

MEASUREMENT OF ^{226}Ra IN MICE

by

V. LENGER

Investigations of the dose-response relationship of certain bone-seeking nuclides suggested that the problem of the rapid and sufficiently precise measurement of ^{226}Ra activities in injections should be solved. It also appeared desirable to follow up dynamic changes of this nuclide in experimental animals, for example, mice, in which it is impossible to achieve equilibrium and in which the fraction of expired radon is unknown. The amount of ^{226}Ra activity is usually ascertained by measurement of the gamma RaC (^{214}Bi) activity in equilibrium. The same lines of RaC (^{214}Bi) deposited in the body of the subject measured are mostly used in measuring incorporated activities *in vivo* and the results achieved corrected by the ^{222}Rn emanating fraction. The period required for establishment of equilibrium is a hindrance and the procedure described is only accurate if the assumption is correct that the amount of radon exhaled by the object measured equals the amount released from radium deposits in the body. The uncertainty of this assumption causes the results to be considerably weighted.

LENGER & THOMAS (1971) attempted to explain the new spectrometric method of measuring ^{226}Ra activity in a nonequilibrium state consisting in the regression analysis of the time course of counting rates in the 187 keV emitted from the ^{226}Ra and 1764 keV emitted from RaC (^{214}Bi) bands. This method was applied in the undermentioned measurement in mice with ^{226}Ra incorporated *in vivo*.

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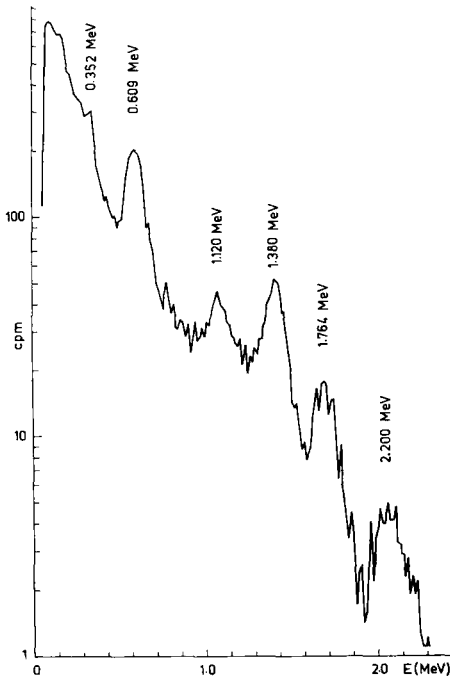


Fig. 1. Complex spectrum of incorporated ^{226}Ra in man.

Material and Method. The possibility of determining the retained ^{226}Ra and ^{222}Rn directly from the spectrum measured in the experimental animal is demonstrated in Figs 1 and 2. If ^{226}Ra is at a low degree of equilibrium with its products (< 50 per cent) or if not a strongly scattering medium, the 187 keV line may well be recorded in spite of its origin from a 50 per cent conversion with a mere six per cent probability of emission. As absolute deemanation is not practicable, even the slightest activity of daughter products affects the 187 keV line by Compton scattering and direct quantitative evaluation is only possible if this superposition is deducted. As reported previously this may be carried out because the ratio of the counting rate pertaining to the Compton effect in the band of the 187 keV line to the counting rate recorded in the 1764 keV band must be constant. It is quite sufficient for calibration to carry out several measurements and to calculate the relation R from linear equations of the type:

$$N_2 = A + RN_1$$

where N_1 and N_2 are the counts measured in the region of the gamma ray line 1764 and 187 keV, respectively, and A is the counting rate in the energy band of 187 keV due to pure ^{226}Ra .

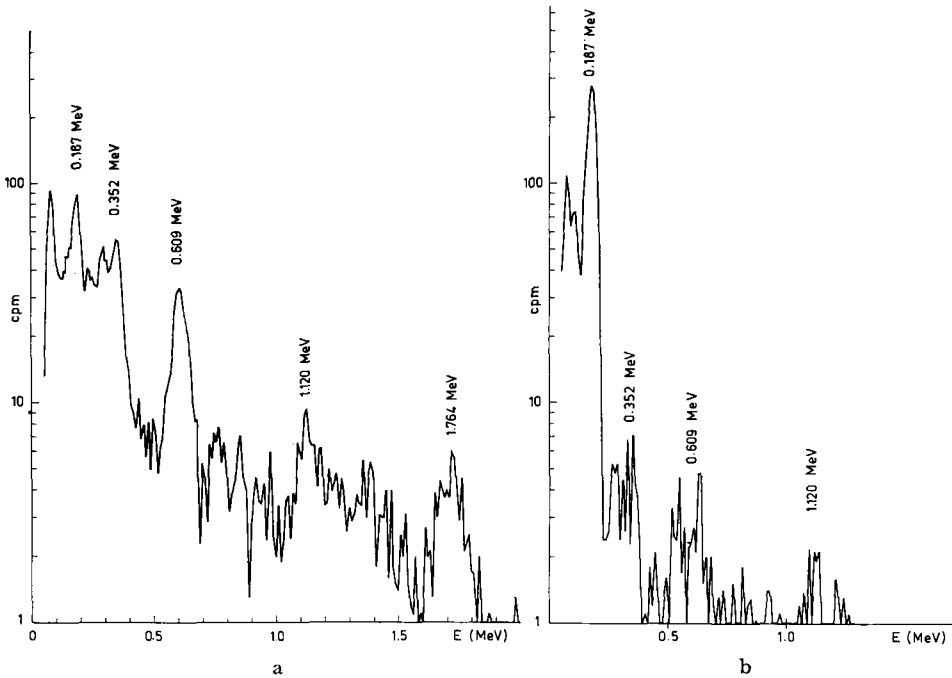


Fig. 2. a) ^{226}Ra spectrum in mice 205 days after single administration. b) ^{226}Ra spectrum in mice 10 minutes after single administration.

The precision may be controlled by determining that $R = \text{const.}$

The mice injected with ^{226}Ra were divided into groups of ten. This number was limited by the geometry with the compromise that the angular dependence should be of the least possible effect and that the sensitivity should be relatively high at a comparatively short period of measurement (15 minutes). Coaxial arrangement of the two scintillation crystals NaI (T1) $5 \times 4''$ ($12.5 \text{ cm} \times 10 \text{ cm}$) was decided upon to balance the effect of nonhomogeneous distribution.

Quantitative evaluation made it necessary to carry out calibration measurements. In principle, one of the two methods known in the problem of in vivo measurement, could be applied. It was possible to apply the known amount of radioactive substance in one. However, due to the kinetics and the metabolism of the members of the series, it was difficult to control the degree to which the Compton scattering contributed in the band of the 187 keV line. A phantom in which the system of non-uniformly distributed activity in strongly heterogeneous medium was replaced by a physically simpler and better defined system was therefore constructed. The accuracy of this phantom is imperative if the evalu-

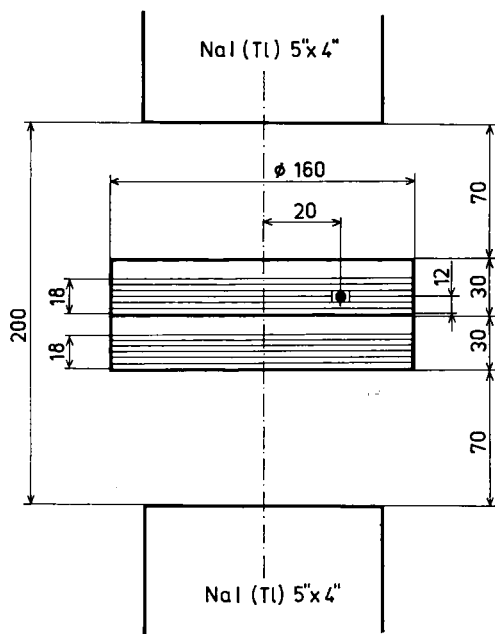


Fig. 3. Phantom used for calibration. Each cylinder held 10 mice during the experiments.

ation is to be correct and precise. The basic part of the phantom consisted of a cylindrical container into which the mice with the radium injected were placed; the basic dimensions were thus fixed. It was necessary to decide upon the optimal position of the reference source and upon the quality and amount of the scattering medium. The container was designed for effective ventilation during the measurement so that the exhaled radon was expelled.

It was decided to experiment with mice of 40 g live weight, the expected maximum. (The lowest limit was laid down as 20 g.) Experience with similar phantoms in spectrometric evaluation of whole-body activities in man suggested the use of Masonite (1g cm^{-3}) and approximation of the quasipoint secondary standard (WENGER et coll. 1968). Because it was necessary to expect migration if one or several mice should die, it would not have been correct to place the reference source mentioned into the centre of the geometry. For this reason a 'point' was selected that represented the mean yield from the central and marginal position of the mouse in the container. The reference source of ^{226}Ra was measured for this purpose in equilibrium in a sealed ampoule at the edge and centre of the container. The spatial angle was related to the effective centre of the crystal. Counts in the band of 187 keV line differed in these cases by 25 per cent. By projecting the 'isocounts curves' obtained into a level vertical to the

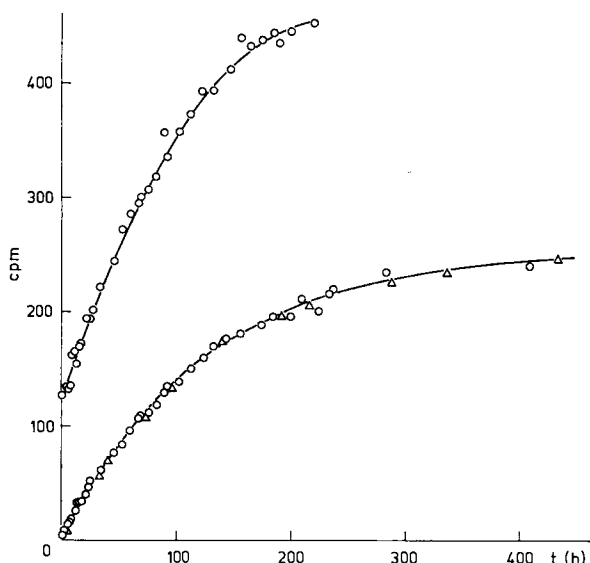


Fig. 4. Calibration curves. The upper curve denotes the time course of counts in the 187 keV line band including Compton scattering, the lower curve being the time course of RaC (^{214}Bi) (Δ denotes the theoretic values).

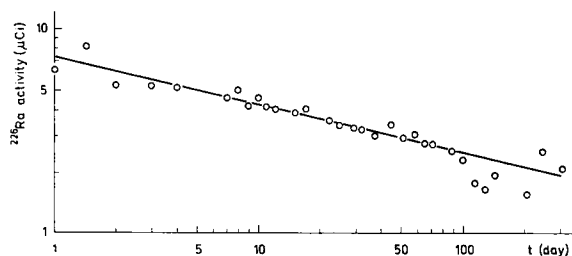


Fig. 5. ^{226}Ra retention curve for mice with single administration.

window of the crystal, the active centre was determined, i.e. the point at a certain distance from the centre of the system where the counting rate measured was identical with the mean value measured in the regions and marginal positions mentioned.

The 'area density' of the average mouse had to be known in order to ascertain the quantitative effect of the absorbing and scattering matter, in this case Masonite. A point source of ^{57}Co (122 keV gamma rays) was therefore measured below and above, and in contact with the anaesthetized mouse. The mean counting rates of these measurements were compared with values measured with the same geometry in air. The difference in these values corresponded to the effect to the absorption of the point source localized in the mouse. By transferring this difference into the relation of absorption obtained for the same emitter in similar geometry, the 'area density' of the complex tissue in mice was obtained. The

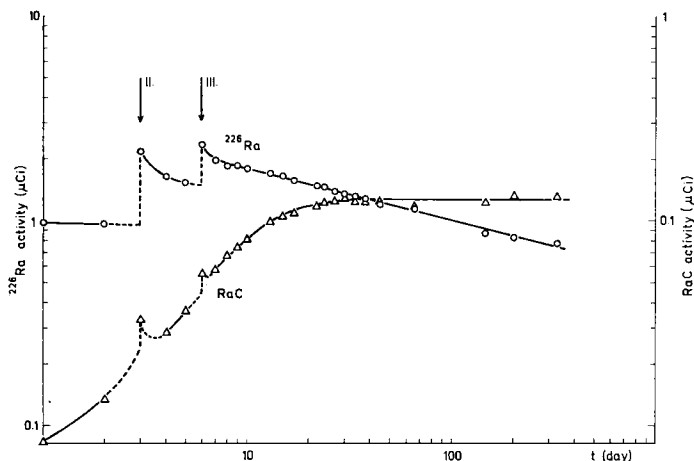


Fig. 6. ^{226}Ra retention curve for mice after triple administration (dotted line is the assumed trend).

effect of the energy difference between ^{57}Co 122 keV and ^{226}Ra 187 keV was taken into consideration when the true value of the area density (or the 'cross-section') was ascertained. The values thus obtained could then be easily substituted by an artificial absorber, in the present case by Masonite. The arrangement is demonstrated in Fig. 3.

Results

The model thus constructed was used for a series of calibration measurements (Fig. 4). The latter were processed according to the linear equations mentioned and the constant $R = 3.84 \pm 0.05$ was calculated. The calibration curves or the value of the R constant count only for a single arrangement (geometry and absorbing medium). If the activity of an unknown sample is to be determined one measurement will suffice if the counts in the 187 keV and 1764 keV bands are known. The respective counting rate of ^{226}Ra and thus also its activity may then be obtained with the help of R . The retention curves measured by the method described are plotted in Figs 5 and 6; their biologic importance will be discussed in a separate paper.

The kinetics of ^{226}Ra immediately after its injection at different states of equilibrium were investigated for the biologic interpretation of the results. A solution of ^{226}Ra in equilibrium was injected into the mouse intraperitoneally — this being a marginal case. The mouse was placed in a container in which

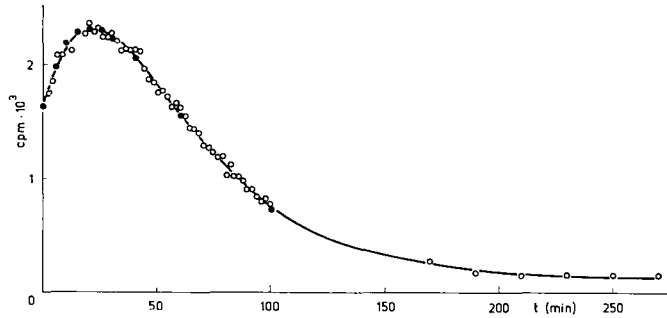


Fig. 7. The time change of RaC (^{214}Bi) in mice after single application of ^{226}Ra in equilibrium (filled circles denote the theoretic values).

ventilation was efficiently solved by a double stream of air to prevent interference by the exhaled radon fraction and its daughter products. The first measurement was made at two minutes, the evaluation being performed in the bands of 187 keV and 1764 keV lines. There was no excretion by the mouse during the measurement so that the effect of radon exhalation and that of decay and increase of the individual daughter products of radon could be observed.

It is interesting that kinetic equilibrium occurs only as late as 4 hours after administering ^{226}Ra in equilibrium. The most important of the curves obtained (Fig. 7) indicates the trend of RaC (^{214}Bi) as the time function. This is caused by the superposition of the decay $\text{Ra/B} \rightarrow \text{C/}$ and the growing of RaC (^{214}Bi) out of RaB. The right descending branch plots the transient equilibrium. The RaC (^{214}Bi) trend was calculated to prove the relations measured under the assumption that the Rn retention is zero and that the RaA incorporation is also negligible ($\text{RaA} = 0$). This theoretic trend is practically identical with the curve measured and is therefore sufficient proof of a rapid exhalation of radon. The practical importance of this finding is apparent when the uncertainty in measuring an experimental animal immediately after it has been treated is considered.

The reliability of the method was verified by measurement of five experimental objects — mice in which unknown ^{226}Ra activity was injected intraperitoneally. At first all five mice were measured collectively during an unknown time after the administration. The mice were then killed and mineralized, the mineralisate being sealed and measured individually in a nonequilibrium state (Table A). After establishing equilibrium the ampoules containing the mineralisates were again measured (B). The evaluation of these last measurements were carried out by comparing the 1764 keV line with the standard.

Table

Check on the reliability of the method. A: mineralized mice individually, B: mineralized mice individually in equilibrium.

Measurement	Counting rate (cpm) in the band		Activity (μCi)
	187 keV	1764 keV	
A	2473	200	0.0303
	2154	116	0.0262
	2573	174	0.0292
	3015	218	0.0334
	2679	131	0.0334
		Total	0.153
B			0.0332
			0.0253
			0.0337
			0.0329
			0.0353
		Total	0.160

It is evident that the error amounts to 3.1 per cent although the experiment covers three different geometries (5 mice in vivo \times 1 ampoule in phantom \times 1 ampoule in the air in the axis of the crystal). The reproducibility was ascertained from measurements of 10 mice at the 240 and 251 day after injection. The mean was calculated from ^{226}Ra and RaC (^{214}Bi) values for ten measurements, the standard deviation and the relative error being calculated according to normal relations. The square of relative errors from the statistics of radioactive decay was subtracted from the squares of relative errors for ^{226}Ra and RaC (^{214}Bi). The resulting relative error thus includes for both isotopes the effect of the geometry variation and the stability of measurement conditions for both isotopes; for ^{226}Ra this error amounts to ± 3.4 per cent and for RaC (^{214}Bi) ± 0.9 per cent.

SUMMARY

Low Compton scattering affords means of direct measurement of the ^{226}Ra 187 keV line, the quantitative evaluation being based on the phantom calibration procedure. The non-equilibrium state is an advantage. The retention curves of ^{226}Ra in mice during a period of up to 352 days are presented and the kinetics of daughter products, especially of ^{222}Rn , proved.

ZUSAMMENFASSUNG

Niedrige Compton Streuung gestattet direkte Messungen der ^{226}Ra 187 keV Linie, deren quantitative Berechnung sich auf Phantom Kalibrierungen stützt. Der Nicht-Gleichgewichtszustand ist ein Vorteil. Die Retentionskurven von ^{226}Ra in der Maus während einer Periode bis zu 352 Tagen werden gegeben und die Kinetik der Tochterprodukte, besonders von ^{222}Rn , dargelegt.

RÉSUMÉ

La diffusion Compton de faible énergie fournit un moyen de mesure directe de la ligne de 187 keV du ^{226}Ra , l'évaluation quantitative étant basée sur la technique d'étalonnage sur fantôme. L'état de non équilibre est un avantage. L'auteur présente les courbes de rétention de ^{226}Ra sur des souris pendant une période allant jusqu'à 352 jours; il montre la cinétique de ces produits descendants, en particulier du ^{222}Rn .

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