Dosimetry of Iodine-123-Epidepride: A Dopamine D2 Receptor Ligand

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Substituted benzamides have been shown to have very high affinity and specificity for the dopamine D2 receptor. One of these is radiolabeled epidepride, an iodine-substituted benzamide currently under evaluation as a SPECT imaging agent. Detailed estimates of the radiation absorbed dose to 26 organs and the whole body from [^{123}I]epidepride have been calculated. **Methods:** The dosimetry calculations use a combination of in vivo uptake and biodistribution data from one rhesus monkey and seven humans to estimate residence times in eight organs. The computer program MIRDOSE2 was used to calculate the dosimetry. **Results:** Results indicate that 75% of the radioactivity is cleared through the urinary tract while the remaining radioactivity clears through the gallbladder and intestinal tract. The radiation absorbed dose can be minimized by administering a high lipid content meal 1.5 hr postinjection to empty the gallbladder and by giving large volumes of fluids throughout the study to induce increased urinary output. **Conclusion:** By emptying the gallbladder and urinary bladder, the lower large intestine becomes the critical organ, 0.102 mGy/MBq (0.38 rad/mCi) followed by the upper large intestine, 0.092 mGy/MBq (0.34 rad/mCi). The effective dose equivalent is 0.025 mSv/MBq (0.092 rem/mCi).

Key Words: iodine-123-epidepride; dosimetry; single-photon emission computed tomography; dopamine D2 receptor

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Labeled substituted benzamides show great potential for investigating the dopamine neurotransmitter system. Epidepride, (S)-(-)-N-[(1-ethyl-2-pyrrolidinyl)methyl]-5-[^{123}I]iodo-2,3-dimethoxybenzamide, has been reported as a very potent dopamine D2 receptor antagonist (*1*). This agent and its corresponding 5-fluoroalkyl substituted analogs promise to be valuable in studying dopaminergic neurotransmission and its relation to various disease states (*2*). Possible applications include Parkinson's disease (*3*), progressive supranuclear palsy (*4*), schizophrenia (*5*), affective disorders (*6*) and tardive dyskinesia (*7*). The extremely high specificity and affinity of epidepride for the dopamine D2 receptor allows investigation of both striatal and extrastriatal receptors (*8*).

In anticipation of its use in human studies, the dosimetry of [^{123}I]epidepride has been calculated. Radiation absorbed dose estimates for 26 organs are presented. Since commercially supplied ^{123}I may contain ^{124}I and ^{125}I as contaminants, the absorbed doses from [^{124}I]epidepride and [^{125}I]epidepride were also calculated.

METHODS

Preparation of Iodine-123-Epidepride and Iodine-125-Epidepride

Epidepride was radioiodinated in 60%–70% radiochemical yields from the corresponding 5-(tributyltin) derivative (*9*) using Na^{123}I with a specific radioactivity of 3000 Ci/mmole, oxidized in situ at 20°C with chloramine-T, and the reaction was quenched with bisulfite after 3 min. Iodine-125-Epidepride was prepared in the same way at 2000 Ci/mmole specific radioactivity using Na^{125}I as the radionuclide (*10*). Iodine-123 was supplied by Amersham/Medi-Physics (Arlington Heights, IL) with a specified radionuclidic purity greater than 99.99%.

Biodistribution Data

Monkey Data. An adult female rhesus monkey (Macaca Mulatta, 9 kg) was used to measure the biodistribution of ^{123}I epidepride 3 hr postinjection. Prior to the experiment, the monkey was on her normal feeding schedule. Following 10 mg/kg ketamine i.m., 185 MBq (5 mCi) [^{123}I]epidepride was administered intravenously. Urine and stools were collected for 3 hr, at which time the animal was killed. Twenty-six whole organs were dissected and assayed for ^{123}I radioactivity. The assays took place in a shielded room with very low background using a large NaI detector. Organs were placed 2 m from the detector to reduce variations in the detected activity due to geometrical effects. The detector was calibrated by counting 30-μCi, 100-μCi, and 300-μCi samples of the injected compound at the same location. To ensure that deadtime was not affecting the counting results, all samples were assayed at 6 and 24 hr postinjection and compared for consistency.

Human Data. Seven healthy adult male volunteers were used to measure the clearance of activity through the urinary bladder. The volunteers were nominally injected intravenously with 150 MBq (4.0 mCi; range was 3.8–4.2 mCi) [^{123}I]epidepride. Large

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TABLE 1
Biodistribution of Iodine-123-Epidepride in Rhesus Monkey Three Hours Postinjection

Organ	Fraction of injected dose
Gallbladder w/content	0.46
Remaining body	0.30
Small intestine w/contents	0.15
Bladder	0.067
Stomach w/contents	0.051
Upper large intestine w/content	0.021
Liver	0.019
Thyroid thalmus	0.015
Eye (one)	0.012
Kidney	0.0076
Brain	0.0076
Muscle (large mass)	0.0067
Urine (pre 2 hr)	0.0063
Lungs	0.0041
Blood (large sample)	0.0031
Feces (pre 2 hr)	0.0026
Cortical bone (femur)	0.0022
Lower large intestine w/content	0.0017
Parotid glands	0.0015
Heart	0.0009
Cancellous bone (skull)	0.0007
Breast	0.0006
Pancreas	0.0005
Ovaries	0.0005
Uterus	0.0003
Spleen	0.0003
Adrenals	0.0003
Red marrow	0.0001

volumes of fluids were given prior to and during the study to facilitate emptying of the urinary bladder. A high lipid content meal (typically pizza) was given to the volunteers 1.5 hr after injection to empty the gallbladder. Prior to the study, the volunteers were given no special dietary instructions. At 1 hr preinjection, 100 mg of Lugol's solution was administered. Urine was collected for 7 hr postinjection and assayed for ^{123}I activity.

Time-activity curves for several regions of the brain, including the basal ganglia, have been previously published (*11*), however, data presented in that report were found to be in error by a scale factor. To determine the correct calibration factor, the three-dimensional Hoffman brain phantom (Data Spectrum, Inc., Chapel Hill, NC) was filled with a known activity concentration, imaged, attenuation corrected and reconstructed using the same parameters as the human study. Comparison of the counts per pixel in the basal ganglia of the phantom to the known radioactivity concentration revealed that the previously reported numbers were a factor of 11.6 too large. The data in the previous report were scaled and used herein.

Residence Time Calculations

The primate biodistribution data (Table 1) indicates that there are two primary excretory pathways by which epidepride is cleared from the body. Therefore, the dosimetric model used consists of two separate excretory pathways and a separate calculation for the basal ganglia. The first pathway describes the

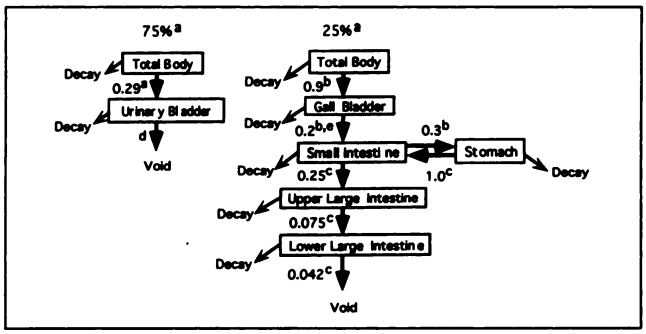

FIGURE 1. Model used to calculate residence times for the various organs. The arrows indicate first order rate constants with values indicated in units of 1/hr. [a]Fraction of injected activity entering this pathway as determined from the urine study. [b]Value determined to agree with the Rhesus Monkey biodistribution experiment. [c]Values from ICRP 30. [d]The urinary bladder is voided at regular intervals (see text). [e]The gallbladder contents are transferred to the small intestine at various times (see text).

clearance of a fraction of the injected activity through the urinary bladder. The second pathway describes clearance of the remainder of the activity through the gastrointestinal tract. Finally, since [^{123}I]epidepride has an extremely high affinity for the dopamine D2 receptor, the dose to the basal ganglia is calculated separately.

The model of the urinary tract is supported by the calculated curve in Figure 2. The dosimetric model for the gastrointestinal tract is a modification of the model presented in ICRP 30 (*12*). That report included compartments and forward rate constants for the stomach, small intestine and upper and lower large intestine exactly as depicted in Figure 1. The dosimetric model is also shown in Figure 1. The boxes represent standard, well mixed compartments connected by first order rate constants of the indicated value in units of 1 hr. The biodistribution data from the rhesus monkey indicate that additional compartments are needed to calculate the dosimetry of epidepride.

The monkey data indicates that radiotracer enters the gastrointestinal tract at the small intestine through the gallbladder and that there is a small amount in the stomach. For calculation purposes, it was assumed that activity entered the stomach by reflux from the small intestine only. Reabsorption into the total body from the gut was not considered for two reasons: (1) data

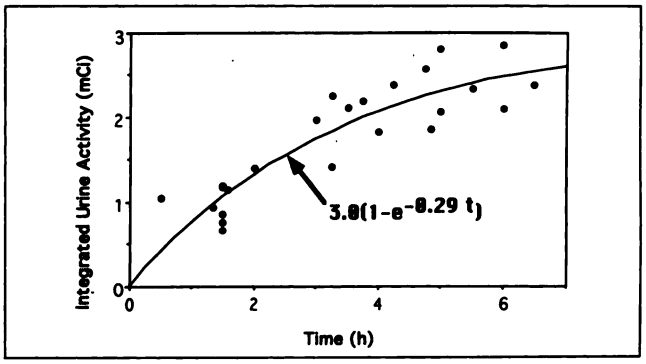

FIGURE 2. Integrated urine activity as a function of time. The data are a compilation of results from seven normal human volunteers each of whom received a 150-MBq (4.0 mCi) injection of [^{123}I]epidepride. The curve is the least squares best fit to the indicated function.

does not exist that would support this complication to the model; and (2) the monkey biodistribution data suggest that the critical organs are in the gut. Therefore, not considering reabsorption sets an upper limit to the dose to these organs and is the conservative approach.

Based on the monkey data, a compartment for the gallbladder was added to the ICRP model along with a reverse rate constant from the small intestine to the stomach. This rate constant and the rate constants that connect the total body to the gallbladder, and the gallbladder to the small intestine were determined so that at 3 hr postinjection, the calculated biodistribution ratios in the human gastrointestinal tract agree with the measured biodistribution ratios in the monkey. Since 45% of the injected dose was found in the monkey gallbladder but only 25% of the injected dose was excreted through the intestines in humans, the rate constants were determined so that the calculated ratios of radioactivity (rather than absolute values) in the human gallbladder, stomach and small intestine were made to agree with the ratios measured in the monkey experiment.

The dosimetric model for calculating residence times was implemented on a Macintosh computer using the program STELLA II (High Performance Systems, Inc., Hanover, NH). Several gallbladder and urinary bladder voiding schemes were used. At a specified time postinjection, coincident with the high lipid content meal, the model transfers the gallbladder contents to the small intestines. The timing effect of this transfer was evaluated by repeating the calculation for several different meal schedules. Similarly, the urinary bladder was emptied at regular intervals and the calculation was repeated for several different voiding intervals. Each compartment for each of the above conditions was integrated to give the residence time. The computer program MIRDOSE2 (*13*) was used to calculate the radiation absorbed dose to an adult (reference man) given the residence times.

The radiation adsorbed dose to the basal ganglia is calculated as the sum of two parts: the dose received from whole brain as calculated above and the dose from irradiation of the basal ganglia by itself. The putamen time-activity curve published by Kessler et al. (*11*) and modified as above was used to calculate the residence time in the basal ganglia. First, the data points were decreased by the appropriate physical decay factor and then the curve was integrated using trapezoidal integration. After the last published data point, the activity was assumed to clear at the combined biological and physical clearance rate and the residence time was calculated. Kessler et al. reported that the biological clearance time from the basal ganglia estimated curve was 20 hr (*11*). S factors for the basal ganglia irradiating basal ganglia have not been published. Since the testes are approximately the same size as the basal ganglia, the published S factors for the testes were used. The basal ganglia dose was estimated by entering the residence time for the basal ganglia as the testes residence time in a separate run of MIRDOSE2. The output of this run is an underestimate of the dose to the basal ganglia because the radiations are averaged over the testes mass (35 g) rather than the basal ganglia mass (26 g) (*14*). To correct this, the dose is scaled by the ratio of the basal ganglia and testes masses.

The radiation adsorbed dose to the brain is also calculated as the sum of two parts: the dose received from the whole brain as calculated above and the dose from irradiation by the basal ganglia. To calculate the later contribution, it is assumed that the dose to the brain from the basal ganglia is uniform throughout the brain and due to disintegration photons only. The shorter-range electrons are considered to contribute only to the basal ganglia dose as described above. To obtain the dose, the residence time is multiplied by the average photon energy per disintegration (^{123}I: 173 keV; ^{124}I: 852 keV; ^{125}I: 42.3 keV) (*15*) and divided by the mass of the brain (taken as 1.4 kg).

RESULTS

Biodistribution

The biodistribution of [^{123}I]epidepride in the rhesus monkey at 3 hr postinjection is shown in Table 1. The total of all activity measured in the dissected tissues and the remainder of the body was 110% of the injected dose. This overestimate is considered within the experimental error (see Discussion). All of the injected activity that was cleared, was cleared through either the urinary or intestinal tracts.

Accumulated activity that passed through the human urinary bladder is shown in Figure 2 which includes data from seven human volunteers. The solid line is the theoretical curve from a model assuming first order clearance from the total body into the urinary bladder (Fig 1). The curve, $3.0(1 - e^{-0.29t})$ where t is the time postinjection in hours, was determined to be the best least-squares fit of the model equation to the data. This indicates that 75% of the activity is cleared through the urinary bladder in humans and that the clearance rate from the body to the bladder is 0.29/hr.

Dosimetry

Residence times for radiolabeled epidepride in various source organs for several different urinary bladder and gallbladder voiding intervals are shown in Table 2. The residence time in organs of the lower gastrointestinal tract tract and stomach are relatively insensitive to the gallbladder emptying schedule. If the gallbladder is to be emptied once, the minimum in residence time for the gallbladder occurs with a void between 1.5 and 2 hr postinjection. Voiding the gallbladder at regular 1.5-hr intervals reduces the gallbladder residence time by a factor of two, from 0.36 to 0.19 hr, over a single void at 2 hr. To determine how many voids are necessary, the residence time was calculated with voids at 1.5, 3 and 4.5 hr and found to be 0.21 hr. The urinary bladder residence time increases from 0.35 to 1.07 hr as the urinary bladder emptying interval is increased from 1 to 3 hr.

Iodine-123-epidepride radiation absorbed dose estimates for the 6 organs affected by different urinary bladder and gallbladder voiding schedules are given in Figure 3A and the remaining 20 organs are given in Figure 3B. The critical organs are the intestinal tract with the lower large intestine receiving the largest dose, 0.10 mGy/MBq (0.38 rad/mCi) followed by the upper large intestine, the urinary bladder and gallbladder and the small intestine. Varying the voiding schedule varies the dose to the gallbladder or urinary bladder but the dose to other organs remains constant. When the gallbladder and urinary bladder are emptied at regular intervals, their dose is reduced by a factor of two. If the gallbladder is not emptied postinjection, it will be the critical organ, 0.11 mGy/MBq (0.4 rad/mCi). Table 2 contains

TABLE 2
Residence Times for Radiolabeled Epidepride in Various Source Organs for Various Gallbladder and Urinary Bladder Voiding Schedules

GB void interval (hr)	1.5*	1.0*	2.0*	3.0*	1.0†	1.5†	1.5‖	1.5†
UB void interval (hr)‡	2	2	2	2	2	2	1	3
[^{123}I]epidepride								
GB (hr)	0.37	0.44	0.36	0.41	0.13	0.19	0.19	0.19
LLI (hr)	1.10	1.09	1.11	1.09	1.17	1.15	1.15	1.15
SI (hr)	0.69	0.68	0.69	0.68	0.73	0.72	0.72	0.72
ST (hr)	0.20	0.19	0.20	0.19	0.21	0.21	0.21	0.21
UB (hr)	0.70	0.70	0.70	0.70	0.70	0.70	0.35	1.07
ULI (hr)	1.37	1.35	1.37	1.36	1.45	1.43	1.43	1.43
Basal ganglia§	0.02							
TB (hr)	2.46	2.46	2.46	2.46	2.46	2.46	2.46	2.46
[^{124}I]epidepride								
GB (hr)	0.46	0.56	0.43	0.47	0.14	0.21	0.21	0.21
LLI (hr)	4.42	4.41	4.43	4.42	4.46	4.45	4.45	4.45
SI (hr)	0.95	0.94	0.95	0.95	0.95	0.95	0.95	0.95
ST (hr)	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28
UB (hr)	0.82	0.82	0.82	0.82	0.82	0.82	0.40	1.27
ULI (hr)	2.89	2.89	2.89	2.89	2.91	2.91	2.91	2.91
Basal ganglia§	0.04							
TB (hr)	2.80	2.80	2.80	2.80	2.80	2.80	2.80	2.80
[^{125}I]epidepride								
GB (hr)	0.47	0.59	0.44	0.48	0.14	0.21	0.21	0.21
LLI (hr)	5.82	5.82	5.82	5.82	5.82	5.82	5.82	5.82
SI (hr)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
ST (hr)	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
UB (hr)	0.84	0.84	0.84	0.84	0.84	0.84	0.84	0.84
ULI (hr)	2.89	2.89	2.89	2.89	2.91	2.91	2.91	2.91
Basal ganglia§	0.04							
TB (hr)	2.86	2.86	2.86	2.86	2.86	2.86	2.86	2.86

*Single void at the indicated time postinjection.
†Regular voiding at the indicated interval (hr).
‡Regular voiding interval for the urinary bladder (hr).
§The basal ganglia residence time is independent of the voiding schedule.
GB = gallbladder; LLI = lower large intestine; SI = small intestine; ST = stomach; TB = total body; UB = urinary bladder; and ULI = upper large intestine.

the radiation dosimetry assuming that the urinary bladder is emptied at 2-hr intervals and the gallbladder is emptied at 1.5-hr intervals. The radiation absorbed dose due to injection of [^{124}I]epidepride and [^{125}I]epidepride are also included.

DISCUSSION

We have determined the dosimetry of [^{123}I]epidepride using residence time calculations and activity concentration measurements in one primate and seven humans. Since epidepride has very high specificity and affinity for dopamine receptors, which are concentrated in the basal ganglia, the dose to the basal ganglia was calculated separately. In the primate experiment, the sum of all activity either excreted through the urine or feces or remaining in the body was 110%. This overestimate is attributed to minor geometrical effects and to cross-calibration of the detectors used for assaying the injected dose and the tissue samples, and is not considered significant. From this, we conclude that all of the activity is excreted through either the urine or feces. The primate experiment also served to demonstrate that activity in the stomach and gallbladder must be accounted for in the dosimetry and hence the ICRP gastrointestinal tract tract model was expanded.

Since only one monkey was killed, sufficient data to determine the existence of a difference between the monkey and human behavior of epidepride in vivo was not met. Because of this, the dosimetry calculations do not rely heavily on the results from testing the monkey. Three conclusions from the primate data were used in the dosimetry calculations:

1. All activity is excreted through the urine or feces.
2. The activity is cleared through the gallbladder and urinary bladder.
3. The ratio of activities in organs of the intestinal tract at 3 hr.

With these findings, the ICRP gastrointestinal tract model (*12*) was slightly modified and used for the human dosimetry calculations.

The fraction of the injected dose that follows each of the

TABLE 3
Radiation Absorbed Dose Following Injection of Radiolabeled Epidepride

Organ	[^{123}I]Epidepride		[^{124}I]Epidepride		[^{125}I]Epidepride	
	mGy/MBq	rad/mCi	mGy/MBq	rad/mCi	mGy/Mbq	rad/mCi
LLI	0.100	0.370	2.27	8.4	0.34	1.27
ULI	0.092	0.340	1.05	3.9	0.14	0.51
Urinary bladder wall*	0.060	0.220	0.40	1.5	0.049	0.18
Gallbladder wall†	0.054	0.200	0.38	1.4	0.041	0.15
Small intestine	0.038	0.140	0.35	1.3	0.041	0.15
Ovaries	0.022	0.082	0.25	0.93	0.032	0.12
Stomach	0.017	0.064	0.15	0.54	0.014	0.053
Uterus	0.015	0.056	0.14	0.51	0.008	0.028
Basal ganglia	0.015	0.054	0.17	0.629	0.024	0.090
Bone surface	0.006	0.023	0.03	0.12	0.005	0.020
Pancreas	0.006	0.023	0.049	0.18	0.002	0.009
Total body	0.005	0.019	0.051	0.19	0.005	0.017
Kidney	0.005	0.019	0.049	0.18	0.002	0.007
Red marrow	0.005	0.019	0.057	0.21	0.003	0.010
Liver	0.005	0.018	0.041	0.15	0.002	0.008
Muscle	0.004	0.016	0.043	0.16	0.003	0.011
Spleen	0.004	0.016	0.038	0.14	0.002	0.006
Testes	0.004	0.015	0.041	0.15	0.002	0.006
Adrenals	0.004	0.014	0.030	0.11	0.001	0.005
Brain	0.003	0.012	0.024	0.090	0.002	0.007
Heart wall	0.003	0.011	0.022	0.080	0.001	0.005
Lungs	0.002	0.009	0.018	0.065	0.001	0.005
Thymus	0.002	0.008	0.016	0.058	0.001	0.004
Thyroid	0.002	0.008	0.014	0.051	0.001	0.005
Skin	0.002	0.008	0.021	0.076	0.001	0.004
Breasts	0.002	0.006	0.014	0.051	0.001	0.004

*The urinary bladder is assumed to empty at 2-hr intervals.
†The gallbladder is assumed empty at 1.5-hr intervals.
See Table 2 for definitions.

excretory routes in humans was determined by measuring the amount of radioactivity in human urine following injection. The remaining radioactivity was assumed to enter the gastrointestinal tract and the dosimetry was calculated using the modified ICRP gastrointestinal-tract model (*12*).

The measured ratios of radioactivity concentrations in the primate gastrointestinal tract at 3 hr postinjection were assumed to approximate closely the ratios in similar human tissue. Absolute values measured in the primate were not used because the fraction of activity in the two excitatory

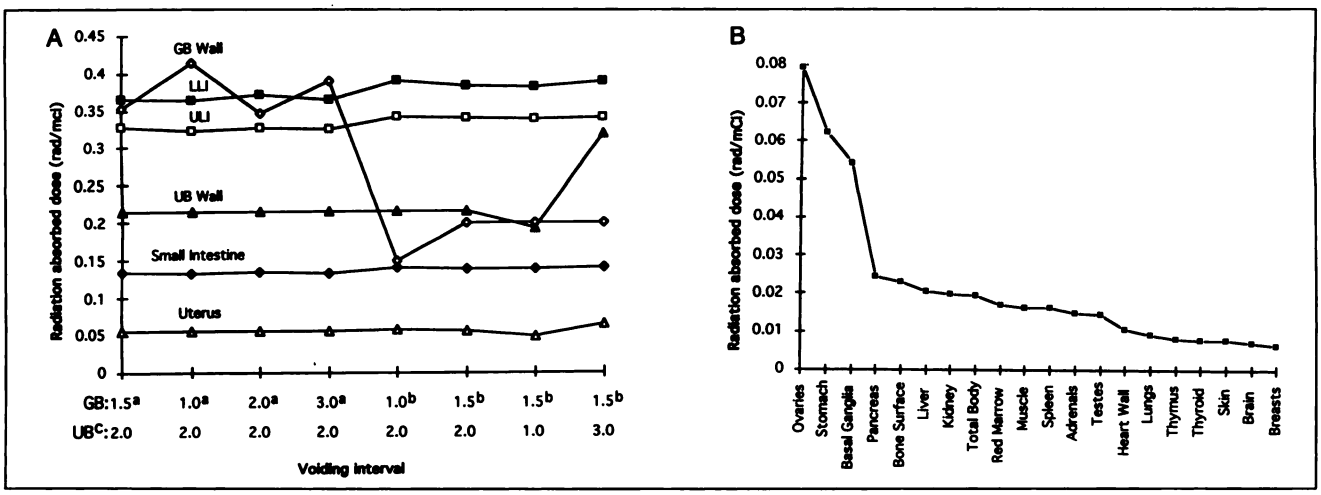

FIGURE 3. (A) Radiation absorbed dose to organs that are affected by the gallbladder and urinary bladder voiding schedule following injection of [^{123}I]epidepride. See Table 2 for definitions. (B) Radiation absorbed dose to organs that are unaffected by the gallbladder and urinary bladder voiding schedule following injection of [^{123}I]epidepride.

routes differed greatly from the human measurements. Reasons for this may include that the primate was not given extra fluids and that the ketamine injection may have altered the distribution of activity that clears through the urine and bowels. It was assumed that of the activity that reached the gastrointestinal tract tract, the ratio of activity in each of the gastrointestinal tract tract organs was similar at 3 hr postinjection in the two species.

A more complete biodistribution model would include compartments for the kidneys and liver which lead into the urinary and gall bladders. This was not done because there was insufficient information to accurately model these compartments. At 3 hr postinjection in the monkey experiment, however, the kidneys contained approximately 10% of the activity in the urinary bladder and the liver contained less that 5% of the activity in the gallbladder. Therefore, the rate constants that connect these compartments are rapid and the residence time in the kidneys and liver will be much less than the residence time in the urinary bladder and gallbladder. To estimate the effect on the calculated dose to the kidneys and liver of omitting specific compartments for these organs, the dose was calculated assuming the residence time was one-third that of the gallbladder or urinary bladder. This produced a dose of 0.0024 and 0.0106 mGy/MBq to the liver and kidney, respectively. These are viewed as upper limits to the dose to these organs and are still well below the doses to the upper and lower large intestines.

Results of the residence time calculations indicate that if the gallbladder is emptied once, it should be emptied between 1.5 and 2 hr postinjection to minimize residence time. The emptying schedule has very little effect on the residence times in the intestinal tract. Voiding the gallbladder three times, at 1.5, 3.0 and 4.5 hr postinjection reduces the residence time by nearly a factor of two. The urinary bladder residence time increases from 0.35 to 1.07 hr as the urinary bladder emptying interval is increased from 1 to 3 hr. Therefore, to minimize the gallbladder dose, it is recommended that the gallbladder be voided three times as indicated above. Since the dose to the urinary bladder decreases with frequent voiding, it is recommended that sufficient fluids be given to facilitate voiding at 1–2-hr intervals.

Estimates from MIRDOSE2 for the radiation absorbed dose to 26 organs are presented in Table 2. Given the residence time for the basal ganglia, S factors for the testes were used to calculate the dose to the basal ganglia. This was done because internal structures of the brain are not included in MIRDOSE2 and because S factors for these structures have not been published. Epidepride accumulates in brain regions other than the basal ganglia but at concentrations that are reduced by an order of magnitude (*11*). Therefore, the dose to these regions is underestimated by the value for the brain given in Table 2, which does not consider the brain irradiating itself, but is on the order of a factor of ten less than the dose to the basal ganglia. The critical organs are the lower and upper large intestines. For purposes of comparison, the effective dose equivalent (*16*) is 0.025 mSv/MBq (0.092 rem/mCi). Based on these considerations, the recommended injection dose is 150 MBq (4 mCi) for clinical imaging. This will provide good imaging conditions for 20 hr and the radiation absorbed dose will be 15 mGy (1.5 rad) or less to all organs.

The radiation absorbed dose from [^{124}I]epidepride and [^{125}I]epidepride have also been calculated because they may be radionuclidic impurities in commercial ^{123}I preparations (Table 3). (When the ^{124}Xe(p,2n) route is used, the ^{124}I impurity is negligible (Medi-Physics).) Also, ^{121}Te can be a contaminant but was not included because the yield of Te-labeled epidepride is negligible. The dose from [^{124}I]epidepride is an order of magnitude greater than from [^{123}I]epidepride because of the positron emission in ^{124}I decay. The dose from [^{125}I]epidepride is a factor of two greater due to its longer half-life. The radionuclidic purity of ^{123}I is specified to be greater than 99.99%, in which case the radiation absorbed dose from impurities will be insignificant.

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REFERENCES

1. Kessler RM, Ansari MS, de Paulis T, et al. High affinity dopamine D2 receptor radioligands. 1. Regional rat brain distribution of iodinated benzamides. *J Nucl Med* 1991;32:1593–1600.
2. Mathis CA, Bishop JE, Gerdes JM, Whitney JM, Brennan KM, Jagust WJ. Synthesis and evaluation of high affinity, aryl-substituted [^{18}F]fluoropropylbenzamides for dopamine D2 receptor studies. *Nucl Med Bio* 1992; 19:571–588.
3. Hornykiewicz O. Dopamine and brain function. *Pharmacol Rev* 1966;18: 925–961.
4. Baron JC, Maziere B, Loch C, et al. Loss of striatal [^{76}Br]bromospiperone binding sites demonstrated by positron tomography in progressive supranuclear palsy. *J Cereb Blood Flow Metab* 1986;6:131–136.
5. Snyder SH. Dopamine and receptors, neuroleptics and schizophrenia. *Am J Psychiatry* 1981;138:460–464.
6. Willner, P. Dopamine and depression: a review of recent evidence: I. Empirical studies. *Brain Res* 1983;6:211–224.
7. Seeman P. Tardive dyskinesia, dopamine receptors and neuroleptic damage to cell membranes. *J Clin Psychopharmacol* 1988;8[Suppl]:35–95.
8. Kessler RM, Ansari MS, Schmidt DE, et al. High affinity dopamine D2 receptor radioligands. II. [125-I]epidepride, a potent and specific radioligand for the characterization of striatal and extrastriatal dopamine D2 receptors. *Life Sci* 1991;49:617–628.
9. de Paulis T, Smith ME. Facile preparation of (S)-N-[(1-ethyl-2-pyrrolidinyl)-methyl]-2,3-dimethoxy-5-(tributyltin)benzamide from isoremoxipride: the precursor of [^{125}I]- and [^{123}I]epidepride. *Synth Commun* 1991;21:1091–5.
10. Clanton JA, dePaulis T, Schmidt DE, et al. Preparation of [^{123}I]- and [^{125}I]epidepride: a dopamine D2 receptor antagonist radioligand. *J Lab Compd Radiopharm* 1991;29:745–751.
11. Kessler RM, Mason NS, Votaw JR, et al. Visualization of extrastriatal dopamine D2 receptors in the human brain. *Eur J Pharmacol* 1992;223:105–107.
12. ICRP Publication 30. *Limits for intakes of radionuclides by workers*. Oxford: Pergamon Press 1979;30–34.
13. Watson EE, Stabin M, Bolch WE. *MIRDOSE ver2*. Oak Ridge, TN: Oak Ridge Associated Universities; 1988.
14. Blinkov SM, Glezer II. *The human brain in figures and tables a quantitative handbook*. New York Basic Books, Inc. Plenum Press 1968;166.
15. Browne E, Firestone RB. *Table of radioactive isotopes*. Shirley VS, ed. New York: John Wiley & Sons; 1986;123–125.
16. ICRP. *Recommendations of the ICRP*. ICRP pub 26. *Annals of ICRP*, volume 1, number 3. Oxford: Pergamon Press; 1977.