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ABSTRACT

The Medical Internal Radiation Dose Committee method was used to calculate the radiation dose to the skeleton, bone marrow, kidneys, liver and whole body for a 10 mCi dose of ^{99m}Tc in the form of 'Skeltec' a thermostable technetium compound for bone scanning. Activity concentration in these organs was determined from both published and unpublished results of phantom, biopsy, and animal experiments.

The calculated doses compare favourably with those published for the widely used bone scanning agent ^{18}F.

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ANIMALS; BIOPSY; BODY; BONE MARROW; DOSIMETRY; INTAKE; INTERNAL IRRADIATION; ISOMERIC NUCLEI; KIDNEYS; LABELLED COMPOUNDS; LIVER; PHANTOMS; RADIATION DOSES; SKELETON; TECHNETIUM 99

CONTENTS

1. INTRODUCTION

Radiation doses to the skeleton, bone marrow, kidneys, liver and whole body have been calculated for a 10 mCi dose of ^{99m}Tc in the form of Skeltec (Murray et al. 1972). The calculations use the equations and terminology of the Medical Internal Radiation Dose Committee (MIRD) method (Loevinger and Berman 1968, and Brownell, Ellett and Reddy 1968), and the 'Standard Man' organ masses quoted by Snyder et al. (1969). The activity concentrated in the organs of interest was determined from a combination of phantom and biopsy measurements and animal studies.

2. DETERMINATION OF ACTIVITY DISTRIBUTION

The distribution of Skeltec in the body was estimated from animal measurements and from measurements using a gamma camera calibrated against simple organ phantoms. It was found that the principal organs involved were the skeleton, bone marrow, liver and kidneys. Activity which could not be accounted for in these organs was assumed to be uniformly distributed in the whole body.

2.1 Skeleton and Bone Marrow

Animal measurements (Murray et al. 1972) showed that approximately 35% of the injected activity is deposited in the skeleton. Hence for a 10 mCi dose 3.5 mCi was taken up by the skeleton. Biopsy measurements (I.P.C. Murray 1972, private communication) showed that of the activity in the skeleton 10.7% concentrated in the bone marrow. Estimates were obtained for cumulated activity* in the skeleton from gamma camera phantom measurements and by calculation using an initial activity of 3.5 mCi and assuming removal by radioactive decay only. The skeletal uptake was based on gamma camera results obtained by the Department of Nuclear Medicine at the Prince of Wales Hospital, Sydney, related to a series of measurements with a phantom and assumed that the concentration of activity per unit mass of skeleton was the same as that determined for the femur. A phantom thigh was used to calibrate the camera so that total counts over the area of interest could be converted to activity present in the bone.

The phantom consisted of a central tube 'femur' surrounded by a container filled with water containing ^{99m}Tc to simulate the thigh of a person to whom Skeltec had been administered. The activity concentration used was that expected from volunteer blood sample results supplied by the Department of Nuclear Medicine at the Prince of Wales Hospital. The gamma camera count rate due to this activity was then determined. It was assumed that the equal activity in an actual thigh would produce the same count, and additional counts would be due to activity in the bone. A known activity was then added to the 'femur' portion of the phantom and a new total count obtained with the camera. It was thus possible to determine the count rate per unit activity in the femur for a given activity in the remainder of the thigh, enabling the activity in the femur to be determined in the presence of the extra-skeletal background.

By combining phantom measurements and gamma camera results provided by the Department of Nuclear Medicine, it was possible to determine the activity present in a patient's femur at convenient times up to six hours after the administration of 10 mCi ^{99m}Tc in the form of Skeltec.

The activity present was plotted against time of measurement (Figure 1). The curve was extrapolated to infinite time and the area under it found to obtain the cumulated activity in microcurie-hours. This was 924 μCi-h. for an estimated bone mass of 150 grams which corresponds to 61.6 mCi-h for a 10 kg 'Standard Man' skeleton. Since 10.7% of the skeletal activity is concentrated in the marrow the cumulated activity in the 150 g portion of femur was 99 μCi-h. The mass of marrow involved is 45 g which corresponds to 6.6 mCi-h for the 'Standard Man' marrow mass of 3 kg.

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* MIRD term for time integrated activity.

2.2 Liver

The activity concentration in the liver was estimated from rabbit studies. It has been found that up to 10% of the injected activity concentrated in the liver (Murray et al. 1972 and R.E. Boyd 1972, private communication). For a 10 mCi dose the upper limit to the uptake would be 1.0 mCi. Other measurements (R.E. Boyd 1972, private communication) showed that the activity in the skeleton was 4.7 times that in the liver giving a liver activity of 0.75 mCi. The dose calculations use the higher of these estimates (1.0 mCi).

2.3 Kidneys

Figure 2 shows the organ retention curve for activity in the kidneys determined from gamma camera-phantom measurements. The cumulated activity determined from this curve was 5.64 mCi-h. After the initial rapid removal the activity present in the kidney settled down to a base level which was depleted by normal radioactive decay. It was assumed that the initial value of this component (approximately 650 μCi) should be included with the 60% of injected activity retained by the body (McKay et al. 1972).

2.4 Whole Body

Of the 60% of activity retained all but 0.85 mCi can be accounted for in the organs considered above (skeleton 3.5 mCi; liver 1.0 mCi; long term kidney component 0.65 mCi). It was assumed that this activity was uniformly distributed in the whole body. These results are summarised in Table 1.

3. DOSIMETRIC DATA AND METHOD OF CALCULATION

The ^{99m}Tc decay scheme and absorbed dose constants Δ_i for all emissions are taken from Dillman (1969). In the calculation of doses to an organ due to activity deposited in that organ, an absorbed fraction of unity was assumed for the low energy X-ray and electron emissions. Hence these emissions will contribute only to the dose to the organ in which the activity is deposited. Except where actual cumulated activity measurements were made using the gamma camera it was assumed that removal of activity from an organ was by radioactive decay only. Provided there is no significant transfer of activity to that organ from elsewhere in the body this assumption gives the maximum dose estimate.

In terms of the MIRD method of calculation the general equation for the absorbed dose is

$$D_{(v \leftarrow r)} = \frac{\tilde{A}_r}{M_v} \Sigma \Delta_i \ \phi_{i(v \leftarrow r)} \ \text{rad} \qquad (1)$$

where $D_{(v \leftarrow r)}$ = average absorbed dose to a volume v from a source r

$\tilde{A}_r$ = cumulated activity in a region, r, in microcurie-hours

M_v = mass of target volume, v, in grams

Δ_i = absorbed dose constant for the i-th emission from the source r in g-rad/mCi-h

$\phi_{i(v \leftarrow r)}$ = absorbed fraction for the i-th emission with the source in region r and v the target volume.

In the case of self irradiation of an organ by activity deposited in that organ Equation 1 becomes

$$D_{(v \longleftrightarrow v)} = \frac{\tilde{A}_v}{M_v} \Sigma \Delta_i \ \phi_{i(v \longleftrightarrow v)} \ \text{rad} \qquad (2)$$

Where $\tilde{A}_v$ = cumulated activity in target volume v,

M_v = mass of organ containing activity

and $\phi_{(v \leftrightarrow v)}$ = absorbed fraction for the i-th emission for irradiation of organ volume v by activity distributed in that organ.

All doses were calculated using Equations 1 and 2 and the absorbed fractions used were taken from the tabulations of Snyder et al. 1969.

The calculation of $\Sigma \Delta_i \phi_{i(v \leftrightarrow v)}$ for the organs considered is summarised in Table 2. All values of $\Delta_i \phi_{i(v \leftarrow r)}$ involve only the 0.1405 MeV photon emission and the relevant values are given below. Final results of dose calculations have been rounded off to one significant figure to be more consistent with the accuracy of the various assumptions.

The calculation of doses to the organs for which data was obtained is summarised below. A backscatter contribution to the photon component of $D_{(v \leftrightarrow v)}$ for central organs is included where applicable.

4. ORGAN DOSE CALCULATIONS

4.1 Skeleton (Brownell, Ellett and Reddy 1968)

Irradiation by activity deposited in the skeleton

(a) Calculation using phantom estimate of cumulated activity in the skeleton.

Skeleton mass	=	10 kg
Cumulated activity	=	61.6 mCi-h
$\Sigma \Delta_i \phi_{i(v \leftrightarrow v)}$	=	0.0789 g-rad/μCi-h (Table 2)
From Equation 2 $D_{(v \leftrightarrow v)}$	=	0.49 rad
Backscatter dose	=	0.04 rad
Total internal dose	=	0.53 rad

The external dose to the skeleton is due to irradiation by 0.1405 MeV photons from sources in the kidney, liver and general whole body distribution. For this energy Δ_i = 0.2643 g-rad/μCi-h and as the absorbed fractions in the skeleton for these source organs are approximately equal to 0.06, only one calculation using Equation 1 was required.

Cumulated external activity A_r	=	21.7 mCi-h
and $\Delta \phi_{(v \leftarrow r)}$	=	0.016 g-rad/μCi-h
From Equation 1 $D_{(v \leftarrow r)}$	=	0.035 rad
Total dose to the skeleton	=	0.6 rad

(b) Calculation using animal measurement estimate of cumulated activity in the skeleton.

Cumulated activity	=	30.4 mCi-h
From Equation 2 $D_{(v \leftrightarrow v)}$	=	0.239 rad
Backscatter dose	=	0.024 rad
Total internal dose	=	0.26 rad
External dose to the skeleton	=	0.035 rad
Total dose to the skeleton	=	0.3 rad

4.2 Bone Marrow

Irradiation by activity deposited in the bone marrow

Bone marrow mass	=	3 kg
Cumulated activity	=	6.6 mCi-h
$\Sigma \Delta_i \phi_{i(v \leftrightarrow v)}$	=	0.0789 g-rad/μCi-h (Table 2)
From Equation 2 $D_{(v \leftrightarrow v)}$	=	0.17 rad which is increased by backscatter to 0.19 rad

To this must be added the dose due to irradiation of the marrow by activity in the skeletal bone, in the kidneys, in the liver and the remaining body distribution.

Irradiation by activity in skeletal bone

Cumulated activity	=	55 mCi-h
$\Delta \phi_{(marrow \leftarrow bone)}$	=	0.0132 g-rad/μCi-h
From Equation 1 $D_{(marrow \leftarrow bone)}$	=	0.24 rad

Irradiation by activity in kidneys

Cumulated activity	=	5.64 mCi-h
$\Delta \phi_{(marrow \leftarrow kidney)}$	=	0.0061 g-rad/μCi-h
From Equation 1 $D_{(marrow \leftarrow kidney)}$	=	0.01 rad

Irradiation by activity in liver

Cumulated activity	=	8.69 mCi-h
$\Delta \phi_{(marrow \leftarrow liver)}$	=	0.0037 g-rad/μCi-h
From Equation 1 $D_{(marrow \leftarrow liver)}$	=	0.01 rad

Irradiation by whole body distribution of activity

Cumulated activity	=	7.39 mCi-h
$\Delta\ \phi_{(\text{marrow} \leftarrow \text{whole body})}$	=	0.0066 g-rad/μCi-h
From Equation 1 $D_{(\text{marrow} \leftarrow \text{whole body})}$	=	0.016 rad

The total dose to bone marrow is therefore 0.5 rad.

4.3 Kidneys

Irradiation by activity deposited in the kidneys

Kidney mass	=	0.29 kg
Cumulated activity	=	5.64 mCi-h
$\Sigma\ \Delta_i\ \phi_{i\,(v \leftrightarrow v)}$	=	0.0565 g-rad/μCi-h (Table 2)
From Equation 2 $D_{(v \leftrightarrow v)}$	=	1.1 rad which is increased by backscatter to 1.2 rad

To this must be added the dose due to irradiation of the kidneys by the activity in the skeleton, in the liver and the remaining body distribution.

Irradiation by activity in the skeleton

Cumulated activity	=	61.6 mCi-h
$\Delta\ \phi_{(\text{kidneys} \leftarrow \text{skeleton})}$	=	2.6×10^{-4} g-rad/μCi-h
From Equation 1 $D_{(\text{kidneys} \leftarrow \text{skeleton})}$	=	0.055 rad

Irradiation by activity in the liver

Cumulated activity	=	8.69 mCi-h
$\Delta\ \phi_{(\text{kidneys} \leftarrow \text{liver})}$	=	0.0011 g-rad/μCi-h
From Equation 1 $D_{(\text{kidneys} \leftarrow \text{liver})}$	=	0.033 rad

Irradiation by whole body distribution of activity

Cumulated activity	=	7.39 mCi-h
$\Delta\ \phi_{(\text{kidney} \leftarrow \text{whole body})}$	=	0.0005 g-rad/μCi-h
From Equation 1 $D_{(\text{kidney} \leftarrow \text{whole body})}$	=	0.013 rad

The total dose to the kidneys is therefore 1.3 rad.

4.4 Liver

Irradiation by activity deposited in the liver

Liver mass	=	1.83 kg
Cumulated activity	=	8.69 mCi-h
$\Sigma \Delta_i \; \phi_{i\,(v \leftrightarrow v)}$	=	0.0810 g-rad/μCi-h (Table 2)
From Equation 2 $D_{(v \leftrightarrow v)}$	=	0.38 rad which is increased by backscatter to 0.42 rad

To this must be added the dose due to irradiation of the liver by the activity in the skeleton, in the kidneys and the remaining body distribution.

Irradiation by activity in the skeleton

Cumulated activity	=	61.6 mCi-h
$\Delta \; \phi_{(liver \leftarrow skeleton)}$	=	0.0012 g-rad/μCi-h
From Equation 1 $D_{(liver \leftarrow skeleton)}$	=	0.04 rad

Irradiation by activity in the kidneys

Cumulated activity	=	5.64 mCi-h
$\Delta \; \phi_{(liver \leftarrow kidney)}$	=	0.0066 g-rad/μCi-h
From Equation 1 $D_{(liver \leftarrow kidney)}$	=	0.02 rad

Irradiation by whole body distribution of activity

Cumulated activity	=	7.39 mCi-h
$\Delta \; \phi_{(liver \leftarrow whole\ body)}$	=	0.0026 g-rad/μCi-h
From Equation 1 $D_{(liver \leftarrow whole\ body)}$	=	0.01 rad

The total dose to the liver is therefore 0.5 rad.

4.5 Whole Body

Irradiation by whole body distribution of activity

Whole body mass	=	70 kg
Cumulated activity	=	7.39 mCi-h
$\Sigma \Delta_i \; \phi_{i\,(v \leftrightarrow v)}$	=	0.1317 g-rad/μCi-h (Table 2)
From Equation 2 $D_{(v \leftrightarrow v)}$	=	0.014 rad

To this must be added the dose due to activity in the skeleton, in the kidneys and in the liver.

Irradiation by activity in the skeleton

Cumulated activity = 61.6 mCi-h

$\Delta \phi_{(\text{whole body} \leftarrow \text{skeleton})}$ = 0.0925 g-rad/μCi-h

From Equation 1 $D_{(\text{whole body} \leftarrow \text{skeleton})}$ = 0.08 rad

Irradiation by activity in the kidneys

Cumulated activity = 5.64 mCi-h

$\Delta \phi_{(\text{whole body} \leftarrow \text{kidney})}$ = 0.1084 g-rad/μCi-h

From Equation 1 $D_{(\text{whole body} \leftarrow \text{kidney})}$ = 0.009 rad

Irradiation by activity in the liver

Cumulated activity = 8.69 mCi-h

$\Delta \phi_{(\text{whole body} \leftarrow \text{liver})}$ = 0.111 g-rad/μCi-h

From Equation 1 $D_{(\text{whole body} \leftarrow \text{liver})}$ = 0.014 rad

The total whole body dose is therefore 0.1 rad.

5. CONCLUSION

The results are summarised in Table 3 together with doses calculated from published data (Trott et al. 1969) for a typical 3.0 mCi administration of the widely used bone scanning agent ^{18}F. It can be seen that a lower patient dose is achieved by the use of Skeltec.

The accuracy of the dose estimates is limited by the accuracy of uptake measurements and the reliance on assumptions which cannot be verified, and by the accuracy of the absorbed fractions used. Although it is generally preferred to base dose calculations on actual human uptake data rather than extrapolate from animal results, the assumptions which have been made here, for example, that the concentration of activity in the femur is representative of that in the whole skeleton, are such that the results of the two methods probably have comparable accuracy. Overall the values obtained are generally much better than order of magnitude estimates and should serve as a useful guide to the dosimetry of this scanning agent.

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TABLE 1

ORGAN UPTAKE ACTIVITIES AND CUMULATED ACTIVITIES USED IN DOSE CALCULATIONS

Organ	Initial Activity (mCi)	Cumulated Activity (mCi-h)	Method
Skeleton	–	61.6	Phantom
Skeleton	3.5	30.4	Animal
Bone marrow	–	6.6	Phantom
Bone only	–	55.0	Phantom
Kidney	0.65	5.64	Phantom
Liver	1.0	8.69	Animal
Whole body	0.85	7.39	Animal
Total non skeleton	2.5	21.7	Animal

TABLE 2

BASIC DATA USED IN DOSIMETRY CALCULATIONS

Emission	Energy MeV	Δ_i (g-rad/μCi-h)	Skeleton		Whole Body		Kidneys		Liver	
			ϕ_i	$\Delta_i\phi_i$	ϕ_i	$\Delta_i\phi_i$	ϕ_i	$\Delta_i\phi_i$	ϕ_i	$\Delta_i\phi_i$
Gamma 1	.0021	0	0	.0000	0	.0000	0	.0000	0	0
Conversion electron	.0017	.0036	1.0	.0036	1.0	.0036	1.0	.0036	1.0	.0036
Gamma 2	.1405	.2643	0.15	.0396	0.35	.0924	0.065	.0172	0.158	.0417
K conversion	.1195	.0225	1.0	.0225	1.0	.0225	1.0	.0225	1.0	.0225
L conversion	.1377	.0032	1.0	.0032	1.0	.0032	1.0	.0032	1.0	.0032
M conversion	.1401	.0011	1.0	.0011	1.0	.0011	1.0	.0011	1.0	.0011
Gamma 3	.1427	.0001	0.15	.0000	0.35	.0000	0.065	.0000	0.158	.0000
K conversion	.1217	.0025	1.0	.0025	1.0	.0025	1.0	.0025	1.0	.0025
L conversion	.1399	.0009	1.0	.0009	1.0	.0009	1.0	.0009	1.0	.0009
M conversion	.1423	.0003	1.0	.0003	1.0	.0003	1.0	.0003	1.0	.0003
X-ray Kα1	.0184	.0017	1.0	.0017	1.0	.0017	1.0	.0017	1.0	.0017
Kα2	.0183	.0008	1.0	.0008	1.0	.0008	1.0	.0008	1.0	.0008
Kβ1	.0206	.0005	1.0	.0005	1.0	.0005	1.0	.0005	1.0	.0005
Kβ2	.0210	.0001	1.0	.0001	1.0	.0001	1.0	.0001	1.0	.0001
L X-ray	.0024	.0000	1.0	.0000	1.0	.0000	1.0	.0000	1.0	.0000
Auger Electrons	.0155	.0005	1.0	.0005	1.0	.0005	1.0	.0005	1.0	.0005
	.0178	.0002	1.0	.0002	1.0	.0002	1.0	.0002	1.0	.0002
	.0202	.0000	1.0	.0000	1.0	.0000	1.0	.0000	1.0	.0000
	.0019	.0004	1.0	.0004	1.0	.0004	1.0	.0004	1.0	.0004
	.0004	.0010	1.0	.0010	1.0	.0010	1.0	.0010	1.0	.0010
$\Sigma\Delta\phi_i$(g-rad/μCi-h)				.0789		.1317		.0565		.0810

TABLE 3

DOSES DUE TO ADMINISTRATION OF 10 mCi ^{99m}Tc IN THE FORM OF SKELTEC, COMPARED WITH DOSES DUE TO 3 mCi ^{18}F

(Trott et al. 1969)

Organ	Skeltec Dose (rad)	Fluorine-18 Dose (rad)
Skeleton	0.6*	0.7
	0.3**	
Bone marrow	0.5	0.7
Whole body	0.1	0.2
Kidneys	1.3	
Liver	0.5	

* Calculation using phantom estimate of cumulated activity in the skeleton.

** Calculation using animal measurements to estimate cumulated activity in the skeleton.

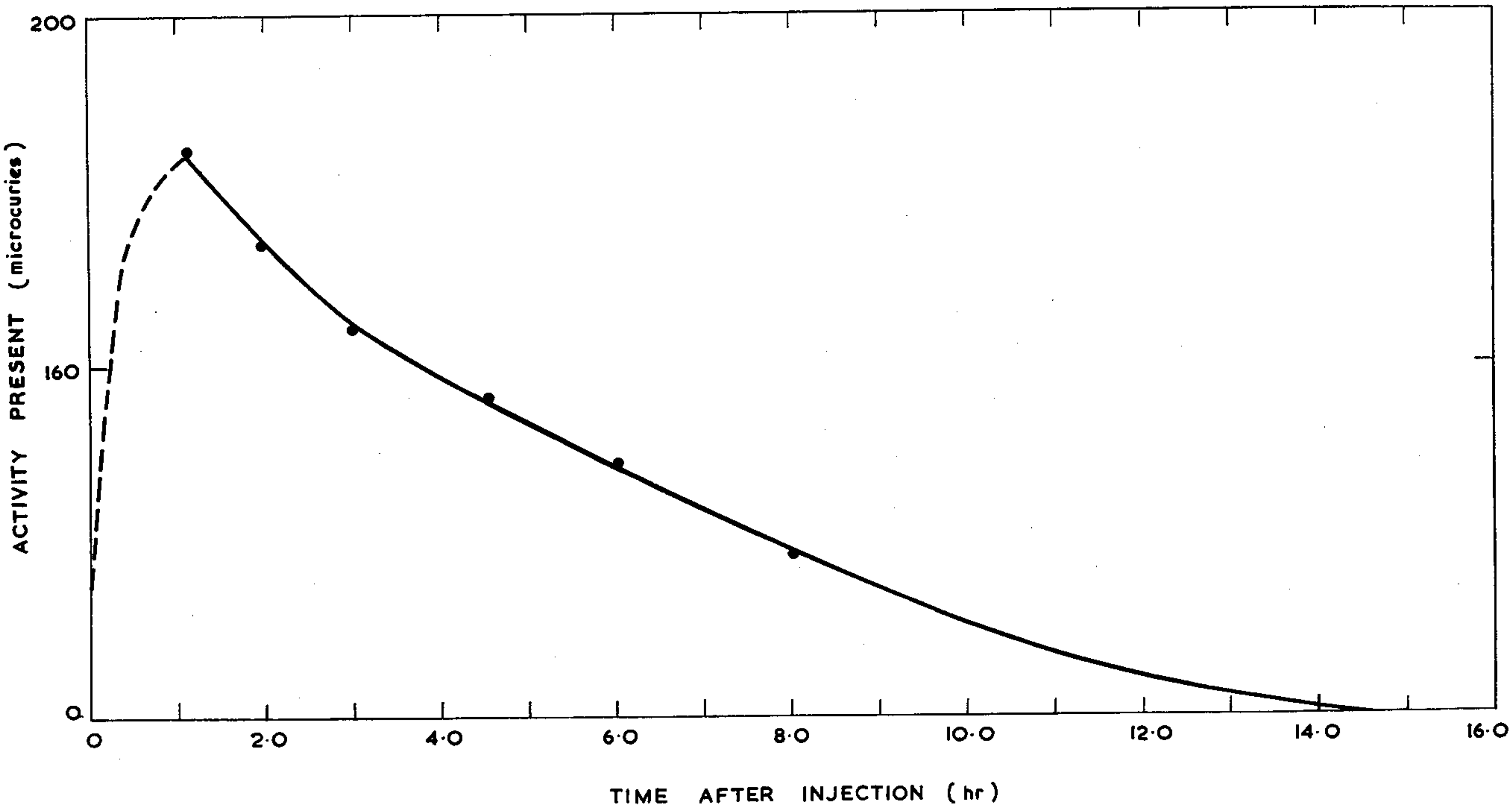

FIGURE 1. RETENTION CURVE FOR ACTIVITY IN FEMUR SECTION (ESTIMATED MASS 150g)

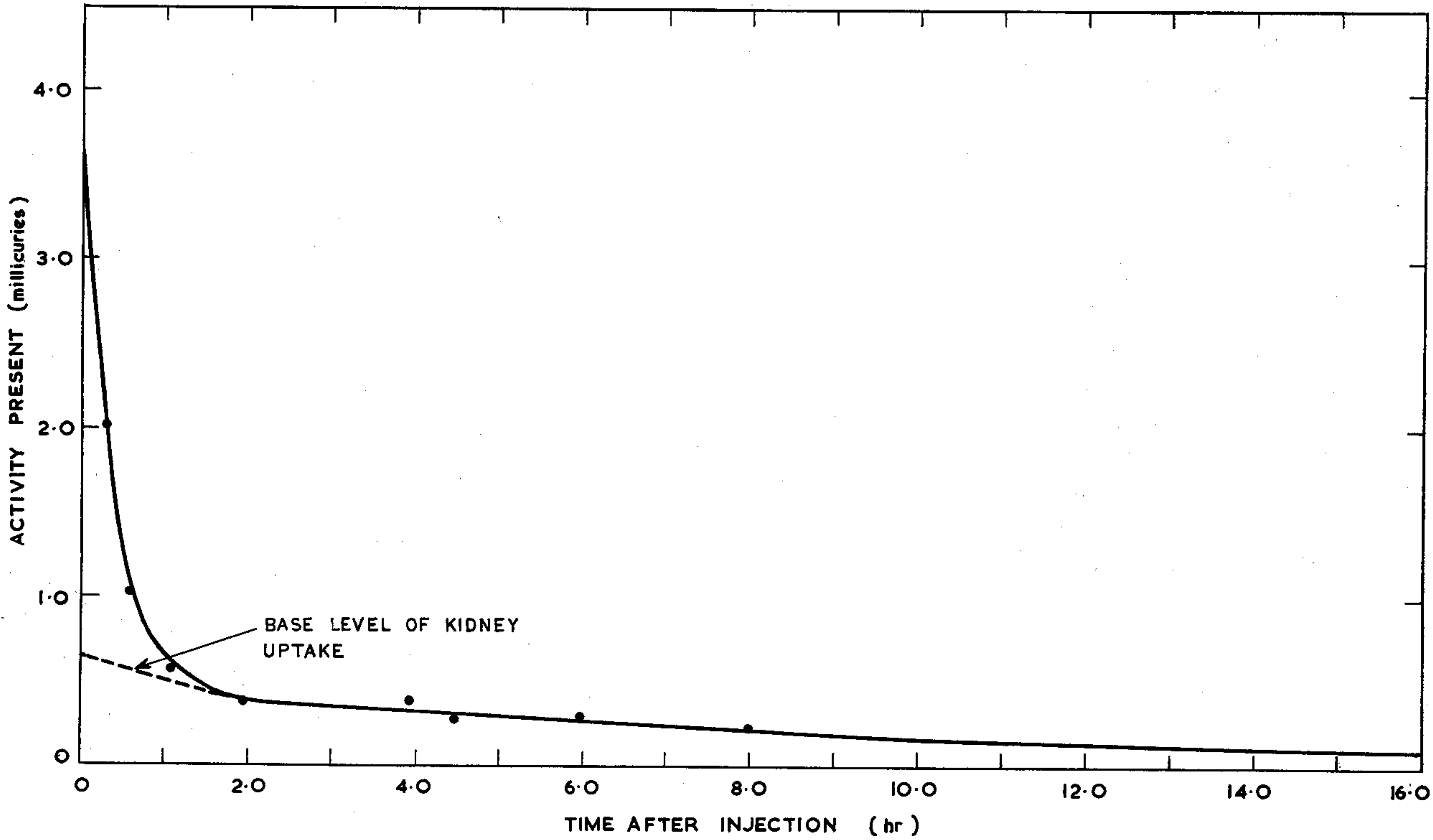

FIGURE 2. RETENTION CURVE FOR ACTIVITY IN KIDNEYS