Radiation Dosimetry for Technetium-99m-MAG_3, Technetium-99m-DTPA, and Iodine-131-OIH Based on Human Biodistribution Studies

Michael Stabin, Andrew Taylor Jr., Dennis Eshima, and Wesley Wooter

Medical Sciences Division, Oak Ridge Associated Universities, Oak Ridge, Tennessee; Emory University Hospital, Atlanta, Georgia; College of Pharmacy (Radiopharmacy) University of New Mexico, Albuquerque, New Mexico; and University of California, San Francisco, Saint Agnes Medical Center, Fresno, California

Radiation dose estimates were calculated for the renal agents ^{99m}Tc-DTPA, ^{99m}Tc-MAG_3, and ^{131}I-OIH from biodistribution data gathered in groups of healthy human volunteers. Biokinetics were evaluated by Anger camera imaging, blood sampling, and urine collection and counting. Collected data were fit to four- or five-compartmental models using the CONversational Simulation, Analysis, and Modeling (CONSAM) software. Radiation dose estimates were performed using standard MIRD techniques. Average residence times in urinary bladder, kidney, and remainder of the body were used to predict radiation dose equivalents and effective dose equivalents for the three agents. Doses for DTPA and MAG_3 were very similar and much lower on a per unit injected activity than OIH. The effective dose equivalents were 3.3 mSv/370 MBq for ^{99m}Tc-DTPA, 3.7 mSv/370 MBq for ^{99m}Tc-MAG_3, and 0.99 mSv/11.1 MBq for ^{131}I-OIH for bladder voiding every 4.8 hr; effective dose equivalents were 2.0 mSv/370 MBq for ^{99m}Tc-DTPA, 1.5 mSv/370 MBq for ^{99m}Tc-MAG_3, and 0.28 mSv/11.1 MBq for ^{131}I-OIH for bladder voiding at 30 min and then every 4.0 hr. Patients should void at the conclusion of the study, as early voiding can reduce the gonadal radiation dose by a factor of 2 to 3.

J Nucl Med 1992; 33:33–40

For a number of years, there have been efforts to synthesize a ^{99m}Tc renal agent with biologic properties comparable to ^{131}I-orthoiodohippurate (OIH) (*1*). In 1986, Fritzberg and others described a new technetium complex, ^{99m}Tc-mercaptoacetyltriglycine (MAG_3) which showed considerable promise in recent animal experiments as a potential ^{99m}Tc replacement for ^{131}I-OIH (*1–3*). Preliminary studies of HPLC-purified ^{99m}Tc-MAG_3 in normal volunteers indicated that plasma clearance was less than that of ^{131}I-hippurate (OIH), the volume of distribution was less than that of OIH, the renogram curves were comparable, and the percent injected activity in urine at 30 min was essentially identical. Furthermore, the ^{99m}Tc-MAG_3 images were of superior quality compared to those of ^{131}I-OIH (*4*). These results have subsequently been confirmed in patients and volunteers using both HPLC-purified MAG_3 and a kit formulation of the complex (*5–9*). The image quality of ^{99m}Tc-MAG_3 also compares very favorably to ^{99m}Tc-DTPA, particularly in patients with impaired renal function (*10–12*). Technetium-99m-diethylenetriaminepentaacetic acid (DTPA) is a popular agent for visualization of the kidneys and measurement of glomerular filtration rate (GFR). Its dosimetry has been well described by the MIRD Committee (*13*).

Since ^{99m}Tc-MAG_3 may be used as a substitute for ^{131}I-OIH or ^{99m}Tc-DTPA, we have determined its dosimetry based on its distribution and retention in a series of healthy adult volunteers and have compared the dosimetry of ^{99m}Tc-MAG_3 with that of ^{131}I-OIH and ^{99m}Tc-DTPA using identical methods of data acquisition and data analysis.

METHODS

The MAG_3 used in this study was supplied as a kit formulation by Mallinckrodt, Inc. (St. Louis, MO). The DTPA came from Syncor, Chatsworth, CA (six patients) and Ackerman Nuclear, Bedford, MA (five patients). Iodine-131-OIH was supplied by Mallinckrodt, Inc.

Eleven volunteers received ^{99m}Tc-DTPA, and eight volunteers were each given ^{99m}Tc-MAG_3 and ^{131}I-OIH as single intravenous injections of the respective radiopharmaceuticals. Patients received about 185 MBq of ^{99m}Tc-MAG_3 and ^{99m}Tc-DTPA and about 11.1 MBq of ^{131}I-OIH. The biokinetics of the agents were determined through Anger camera images acquired posteriorly over the kidneys and stored in a minicomputer at 20 sec per frame for 20 min. The activity in both kidneys as a function of time was estimated from regions of interest. The system was calibrated by imaging a kidney phantom in a water bath with the center of the phantom at depths from 5 to 8 cm. The kidney depth for each volunteer was estimated by the formulas of Tonnesen et al. (*14,15*) and was used in determining the calibration factors.

Blood or plasma samples were taken at about 3–5-min intervals for the first half hour and at about 60, 120, and 180 min. For OIH, whole blood samples were used to be sure that the samples

Received Mar. 18, 1991; revision accepted Jul. 22, 1991.
For reprints contact: Andrew Taylor, Jr., MD, Department of Radiology, Emory University Hospital, 1364 Clifton Rd., N.E., Atlanta, GA 30322.

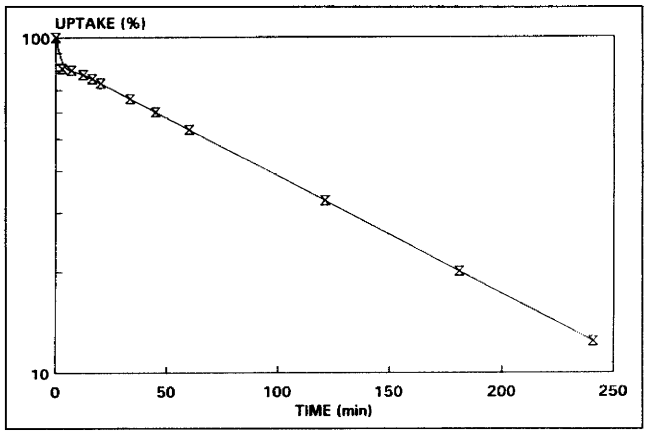

FIGURE 1. Blood time-activity curve for ^{99m}Tc-DTPA.

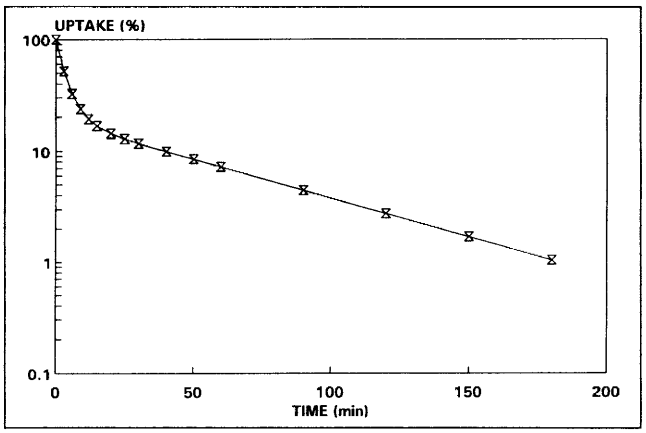

FIGURE 3. Blood time-activity curve for ^{99m}Tc-MAG$_3$.

included any OIH incorporated into the red cells. For DTPA and MAG$_3$, only plasma samples were analyzed for initial retention since neither MAG$_3$ nor DTPA are incorporated into red cells to any significant degree (*1,16*). Urine samples were obtained at 30 min after injection and then again between 180 and 240 min after injection; the percent injected activity in each voided specimen was determined.

Collected data in blood, kidneys, and cumulative urine were reduced to represent percent of injected activity as a function of time after injection. These data were fit to four- or five-compartment models of various configurations using the CONversational Simulation, Analysis, and Modeling (CONSAM) software (*17*) on a VAXstation computer using the VMS operating system. The models for the three agents are shown in the Appendix (Figs. A1–A3). In these tables, F_i is the percent of injected activity in compartment i at time t, L_{ij} is the coefficient for transfer of activity from compartment j to i per unit time (min^{-1}), and C_i is a proportionality constant (dimensionless). In SAAM, multiple compartments may be linked through use of these proportionality constants to fit a single data set.

In all models, compartment 1 is the compartment into which tracer is injected and from which tracer is cleared. This compartment includes the blood, but also includes spaces outside the blood, as indicated by the fact that the volume of distribution of this compartment may be several times the actual blood volume (*18*). Compartment 2 (in the case of OIH, compartments 2 and 3) represents tracer that is distributed throughout the body, but is not available to the kidneys for clearance. Compartment 4 (in the case of DTPA, compartments 3 and 4) represents the kidneys. We have included the kidneys as a compartment (in the case of DTPA, two compartments) only as a convenient mathematical device to fit the curves. The kidneys do not fit the assumptions of a well-mixed compartment, but we are able to take advantage of the SAAM software to produce fitted curves that agree well with the measured time-activity data.

The periodic voiding of the urinary bladder was modeled by adding a separate bladder compartment that was cleared at regular intervals. The original bladder compartment was retained to match the model results to the observed cumulative urinary excretion. A technique within the SAAM software allows the user to simulate this compartment and compensate for the additional transfer pathway by subtracting an equivalent amount from the feeding compartment in real time.

In the SAAM software, a nonlinear least squares regression algorithm adjusts the transfer coefficients (L_{ij}'s in the Appendix, Figs. A1–A3) to obtain the best fit of the model to the observed data. When a solution is converged upon, SAAM will calculate the time integrals of activity in each compartment by numerical integration techniques. If the input data and conversion constants are entered into SAAM in the proper form, these integrals are exactly the values of residence time, τ, needed to calculate radiation dose estimates by the MIRD technique (*19*). Values of τ

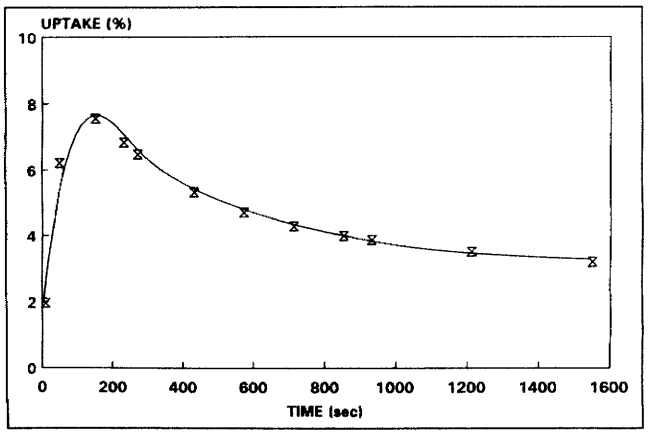

FIGURE 2. Kidney time-activity curve for ^{99m}Tc-DTPA.

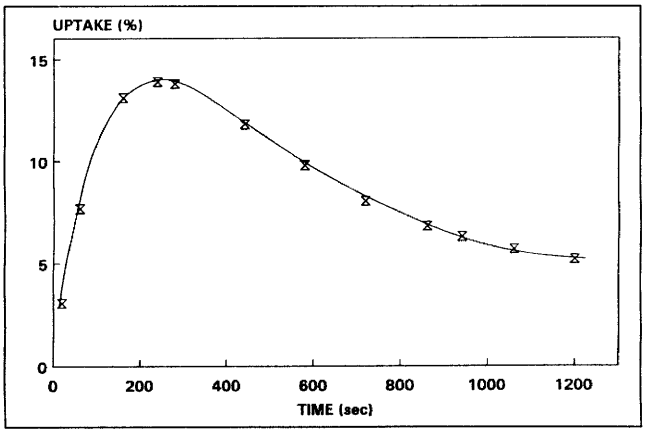

FIGURE 4. Kidney time-activity curve for ^{99m}Tc-MAG$_3$.

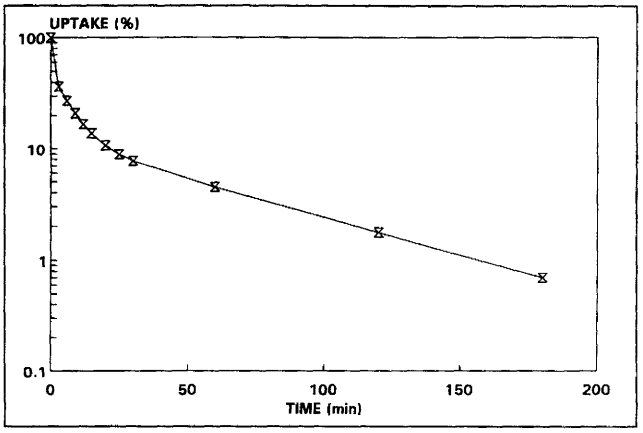

FIGURE 5. Blood time-activity curve for ^{131}I-OIH.

were calculated separately for each individual and averaged for kidney, urinary bladder, and remainder of the body. We used the software MIRDOSE (*20*) for estimating the radiation doses after the average values of τ were obtained from SAAM.

Characteristic equations (coefficients of α_{hi} and biologic disappearance constants λ_i) were derived from averaged values of the transfer coefficients and proportionality constants for each agent by solving simultaneously the differential equations for each compartment. A computer program called DIFFSOL (*21*), developed at Oak Ridge National Laboratory, was used to solve the simultaneous differential equations. Residence times used in the dose calculations were not derived from these characteristic equations, but were averages of the values observed in each individual.

RESULTS

Tables of optimum values of the transfer coefficients, proportionality constants, and residence times for DTPA, MAG_3, and OIH are shown in the Appendix (Tables A1–A3). Plots of the retention of the activity in blood and kidneys for an "average" individual are shown in Figures 1–6. These plots were constructed using arithmetic averages of the transfer coefficients for each agent. Table A4 in the Appendix lists the characteristic solutions for the matrix of averaged transfer coefficients.

Residence times were calculated separately for each individual and then averaged. Table 1 lists dose estimates if the bladder is emptied every 4.8 hr; Table 2 lists dose estimates for voiding at 30 min and every 4 hr thereafter. Tables 3 and 4 list dose estimates for these two bladder voiding schedules for injections of 370 MBq of DTPA or MAG_3 and 11.1 MBq of OIH. The quantity "effective dose equivalent", as defined by the ICRP (*22*), is also shown, to facilitate comparison of the total risk from the use of the different pharmaceuticals.

TABLE 1
Radiation Dose Estimates for Unit Injections of DTPA, MAG_3, or OIH—Slow Voiding

Organ	Estimated radiation dose (mSv/MBq)		
	DTPA	MAG_3	OIH
Kidneys	0.0038	0.0040	0.015
Ovaries	0.0054	0.0058	0.021
Red marrow	0.0015	0.0010	0.0041
Bone surfaces	0.0022	0.0014	0.0031
Testes	0.0038	0.0040	0.016
Urinary bladder wall*	0.094	0.12	1.3
Uterus	0.011	0.013	0.048
Total body	0.0018	0.0014	0.0063
Effective dose equivalent	0.0089	0.010	0.089

* Bladder voiding interval 4.8 hr.

DISCUSSION

Transfer coefficients (L_{ij}'s) for DTPA were remarkably similar. Starting each data set from a common starting point, adjustments in the proportionality constants (C_i's) would produce a good fit in most cases. Residence times for remainder of body and bladder were very uniform and were the primary source organs responsible for the dose

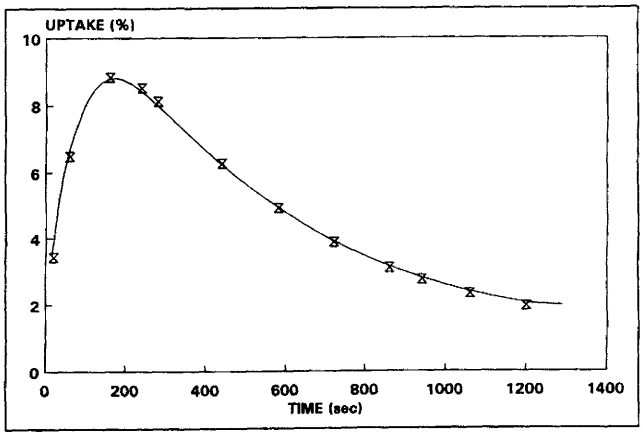

FIGURE 6. Kidney time-activity curve for ^{131}I-OIH.

TABLE 2
Radiation Dose Estimates for Unit Injections of DTPA, MAG_3, or OIH—Rapid Voiding

Organ	Estimated radiation dose (mSv/MBq)		
	DTPA	MAG_3	OIH
Kidneys	0.0037	0.0039	0.014
Ovaries	0.0034	0.0023	0.0062
Red marrow	0.0012	0.00049	0.0016
Bone surfaces	0.0018	0.00067	0.0012
Testes	0.0024	0.0016	0.0046
Urinary bladder wall*	0.052	0.045	0.36
Uterus	0.0066	0.0051	0.014
Total body	0.0013	0.00064	0.0021
Effective dose equivalent	0.0054	0.0042	0.026

* Bladder voided at 30 min, then at 4 hr and every 4 hr thereafter.

TABLE 3
Radiation Dose Estimates for Clinical Injections* of DTPA, MAG_3, or OIH—Slow Voiding

Organ	Estimated radiation dose mSv (rem) DTPA	MAG_3	OIH
Kidneys	1.4 (0.14)	1.5 (0.15)	0.17 (0.017)
Ovaries	2.0 (0.20)	2.2 (0.22)	0.23 (0.023)
Red marrow	0.56 (0.056)	0.37 (0.037)	0.046 (0.0046)
Bone surfaces	0.81 (0.081)	0.52 (0.052)	0.034 (0.0034)
Testes	1.4 (0.14)	1.5 (0.15)	0.18 (0.018)
Urinary bladder wall†	35 (3.5)	44 (4.4)	14 (1.4)
Uterus	4.1 (0.41)	4.8 (0.48)	0.53 (0.053)
Total body	0.67 (0.067)	0.52 (0.052)	0.070 (0.0070)
Effective dose equivalent	3.3 (0.33)	3.7 (0.37)	0.99 (0.099)

* 370 MBq (10 mCi) of DTPA or MAG_3 and 11.1 MBq (30 μCi) of OIH.
† Bladder voiding interval 4.8 hr.

estimates for most organs of interest. Transfer coefficients for MAG_3 were more varied; the proportionality constant for compartment 2 (C2) was very small in most cases and indicated that this compartment is not very important to overall dosimetry. Residence times for MAG_3 were also very similar across the study population for the bladder and remainder of body. Transfer coefficients were also rather nonuniform for OIH, although final residence times were very similar. Volunteer 2 for the OIH group had an almost flat kidney curve, due to a delay in initiating the camera acquisition. This person's kidney residence time was low, although the bladder residence time was very typical.

The multicompartment models employed to fit the data were chosen for their utilitarian value, and, as such, are not useful for making interpretations about the metabolic processes which produced the kinetic data. For this reason, we used the term transfer coefficient rather than transfer rate coefficient. For example, the kidneys do not meet the criteria for being a well mixed space. Therefore, the transfer coefficient from compartment 4 to 1 (L_{14}) for MAG_3 does not indicate recirculation of the radionuclide, but is a mathematical device for causing the compartment model to fit the data. These compartment models provide an adequate vehicle for calculating the radiation dosimetry, but should not be used to project results beyond their scope.

TABLE 4
Radiation Dose Estimates for Clinical Injections* of DTPA, MAG_3, or OIH—Rapid Voiding

Organ	Estimated radiation dose mSv (rem) DTPA	MAG_3	OIH
Kidneys	1.4 (0.14)	1.4 (0.14)	0.16 (0.016)
Ovaries	1.3 (0.13)	0.86 (0.086)	0.068 (0.0068)
Red marrow	0.45 (0.045)	0.18 (0.018)	0.017 (0.0017)
Bone surfaces	0.68 (0.068)	0.25 (0.025)	0.013 (0.0013)
Testes	0.88 (0.088)	0.59 (0.059)	0.051 (0.0051)
Urinary bladder wall†	19 (1.9)	17 (1.7)	4.0 (0.40)
Uterus	2.4 (0.24)	1.9 (0.19)	0.15 (0.015)
Total body	0.49 (0.049)	0.24 (0.024)	0.023 (0.0023)
Effective dose equivalent	2.0 (0.20)	1.5 (0.15)	0.28 (0.028)

* 370 MBq (10 mCi) of DTPA or MAG_3 and 11.1 MBq (30 μCi) of OIH.
† Bladder voided at 30 min, then at 4 hr, then every 4 hr thereafter.

The characteristic solutions are useful in deriving analytical expressions for the time-activity curves in kidneys and blood. Values of τ calculated using these characteristic equations will be slightly different from the values of τ used in the dosimetry calculations, which were averages of the values observed in the individuals studied.

Liver and gallbladder imaging were not performed during this study. Taylor et al. (*9*) noted a liver uptake of 2.6% in the first hour, dropping to about 0.5% by 3 hr, in ten normal volunteers. They noted about 0.5% in the gallbladder in the first hour and also at 3–4 hr postinjection. Radiation dosimetry for these patients agreed well with the estimates generated in this study for the kidneys, bladder, ovaries, testes, and marrow. Their estimates of radiation dose to the liver and gallbladder were 0.0014 mSv/MBq and 0.0041 mSv/MBq, respectively.

Radiation dose estimates obtained for DTPA are in good agreement with those generated by the MIRD Committee in their Dose Estimate Report (*13*). Tables 3 and 4 show the two ^{99m}Tc agents to be very similar in radiation dosimetry on a per unit injected activity basis and ^{131}I to deliver doses from three to ten times higher. Based on typical clinical administrations (Tables 5 and 6), absorbed doses for the ^{99m}Tc agents are about three to ten times higher than those for ^{131}I-OIH, for about thirty times more administered activity. For the 4.8-hr voiding schedule, dose estimates for red marrow and bone surfaces are lower for MAG_3 than for DTPA, but all other organ doses are slightly higher, as is the effective dose equivalent. This uniform 4.8-hr bladder voiding interval is often assumed to represent an average adult voiding schedule with no encouragement to more frequent voiding. Clinically, however, the patient should void at the completion of the study (approximately 30 min postinjection); if the patient voids at 30 min and then at 4-hr intervals, bladder wall, ovaries and testes doses will be reduced by factors of 2 to 3, and kidney dose will be reduced by about 10%. In this case, dose equivalents for most organs are slightly lower for MAG_3 than for DTPA, as is the effective dose equivalent.

We also estimated radiation dose estimates for these agents assuming no clearance from the kidneys after uptake to simulate bilateral renal obstruction. We did not study any patients with this condition, but merely adjusted the kinetic model to prevent outflow from kidneys to

urinary bladder. The kidney doses (rather than dose equivalents, because of the magnitude) from administration of amounts of activity as listed in Tables 5 and 6 are 130 mGy (13 rad) for DTPA, 150 mGy (15 rad) for MAG_3, and 1300 mGy (130 rad) for OIH. As shown by Marcus and Koyle (*23*), absorbed doses from ^{131}I-OIH are typically thousands of mGy (hundreds of rads) for patients with various renal diseases, and conversion to ^{99m}Tc- or ^{123}I-based agents is particularly desirable in patients with impaired renal function. Furthermore, free iodide in the ^{131}I-OIH preparation may deliver an unwanted radiation dose to the thyroid.

APPENDIX

The following tables and figures give details of the model results which were too extensive to be included in the text. Optimal model parameters and residence times for each patient as well as the biologic parameters for unit injections as derived from solution of the differential equations for the average case are presented.

TABLE A-1
Optimal Values of Model Parameters and Residence Times for ^{99m}Tc-DTPA*

Volunteer	L(1,2)	L(2,1)	L(3,1)	L(1,3)	L(4,3)	L(5,4)
1	2.22E − 2	1.88E − 1	3.37E − 1	7.28E − 1	3.23E − 1	3.81E − 2
2	2.71E − 2	2.70E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2
3	2.12E − 2	2.50E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2
4	2.71E − 2	1.90E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2
5	2.71E − 2	1.90E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2
6	4.11E − 2	2.20E − 1	3.79E − 1	8.37E − 1	1.38E − 1	5.99E − 2
7	2.71E − 2	1.90E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2
8	2.71E − 2	1.90E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2
9	2.71E − 2	1.90E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2
10	2.30E − 2	2.10E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2
11	2.71E − 2	1.90E − 1	3.34E − 1	7.30E − 1	3.17E − 1	3.85E − 2

Volunteer	C1	C2	C3	C4
1	1.05E00	1.21E00	3.06E − 1	4.26E − 2
2	1.00E00	1.14E00	5.32E − 1	9.08E − 2
3	1.01E00	1.13E00	4.08E − 1	3.30E − 1
4	1.02E00	1.34E00	4.33E − 1	9.06E − 2
5	1.02E00	1.37E00	3.91E − 1	1.01E − 1
6	9.81E − 1	8.04E − 1	2.95E − 1	1.55E − 1
7	1.00E00	1.41E00	4.14E − 1	8.54E − 2
8	1.01E00	1.35E00	4.51E − 1	1.23E − 1
9	1.07E00	1.31E00	3.83E − 1	6.48E − 2
10	1.00E00	1.24E00	3.91E − 1	6.16E − 2
11	1.01E00	1.26E00	3.14E − 1	2.52E − 1

	Residence Times		
Volunteer	Remainder of body	Kidneys	Bladder
1	1.44E00	2.96E − 2	2.30E00
2	1.59E00	5.44E − 2	2.18E00
3	1.78E00	1.28E − 1	2.12E00
4	1.41E00	5.22E − 2	2.36E00
5	1.43E00	5.43E − 2	2.36E00
6	1.28E00	6.27E − 2	2.13E00
7	1.47E00	4.96E − 2	2.36E00
8	1.41E00	6.48E − 2	2.36E00
9	1.38E00	4.07E − 2	2.36E00
10	1.60E00	3.87E − 2	2.25E00
11	1.33E00	1.05E − 1	2.36E00
Mean	1.47E00	6.18E − 2	2.29E00
s.d.	1.42E − 1	2.94E − 2	9.87E − 2

* Values of L are min^{-1}; values of residence time are hr; Cs are dimensionless.

TABLE A-2
Optimal Values of Model Parameters and Residence Times for ^{99m}Tc-MAG$_3$*

Volunteer	L(1,2)	L(2,1)	L(4,1)	L(1,4)	L(5,4)
1	1.96E − 2	5.99E − 2	9.48E − 2	2.47E − 1	2.89E − 1
2	4.50E − 2	1.29E − 1	1.16E − 1	5.68E − 2	1.65E − 1
3	4.34E − 2	1.05E − 1	1.39E − 1	1.12E − 1	1.20E − 1
4	5.66E − 2	1.22E − 1	9.26E − 2	9.87E − 2	2.09E − 1
5	7.00E − 2	1.61E − 1	8.33E − 2	4.61E − 2	2.70E − 1
6	6.50E − 2	1.33E − 1	8.70E − 2	1.00E − 2	2.50E − 1
7	1.00E − 1	2.48E − 1	8.56E − 2	2.50E − 2	9.65E − 1
8	1.10E − 1	2.30E − 1	1.15E − 1	2.37E − 1	2.10E − 1

Volunteer	C1	C2
1	9.89E − 1	1.13E − 2
2	9.57E − 1	4.25E − 2
3	9.95E − 1	5.27E − 3
4	1.00E00	0.00E00
5	9.89E − 1	1.02E − 2
6	9.65E − 1	3.47E − 2
7	9.65E − 1	3.48E − 2
8	9.77E − 1	2.29E − 2

	Residence Times		
Volunteer	Remainder of body	Kidneys	Bladder
1	2.91E − 1	5.01E − 2	2.70E00
2	1.91E − 1	9.21E − 2	2.94E00
3	2.12E − 1	1.26E − 1	2.89E00
4	2.42E − 1	7.23E − 2	2.89E00
5	2.18E − 1	5.63E − 2	2.95E00
6	1.92E − 1	6.19E − 2	3.07E00
7	2.11E − 1	7.58E − 2	2.93E00
8	2.83E − 1	7.08E − 2	2.79E00
Mean	2.30E − 1	7.57E − 2	2.90E00
s.d.	3.87E − 2	2.40E − 2	1.11E − 1

* Values of L are min^{-1}; values of residence time are hr; Cs are dimensionless.

TABLE A-3 (Continued)
Optimal Values of Model Parameters and Residence Times for ^{131}I-OIH*

Volunteer	L(1,2)	L(2,1)	L(1,3)	L(3,1)	L(1,4)	L(4,1)	L(5,4)
1	7.04E00	9.52E00	3.46E − 2	1.14E − 1	2.37E − 2	1.70E − 1	5.50E − 1
2	3.49E00	6.30E00	3.53E − 2	1.48E − 1	6.90E − 1	2.67E − 1	1.00E00
3	1.00E + 1	1.00E + 1	3.00E − 2	8.56E − 2	2.14E − 1	3.00E − 1	3.88E − 1
4	4.02E00	8.32E00	3.58E − 2	1.70E − 1	0.00E00	1.61E − 1	3.34E − 1
5	8.88E00	1.00E + 1	3.68E − 2	1.09E − 1	5.93E − 3	1.45E − 1	7.01E − 1
6	1.24E00	6.15E00	8.00E − 3	8.51E − 2	0.00E00	3.37E − 1	3.75E − 1
7	2.81E00	1.00E + 1	2.62E − 2	2.22E − 1	0.00E00	3.07E − 1	6.86E − 1
8	6.54E00	1.00E + 1	2.70E − 2	1.83E − 1	0.00E00	2.17E − 1	5.42E − 1

Volunteer	C1	C2	C3
1	1.00E00	3.83E − 1	1.20E − 1
2	1.00E00	1.00E − 1	1.00E − 1
3	1.00E00	8.16E − 1	3.32E − 1
4	1.00E00	1.00E − 1	1.00E − 1
5	1.00E00	1.00E − 1	1.00E − 1
6	1.00E00	1.66E − 1	1.00E − 1
7	1.00E00	1.00E − 1	1.00E − 1
8	1.00E00	1.00E − 1	1.00E − 1

TABLE A-3 (Continued)

Volunteer	Residence Times		
	Remainder of body	Kidneys	Bladder
1	1.94E − 1	3.00E − 2	4.14E00
2	1.67E − 1	1.64E − 2	4.01E00
3	2.36E − 1	4.26E − 2	4.27E00
4	1.72E − 1	4.94E − 2	3.93E00
5	1.62E − 1	2.36E − 2	4.13E00
6	1.41E − 1	4.41E − 2	4.11E00
7	1.25E − 1	2.41E − 2	4.06E00
8	1.31E − 1	3.04E − 2	4.04E00
Mean	1.66E − 1	3.26E − 2	4.09E00
s.d.	3.63E − 2	1.16E − 2	1.02E − 1

* Values of L are min^{-1}; values of residence time are hr; Cs are dimensionless.

TABLE A-4
Biologic Parameters of the Fractional Distribution Function $\hat{A}_h(T)$ for a Single Intravenous Administration of DTPA, MAG_3, or OIH*

I. ^{99m}Tc-DTPA

$\hat{A}_{hi}$

	$\lambda_1 = 2.42$ hr^{-1}	$\lambda_2 = 81.1$ hr^{-1}	$\lambda_3 = 15.2$ hr^{-1}	$\lambda_4 = 0.482$ hr^{-1}
Kidneys	0.019	−0.110	0.060	0.031
Remainder	0	0.23	−0.077	0.86

II. ^{99m}Tc-MAG_3

α_{hi}

	$\lambda_1 = 0.966$ hr^{-1}	$\lambda_2 = 12.76$ hr^{-1}	$\lambda_3 = 24.2$ hr^{-1}
Kidneys	0.064	0.41	−0.47
Remainder	0.20	0.40	0.38

III. ^{131}I-OIH

α_{hi}

	$\lambda_1 = 14.52$ hr^{-1}	$\lambda_2 = 0.138$ hr^{-1}	$\lambda_3 = 0.706$ hr^{-1}	$\lambda_4 = 0.0154$ hr^{-1}
Kidneys	−0.011	0.14	−0.14	0.015
Remainder	0.48	0.39	0.014	0.14

* $\alpha_h(t) = \sum \alpha_{hi} \exp(-\lambda_i t)$.

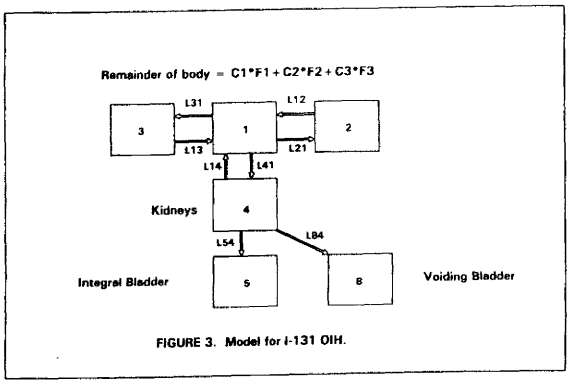

FIGURE A-1. Model for ^{131}I-OIH.

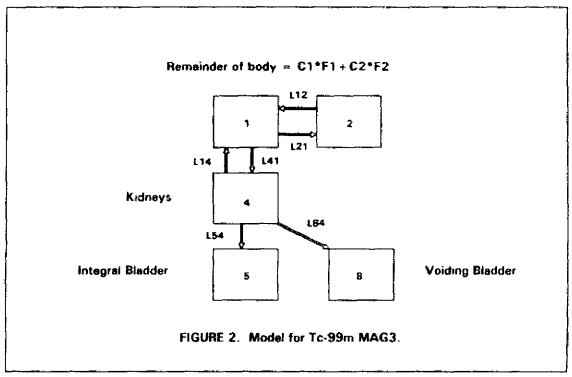

FIGURE A-2. Model for ^{99m}Tc-MAG_3.

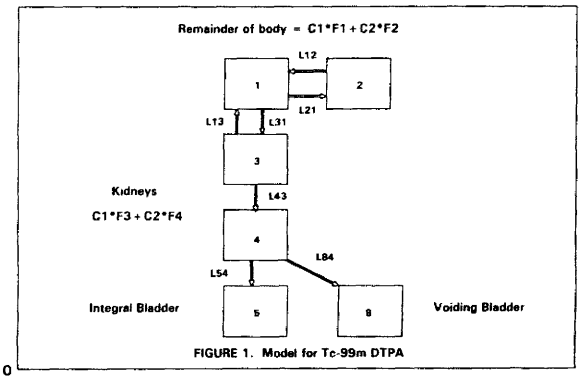

FIGURE A-3. Model for ^{99m}Tc-DTPA.

ACKNOWLEDGMENTS

This work was supported by a grant from the National Institutes of Health (DK 38842-04) and a grant from Mallinckrodt, Inc., St. Louis, Missouri. The work was also performed for the U.S. DOE under contract DE-AC05-76OR00033 and Interagency Agreement No. FDA 224-75-3016, DOE 40-286-71.

The submitted manuscript has been authored by a contractor of the U.S. Government under contract DE-AC05-760R00033. Accordingly, the U.S. Government retains a nonexclusive, royalty-free license to publish or reproduce the published form of

the contribution, or allow others to do so, for U.S. Government purposes.

REFERENCES

1. Eshima D, Fritzberg AR, Taylor Jr A. ^{99m}Tc renal tubular agents: current status. *Semin Nucl Med* 1990;20:28–40.
2. Fritzberg AR, Kasina S, Eshima D, Johnson DL. Synthesis and biological evaluation of technetium-99m-MAG_3 as a hippuran replacement. *J Nucl Med* 1986;27:111–116.
3. Taylor Jr. A, Eshima D. Effects of altered biochemical physiologic states on the clearance and biodistribution of technetium-99m-MAG_3, iodine-131-OIH and iodine-125-iothalamate. *J Nucl Med* 1988;29:669–675.
4. Taylor Jr. A, Eshima D, Fritzberg AR et al. Comparison of I-131-OIH and Tc-99m-MAG_3 renal imaging in volunteers. *J Nucl Med* 1986;27:795–803.
5. Taylor Jr. A, Ziffer JA, Steves A, et al. Clinical comparison of I-131 OIH and the kit formulation of Tc-99m mercaptoacetyltriglycine. *Radiology* 1989;170;721–725.
6. Jafri RA, Britton KE, Nimmon CC, et al. Technetium-99m-MAG_3: a comparison with iodine-123- and iodine-131-orthoiodohippurate in patients with renal disorders. *J Nucl Med* 1988;29:147–158.
7. Russell CD, Thorstad B, Yester MV, et al. Comparison of technetium-99m-MAG_3 with iodine-131-hippuran by a simultaneous dual-channel technique. *J Nucl Med* 1988;29:1189–1193.
8. Bubeck B, Brandau W, Steinbacher M, et al. Technetium-99m-labeled renal function agents. II. Clinical evaluation of Tc-99m MAG3 (Tc-99m mercaptoacetyltriglycine). *Nucl Med Biol* 1988;15:109–118.
9. Taylor Jr. A, Eshima D, Christian P, et al. Technetium-99m-MAG3 kit formulation: preliminary results in normal volunteers and patients with renal failure. *J Nucl Med* 1988;29:616–622.
10. Al-Nahhas AA, Jafri RA, Britton KE, et al. Clinical experience with ^{99m}Tc-MAG_3, mercaptoacetyltriglycine, and a comparison with ^{99m}Tc-DTPA. *Eur J Nucl Med* 1988;14:453–462.
11. Taylor Jr. A, Eshima D, Christian PE, et al. Evaluation of Tc-99m mercaptoacetyltriglycine in patients with impaired renal function. *Radiology* 1987;162:365–370.
12. Taylor Jr. A, Ziffer JA, Eshima D. Comparison of Tc-99m MAG3 and Tc-99m DTPA in renal transplant patients with impaired renal function. *Clin Nucl Med* 1990;15:371–378.
13. Thomas SR, Atkins HL, McAfee JG, et al. MIRD dose estimate report no. 12: technetium-99m-diethylenetriaminepentaacetic acid. In: *MIRD primer for absorbed dose calculations.* New York: Society of Nuclear Medicine; 1988.
14. Tonnesen KH, Munck O, Hald T, et al. Influence on the radiorenogram of variation in skin-to-kidney distance and the clinical importance thereof. In: Winkel SUM, Blaufox MD, Bretano JLF, eds. *Radionuclides in nephrology.* Stuttgart: Georg Thieme; 1975:76–86.
15. Tanasescu DE, Resser K, McLurkin B et al. Comparison of kidney depth determination using Tonnesen formula versus ultrasound. *J Nucl Med* 1987;28:647.
16. Muller-Suur M, Muller-Suur C. Renal and extrarenal handling of a new imaging compound (^{99m}Tc-MAG3) in the rat. *Eur J Nucl Med* 1986;12:438–442.
17. Robertson J. *Compartmental distribution of radiotracers.* Orlando: CRC Press; 1983:73–142.
18. Blaufox MD, Orvis AL, Owen CA. Compartmental analysis of the radio renogram and distribution of I-131-hippuran in dogs. *Am J Physiol* 1963;204:1059–1064.
19. Loevinger R, Budinger T, Watson E. *MIRD primer for absorbed dose calculations.* New York: Society of Nuclear Medicine; 1988.
20. Watson E, Stabin M. Basic alternative software package for internal radiation dose calculations. In: Kathren RL, Higby DP, McKinney MA, eds. *Computer applications in health physics. Proceedings of the 17th midyear topical symposium of the Health Physics Society.* Richland, WA: Columbia Chapter, HPS; 1984:7.79–7.86.
21. Killough GG, Eckerman KF. A conversational Eigen analysis program for solving differential equations. In: Kathren RL, Higby DP, McKinney MA, eds. *Computer applications in health physics. Proceedings of the 17th midyear topical symposium of the Health Physics Society.* Richland, WA: Columbia Chapter, HPS; 1984:4.49–4.58.
22. International Commission on Radiological Protection. *Limits for intakes of radionuclides by workers.* ICRP Publication 30. New York: Pergamon Press; 1979.
23. Marcus C, Koyle M. Dosimetry considerations in patients with renal pathology. In: Schlakfe-Stelson A, Watson E, eds. *Fourth international radiopharmaceutical dosimetry symposium.* Oak Ridge, TN: Oak Ridge Associated Universities; 1986.