Radiation Dosimetry of Technetium-99m-DMSA in Children

Terry Smith, Kenneth Evans, Mark F. Lythgoe, Peter J. Anderson and Isky Gordon
Departments of Medical Physics and Radiology, Great Ormond Street Hospital for Children NHS Trust and Institute of Child Health, Great Ormond Street, London

Radiation dosimetry was performed on 24 children (aged 5 wk to 14.8 yr) who were undergoing routine diagnostic investigation of renal impairment with ^{99m}Tc-DMSA. **Methods:** Organ doses were calculated using MIRDOSE 3 with biokinetic data obtained in previously described studies, and effective doses and effective dose equivalents were estimated. Interpolation by inverse weight between pediatric anthropomorphic phantoms was compared with age-matching to discrete phantoms. Administered activities were scaled by body surface area from the adult activity of 100 MBq and the resulting radiation doses in normal children were compared with those that would have resulted from a schedule based on body weight. **Results:** The effective doses estimated by interpolation differed by up to 46% from those based on discrete phantoms and showed less variation. In children with normal bilateral renal function, the mean effective dose per administered activity was 0.91 ± 0.08 mSv or 0.98 ± 0.29 mSv by the two methods, respectively. Renal pathology reduced the effective dose, on average, by 15% of the value for normal patients. **Conclusion:** Over the pediatric age range, the uniformity of effective dose values was improved by scaling the administered activity according to body surface area rather than to body weight.

Key Words: technetium-99m-DMSA; pediatrics; internal dosimetry; effective dose; effective dose equivalent

J Nucl Med 1996; 37:1336–1342

The results of biokinetic studies on children of differing age and degree of renal dysfunction after the administration of ^{99m}Tc-DMSA have been presented (*1*). It was concluded that, other than lower values of excreted activity and uptake in knees in children less than 1 yr of age, there was little evidence of age dependency. For purposes of radiation dosimetry of ^{99m}Tc-DMSA in normal children, a single biokinetic model would therefore seem acceptable provided that the known age-dependency of bladder voiding periods was taken into account.

In children with renal abnormalities, the expected finding of reduced kidney uptake of ^{99m}Tc-DMSA was accompanied in most cases by increased urinary excretion. In view of the recognized implications of the radiation effects of radioactive bladder contents on other organs, especially gonads, it is not immediately obvious to what extent renal pathology influences estimates of effective dose compared with normal physiology.

The purpose of the present paper was to estimate individual radiation burdens from ^{99m}Tc-DMSA administered to 15 children with normal renal function and 9 with renal abnormalities. The measured biokinetic data were used to make radiation dose estimates for each child, but the period of bladder voiding appropriate for age was taken from a published model (*2*). Reference was made to one of five pediatric anthropomorphic phantoms chosen to represent the closest match to the physical and anatomical characteristics of a given child (*3*). In view of the inability to match perfectly each child to such a small series of discrete phantoms, a method of interpolation between dose estimates derived from adjacent pairs of phantoms was also investigated in these children.

Differences between the two methods have been assessed. Additionally, the overall success of the aim to equalize pediatric radiation burdens, using the amounts of administered activity scaled according to body surface area, was evaluated and compared with that of a method based on body weight alone.

Received Mar. 7, 1995; revision accepted Sept. 6, 1995.
For correspondence or reprints contact: Isky Gordon, FRCR, Consultant Radiologist, Department of Radiology, Great Ormond Street Hospital for Children NHS Trust, Great Ormond Street, London WC1N 3JH.

MATERIALS AND METHODS

Biodistribution

The time-course of biodistribution of ^{99m}Tc-DMSA in 24 children (15 normals, 9 abnormals) undergoing routine diagnostic imaging at Great Ormond Street Hospital NHS Trust was investigated as previously described (*1*). In summary, patients were imaged with a gamma camera up to 30 hr after injection of an amount of ^{99m}Tc-DMSA calculated by scaling the adult activity (100 MBq) according to relative body surface area. An attenuation-corrected conjugate counting technique was used to estimate the absolute activities in six organs (kidneys, liver, spleen, bladder contents, knees and whole body). After correction for radioactive decay, these were expressed as biological retention data relative to the amount of administered activity. The observed uptake of ^{99m}Tc-DMSA in knees has been assumed to concentrate in the metaphyses of the long bones. The rates of renal uptake and elimination, and the urinary excretion of ^{99m}Tc-DMSA were also measured.

Dose Estimation

The MIRDOSE 3 dose calculation program, based on the Medical Internal Radiation Dose (MIRD) Committee formalism (*4*) was used to estimate radiation doses ($rad \cdot mCi^{-1}$ or $mGy \cdot MBq^{-1}$) in 24 target organs following the input of our observed residence times in source organs kidneys, liver, spleen and remaining body. The dose to the metaphyseal growth complexes, however, had to be calculated separately.

Residence Times

Biological distribution data for the whole body (less bladder contents), kidneys, liver and spleen (*1*) were expressed in terms of single- or bi-exponential equations. Residence times (hr) in organs and tissues were estimated by integration of their effective retention curves. During the period of study, the measured uptake in knees was assumed to be retained with an elimination half-time which was large in relation to the radioactive half-life. Residence time in whole body was calculated from measured whole-body retention data after subtraction of the activity in bladder contents at each measurement time. The required residence time in remaining body was obtained by subtracting the sum of residence times in kidneys, liver and spleen from the whole body residence time. Residence time in bladder contents was automatically calculated by the MIRDOSE 3 program after inputting values of the retention parameters (magnitude and half-times of components) derived

from equations of observed whole-body retention after subtraction of bladder activity, together with the appropriate bladder voiding period for a given child.

Pediatric Phantoms and S-values

S-values for ^{99m}Tc and source organs kidneys, liver, spleen and bladder contents are incorporated in the MIRDOSE 3 program which also calculates the S-value for remaining body. S-values are available for five differently sized pediatric anthropomorphic phantoms (*3,5*) representing children of age 15, 10, 5, 1 yr weighing 55.6, 32.4, 18.6, 9.9 kg, respectively and the neonate weighing 3.4 kg. Children in the present study were related to the nearest representative phantom by age. The bladder voiding periods used with the MIRDOSE 3 dynamic bladder model (*6*) were 2 hr for the neonate, 1 and 5 yr phantoms; 3 hr for the 10 yr phantom; and 3.5 hr for the 15 yr phantom (*2*). An S-value for the metaphyseal growth complexes is not generally available and consequently the S-value for self-dose in this tissue was calculated following the method of Gelfand et al. (*7*). This method assumes that the combined volume of the complex can be described by a right cylinder of height 3-to-4 mm, diameter 2-to-4 cm and density 1.3 $g \cdot cm^{-3}$. Physical data for ^{99m}Tc were taken from ICRP publication 38 (*8*). The self-absorbed fraction was assumed to be 1.0 for particulate radiation and values for penetrating radiation were estimated from the data of Widman and Powsner (*9*). A simple linear relationship with age was assumed for the variations in height (3–4 mm) and diameter (2–4 cm) of the right cylindrical model of the growth complex (*7*). The resulting S-factor for self-dose to the metaphyseal growth complex decreased with increasing age, ranging from 3.0 E−2 for the 5-wk-old child to 5.9 E−3 for the 14.8-yr-old child. It was assumed that the observed uptake in pairs of knees was equally divided among four metaphyseal growth complexes. Doses to other organs from the activity in the metaphyseal growth complexes and doses to the latter from other organs will be small and have been ignored.

Unilateral and Disproportionate Uptake in Kidneys

In the four patients who had unilateral renal uptake, the dose to the functioning kidney was assumed to be twice the value yielded by the MIRDOSE 3 program for a pair of normally functioning kidneys. This allows for the fact that all the kidney residence time in such cases is associated with a single kidney, but is probably a worst-case consideration since renal hypertrophy, if present, will reduce this increase in dose. Patients 8 and 20 showed large disproportionality in renal uptake. The higher kidney dose estimate has been used for dosimetry purposes. In the absence of S-values for the individual kidneys, the effect of these disproportionate renal uptakes on doses to other organs has not been considered.

Equivalent Dose, Effective Dose and Effective Dose Equivalent

From values of equivalent dose to 24 target organs calculated using MIRDOSE 3, the effective dose (E) and the effective dose equivalent (H_e) were calculated for each patient using relevant tissue weighting factors (*10,11*). It should be noted that these weighting factors are derived from a population consisting mostly of adults and are intended primarily for radiation workers. Our values of E and H_e for children should be interpreted with caution. Following current practice, they are presented to allow a single figure dose comparison with other radiopharmaceuticals used in pediatric investigations. In the calculation of E, we have assumed the dose to the thymus to represent the dose to the esophagus (*12*), the colon dose to be given by 0.57 ULI dose + 0.43 LLI dose (*13*), and used the appropriate gonad dose for individual children.

Interpolated Doses

In an attempt to reduce errors in dose estimates arising from mismatch of a given patient to one of five discrete pediatric anthropomorphic phantoms, dose calculations were repeated using an interpolation method based on inverse body weight. The MIRDOSE 3 program was used to determine dose estimates for each child using the two adjacent phantoms whose differential weight range included the weight of the child. For this purpose, the adult phantom was used where necessary. A computer program was written to perform linear interpolation on the basis of inverse body weight between organ doses calculated using the two phantoms. In two cases, it was necessary to extrapolate beyond the extremes of the available range of phantoms. E and H_e were recalculated using the interpolated or extrapolated equivalent organ doses. It is acknowledged that this simple method does not provide a true correction, since the physical parameters necessary for dose calculation are not dependent on body weight alone.

Statistics

Summary statistics of measured data are presented as mean ± 1 s.d. and differences between mean values for different groups were tested for significance using Student's t-test. Correlation coefficients between various data sets were calculated and tested for significance by t-test.

RESULTS

Residence Times

In 15 children with normal renal function, the residence times in the kidneys, liver, spleen, bladder and remaining body were 3.01 ± 0.41 hr, 0.35 ± 0.16 hr, 0.13 ± 0.08 hr, 0.18 ± 0.09 hr and 4.08 ± 0.49 hr, respectively. There was no significant correlation between kidney, liver or spleen residence times and age or weight. There were, however, significant correlations between remaining body residence time (τ_{rb}) and both age and weight. The regression equations were

$$\tau_{rb}\,(\text{hr}) = 4.43 - 0.014 \times \text{weight (kg)} \quad (r = -0.73;\ p < 0.005) \text{ and}$$

$$\tau_{rb}\,(\text{hr}) = 4.45 - 0.065 \times \text{age (yr)} \quad (r = -0.74;\ p < 0.005).$$

We have previously shown (*1*) that children younger than 1 yr excrete a significantly lower proportion of the administered activity in urine than children older than 1 yr. This would lead to an increase in remaining body residence time in children under 1 yr.

In the nine children with renal pathology, the mean residence times in kidneys, liver, spleen, bladder and remaining body were 1.07 ± 0.60 hr, 0.39 ± 0.15 hr, 0.10 ± 0.07 hr, 0.23 ± 0.12 hr and 5.39 ± 0.83 hr, respectively.

Differences between Two Dose Estimation Methods

Radiation dose estimates obtained both by reference to discrete pediatric phantoms by age and by interpolation between phantoms by inverse weight are given in Tables 1 and 2 for children with normal renal function and for those with renal pathology, respectively. Differences between effective doses calculated by the two methods were within ±10% in 6 patients and within ±20% in 13. In the remaining 11 children, larger differences of up to +46% were observed. The largest increase occurred in the youngest child, (Patient 20) aged 5 wk, whose weight of 2.2 kg was substantially lower than that of the neonate phantom. On the other hand, the largest decrease (−42%) occurred in a 4-mo-old child (Patient 5) whose weight of 6.6 kg was halfway between those of the neonate and 1-yr phantoms while a similar decrease (−39%) was observed in an 11-yr-old

TABLE 1
Dosimetry of Technetium-99m-DMSA in 15 Children with Normal Renal Function

	Patient no.						
	3	5	4	24	13	9	12
Sex	M	M	F	M	M	F	M
Age	7 wk	4 mo	5 mo	6 mo	8 mo	11.5 mo	1.3 yr
Weight (kg)	4.2	6.6	4	4.1	6.5	7.6	8
Height (cm)	54	61	57	63	63	64	76
Surface area (m^2)	0.238	0.316	0.243	0.264	0.322	0.347	0.402
Max % kidney uptake (L/R)	19.5/19.9	23.0/19.1	19.4/19.6	22.4/26.0	15.8/16.5	23.5/25.9	19.5/18.6
Administered activity (MBq)	14	20	14	14	19	22	23
Residence Times (hr)							
Kidneys	2.9	2.91	2.79	3.37	2.18	3.56	2.64
Liver	0.1	0.53	0.57	0.511	0.103	0.4	0.23
Spleen	0.11	0.071	0.11	0.121	0.076	0.2	0.05
Bladder	0.133	0.045	0.228	0.027	0.189	0.052	0.194
Remaining body	5.07	4.61	4.24	4.44	4.68	3.77	4.19
Discrete Phantom Method							
Pediatric phantom used	Neonate	Neonate	Neonate	Neonate	1 yr	1 yr	1 yr
Organ dose ($mSv \cdot MBq^{-1}$)							
Adrenals	1.1E−01	1.1E−01	1.0E−01	1.2E−01	4.4E−02	6.2E−02	4.9E−02
GB wall	6.1E−02	6.7E−02	6.5E−02	6.9E−02	2.3E−02	3.3E−02	2.6E−02
Kidneys	1.5E+00	1.5E+00	1.5E+00	1.8E+00	4.5E−01	7.4E−01	5.5E−01
Liver	4.6E−02	9.6E−02	9.9E−02	9.7E−02	2.0E−02	4.1E−02	2.8E−02
Pancreas	7.4E−02	7.4E−02	7.2E−02	8.0E−02	3.1E−02	4.2E−02	3.3E−02
Bone surface	6.8E−02	6.5E−02	6.2E−02	6.7E−02	2.9E−02	3.0E−02	2.8E−02
Spleen	2.1E−01	1.6E−01	2.1E−01	2.3E−01	6.6E−02	1.4E−01	5.7E−02
UB wall	9.6E−02	5.1E−02	1.4E−01	4.2E−02	5.3E−02	2.4E−02	5.3E−02
Gonads	3.4E−02	3.0E−02	4.8E−02	2.9E−02	1.4E−02	2.1E−02	1.3E−02
GI tract (range)	4.5E−02	4.1E−02	4.2E−02	4.2E−02	2.1E−02	1.9E−02	2.0E−02
	5.8E−02	5.7E−02	5.5E−02	5.8E−02	2.4E−02	2.7E−02	2.5E−02
Others (range)	2.9E−02	2.8E−02	2.6E−02	2.7E−02	1.1E−02	1.0E−02	1.1E−02
	4.2E−02	4.1E−02	5.0E−02	4.2E−02	1.7E−02	2.0E−02	1.6E−02
E (mSv)	1.1E+00	1.6E+00	1.2E+00	1.2E+00	5.7E−01	8.4E−01	7.4E−01
H_e (mSv)	2.0E+00	2.8E+00	2.1E+00	2.3E+00	9.4E−01	1.6E+00	1.3E+00
Interpolated Phantom Method							
Organ dose ($mSv \cdot MBq^{-1}$)							
Adrenals	9.2E−02	6.9E−02	9.2E−02	1.0E−01	5.5E−02	7.1E−02	5.5E−02
GB wall	5.1E−02	4.1E−02	5.7E−02	6.0E−02	3.1E−02	3.8E−02	3.0E−02
Kidneys	1.2E+00	8.4E+01	1.3E+00	1.5E+00	6.4E−01	9.1E−01	6.5E−01
Liver	4.0E−02	5.9E−02	8.7E−02	8.4E−02	2.6E−02	4.7E−02	3.2E−02
Pancreas	6.3E−02	4.8E−02	6.4E−02	7.0E−02	3.9E−02	4.7E−02	3.7E−02
Bone surface	5.8E−02	4.0E−02	5.5E−02	5.8E−02	3.7E−02	3.5E−02	3.2E−02
Spleen	1.7E−01	9.3E−02	1.8E−01	2.0E−01	8.9E−02	1.7E−01	6.5E−02
UB wall	8.0E−02	3.1E−02	1.2E−01	3.6E−02	7.1E−02	2.8E−02	6.1E−02
Gonads	2.8E−02	1.8E−02	4.2E−02	2.5E−02	1.9E−02	2.4E−02	1.5E−02
GI tract (range)	3.9E−02	2.6E−02	3.7E−02	3.6E−02	2.6E−02	2.1E−02	2.2E−02
	4.9E−02	3.5E−02	4.8E−02	5.1E−02	3.1E−02	3.1E−02	2.8E−02
Others (range)	2.4E−02	1.6E−02	2.3E−02	2.3E−02	1.5E−02	1.2E−02	1.2E−02
	3.5E−02	2.5E−02	4.4E−02	3.6E−02	2.2E−02	2.3E−02	1.9E−02
E (mSv)	9.4E−01	9.2E−01	1.0E+00	1.0E+00	7.6E−01	1.0E+00	8.5E−01
H_e (mSv)	1.7E+00	1.6E+00	1.8E+00	1.9E+00	1.3E+00	2.0E+00	1.5E+00

GB = gallbladder; UB = urinary bladder; GI = gastrointestinal.

child (Patient 10) for whom the 10-yr phantom was used but whose weight of 65 kg approached that of the adult phantom. In 14 normal patients, excluding one with unilateral compensatory hypertrophy, the mean value of E was 0.98 ± 0.29 mSv using discrete phantoms and 0.91 ± 0.08 mSv using the interpolated method. The s.d. was reduced considerably by application of the interpolated method. With either method, the values of effective dose equivalent (H_e), 1.8 ± 0.6 and 1.7 ± 0.2 mSv, respectively, were almost double the values of E, reflecting the changes in tissue weighting factors between ICRP 60 (*10*) and ICRP 26 (*11*) particularly for kidneys, which receive the highest dose.

In children with renal pathology, the mean values of E were

TABLE 1 (Continued)

Patient no.							
22	1	16	21	10	2	18	11
F	F	F	M	M	M	F	F
4.1 yr	6.1 yr	8.2 yr	10.2 yr	11.0 yr	12.8 yr	13.0 yr	14.8 yr
15	16.5	20	35	65	41	56	80
103	111	125	149	155	168	141	179
0.654	0.72	0.850	1.23	1.64	1.43	1.44	1.99
20.7/21.9	0/44	18.6/22.1	17.0/20.2	22.9/24.2	27.0/22.4	18.8/18.6	24.2/25.2
38	42	46	70	98	77	92	100
2.97	3.1	3.02	2.66	3.26	3.58	2.63	3.64
0.361	0.31	0.17	0.441	0.44	0.177	0.509	0.38
0.141	0.03	0.129	0.206	0.27	0.04	0.259	0.21
0.173	0.169	0.339	0.235	0.247	0.188	0.347	0.201
3.97	4.14	3.62	3.99	3.42	4.1	3.4	3.54
5 yr	5 yr	10 yr	10 yr	10 yr	15 yr	15 yr	15 yr
3.2E−02	3.2E−02	2.1E−02	2.0E−02	2.3E−02	1.6E−02	1.3E−02	1.6E−02
2.1E−02	2.1E−02	1.3E−02	1.4E−02	1.5E−02	1.0E−02	9.2E−03	1.1E−02
3.5E−01	7.3E−01	2.5E−01	2.2E−01	2.7E−01	2.1E−01	1.6E−01	2.2E−01
2.2E−02	2.1E−02	1.2E−02	1.7E−02	1.8E−02	8.6E−03	1.2E−02	1.2E−02
2.3E−02	2.2E−02	1.5E−02	1.6E−02	1.8E−02	1.2E−02	1.1E−02	1.3E−02
1.6E−02	1.6E−02	9.9E−03	1.0E−02	1.0E−02	7.5E−03	6.4E−03	7.1E−03
6.1E−02	3.2E−02	3.9E−02	5.2E−02	6.5E−02	1.7E−02	4.0E−02	3.7E−02
2.6E−02	2.6E−02	3.0E−02	2.2E−02	2.3E−02	1.3E−02	2.1E−02	1.4E−02
1.2E−02	1.2E−02	7.6E−03	4.5E−03	4.0E−03	2.9E−03	4.8E−03	4.9E−03
1.1E−02	1.1E−02	7.4E−03	7.4E−03	7.0E−03	4.8E−03	4.5E−03	4.5E−03
1.5E−02	1.6E−02	1.0E−02	1.1E−02	1.1E−02	7.1E−03	6.6E−03	7.4E−03
5.6E−03	5.8E−03	3.2E−03	3.6E−03	3.2E−03	2.4E−03	2.0E−03	2.0E−03
1.2E−02	1.3E−02	9.0E−03	8.6E−03	6.0E−03	4.2E−03	5.6E−03	5.2E−03
7.9E−01	1.3E+00	6.6E−01	9.2E−01	1.4E+00	8.0E−01	8.8E−01	1.1E+00
1.4E+00	2.4E+00	1.2E+00	1.7E+00	2.7E+00	1.4E+00	1.6E+00	2.1E+00
3.8E−02	3.6E−02	2.9E−02	1.9E−02	1.3E−02	2.0E−02	1.3E−02	1.0E−02
2.4E−02	2.3E−02	1.9E−02	1.3E−02	8.9E−03	1.2E−02	9.5E−03	7.7E−03
4.3E−01	8.2E−01	3.4E−01	2.1E−01	1.7E−01	2.5E−01	1.6E−01	1.6E−01
2.6E−02	2.3E−02	1.5E−02	1.6E−02	1.0E−02	1.1E−02	1.2E−02	8.0E−03
2.7E−02	2.5E−02	2.1E−02	1.5E−02	1.1E−02	1.4E−02	1.1E−02	8.9E−03
1.9E−02	1.8E−02	1.4E−02	9.6E−03	5.9E−03	9.3E−03	6.5E−03	5.0E−03
7.4E−02	3.5E−02	5.6E−02	4.8E−02	3.6E−02	2.1E−02	4.1E−02	2.2E−02
3.3E−02	3.0E−02	4.2E−02	2.1E−02	1.3E−02	1.6E−02	2.1E−02	8.5E−03
1.5E−02	1.4E−02	1.2E−02	4.2E−03	2.2E−03	3.6E−03	4.8E−03	3.2E−03
1.3E−02	1.3E−02	1.1E−02	6.9E−03	3.7E−03	6.2E−03	4.5E−03	2.9E−03
1.8E−02	1.7E−02	1.5E−02	9.8E−03	6.3E−03	9.1E−03	6.6E−03	5.5E−03
7.1E−03	6.6E−03	5.2E−03	3.3E−03	1.7E−03	3.0E−03	2.0E−03	1.4E−03
1.5E−02	1.4E−02	1.3E−02	5.8E−03	3.4E−03	5.2E−03	5.6E−03	3.6E−03
9.5E−01	1.4E+00	9.3E−01	8.7E−01	8.5E−01	9.7E−01	8.9E−01	7.8E−01
1.7E+00	2.7E+00	1.7E+00	1.6E+00	1.6E+00	1.7E+00	1.6E+00	1.5E+00

0.90 ± 0.21 mSv using discrete phantoms and 0.77 ± 0.13 mSv using the interpolated method. The values of H_e were again greater than E, but by a smaller factor than in normals because of lower values of kidney uptake and dose. The values of E from the interpolated method were significantly higher in children with normal renal function than in children with renal pathology showing that, in the latter group, the effects of reduced kidney uptake and faster elimination of radioactivity, which tend to reduce the E value, outweigh the effects of raised urinary bladder cumulated activity, which tend to increase it.

DISCUSSION

Relationship between Effective Dose and Body Weight

At this hospital, the amount of administered ^{99m}Tc-DMSA is calculated according to a schedule (*14*) based on the body

TABLE 2
Dosimetry of Technetium-99m-DMSA in Nine Children with Renal Pathology

Patient	20	19	15	6	7	23	8	14	17
Sex	M	F	M	M	M	M	F	M	M
Age	5 wk	3.5 mo	2.3 yr	2.7 yr	5.1 yr	5.2 yr	7 yr	11.2 yr	12.4 yr
Weight (kg)	2.2	4.3	15	16.2	21.4	18	32	34	38
Height (cm)	50	53	96	100	115	120	122	142	145
Surface area (m^2)	0.171	0.238	0.621	0.661	0.824	0.789	1.02	1.17	1.24
Max % kidney uptake (L/R)	1.7/4.5	6.7/9.0	0/9.1	0/5.1	13.1/12.1	0/28.1	2.9/18.0	11.3/8.0	5.7/7.0
Administered activity (MBq)	10	15	38	41	49	44	65	68	73
Residence Times (hr)									
Kidneys	0.425	1.12	0.57	0.36	1.8	1.97	1.4	1.35	0.662
Liver	0.447	0.502	0.58	0.291	0.171	0.399	0.229	0.29	0.561
Spleen	0.142	0.029	0.043	0.131	0.034	0.03	0.168	0.21	0.137
Bladder	0.167	0.189	0.239	0.351	0.227	0.26	0.129	0.473	0.071
Remaining body	6.17	5.47	5.53	4.94	4.92	4.4	5.85	4.38	6.87
Discrete Phantom Method									
Pediatric phantom used	Neonate	Neonate	1 yr	1 yr	5 yr	5 yr	5 yr	10 yr	10 yr
Organ dose ($mSv \cdot MBq^{-1}$)									
Adrenals	5.7E−02	6.8E−02	2.7E−02	2.2E−02	2.3E−02	2.4E−02	2.2E−02	1.3E−02	1.3E−02
GB wall	5.6E−02	5.7E−02	2.3E−02	1.7E−02	1.7E−02	1.9E−02	1.8E−02	1.1E−02	1.3E−02
Kidneys	3.5E−01	6.0E−01	2.6E−01	1.7E−01	2.2E−01	4.7E−01	2.9E−01	1.1E−01	6.0E−02
Liver	7.2E−02	8.2E−02	4.1E−02	2.4E−02	1.4E−02	2.1E−02	1.5E−02	1.1E−02	1.7E−02
Pancreas	5.7E−02	5.8E−02	2.6E−02	2.2E−02	1.8E−02	1.8E−02	1.9E−02	1.2E−02	1.3E−02
Bone surface	6.3E−02	6.1E−02	2.8E−02	2.4E−02	1.5E−02	1.5E−02	1.7E−02	9.5E−03	1.3E−02
Spleen	2.1E−01	7.6E−02	3.7E−02	7.6E−02	2.5E−02	2.5E−02	6.1E−02	4.7E−02	3.2E−02
UB wall	1.1E−01	1.2E−01	6.4E−02	8.5E−02	3.3E−02	3.6E−02	2.3E−02	4.0E−02	1.2E−02
Gonads	3.9E−02	4.9E−02	1.7E−02	1.6E−02	8.3E−03	7.8E−03	1.4E−02	5.6E−03	6.3E−03
GI tract (range)	4.8E−02	4.5E−02	2.1E−02	1.8E−02	1.2E−02	1.1E−02	1.3E−02	8.2E−03	9.5E−03
	5.2E−02	5.1E−02	2.3E−02	2.1E−02	1.4E−02	1.4E−02	1.5E−02	8.8E−03	1.1E−02
Others (range)	3.1E−02	2.9E−02	1.2E−02	1.1E−02	6.1E−03	5.7E−03	6.9E−03	3.5E−03	4.9E−03
	4.2E−02	5.1E−02	1.8E−02	1.5E−02	9.2E−03	9.0E−03	1.4E−02	5.6E−03	7.9E−03
E (mSv)	5.5E−01	9.4E−01	1.0E+00	9.7E−01	8.0E−01	1.0E+00	1.3E+00	7.4E−01	7.3E−01
H_e (mSv)	7.6E−01	1.3E+00	1.4E+00	1.4E+00	2.1E+00	1.8E+00	2.1E+00	1.2E+00	9.5E−01
Interpolated Phantom Method									
Organ dose ($mSv \cdot MBq^{-1}$)									
Adrenals	8.2E−02	5.7E−02	1.9E−02	1.4E−02	2.1E−02	2.5E−02	1.5E−02	1.3E−02	1.1E−02
GB wall	8.4E−02	4.7E−02	1.9E−02	1.4E−02	1.6E−02	1.9E−02	1.2E−02	1.0E−02	1.2E−02
Kidneys	5.3E−01	4.8E−01	1.8E−01	1.1E−01	2.0E−01	4.9E−01	2.0E−01	1.1E−01	5.4E−02
Liver	1.0E−01	6.8E−02	2.8E−02	1.6E−02	1.3E−02	2.2E−02	1.1E−02	1.1E−02	1.5E−02
Pancreas	8.3E−02	4.8E−02	1.8E−02	1.5E−02	1.6E−02	1.9E−02	1.3E−02	1.1E−02	1.1E−02
Bone surface	9.1E−02	5.1E−02	1.9E−02	1.5E−02	1.4E−02	1.6E−02	1.2E−02	9.1E−03	1.1E−02
Spleen	3.1E−01	6.3E−02	2.6E−02	4.9E−02	2.3E−02	2.6E−02	4.0E−02	4.5E−02	2.8E−02
UB wall	1.7E−01	1.0E−01	4.3E−02	5.3E−02	3.0E−02	3.8E−02	1.6E−02	3.8E−02	1.1E−02
Gonads	5.7E−02	4.0E−02	1.1E−02	1.0E−02	7.4E−03	8.1E−03	8.7E−03	5.3E−03	5.6E−03
GI tract (range)	6.8E−02	3.8E−02	1.5E−02	1.2E−02	1.1E−02	1.2E−02	8.7E−03	7.8E−03	8.2E−03
	7.5E−02	4.3E−02	1.6E−02	1.3E−02	1.3E−02	1.4E−02	1.0E−02	8.4E−03	9.3E−03
Others	4.7E−02	2.4E−02	8.0E−03	6.8E−03	5.4E−03	6.1E−03	4.3E−03	3.3E−03	4.2E−03
	6.1E−02	4.2E−02	1.2E−02	9.7E−03	8.4E−03	9.5E−03	9.2E−03	5.4E−03	7.0E−03
E (mSv)	8.1E−01	7.7E−01	7.2E−01	6.3E−01	7.3E−01	1.1E+00	8.7E−01	7.1E−01	6.4E−01
H_e (mSv)	1.0E+00	1.1E+00	9.7E−01	8.7E−01	1.1E+00	1.9E+00	1.5E+00	1.1E+00	8.4E−01

GB = gallbladder; UB = urinary bladder; GI = gastrointestinal.

surface area of a child, relative to that of the adult value of 1.73 m^2, and an adult administered activity of 100 MBq. Figure 1, curve (A), shows the relationship between effective dose, calculated by the interpolated method, and body weight which results from the use of this schedule in 14 children with normal bilateral renal function. The effective dose was reasonably constant in these children and the variation with body weight was not significant ($p > 0.05$) from these data. One child weighing 80 kg (Patient 11) was given the adult maximum administered activity of 100 MBq although dose estimates were made by extrapolation beyond the adult 70 kg phantom. Using this schedule, children weighing less than 3 kg were given the minimum activity of 10 MBq.

Figure 1, curve (B), shows the relationship between E and body weight that would have resulted if a body weight scaling factor had been used to calculate the administered activity. In this case, the effective dose decreases significantly with decreasing weight. This raises the question as to whether the

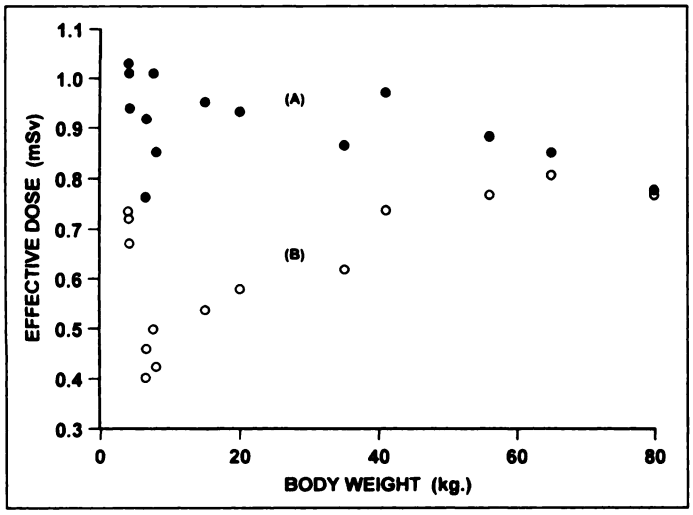

FIGURE 1. Relationship between effective dose and body weight following administration of ^{99m}Tc-DMSA to 14 children with normal bilateral renal function. Administered activity scaled according to relative body surface area (A) or relative body weight (B).

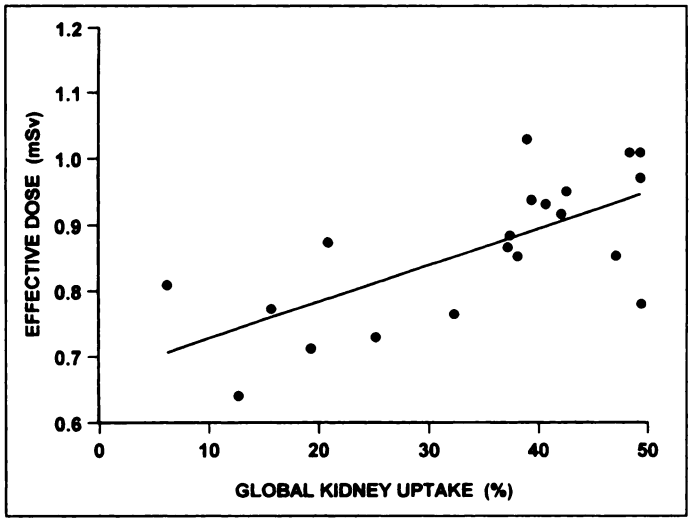

FIGURE 2. Relationship between effective dose and maximum global kidney uptake of ^{99m}Tc-DMSA in 20 children with bilateral renal function. The regression line is shown (see text).

reduced activities administered to children below about 40 kg, although leading to progessively lower effective doses, would result in unsatisfactory clinical images. If this schedule had been used in the present study, five normal children weighing less than 7 kg would have required the minimum administered activity of 10 MBq, resulting in a return to larger values of E for these children as indicated in Figure 1, curve (B).

Highest Doses to Organs and Tissues

The kidneys received the highest dose. In normal children with bilateral function, the kidney dose of 16.7 ± 2.3 mSv per administered activity contributed 0.42 ± 0.06 mSv to the effective dose of 0.91 ± 0.08 mSv. In one child with unilateral compensatory hypertrophy the kidney dose was 35 mSv. In renal pathology, kidney dose was lower on average and more variable (8.8 ± 5.5 mSv). The next highest discrete organ dose was observed in spleen (2.5 ± 0.8 mSv in normals and 1.6 ± 0.9 mSv in pathological cases). The estimated dose to the metaphyseal growth complexes, however, ranged from 0.93 to 14.7 mSv in all 24 patients with a mean value of 5.0 ± 3.4 mSv. There was a significant positive correlation between dose to growth complex and age of the patient ($r = +0.46$; $p < 0.025$).

Effective Dose in Normal and Abnormal Renal Function

Figure 2 shows E as a function of global renal uptake in 20 children with bilateral kidney function. There was a significant correlation between E and global renal uptake ($r = 0.69$; $p < 0.001$) and the regression is given by:

$$E\ (mSv) = 0.67 + 0.0056 \times \text{global kidney uptake (\%)}.$$

As previously shown (*1*) the accumulated activity in urine was significantly higher in patients with low renal uptake than those with normal uptake. These factors lead to reduced radiation doses in our abnormal patients compared with those for normal children. This is contrary to the increase in radiation dose in patients with poor renal function when agents such as DTPA and MAG3 are used to assess renal function.

Proposed Model for Technetium-99m-DMSA in Normal Children

Our results have shown little age-dependency of biokinetic parameters in children aged 7 wk to 14.8 yr, suggesting that biokinetic models based on adult studies may be directly applicable to pediatric dosimetry. This finding lends support, for this radiopharmaceutical at least, for the validity of the principle adopted in ICRP publication 53 (*15*) where doses were estimated for children of four different ages using biokinetic data gleaned largely from studies on adults. Not surprisingly, our data differ slightly in detail from the ICRP 53 model since they are based on an ad hoc study and no similarly detailed body of information was available when ICRP 53 was compiled. Our value of 0.45 for the fractional distribution (F_s) of kidneys is lower than that used in ICRP 53 (0.5) and thereafter shows distinct elimination from the kidneys with a mean half-time of 3.2 days. This leads to a value of 0.424, our observed mean maximal kidney uptake, at the observed mean time-to-maximum of 6.8 hr. The renal uptake half-time, however, was identical in the two models (1 hr). The overall effect is to give a lower value for kidney residence time (3.1 hr) compared with that of the ICRP 53 model (3.7 hr). Our mean values for uptake in liver (0.046) and spleen (0.019) also differ from the ICRP 53 values of 0.1 and 0.01, respectively.

We saw no evidence of buildup in these organs similar to that in kidneys and have ascribed only a single experimentally observed exponential component to describe elimination from them. One of the main differences is in the value of residence time in remaining body, where our value of 3.9 ± 0.5 hr is substantially higher than that derived from the ICRP 53 model (2.6 hr) and arises mainly because of a larger whole-body residence time and smaller kidney residence time. The consequence of this is to imply larger doses to those organs not specified in the model as source organs. From the results of the present study, a biokinetic model, applicable for dosimetry in children of all ages with normal renal function, is presented in the format of ICRP 53 (Table 3). When applied to our group of 14 normal children (excluding one with unilateral kidney function), the model predicts a mean effective dose of 0.92 ± 0.07 mSv using the described method of interpolating organ doses between phantoms, compared with the actual mean value of 0.91 ± 0.08 mSv. The mean paired difference was 0.005 ± 0.054 mSv ($p > 0.7$). The model gives a mean value of 1.7 ± 0.13 mSv for H_e, compared with the actual value of 1.7 ± 0.18 mSv.

CONCLUSION

Two different methods were used to estimate pediatric radiation dosimetry of ^{99m}Tc-DMSA from biokinetic studies in children aged from 5 wk to 14.8 yr. A method of interpolating

TABLE 3
Biokinetic Model for Dosimetry of Technetium-99m-DMSA in Children with Normal Renal Function

Organ	F_S	T	a	τ
Total body (excluding bladder contents)	1.0	50 min 4.9 d	0.11 0.89	7.47 hr
Kidneys	0.45	1 hr 3.2 d	−1.0 1.0	3.07 hr
Liver	0.046	1.6 d	1.0	20.8 min
Spleen	0.019	17 hr	1.0	7.2 min
Remaining body				3.93 hr
Urinary bladder contents	(2 hr void) (3 hr void) (3.5 hr void)			9.4 min 14.5 min 17.0 min

F_S = fraction distribution.
T = biological half-time of retention components.
a = fractional retention component (−ve sign indicates uptake).
τ = residence time.

between pediatric phantoms on the basis of inverse body weight showed large differences in effective dose of up to 46% compared with the use of discrete phantoms based on age. A schedule for calculating the amounts of activity to be administered to normal children of different age and size based on an adult activity of 100 MBq, scaled for relative body surface area, yields a fairly uniform dose over the complete range of children investigated. The mean effective dose was 0.91 ± 0.08 mSv per administered activity, using the interpolated method, with kidneys receiving the highest dose (17 ± 2 mSv). Renal pathology reduced the effective dose to about 85% of that estimated for children with normal renal function. A biokinetic model, based on these studies, is presented in the ICRP 53 format and is applicable for pediatric dosimetry of ^{99m}Tc-DMSA independent of age below 15 yr in normal children.

ACKNOWLEDGMENTS

We thank Michael Stabin of the Radiation Internal Dose Information Center, Oak Ridge Institute for Science and Education for his help with this work and for supplying the MIRDOSE 3 program. We also thank members of the MIRD committee for their very helpful suggestions. We are grateful to the CEC Nuclear Fission Safety Program for a grant which partially supported this work (contract F13P-CT920052).

REFERENCES

1. Evans K, Lythgoe MF, Anderson PJ, et al. The biokinetic behavior of ^{99m}Tc-DMSA in children. *J Nucl Med* 1996;37:1331–1335.
2. International Commission on Radiological Protection. Radiological Protection in Biomedical Research. ICRP Publication 62. *Ann ICRP* Oxford: Pergamon Press, 1991;22.
3. Cristy M. Mathematical phantoms representing children of various ages for use in estimates of internal dose. ORNL/NUREG/TM-367, Oak Ridge, TN: Oak Ridge National Laboratory; 1980.
4. Loevinger R, Berman M. A revised schema for absorbed radiation dose calculations for biologically-distributed radionuclides. *MIRD pamphlet no. 1, revised.* New York: Society of Nuclear Medicine; 1976.
5. Cristy M, Eckerman K. Specific absorbed fractions of energy at various ages from internal photon sources, ORNL/TM-8381. Oak Ridge, TN: Oak Ridge National Laboratory; 1987.
6. Cloutier RL, Smith SA, Watson EE, et al. Dose to the fetus from radionuclides in the bladder. *Health Phys* 1973;25:147–161.
7. Gelfand MJ, Thomas SR, Kereiakes JG. Absorbed radiation dose from routine imaging of the skeleton in children. *Ann Radiol* 1983;26:421–423.
8. International Commission on Radiological Protection. Radionuclide transformations: energy and intensity of emissions. ICRP Publication 38. Oxford: Pergamon Press, *Ann ICRP* 1983;11–13.
9. Widman JC, Powsner ER. Energy absorption in cylinders containing a uniformly distributed source. *J Nucl Med* 1967;8:179–186.
10. International Commission on Radiological Protection. Recommendations of the ICRP. ICRP Publication 60. Oxford: Pergamon Press, *Ann ICRP* 1990;21.
11. International Commission on Radiological Protection. Recommendations of the ICRP. ICRP Publication 26. Oxford: Pergamon Press; 1977.
12. International Commission on Radiological Protection. Annual limits on intake of radionuclides by workers based on the 1990 recommendations. *Ann ICRP* 1990;20:21.
13. International Commission on Radiological Protection. Age-dependent doses to members of the public from intake of radionuclides: part 2. ICRP Publication 67. *Ann ICRP* 1993;23:3–4.
14. Pediatric Task Group of the European Association of Nuclear Medicine. A radiopharmaceuticals schedule for imaging in pediatrics. *Eur J Nucl Med* 1990;17:127–129.
15. International Commission on Radiological Protection. Radiation dose to patients from radiopharmaceuticals. ICRP Publication 53. Oxford: Pergamon Press, *Ann ICRP* 1987;18.