camera investigation. Using an exponential model for washin and washout of gas, it is shown that the specific activity-time relationship is always equal to the product of the spirometer concentration and the rebreathing period.

It is concluded that of the three radionuclides ^{127}Xe gives the lowest radiation dose during a typical lung function study.

Since the original description of ^{133}Xe for pulmonary function investigations by Knipping (1), various alternative radioactive gases have been considered for this purpose (2-5). The most suitable have been the radioisotopes of nitrogen, oxygen, or carbon but all of these have short physical half-lives which demand close proximity to a cyclotron.

Xenon has a number of radionuclides but until recently ^{133}Xe has been used almost exclusively for regional lung function. The increased use of scintillation cameras for these measurements has prompted an interest in ^{127}Xe (6) and ^{125}Xe .

The mean total beta and electron energy per transformation (E_{β}) of both ^{125}Xe and ^{127}Xe is approximately 25% of that for ^{133}Xe in spite of the positron emission of ^{125}Xe . Both have principal electromagnetic emissions of about 200 keV, an energy closer to the optimum value for intrinsic scintillation camera sensitivity and spatial resolution than the 81 keV of ^{133}Xe and both have an almost threefold advantage over ^{133}Xe in useful photon yield. The effective half-lives of all xenon radionuclides are likely to be unaffected by differences in physical half-life since the residence time of the gas in the body is short for most pulmonary studies. For regular hospital use

the longer physical half-life of ^{127}Xe could be an advantage insofar that wastage from radioactive decay is minimized.

This paper is concerned with a comparison of the dosimetry of ^{133}Xe , ^{127}Xe , and ^{125}Xe when these gases are used for regional pulmonary function measurement.

PHYSICAL PROPERTIES OF ^{133}Xe , ^{127}Xe , AND ^{125}Xe

Tables 1 and 2 list physical data for the three radionuclides summarized from figures supplied by the Oak Ridge National Laboratory (7). Notable are the low values for the mean total electron energy per transformation for both ^{125}Xe and ^{127}Xe . Photons are emitted abundantly at 172 keV and 203 keV for ^{127}Xe (36.4 days) and at 188 keV and 243 keV for ^{125}Xe (17.0 hr). The gamma emission of ^{133}Xe (5.31 days) is 81 keV at only 37% abundance.

TYPICAL TECHNIQUE FOR THE INVESTIGATION OF REGIONAL LUNG FUNCTION

In order that dosimetry calculations can be made, a standard technique is described for lung function investigation.

The subject is connected to a spirometer containing radioactive xenon in 100% oxygen; the circuit contains a mixing pump and carbon dioxide absorbent. After total expiration to residual volume (RV), the subject takes a full inspiration of gas to total lung capacity (TLC) from the spirometer and holds his breath for 30 sec. Then he is switched to room air and the radioactive gas is washed out through exhaust tubing. The subject then breathes quietly (at tidal volume) in closed circuit with the spirometer for 3 min after which he is again switched to room air for washout of radioactive gas.

Received Oct. 16, 1973; revision accepted Feb. 26, 1975.

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TABLE 1. PRINCIPAL BETA AND CONVERSION ELECTRON EMISSIONS

Radionuclide	Beta* (MeV)	Conversion electrons* (MeV)	Auger electrons* (KeV)	Mean total beta and electron energy per transformation \bar{E}_β (MeV)
^{135}Xe	0.34 (98%)	0.045 (53.0%) 0.078 (11.0%)	3.1 (49%) 0.9 (118%)	0.138
^{137}Xe	—	0.025 (16.0%) 0.112 (1.4%) 0.139 (4.0%) 0.170 (6.6%) 0.198 (1.0%)	3.1 (94%) 0.9 (224%)	0.0336
^{138}Xe	0.50 (0.7%) (Positrons)	0.022 (22.0%) 0.050 (3.2%) 0.054 (1.1%) 0.155 (6.3%) 0.210 (1.9%)	3.1 (107%) 0.9 (256%)	0.0363

* Summarized Oak Ridge National Laboratory data (7).

TABLE 2. PRINCIPAL GAMMA EMISSIONS

Radionuclide	Photon intensity* (%)						
	0.004 MeV	0.025-0.036 MeV	0.05-0.06 MeV	0.07-0.09 MeV	0.14-0.24 MeV	0.3-0.5 MeV	>0.5 MeV
^{135}Xe	8	47	—	37	—	—	—
^{137}Xe	14	88	1.4	—	97	18	—
^{138}Xe	16	102	5.3	0.1	84	4.5	4.7

* Summarized Oak Ridge National Laboratory data (7).

Subsequently an intravenous injection of xenon in saline is given to show the distribution of pulmonary arterial blood flow perfusing the lungs. This distribution is displayed by xenon evolved into perfused alveoli at TLC breathhold, the gas being later washed out by tidal breathing.

Calculation of the specific activity-time integral for the rebreath and washout procedure. The principal tissue dose delivered during the technique described is accumulated during the washin and washout of xenon.

It was assumed that each region of the lung acts as a single compartment system (Fig. 1), so that both washin and washout of gas can be described by a single exponential function, the rate constants of which are the same.

For the general case:

$$A_t = A_0 (1 - e^{-kt})$$

where A_t is the specific activity of xenon in the lung air at time t (min), A_0 is the specific activity of xenon in the spirometer ($\mu\text{Ci}/\text{ml}$), and k is the rate constant for washin of xenon. The specific activity-time integral, I_t , over the washin period is given by

$$I_t = A_0 \int_0^T (1 - e^{-kt}) dt = A_0 \left(T - \frac{1}{k} + \frac{e^{-kT}}{k} \right) \quad (1)$$

where T is the rebreath period. For washout (which

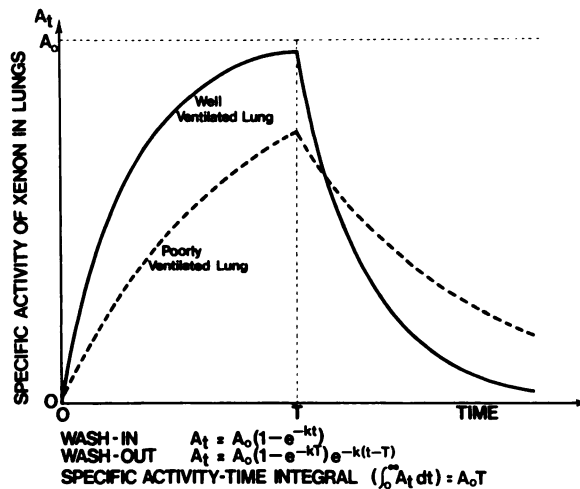


FIG. 1. Variation of specific activity of xenon in lungs with time during rebreath and washout assuming single closed compartment system.

has the same rate constant, k , as for washin) the specific activity–time integral, I_0 , is given by

$$\begin{aligned} I_0 &= A_0 (1 - e^{-kT}) \int_T^{\infty} e^{-k(t-T)} dt \\ &= A_0 (1 - e^{-kT}) \frac{1}{k}. \end{aligned} \quad (2)$$

Therefore the specific activity–time integral for the total washin and washout procedure, $(I_1 + I_0)$, is given by summing Eqs. 1 and 2;

$$I_1 + I_0 = A_0 T (\mu\text{Ci} - \text{min/ml}). \quad (3)$$

This result shows that when the rate constant for washin and washout is the same, the integral value for the specific activity–time relationship depends only on the spirometer concentration, A_0 (assumed here to remain constant during the period of rebreathe) and the rebreathing period, T . This is true whether or not the lung (or region of lung) attains the spirometer concentration during rebreathing (Fig. 1). Thus, in regions where washin is poor, washout will be prolonged and therefore specific activity–time integral will be the same as that for well-ventilated parts of the lung.

METHOD

To calculate the total beta and electron dose to tissues, not including major airway mucosa, the following equation was used:

$$\text{Dose}_{(\text{beta})} = 35.5 \bar{E}_\beta (\text{CT}) (\text{mrad})$$

where \bar{E}_β is the mean total electron energy per transformation (MeV) and (CT) is the specific activity–time integral ($\mu\text{Ci-min/gm}$).

To calculate the gamma radiation dose to different tissues, the formulations used by the MIRD Committee using the concept of absorbed fraction were employed (8,9). The expression for the gamma dose is written as follows:

$$\text{Dose}_{(\text{gamma})} = 35.5 (\text{CT}) \sum_{i=1}^n \phi_i n_i E_i \text{ rad}$$

where n_i is the number of emissions per disintegration of photons of energy E_i (MeV) and ϕ_i is the absorbed fraction of photons of this energy, obtained from the MIRD tables (9) for a particular organ.

Absorbed fractions are also given for situations when source and target organs are not the same (9). By use of the reciprocity principle (8), these figures enabled calculation of gamma doses to gonads from xenon in the lungs and fat.

In the calculation of gamma dose to fat and blood, values of absorbed fraction for the whole body were taken, assuming that the body contains 10 kg of fat and 5 liters of blood. The gamma dose to lung includes a contribution from xenon in fat, blood dose

includes contributions from lung and fat, and gonad dose includes contributions from lungs, fat, and blood.

Specific activity for lung during the rebreathe and washout procedures. The following assumptions were made: mass of lungs, 1,000 gm; concentration of spirometer (A_0), 1 mCi/liter; mean density of lungs, 0.3 gm/cm³; rebreathe time (T), 3 min; vital capacity, 5 liters; functional residual capacity (FRC), 2 liters; and mean tidal volume (v), 1 liter. During the rebreathe period the subject breathes quietly. A mean volume of 2.5 liters (FRC + 0.5 v) was assumed.

Therefore, when the lung is at near equilibration with the spirometer it will contain 2.5 mCi of radioactive xenon in 1,000 gm of tissue or a specific activity of 2.5 $\mu\text{Ci/gm}$. At other times, the mean specific activity will vary; from Eq. 3 it will be seen that the mean specific activity–time integral for lung tissue will be given by 2.5 $A_0 T$ ($\mu\text{Ci-min/gm}$). It was assumed throughout that no dilution of the spirometer takes place.

Specific activity–time integral for blood and other tissues (not fat) during the rebreathe and washout procedure. As the concentration of xenon in the lungs rises during the rebreathe period, the concentration of dissolved xenon in blood will also increase and at any moment will be equal to the product of that in the lung and the partition coefficient of xenon between blood and air.

It was assumed that activity in the blood equilibrates with that in alveolar air in a single passage through the lungs. Then

$$\int_0^{\infty} C_B dt = \lambda_B A_0 T (\mu\text{Ci-min/ml})$$

where C_B is the specific activity of blood and λ_B is the xenon partition coefficient between blood and air. The value of λ_B varies with hematocrit (10); a mean value of 0.2 was taken. All tissues including the gonads and bone marrow (but excluding fat, see next section) have a partition coefficient with blood of unity or less; thus the radiation dose to these tissues from xenon dissolved in blood is not greater than that calculated for blood.

Specific activity–time integral for fat during the rebreathe and washout procedure. The partition coefficient of xenon between fat and blood is high, 8.0 (10). This requires that fat be treated as a special case for the calculation of radiation dose from dissolved xenon.

The buildup and clearance of xenon in fat obey the rule set out for the general case given by Eq. 3. The specific blood flow to fat is low so that equilibration with the spirometer is not attained for short rebreathe periods. However, the specific activity–

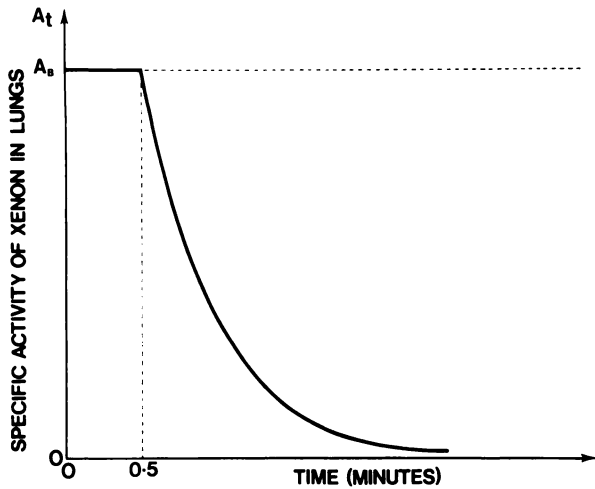


FIG. 2. Variation of specific activity of xenon in lungs with time for single breath and washout.

time integral is independent of blood flow and is given by:

$$\lambda_F \lambda_B A_0 T \text{ (}\mu\text{Ci-min/gm)}$$

where λ_F is the partition coefficient between fat and blood.

Specific activity–time integral for a single breath (total lung capacity) from the spirometer. Figure 2 shows the relationship between lung specific activity and time for this procedure. The following assumptions were made: specific activity within the spirometer, 1 mCi/liter; single breath from RV to TLC, 5 liters; residual volume in the lung, 1 liter; mass of lungs, 1,000 gm; overall density of lung, 0.14 gm/cm³; breathhold time, 0.5 min, and half period of washout of gas, 0.5 min.

After a single breath from the spirometer of 5 liters, 5 mCi of xenon are mixed in a total lung volume of 6 liters of gas. The specific activity in lung (A_B) is 5 $\mu\text{Ci/gm}$ and the concentration of activity in lung air (A_s) is 0.83 $\mu\text{Ci/ml}$. Although the assumed value of washout half-period is that shown by normal lungs, prolonged washout due to abnormal airway resistance may result also in reduced washin and a situation exists analogous to the rebreathe procedure.

The concentration–time integral is equal to the area under the curve, which is the sum of the breathhold specific activity–time integral and the subsequent washout specific activity–time integral. This is given by

$$(0.5 \times A_B) + (1.44 \times 0.5 \times A_B) = 6 \mu\text{Ci-min/gm}$$

Similarly, the values of the specific activity–time integral for blood and fat are:

$$\lambda_B [(0.5 \times A_s) + (1.44 \times 0.5 \times A_s)] = 0.2 \mu\text{Ci-min/ml blood}$$

$$\lambda_F \lambda_B [(0.5 \times A_s) + (1.44 \times 0.5 \times A_s)] = 1.6 \mu\text{Ci-min/gm fat.}$$

Specific activity–time integral for an intravenous administration of an injection of xenon in saline. For this calculation it was assumed that 1 mCi of xenon in a volume of 10 ml of saline is injected. It was assumed also that in the 10 sec needed to reach the lung, the bolus is not spread in the blood during transit. Breathhold is maintained for 30 sec while a measurement is made. The activity–time relationship is shown in Fig. 3. It was assumed also that all xenon is cleared in one passage through the lung.

In this case the specific activity–time integral in blood is: 16.7 $\mu\text{Ci-min/ml}$.

Specific activity–time integral for lung. For normal lung a washout half-period of 0.5 min was assumed. For abnormal lung, it is taken to be 5 min. Gas arising in perfused alveoli is trapped and subsequently cleared with this half-period. The specific activity–time integral for air in the lungs is given in this worst case by:

$$(0.5 \times A_p) + (1.44 \times 5 \times A_p)$$

where A_p is the maximum specific activity in lung (1 mCi in 6 liters). Therefore, the total specific activity–time integral is 7.7 $\mu\text{Ci-min/gm}$.

The values of the specific activity–time integral for blood and fat are, respectively:

$$\lambda_B [(0.5 \times A_p) + (1.44 \times 5 \times A_p)] = 0.26 \mu\text{Ci-min/ml}$$

$$\lambda_F \lambda_B [(0.5 \times A_p) + (1.44 \times 5 \times A_p)] = 2.1 \mu\text{Ci-min/gm.}$$

Incident radiation doses to the mucosal layer of the major airways for the single breath, rebreathe, and intravenous procedures. The variation of specific

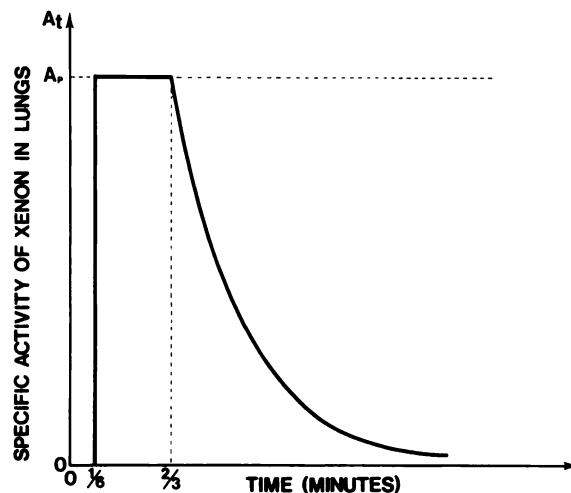


FIG. 3. Variation of specific activity of xenon in lungs with time for intravenous administration of injection of xenon in saline and washout.

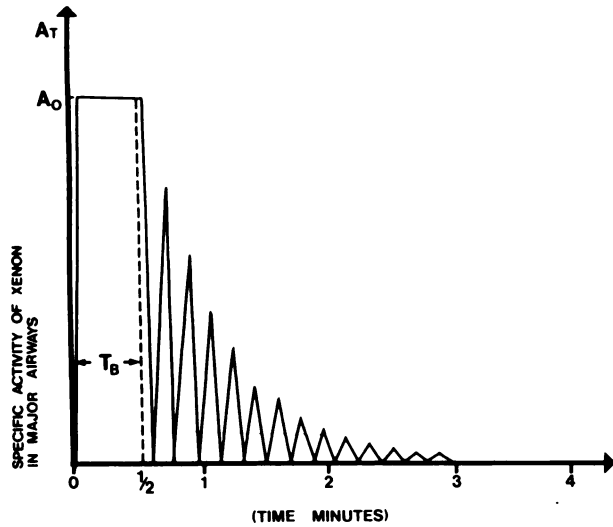


FIG. 4. Variation of specific activity of xenon in major airways for single breath and washout.

activity of xenon in the major airways during single breath and rebreath is shown in Figs. 4 and 5. It was assumed that the specific activity in the major airways immediately attains the spirometer concentration ($A_0 \mu\text{Ci/ml}$) and remains at this value for the period of breathhold (T_B). Diffusion of xenon into distal parts of the lung was assumed not to take place during this period so that the first exhalation of the clearance period, after the subject is switched to room air, gives a reduction in concentration. Subsequent tidal breathing produces an envelope which is a curve of exponential decay. The specific activity–

time integral during the breathhold is $A_0 T_B$. During the subsequent clearance of this activity (half-clearance = 0.5 min), the specific activity–time integral will be less than $1.44 \times 0.5 \times A_0$ ($\mu\text{Ci-min/ml}$). The total specific activity–time integral for the single breath procedure is therefore less than $A_0 (0.72 + T_B) \mu\text{Ci-min/ml}$.

Upon reconnection to the spirometer, further tidal breaths increase the specific activity until a value is attained close to that of the spirometer concentration (A_0).

Following the rebreath period when the subject is switched to room air, the specific activity falls again. It is seen that for the specific activity–time curve the washout relationship is the inverse of the washin phase during tidal breathing, and the specific activity–time integral for this period equals $A_0 T$ ($\mu\text{Ci-min/ml}$) (see Eq. 3).

For the intravenous injection of 1 mCi of xenon, all the activity was assumed to be deposited in the alveolar gas during the breathhold without diffusion to the upper airways. As previously, the half-clearance is assumed to be 5 min, and therefore the maximum possible value for the specific activity–time integral equals $1.44 \times 5 \times A_p$ ($\mu\text{Ci-min/ml}$).

To calculate the beta/electron dose to mucosal surfaces, a hemicylindrical airway of 1.5-cm radius was assumed. The empirical function representing the beta-ray point source dose distribution in air and tissue derived by Loevinger, et al (11) on the basis of experimental results has been applied to monoenergetic electrons and integrated over a 10-cm length of airway. The absorption coefficients required

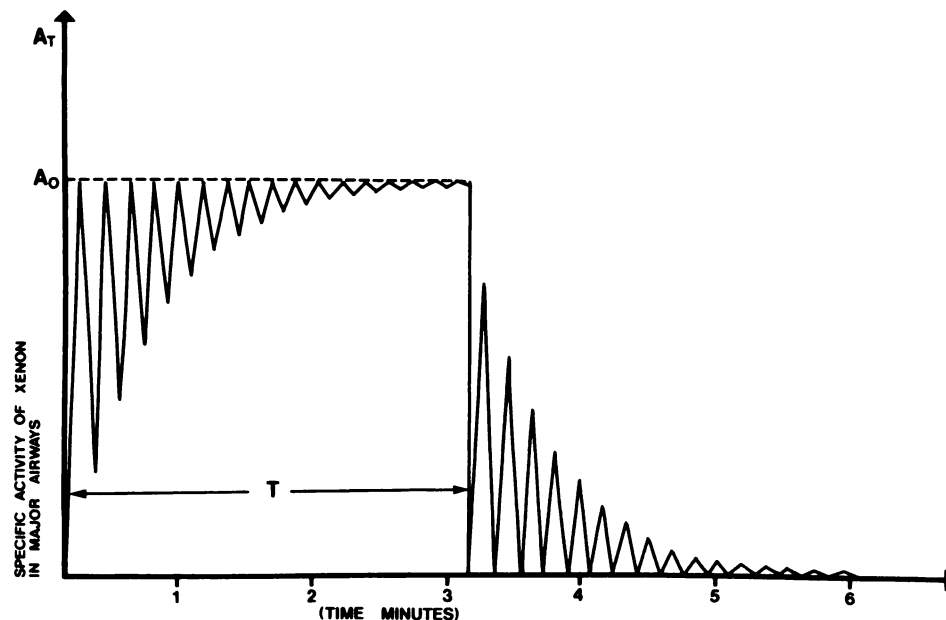


FIG. 5. Variation of specific activity of xenon in major airways for rebreath and washout procedure.

TABLE 3. BETA/ELECTRON AND GAMMA DOSES (MILLIRAD) TO LUNGS, BLOOD, FAT, AND GONADS

Radionuclide	Procedure	Radiation	Lung	Blood	Fat	Gonads
¹³³ Xe	RB and WO	β/electron	37	3.0	24.0	3.0
		γ	2	0.7	0.7	0.7
	SB and WO	β/electron	29	1.0	8.0	1.0
		γ	1	0.3	0.3	0.3
IVI and WO	β/electron	38	82.0†	10.0	1.0	
	γ	2	0.4†	0.4	0.3	
¹²⁵ Xe*	RB and WO	β/electron	9	0.7	6.0	0.7
	SB and WO	γ	8	3.0	3.0	4.0
¹²⁷ Xe	IVI and WO	β/electron	7	0.2	2.0	0.2
		γ	5	1.0	1.0	1.0
		β/electron	9	20.0†	3.0	0.3
		γ	6	2.0†	2.0	2.0

RB = rebreath, WO = washout, SB = single breath, and IVI = intravenous injection.
 * Doses for ¹²⁵Xe and ¹²⁷Xe differ by less than 10%.
 † Doses for 10-ml volume.

TABLE 4. BETA/ELECTRON AND GAMMA RADIATION DOSES (MILLIRAD) TO MAJOR AIRWAY MUCOSA

Radionuclide	Procedure	Beta/ electron	Gamma
¹³³ Xe	RB and WO	640	2
	SB and WO	260	1
	IVI and WO	256	1
¹²⁷ Xe	RB and WO	71	8
	SB and WO	29	5
	IVI and WO	29	5
¹²⁵ Xe	RB and WO	130	8
	SB and WO	53	5
	IVI and WO	52	5

RB = rebreath, WO = washout, SB = single breath, and IVI = intravenous injection.

TABLE 5. TOTAL PROCEDURE RADIATION DOSES (MILLIRAD)

Radio- nuclide	Lung	Blood	Fat	Gonads	Major airway mucosa	Thy- roid
¹³³ Xe	108	91	43	6	1,160	
¹²⁷ Xe	44	34	16	8	150	
¹²⁵ Xe	46	36	17	6	250	1,500*

* Radiation dose from daughter ¹²⁵I (14).

in the function have been obtained from tables compiled by Berger and Seltzer (12). A 5-micron layer of mucus was assumed to line the mucosal surface (13) and corrections for absorption through this layer were made. Beta and conversion electrons incident upon this layer were assumed to have energies equal to their initial value. Backscatter was assumed to be negligible. Calculations of dose were made for each electron energy weighted proportionally to in-

dividual intensities. A₀ was taken to be 1 μCi/ml, T_B and T to be 0.5 and 3 min, respectively.

Gamma dose was calculated assuming the major airways to be at the center of the lungs.

RESULTS

Beta and gamma doses to various tissues for each procedure are given in Tables 3 and 4. Total doses are given in Table 5.

DISCUSSION

Previous assessments (15,16) of radiation doses from ¹³³Xe to lung, fat, blood, and gonads are similar to those calculated here. In spite of the different methods and assumptions employed in each case, the final figures differ by no more than 30%. Only two references give radiation doses for ¹²⁷Xe (6,17) but neither explains the basis for his calculation. There is no available literature for ¹²⁵Xe dosimetry. Although the radiation doses from ¹²⁵Xe gas are similar to those from ¹²⁷Xe, ¹²⁵Xe has the serious disadvantage that it decays to ¹²⁵I. We calculate that, for a typical lung investigation, about 1 μCi of ¹²⁵I would be deposited in the body and this would then result in a radiation dose of 1.5 rad to the thyroid gland and 4 mrad to the whole body (14).

It has been reported by Lassen (16) that the radiation dose delivered to mucosal surfaces of airways by local beta irradiation is higher than that for the lung as a whole calculated on the basis of uniform energy deposition within tissue. Our result for the dose to the mucosal surface of major airways is twice that given by Lassen. This is because we have calculated the beta and electron dose incident upon the mucosal surface under a 5-micron thickness of mucus (13), whereas Lassen's value was for the mean dose to a layer 100 microns in thickness. Recalculation of our data as a mean dose over this thickness gives

a value similar to Lassen's although his calculation was quite differently based. For 5 microns of mucus the beta/electron dose attenuation factor is 0.7 for ^{133}Xe and 0.25 for ^{127}Xe . These figures are dictated mainly by the contribution to total dose by Auger electrons. Thus the value chosen for thickness of mucus will have an important effect on the overall result, particularly in the case of ^{127}Xe and ^{125}Xe .

The surface incident beta/electron dose from a xenon-filled air cavity may also be applied to smaller airways and calculation shows that the mucosal dose is approximately proportional to their diameter. In these calculations of surface dose, we have assumed that electrons incident on the surface possess their initial energy. This leads to an overestimation of the dose, which is probably balanced by the fact that no allowance has been made for the change in backscatter conditions which pertain at the surface. It has also been necessary to apply the measured values for mean beta dose of Loevinger (11) to monoenergetic electrons since no other data are available in the literature.

In summary, the dose to cells lining the major airways is higher than that received by other tissues in the body. The radiobiologic significance of such a highly localized dose is not the subject of this paper.

For the perfusion investigation most xenon is cleared rapidly from the blood in the first passage through the lungs. Thus the dose calculated for the small volume of blood carrying the activity greatly exceeds that for whole blood and bone marrow. For this calculation the gamma photon absorption fraction was taken as zero and that for beta/electrons was assumed to be unity.

The value of the model proposed in this paper is that radiation doses are not increased during re-breathing and clearance of xenon if the turnover of gas in the lung is slow, because the specific activity-time integral is independent of the rate constants for washin and washout, provided that these are the same. This holds true also for multiexponential functions, provided that exchange of xenon is freely reversible between compartments and that no active concentration takes place, which is a reasonable assumption. Mixing of xenon with more slowly exchanging compartments outside the lung, e.g., blood or other tissues, will not therefore affect the specific activity-time integral.

We conclude that the advantageous dosimetry of ^{127}Xe , together with its better gamma emission for the scintillation camera, make it the xenon radionuclide of choice for lung function studies.

ACKNOWLEDGMENTS

We thank Ed Smith for his helpful criticism; Mary Ford, Oak Ridge National Laboratory, for the latest figures on

the xenon radionuclides; and Jack Vennart, Medical Research Council, Radiobiological Unit, Harwell, for the details of the ICRP reference data. Linda Downer kindly typed the manuscript.

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