Biodistribution, Radiation Dosimetry and Pharmacokinetics of ^{111}In-Antimyosin in Idiopathic Inflammatory Myopathies

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In view of the established role of ^{111}In-antimyosin in the detection of heart muscle pathology, radiation dose estimates were made for this substance. Biodistribution and biokinetic data were obtained from our studies, which failed to show abnormal uptake of ^{111}In-antimyosin in localized sites of skeletal muscle involvement in patients with idiopathic inflammatory myopathies. **Methods:** After intravenous administration of 74 MBq (2 mCi) ^{111}In-antimyosin, gamma camera scintigraphy was performed in 12 adult patients with inflammatory muscle disease and in 2 control patients. Six whole-body scans were performed over 72 h, and uptake of ^{111}In-antimyosin in organs was quantified using an attenuation-corrected conjugate counting method. Residence times in source organs were used with MIRDOSE software to obtain radiation dose estimates. Pharmacokinetic parameters were derived from serial whole-blood and plasma ^{111}In concentrations. **Results:** The tracer cleared slowly from the circulation, and highest organ uptakes were found in the marrow and liver; kidneys showed the highest concentrations. Uptake was also evident in spleen, the facial image and male genitalia. **Conclusion:** For a typical administered activity of 74 MBq ^{111}In-antimyosin, the kidneys receive the highest dose (58 mSv), and the effective dose is 11 mSv. Radioactivity was cleared from plasma at an average rate of 136 mL/h, and the mean steady-state distribution was approximately 5 L plasma.

Key Words: ^{111}In-antimyosin; idiopathic inflammatory myopathies; internal dosimetry; effective dose; pharmacokinetics

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Immunoscintigraphy with ^{111}In-labeled antimyosin antibody has been used in the imaging of myocardial necrosis and inflammation in situations such as myocardial infarction (*1*), myocarditis and cardiac rejection (*2*). It has been shown in animal experiments and in postmortem human studies that the antibody to myosin specifically binds to myocytes. In addition to documenting myocardial necrosis, immunoscintigraphy may localize the site in cases of patchy inflammation and necrosis. So far this technique has been applied largely to the imaging of myocardial inflammation. Whether this antibody binds to exposed myosin in inflamed or necrotic skeletal muscle is a relatively unanswered question that deserves further study. Although De Geeter et al. (*3*) showed evidence for the detection of muscle necrosis in dermatomyositis using ^{111}In-antimyosin Fab fragments, our own studies failed to show evidence of concentration of this substance in affected skeletal muscles in patients with idiopathic inflammatory myopathies (IIMs). Although the clinical aspects of our studies will be described elsewhere, the biodistribution and biokinetic data are used in this article to derive radiation dose estimates. In view of the absence of significant effects on biodistribution in our patients with muscle disease, we suggest that these dose estimates are applicable to healthy subjects.

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MATERIALS AND METHODS

Patients

This dosimetry study is based on scintigraphic measurements on 12 patients with IIM (5 men, 7 women; age range 23–67 y) seen at the Rheumatology Departments at Southend, St. George's and Guy's Hospitals.

They fulfilled the criteria of Bohan et al. (*4*) for polymyositis/dermatomyositis and, in addition to symptoms and signs of myositis, they had increased creatinine phosphokinase levels, positive electromyography and positive muscle biopsy. Similar scintigraphic measurements on 2 control patients (men) aged 53 and 66 y without muscle disease who were undergoing evaluation of a primary cardiac problem were also included in the study. All patients were admitted to Northwick Park Hospital for 3 d. Approval for these studies was obtained from the ethical committees of these hospitals.

^{111}In-Antimyosin Injection and Standard Solutions

Antimyosin Fab antibodies (Myoscint) obtained from Centocor Inc. USA (Malvern, PA) were mixed with citrate buffer and incubated with 100 MBq ^{111}In (Amersham International, Amersham, UK) for 10 min at room temperature. Chromatographic quality control was performed by using sodium citrate and measuring the relative amounts of activity remaining at the origin and at the solvent front. Only if the proportion remaining at the origin, representing the degree of incorporation of the label, was greater than 90% was the preparation used in vivo. Patients were injected through an antecubital vein with approximately 74 MBq

(2 mCi) of the labeled antibodies, the injection syringe was measured in an ionization chamber (Capintec Inc., Ramsey, NJ) before and after the injection.

A small residue of the labeled antibodies was retained for preparation of standard solutions for the quantification of sample counting. For this purpose, an accurately measured quantity (about 20 MBq [0.5 mCi]) was diluted volumetrically using 1% bovine serum albumin to prevent adherence of activity to the walls of glass vessels.

Gamma Camera Measurements

Whole-body scans were performed using an IGE 400AT gamma camera (International General Electric Medical Systems, Slough, UK) with a medium-energy collimator. Counts were obtained in 20% windows set over each of the gamma ray peaks at 171 and 245 keV. The camera was used over the couch at all times; patients were turned to the prone position for posterior measurements, and two separate overlapping scans were made for both anterior and posterior views to accommodate the full width of the body. Care was taken to align patients straight along the couch for all scans.

Anterior and posterior whole-body scans were performed 5 min, and 2, 7, 24, 48 and 72 h after the injection of ^{111}In-antimyosin. For the first 5 patients, scans were also performed 30 min postinjection.

Blood Activity

Blood samples (10 mL) were drawn at 5 and 30 min and 2, 7, 24, 48 and 72 h from the patients' arms contralateral to the ones used for injection. Samples were centrifuged and duplicate 1-mL aliquots of plasma were placed in plastic counting tubes and counted in an automatic gamma counter. Duplicate 1-mL aliquots of the counting standard were measured at the same time to determine the percentage of the administered activity in each sample of plasma. In seven studies, aliquots of whole blood were also counted in a similar manner and hematocrit values were measured.

Urine Collection and Analysis

Complete collections of urine were obtained throughout the study periods. Patients were provided with plastic bottles (2.5 L) containing approximately 50 mL 1% bovine serum albumin and were instructed to collect all urine in separate bottles for the periods 0–2, 2–4, 4–7, 7–24, 24–48 and 48–72 h. The bottles were counted in a fixed-geometry jig using a single large NaI detector (10.2 cm diameter × 7.6 cm). An aliquot of the standard solution was diluted in a similar container and counted under the same conditions at each volume. From these measurements, the percentage of the administered activity present in each urine bottle was determined. No evidence of endogenous radioactivity in the gastrointestinal tract was observed, and therefore no attempt was made to collect fecal samples.

Image Analysis

Complete whole-body scans were analyzed using a rectangular region of interest (ROI). For the two overlapping scans observed for each anterior and posterior view, the ROI was carefully fixed on image landmarks so that the two ROIs could be linearly juxtaposed; thus, the sum of counts in the two ROIs represented the total whole-body counts for that view. Complete whole-body scans were used to obtain whole-body retention data; therefore, the total counts from the whole-body ROIs were corrected for background using average pixel counts from four regions outside the body. Irregular ROIs were drawn to estimate counts in six source organs: heart, lungs, liver, spleen, kidneys and bladder as well as the L2 and L3 lumbar vertebrae. Counts from an organ ROI were corrected for background tissue activity using the average pixel count from small rectangular ROIs positioned adjacent to the organ ROI. Additionally, ROIs were drawn around other regions showing enhanced uptake of activity, such as the facial image (presumably soft tissues of the mouth and nasopharynx) and male genitalia. ROIs were selected to represent the whole organ from one of the overlapping whole-body images and were saved for analysis. Because the injected material resides initially in the blood pool, intense activity in the heart and large blood vessels in the chest made measurement of lung uptake difficult. For this reason, lung ROIs were drawn to obtain the organ size (pixels), and smaller regions were sampled within these ROIs but clear of the large vessel activity to obtain a mean lung pixel count. Because the right kidney overlaps the liver image, making separate assessment of its uptake difficult, the total counts in both kidneys were calculated as twice the counts estimated for the left kidney. Counts caused by the liver were estimated using an ROI drawn including the liver and the complete right kidney and subtracting the measured counts in the left kidney. According to the method of Mardirossian et al. (unpublished data) and Mardirossian et al. (*5*), an attempt was also made to estimate activity in bone marrow on the assumption that counts recorded from a rectangular ROI over the position of the L2 and L3 lumbar vertebrae were caused by ^{111}In activity of the marrow content. The background-corrected counts were used to make a rough estimate of the total red marrow uptake by multiplying by the ratio of total red marrow mass to that in the two measured vertebrae based on data for marrow distribution (*6*) and assuming uniform marrow uptake. At each scanning session, all background-corrected counts in the total body and individual organs were decay corrected to the time of the first scan after injection, and geometric means of conjugate images were calculated. The latter values were converted to absolute organ activity content using the results of phantom studies to assess the counting efficiency of the system and a transmission imaging method to correct for variable gamma-ray attenuation in the body at different organ sites. Finally, the absolute organ uptakes were translated to percent of administered activity by reference to the measured injected activity.

Dosimetry Methods

The time course of biological retention in whole body and selected organs was described by multiexponential equations of the form

$$R_t = \Sigma\, a_i e^{(-\lambda_i t)},$$

from which residence times (τh) were determined using the radioactive decay constant (0.0102/h) of ^{111}In. Net whole-body residence time not accounted for by the sum of residence times in specified organs was assumed to be uniformly distributed in the remaining body. MIRDOSE 3 software (Oak Ridge Institute for Science and Education, Oak Ridge, TN) (*7*) was used to calculate, for each patient, absorbed doses to 25 organs based on the MIRD formalism (*8*). Means and SDs of the target organ doses were calculated from 14 sets of data and used to determine effective dose (E) (*9*) values for ^{111}In-antimyosin. In these dose calculations, a dynamic bladder model was used with a bladder voiding period of 3.5 h, which was found to be the mean value for bladder emptying (*10*). This conforms with International Commission on Radiological Protection policy (*11*), but additional calculations were made to

observe the effect on effective dose of an alternative bladder voiding period of 4.8 h. Of the estimated residence time in the heart, 90% was allocated to the contents and 10% to the wall, based on the relative blood distribution in the contents and the walls (*6*).

Pharmacokinetic Analysis

From measurements of ^{111}In activity concentrations in plasma (14 patients) and whole blood (7 patients), pharmacokinetic parameters associated with tracer kinetics and clearance of the radiolabel were derived from fitting the results to an open two-compartment model. However, immunoassay for Fab antibodies in these samples was not performed. Serial plasma and whole blood counting data were fitted by biexponential equations of the form

$$R_t = ae^{(-\alpha t)} + be^{(-\beta t)},$$

where a and b represent the fractions of injected ^{111}In activity per liter plasma or whole blood at zero time and have rate constants (h^{-1}) of α and β, respectively. These equations were determined using SAAM II software (SAAM Institute, Seattle, WA), with values weighted by the SD of observed data. The pharmacokinetic parameters obtained from these equations were as follows (Mardirossian et al., unpublished data):

$$\text{Clearance, CL (L h}^{-1}) = (a/\alpha + b/\beta)^{-1}$$

$$\text{Initial volume of distribution, } V_{init}\text{ (L)} = (a + b)^{-1}$$

$$\text{Steady state volume of distribution, } V_{ss}\text{ (L)} = (CL)^2(a/\alpha^2 + b/\beta^2).$$

Values of V_{init} were compared with expected blood and plasma volumes calculated by height and weight.

RESULTS

Retention of ^{111}In-Antimyosin in Plasma and Whole Blood

Changes over time in concentration of injected ^{111}In-antimyosin in plasma (% administered activity/L) are shown in Figure 1 as mean values (±1 SD). Using SAAM II software, the data were fitted by the following equation:

$$\text{Plasma concentration (\% administered activity/L)} = 23.0e^{(-0.22t)} + 15.7e^{(-0.022t)},$$

where t (h) is the time postinjection.

In seven of the studies in which whole-blood radioactivity concentration was measured as well as the patient's hematocrit (hct), it was concluded that ^{111}In was confined to the plasma space. The average hematocrit was 0.41; Figure 1 shows that the observed values of whole-blood concentration are well fitted by the plasma retention equation multiplied by 0.59 (i.e., 1 − hct). However, the data can be fitted by the following equation:

$$\text{Whole-blood concentration (\% administered activity/L)} = 14.8e^{(-0.19t)} + 8.2e^{(-0.021t)}.$$

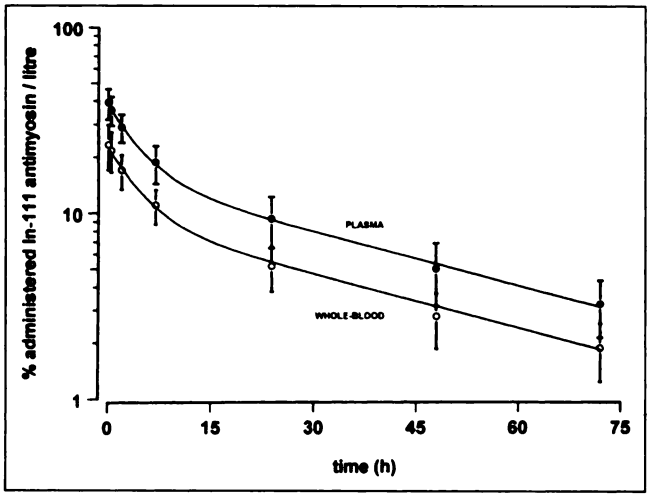

FIGURE 1. Retention of ^{111}In-antimyosin (% of administered activity/L) in plasma and whole blood. Mean values (±1 SD) are shown. Curves represent equations given in text.

TABLE 1
Total-Body and Organ Retention of ^{111}In-Antimyosin

Organ	Measurement time						
	5 min	30 min	2 h	7 h	24 h	48 h	72 h
Heart	5.8	4.6	4.9	3.6	2.2	1.4	0.94
	(2.0)	(1.8)	(1.6)	(1.3)	(0.89)	(0.57)	(0.48)
Lungs	5.0	5.6	4.3	3.2	2.0	1.4	1.2
	(1.3)	(1.0)	(1.2)	(0.92)	(0.73)	(0.56)	(0.44)
Spleen	2.2	2.2	1.9	1.5	1.40	1.3	1.3
	(0.64)	(0.87)	(0.77)	(0.55)	(0.72)	(0.79)	(0.71)
Liver	9.4	8.2	8.6	8.6	10.3	12.6	13.0
	(1.9)	(1.1)	(2.0)	(2.5)	(2.9)	(5.3)	(5.4)
Kidneys	3.8	4.0	5.3	6.4	6.7	6.4	5.4
	(1.3)	(0.77)	(2.4)	(3.0)	(3.7)	(2.9)	(2.7)
Marrow	—	—	—	15.9	12.0	11.3	11.2
				(6.7)	(5.5)	(2.9)	(3.7)
Total body	98.9	97.6	91.0	84.1	75.7	69.0	63.7
	(0.52)	(1.4)	(2.9)	(6.4)	(7.7)	(8.2)	(9.0)

Results are given as mean (SD) percent of ^{111}In-antimyosin administered in 14 patients at various times.

Whole-Body and Organ Retention of ^{111}In-Antimyosin

Table 1 shows mean (±1 SD) for whole-body and organ retention values for the 14 patients. The estimated uptake values for the site of the L2 and L3 vertebrae were multiplied by 22.9, the ratio of total marrow (1046 g) to the marrow content of L2 and L3 (45.7 g) (*6*). Bearing in mind this large correction factor, the estimated level of radioactivity in total bone marrow was higher than that in the measured organs, except at late imaging times, when it was similar to that in liver. One patient had a single kidney; kidney retention data for that patient were excluded from the statistical analysis. The maximum uptake in this patient's single kidney (9.0%) exceeded the mean value for both kidneys in the other 13 patients. The mean values and SDs of uptake components a_i (fraction of administered activity) and their respective biological elimination rates $\lambda_i(h^{-1})$ for

whole-body and organ retentions are given in Table 2, and the equations and mean retention values are plotted in Figure 2. Table 2 also includes estimated residence times (τh). In addition to the organs listed above, the average uptake was estimated to be approximately 1.3% in the face and approximately 0.5% in the male genitalia.

Urinary Excretion of ^{111}In

Approximately 10% of administered ^{111}In was excreted in urine by 2 h postinjection and, on average, approximately one third (18%–50%) was eliminated over 72 h. In Figure 3, the mean cumulative urine excretion data are shown together with the curve describing 100 − % whole-body retention, illustrating the good agreement between the two methods of estimating excretion.

Absorbed Dose Calculations

Absorbed doses (mGy/MBq) estimated for 25 target organs are shown in Table 3. The effective dose (E) was calculated to be 0.15 (±0.02) mSv/MBq. Use of a bladder voiding period of 4.8 h rather than 3.5 h would increase this value by approximately 2%. In these calculations, the observed retention of ^{111}In in male genitalia was included as part of the remaining body activity because the present studies did not establish the uptake, if any, in testes. Thus the dose to testes shown in Table 3 may be an underestimate. Based on the supposition that there was uniform distribution in the male genitalia, it can be estimated roughly that the testes dose would be increased to 0.14 mGy/MBq. As a result, E values for men would increase to 0.16 mSv/MBq. However, further studies are needed to determine the extent to which observed uptake of ^{111}In-antimyosin in male genitalia affects the dose to the gonads.

Pharmacokinetics

Table 4 shows the mean values of a, b, α and β calculated from equations of ^{111}In activity concentrations in plasma (n = 14) and whole blood (n = 7). Derived pharmacokinetic parameters are shown in Table 5 and include the half-times of the plasma and whole blood retention components ($T_{1/2\ (1)}$ and $T_{1/2\ (2)}$); the ratio of V_{init} to expected values of plasma volume (EPV) and whole-blood volume (EBV); clearance (CL); and steady-state volume of distribution (V_{ss}). Comparable data in Tables 4 and 5 were not significantly different from values found by Mardirossian et al. (unpublished data) (all P values >0.05).

DISCUSSION

The pattern of biodistribution in 12 patients with IIM was similar to that in 2 control patients with primary cardiac problems but without general muscle disease. For this reason, the 14 adult patients were considered to form a single group for purposes of establishing biodistribution and dosimetry data after intravenous administration of ^{111}In-antimyosin. Furthermore, because there was no evidence of abnormal concentration of ^{111}In-antimyosin in affected skeletal muscles in these patients, it is reasonable to suppose that radiation absorbed doses estimated from this study are applicable to the normal subject.

Intravenously administered ^{111}In-antimyosin was retained for a long time in the blood pool and images up to 2 h were characterized by activity in the vascular tree. Approximately 60% of administered activity left the blood with a $T_{1/2}$ of about 3 h and 40% with a $T_{1/2}$ of about 30 h; activity was confined to the plasma space. Excretion of the radioactive label occurred almost entirely via the renal system; no scintigraphic evidence of significant activity in the gastrointestinal tract was observed. After 72 h, the duration of our investigation, the average amount excreted in urine was 32.1% (±9.1%), although there was wide variation. Thus, taking radioactive decay into account, the patients still retained 33% of the administered radioactivity on average at

TABLE 2
a_i and λ_i Values for Total-Body and Organ Retentions, Together with Residence Times

Organ	a_1	λ_1	a_2	λ_2	a_3	λ_3	τ h
Heart	0.031	0.29	0.032	0.017			1.26
	(0.014)	(0.25)	(0.013)	(0.006)			
Lungs	0.016	0.51	0.021	0.081	0.019	0.0063	1.41
	(0.011)	(0.33)	(0.013)	(0.025)	(0.0091)	(0.0047)	
Spleen	0.0052	0.59	0.0065	0.14	0.013	0.00081	1.25
	(0.0067)	(0.44)	(0.0058)	(0.17)	(0.0072)	(0.0018)	
Liver	0.034	0.37	−0.072	0.05	0.13	−0.00004	12.0
	(0.020)	(0.23)	(0.061)	(0.031)	(0.052)	(0)	
Kidneys	−0.021	0.69	−0.03	0.084	0.087	0.0061	5.0
	(0.017)	(0.37)	(0.026)	(0.078)	(0.043)	(0.0013)	
Marrow	0.10	0.089	0.11	0.00078			11.2
	(0.12)	(0.092)	(0.032)	(0.0014)			
Total body	0.054	1.09	0.13	0.18	0.82	0.0035	60.4
	(0.032)	(0.41)	(0.052)	(0.047)	(0.075)	(0.0010)	

Results are given as mean (SD). a_i = fraction of administered activity; λ_i = biological elimination rate (h^{-1}); τ h = estimated residence time.

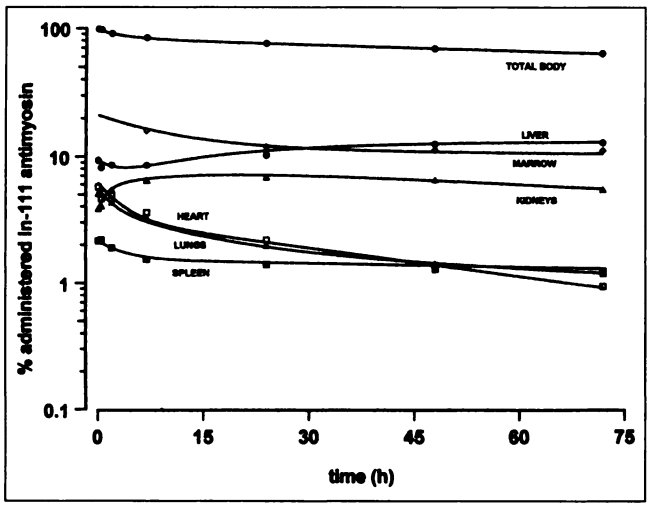

FIGURE 2. Retention of ^{111}In-antimyosin in whole body and various organs in humans. Data points are mean values for 14 patients; curves are described by mean values of a_i and λ_i derived from individual patient curves.

the end of our studies. The initial biodistribution pattern reflected the protracted retention in blood, with intense uptake in the heart and major vessels in the chest, making accurate analysis of the uptake in lungs difficult. The highest organ radioactivity level was estimated for bone marrow but, on average, of the organs that were measured completely, highest uptake was found in liver, with lesser amounts in kidneys and spleen. There were indications of competition for ^{111}In-antimyosin between liver and the renal system; the patient with the lowest liver uptake (6% at 24 h) had the highest kidney uptake (17.4% at 24 h) and also excreted the most activity (50% at 72 h). Apart from marrow, the highest uptake (% of administered substance) was observed in the liver (about 10% at 24 h). Liver uptake continued to increase from 7 h until 72 h in all patients except the one whose liver activity slowly declined. However, the highest organ concentration was found in the kidneys with a mean uptake of 6.4% at 7 h decreasing only slightly in the last 24 h. After the kidneys and liver, the highest activity concentration was observed in the spleen, although the early uptake of about 2.2% in this organ had slowly reduced to half this value by 72 h. The observation of marrow uptake became more obvious in scans after 7 h as the initial high blood background diminished, prompting an attempt to estimate

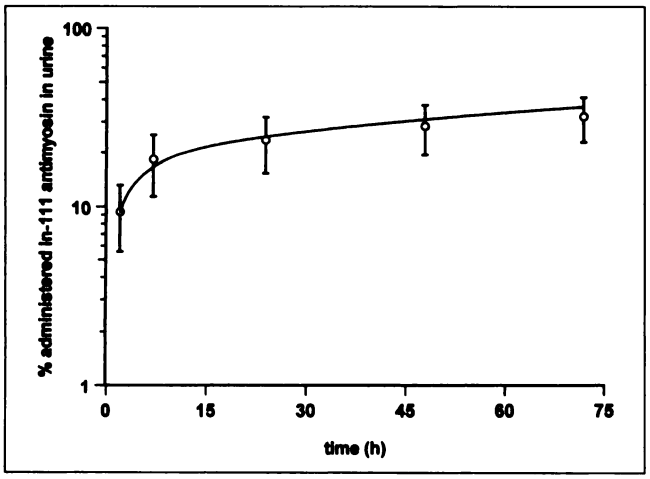

FIGURE 3. Cumulative urinary excretion of ^{111}In-antimyosin in humans. Data points are mean values for 14 patients. Curve represents 100 − whole-body retention curve shown in Figure 2.

TABLE 3
Radiation Absorbed Doses from ^{111}In-Antimyosin

Organ	Dose in mGy/MBq (bladder voiding period 3.5 h)
Adrenals	0.19 (0.02)
Brain	0.051 (0.012)
Breast	0.057 (0.009)
Gallbladder wall	0.21 (0.042)
LLI	0.091 (0.015)
Small intestine	0.11 (0.014)
Stomach	0.11 (0.014)
ULI	0.11 (0.013)
Heart wall	0.16 (0.04)
Kidney	0.78 (0.30)
Liver	0.47 (0.17)
Lungs	0.13 (0.02)
Muscle	0.075 (0.010)
Ovaries	0.098 (0.016)
Pancreas	0.17 (0.022)
Red marrow	0.24 (0.05)
Bone surface	0.20 (0.04)
Skin	0.044 (0.007)
Spleen	0.40 (0.17)
Testes*	0.051 (0.012)
Thymus	0.081 (0.013)
Thyroid	0.061 (0.013)
UB wall	0.14 (0.01)
Uterus	0.096 (0.014)
Total body	0.097 (0.012)
Effective dose	0.15 (0.02)

*For discussion of testes dose, see text.

Results are given as mean (SD) absorbed dose (bladder voiding period 3.5 h). LLI = lower large intestine; ULI = upper large intestine; UB = urinary bladder.

TABLE 4
Retention Parameters for ^{111}In-Antimyosin in Plasma and Whole Blood

	a (L^{-1})	b (L^{-1})	α (h^{-1})	β (h^{-1})
Plasma (n = 14)	0.234 (0.072)	0.159 (0.062)	0.264 (0.146)	0.0232 (0.0044)
Whole blood (n = 7)	0.146 (0.045)	0.0894 (0.035)	0.227 (0.0954)	0.0229 (0.0054)

Results are given as mean (SD). a and b represent fractions of ^{111}In activity per 1 plasma or whole blood at zero time; α and β are their respective rate constants.

TABLE 5
Derived Pharmacokinetic Values for ^{111}In-Antimyosin in Plasma and Whole Blood

	V_{init}/EV*	$T_{1/2(1)}$ (h)	$T_{1/2(2)}$ (h)	CL (mL/h)	V_{ss} (mL)
Plasma	1.02	3.45	26.3	136	4967
(n = 14)	(0.11)	(1.90)	(9.50)	(55)	(1115)
Whole blood	1.02	3.52	31.9	225	8698
(n = 7)	(0.11)	(1.42)	(8.0)	(51)	(2228)

*Expected volume of plasma (EPV) or whole-blood (EBV).
V_{init} = initial volume; EV = expected volume; $T_{1/2}$ = half-life; CL = clearance; V_{ss} = steady-state volume of distribution.

total marrow uptake. The adopted method, however, in which uptake at a small site (L2 and L3 vertebrae) was multiplied by a large correction factor estimated from the marrow content of the measurement site and of the total body, was subject to large errors but suggested a total marrow uptake of 12% after 24 h, similar to that in liver at late imaging times. Uptake in marrow is difficult to explain unless in vivo stripping of the label occurs to some extent. The measured heart uptake declined with a $T_{1/2}$ similar to that of the final blood component. In addition, there was strong and persistent uptake in the facial image amounting to approximately 1.2% at 2 h and obvious uptake of approximately 0.5% in male genitalia.

The highest mean absorbed dose (0.78 mGy/MBq) was calculated for kidneys with doses to the liver (0.47 mGy/MBq) and spleen (0.40 mGy/MBq) substantially higher than doses to other organs. The effective dose was estimated from the mean dose values to be 0.15 mSv/MBq. For the patient with a single kidney, the enhanced compensated uptake led to a relatively high dose of 1.9 mGy/MBq to that kidney.

In this study, we adopted some of the techniques of Mardirossian et al. (unpublished data), who investigated dosimetry and pharmacokinetics in 10 patients with suspected myocardial infarction. These techniques allowed direct comparison of dose estimates from the two studies. Mardirossian et al. also estimated that the highest mean dose was received by the kidneys (0.95 mGy/MBq ^{111}In), and their data suggest an effective dose of 0.17 mSv/MBq. Thus their mean dose values are slightly higher than ours. However, there are wide ranges of variation in biodistribution and dose estimates in both sets of data and in general there is good agreement. In making these comparisons, we recalculated the organ dose values of Mardirossian et al. for ^{111}In alone because those authors took into account the dose effects caused by the presence of ^{114m}In as a contaminant of the ^{111}In used to produce the labeled antimyosin. Their estimations were based on a ^{114m}In content of 0.16%, the maximal proportion at the time of expiration of the ^{111}In. It was found that this level of contamination led on average to 14.1% of the dose to source organs from the combination of both isotopes. The ^{111}In used in our studies was supplied by Amersham International and was stated to contain <0.08% ^{114m}In on the reference date. Our injections were all made on or before the reference date and it can be concluded that the average increase in doses to our patients caused by ^{111}In alone did not exceed 7% as a result of ^{114m}In contamination. However, it is important to estimate and consider the additional dose resulting from ^{114m}In in assessment of the radiation dosimetry of ^{111}In-antimyosin.

Comparable pharmacokinetic parameters for the ^{111}In label were also similar to those observed by Mardirossian et al. (unpublished data). There was good agreement on average between the derived values of V_{init} and plasma or whole blood volumes calculated from heights and weights of the patients. The average rate of clearance of radioactivity from plasma was 136 mL/h, equivalent to 233 mL/h whole blood, and the steady-state volumes of distribution of plasma and whole-blood were 1.8–1.9 times the initial volumes of distribution.

CONCLUSION

After intravenous administration of ^{111}In-antimyosin, the highest mean uptake was observed in bone marrow (estimated to be about 12%) and in liver (10%, increasing to 13%), but the highest mean concentration was found in kidneys (21%/kg). For a typical administered activity of 74 MBq (2 mCi) ^{111}In-antimyosin, the highest mean organ absorbed dose was estimated for kidneys (58 mSv), followed by the liver (35 mSv) and spleen (30 mSv). In view of potential error, the relatively large bone marrow dose estimate (18 mSv) should be considered with circumspection. However, for radiation safety purposes we have used this value to calculate the effective dose (11.0 mSv) resulting from ^{111}In alone. Although the majority of our subjects were patients with IIMs, the absence of evidence of abnormal uptake in diseased muscles (unpublished observations) suggests that the present dose estimates are applicable to healthy adult subjects. Our results on the dosimetry and pharmacokinetics of ^{111}In-antimyosin agree with those of Mardirossian et al. (unpublished data).

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