jnm/INSTRUMENTATION AND PHYSICS

DOSIMETRY OF FOUR HEART-IMAGING RADIONUCLIDES: ^{43}K, ^{81}Rb, ^{129}Cs, AND ^{201}Tl

Paul A. Feller and Vincent J. Sodd

Bureau of Radiological Health, Food and Drug Administration, Cincinnati General Hospital, Cincinnati, Ohio

In conjunction with research into the relative clinical suitability of radionuclides for heart imaging, estimates of the radiation dosimetry for ^{43}K, ^{81}Rb, ^{129}Cs, and ^{201}Tl were calculated. Estimates of absorbed radiation dose for the heart, kidneys, liver, lungs, testes, and whole body of the standard man were computed from published distribution data in rats via the MIRD method by assuming that the concentration in each organ per initial mean whole-body concentration is the same in rats and humans. The whole-body absorbed radiation doses from ^{81}Rb, ^{129}Cs, ^{201}Tl, and ^{43}K are 0.08, 0.17, 0.24, and 0.60 rads/mCi administered intravenously. In general, the organ doses for the four radionuclides follow the same order.

TABLE 1. CUMULATED ACTIVITIES PER MILLICURIE ADMINISTERED INTRAVENOUSLY (μCi-HR)

	^{81}Rb*	^{81m}Kr*	^{129}Cs	^{201}Tl	^{43}K
Whole body†	6,520	6,260	43,600	96,400	30,800
Blood‡	107	103	523	147	172
Heart‡	85	81	278	135	89
Kidneys‡	98	94	332	739	92
Liver‡	308	296	1,450	1,030	608
Lungs‡	118	113	455	240	219
Testes‡	2.7	2.6	18	52	10

* Organ cumulated activities based on cesium distribution. (Cumulated activity of ^{81m}Kr = 0.96 × ^{81}Rb cumulated activity.)

† Based on total-body cesium retention in humans.

‡ Organ cumulated activities extrapolated from rat distribution.

The search for an ideal heart-imaging agent has led to the testing of several radionuclides, four of the most promising being ^{43}K (*1,2*), ^{81}Rb (*3*), ^{129}Cs (*4*), and ^{201}Tl (*5–7*) in their ionic (+1) form. As part of the research into the relative clinical suitability of these agents, information on their comparative dosimetry was desired. Published dosimetry information for ^{129}Cs (*8–10*) has been based on limited biologic data; published data for ^{43}K and ^{81}Rb have consisted only of whole-body values (*2,11,12*); human organ dose estimates for ^{201}Tl based on distribution data in goats have recently been published (*6*). Quantitative biologic distribution data in humans were unavailable for these agents, although some animal data were found.

Reported here are organ dose estimates for several organs of standard man calculated from animal data gathered from the literature.

NUCLIDE PARAMETERS

The physical half-lives and equilibrium absorbed dose constants, Δ, for 22.4-hr ^{43}K, 4.6-hr ^{81}Rb, and its radioactive daughter 13-sec ^{81m}Kr were taken from the work of Dillman (*13*); the Δ values for 32.1-hr ^{129}Cs have been calculated by Feller and Kereiakes (*10*), and for 73.5-hr ^{201}Tl by Feller and Scholz (*14*).

BIOLOGIC DISTRIBUTION AND CUMULATED ACTIVITIES

Table 1 lists the cumulated activities calculated for the four radionuclides. The lack of whole-body retention data for the different radionuclides in humans necessitated that the whole-body cumulated activity for each nuclide be based on human whole-body retention of cesium, i.e., immediate 100% uptake, with 10% and 90% of the activity having biologic half-times of 1.5 days and 110 days, respectively (*15*).

To obtain cumulated activities in human blood, heart, kidneys, liver, lungs, and testes, the biologic

Received April 15, 1975; revision accepted May 31, 1975.

For reprints contact: Paul A. Feller, Nuclear Medicine Laboratory, BRH, FDA, Cincinnati General Hospital, Cincinnati, Ohio 45267.

TABLE 2. ABSORBED DOSE ESTIMATES PER MILLICURIE ADMINISTERED INTRAVENOUSLY (RADS)

	^{81}Rb*	^{129}Cs	^{201}Tl	^{42}K
Total body	0.08	0.17	0.24	0.60
Heart†	0.16	0.25	0.17	0.52
Kidneys†	0.22	0.23	0.39	0.52
Liver†	0.14	0.22	0.15	0.53
Lungs†	0.10	0.16	0.12	0.43
Testes†	0.09	0.21	0.30	0.58

* Includes contribution from ^{81m}Kr daughter.
† Doses in standard man (MIRD Pamphlet No. 5) extrapolated from rat data.

uptake and retention curves for these organs in rats were evaluated. The basic assumption was that the individual organ concentration, per initial mean whole-body concentration, is the same for the two species. Specifically:

$$\left[\frac{A_i(t)/m_i}{A_o/m_{TB}}\right]_{rat} = \left[\frac{A_i(t)/m_i}{A_o/m_{TB}}\right]_{human}, \quad (1)$$

where $A_i(t)$ is the activity present at any time t in organ i; m_i is the mass of organ i; A_o is the injected activity; and m_{TB} is the mass of the whole body. Equating these ratios of concentrations compensates for differences in the sizes of organs relative to whole-body size from species to species.

In evaluating the biologic data in rats, when the maximum uptake in an organ (except testes) was not instantaneous, immediate uptake was assumed, followed by a period of constant activity until the actual time that the maximum occurred. The maximum overestimation of cumulated activity attributable to this assumption is less than 4%. For the testes, a one-component exponential uptake equation was calculated by a least-squares analysis. A one- or two-component exponential equation describing the biologic excretion portion of each curve was also fitted by a least-squares analysis. The incorporation of the nuclide's physical decay constant into each expression, subsequent integration, and multiplication by appropriate mass ratios, yielded a value of cumulated activity for each human organ. The human organ masses used were those of the MIRD phantom (*16*). Special mention should be made of the heart, whose mass of 603 gm is almost equally divided between the heart muscle and contents (blood) (*17*). The rat data were assumed to be for heart muscle only. The cumulated activity in the human heart is the sum of that in the heart muscle plus that in the average fraction of whole-body blood located in the heart. A brief description of the sources of data used in calculating the cumulated activities for the organs follows.

Cesium. Moskalev's reported results (*18*) of an investigation into the distribution of cesium in rats list organ content at 11 time points from 10 min to 64 days after injection of ^{137}Cs. Due to the 30.2-year half-life of this cesium isotope, the data needed no correction for physical decay. These data were in the form:

$$\left[\frac{A_i(t)}{A_o}\right]_{rat}. \quad (2)$$

To obtain the cumulated activity for each human organ, the time integral of each distribution expression for these data was multiplied by:

$$\left[m_{TB}/m_i\right]_{rat} \times \left[m_i/m_{TB}\right]_{human}, \quad (3)$$

where the ratios of masses for the rat were taken from Spector (*19*).

Potassium and thallium. Gehring and Hammond's 1967 publication (*20*) included distribution data in rats for ^{42}K (corrected for physical decay) and for ^{204}Tl (physical decay correction unnecessary) from 2 min to 12 hr after injection. These data were expressed as:

$$\left[\frac{A_i(t)/m_i}{A_o/m_{TB}}\right]_{rat}, \quad (4)$$

so cumulated activity for each human organ was obtained by multiplying the time integral of each distribution function for these data by:

$$\left[m_i/m_{TB}\right]_{human}. \quad (5)$$

Rubidium. Because insufficient biologic data exist for rubidium, the cumulated activities for ^{81}Rb were calculated assuming the same distribution parameters as for cesium. Ninety-six percent of all ^{81}Rb disintegrations result in the formation of radioactive ^{81m}Kr. Since the half-life of the daughter, 13 sec, is very much shorter than that of the parent, 4.7 hr, secular equilibrium was assumed to exist, and the krypton was assumed to decay within each organ in the same way as the rubidium. Each value of cumulated activity for ^{81m}Kr was thus assumed to be 96% of the corresponding ^{81}Rb cumulated activity.

RESULTS

The estimates of absorbed radiation dose to the whole body and to five organs, from 1 mCi of each of the four nuclides administered intravenously, are listed in Table 2. These values were obtained using a computer code (*21*) that linearly interpolated the absorbed fraction tables of Snyder, et al (*16*) for the specific energy of each emission of the nuclides and computed the dose to a specified organ according to the MIRD schema (*22,23*). Each organ value is

TABLE 3. ABSORBED DOSE CONTRIBUTIONS PER MILLICURIE OF ^{81}Rb + ^{81m}Kr ADMINISTERED INTRAVENOUSLY (RADS)

	Dose to					
Dose from	Heart	Kidneys	Liver	Lungs	Testes	Total body
Heart*	0.060† 0.045	—	0.001	0.002	—	
Kidneys*	—	0.145† 0.036	0.002	—	—	
Liver*	0.004	0.005	0.071† 0.037	0.003	—	
Lungs*	0.003	0.001	0.001	0.050† 0.009	—	
Testes*	—	—	—	—	0.030† 0.005	
Total body						0.040† 0.042
Other	0.046	0.031	0.025	0.032	0.050	
Total	0.16	0.22	0.14	0.10	0.09	0.08

* Doses in standard man (MIRD Pamphlet No. 5) extrapolated from rat data.
† Dose from nonpenetrating radiations.
Dashes denote contributions of <0.001.

TABLE 4. ABSORBED DOSE CONTRIBUTIONS PER MILLICURIE OF ^{129}Cs ADMINISTERED INTRAVENOUSLY (RADS)

	Dose to					
Dose from	Heart	Kidneys	Liver	Lungs	Testes	Total body
Heart*	0.016† 0.065	—	0.002	0.004	—	
Kidneys*	0.001	0.040† 0.067	0.003	0.001	—	
Liver*	0.008	0.012	0.028† 0.095	0.008	—	
Lungs*	0.006	0.001	0.002	0.016† 0.019	—	
Testes*	—	—	—	—	0.017† 0.018	
Total body						0.022† 0.145
Other	0.153	0.109	0.085	0.113	0.173	
Total	0.25	0.23	0.22	0.16	0.21	0.17

* Doses in standard man (MIRD Pamphlet No. 5) extrapolated from rat data.
† Dose from nonpenetrating radiations.
Dashes denote contributions of <0.001.

a sum of dose contributions from (A) activity in the organ itself, (B) activity in the other four organs, and (C) activity assumed to be uniformly distributed in the remainder of the body. These contributions are detailed in Tables 3–6. For the special case of the heart, the self-dose due to penetrating emissions for each nuclide was calculated using a MIRD table entitled "Absorbed Fractions for Uniform Distribution of Activity in Small Spheres and Thick Ellipsoids" (*24*).

DISCUSSION

The results indicate organ dose estimates for ^{129}Cs that are from 5% to 70% lower than those previously stated in the literature (*8–10*). Assuming the validity of the basic premise relating human and rat nuclide distribution, our organ dose estimates for ^{129}Cs are believed to represent an improvement over previous estimates, due to more complete biologic data and the ability to refine the calculations through the use of the computer. Comparing our ^{201}Tl dose

TABLE 5. ABSORBED DOSE CONTRIBUTIONS PER MILLICURIE OF ^{201}Tl ADMINISTERED INTRAVENOUSLY (RADS)

	Dose to					
Dose from	Heart	Kidneys	Liver	Lungs	Testes	Total body
Heart*	0.020† 0.013	—	—	0.001	—	
Kidneys*	—	0.224† 0.064	0.002	—	—	
Liver*	0.002	0.003	0.049† 0.027	0.002	—	
Lungs*	0.001	—	—	0.021† 0.005	—	
Testes*	—	—	—	—	0.120† 0.025	
Total body						0.120† 0.124
Other	0.129	0.098	0.072	0.094	0.151	
Total	0.17	0.39	0.15	0.12	0.30	0.24

* Doses in standard man (MIRD Pamphlet No. 5) extrapolated from rat data.
† Dose from nonpenetrating radiations.
Dashes denote contributions of <0.001.

TABLE 6. ABSORBED DOSE CONTRIBUTIONS PER MILLICURIE OF ^{43}K ADMINISTERED INTRAVENOUSLY (RADS)

	Dose to					
Dose from	Heart	Kidneys	Liver	Lungs	Testes	Total body
Heart*	0.102† 0.071	0.001	0.002	0.003	—	
Kidneys*	0.001	0.222† 0.045	0.002	0.001	—	
Liver*	0.011	0.016	0.230† 0.102	0.010	—	
Lungs*	0.008	0.002	0.004	0.152† 0.022	—	
Testes*	—	—	—	—	0.183† 0.023	
Total body						0.305† 0.293
Other	0.330	0.236	0.189	0.238	0.375	
Total	0.52	0.52	0.53	0.43	0.58	0.60

* Doses in standard man (MIRD Pamphlet No. 5) extrapolated from rat data.
† Dose from nonpenetrating radiations.
Dashes denote contributions of <0.001.

estimates with those calculated by Bradley-Moore, et al (*6*) our values are about 20% lower for the kidneys, 40% lower for the heart, and 25% higher for the testes.

A comparison of the relative dose values for all organs in Table 2 indicates a consistent increase in estimated dose from ^{81}Rb to ^{129}Cs to ^{43}K. The thallium values for the kidneys and testes lie between those for ^{129}Cs and ^{43}K while estimates for the other organs fall between ^{81}Rb and ^{129}Cs. It has been shown that potassium, rubidium, and cesium, all being from the same group in the "Periodic Table of the Elements," behave similarly in animals, and that the relative speed of their migration possibly depends on the relative size of their crystal radii (*20,25*). A comparison of the data curves for cesium and potassium, and the resulting dose estimates in the five organs, supports this hypothesis. Thus, pre-

suming that the rubidium retention curves fall between the cesium and potassium curves, the use of cesium biologic data to compute cumulated activities for rubidium should yield upper-limit values for this nuclide. The thallium curves suggest that a similar relationship might hold between it and the other three elements except in the kidneys and testes, where thallium seems to be handled more slowly than potassium or cesium (*20*).

The largest errors in dose can be expected to occur for the testes, where the maximum uptake for both potassium and thallium was observed at 12 hr. Since no biologic data were available for these elements after 12 hr, the biologic decay constant for cesium was used. Maximum thallium uptake in the kidneys occurred 4 hr after administration, leaving only two subsequent data points and thus introducing possible errors in the elimination constant for those organs.

While the use of cesium data for the rubidium, potassium, and thallium whole-body dose calculations may have resulted in some overestimation of these values, each can probably be considered as an upper limit. These whole-body values for ^{129}Cs, ^{81}Rb, ^{43}K, and ^{201}Tl compare with the previously published values of 0.17 (*10*), 0.10 (*11*), 0.70 (*2*), and 0.07 (*6*) rads/mCi, respectively.

The absorbed dose per imaging examination depends on the quantity of each nuclide needed to obtain an image in a reasonable length of time. Therefore, the administered amount of each nuclide depends in part on the energies and relative abundances of the emissions chosen for detection. When these factors are considered, the estimates of absorbed dose per study will probably result in a different ordering of the nuclides, because a different amount of each radionuclide is needed for imaging (*7*).

The assumption that the individual organ concentrations per initial mean whole-body concentration are the same from species to species is subject to question, and this must be kept in mind. The same holds for many hypotheses that attempt to extrapolate quantitative animal data to humans. The discrepancies between the thallium dose estimates of Bradley-Moore, et al (*6*) and our values are probably due to differences in goat and rat metabolism and accentuate the need for better biologic data for humans. As human data are collected, more reliable dose estimates will be possible.

Radionuclidic purity was assumed in making these dose estimates. Depending on the method of production, small amounts of radiocontaminants may be present in actual preparations, and their effects on absorbed dose should be considered before assuming that these estimates apply.

SUMMARY

Absorbed dose estimates for the heart, kidneys, liver, lungs, testes, and whole body were calculated for ^{43}K, ^{81}Rb, ^{129}Cs, and ^{201}Tl. The organ dose values for ^{129}Cs are substantially lower than previous estimates; ^{201}Tl estimates differ somewhat from other published estimates probably because the data used were collected from different animal species. Finally, dose estimates for ^{43}K and ^{81}Rb represent a first attempt at such calculations for these nuclides.

REFERENCES

1. MARTIN ND, ZARET BL, STRAUSS HW, et al: Myocardial imaging using ^{43}K and the gamma camera. *Radiology* 112: 446–448, 1974

2. HURLEY PJ, COOPER M, REBA RC, et al: ^{43}KCl: A new radiopharmaceutical for imaging the heart. *J Nucl Med* 12: 516–519, 1971

3. MARTIN ND, ZARET BL, MCGOWAN RL, et al: Rubidium-81: A new myocardial scanning agent. Noninvasive regional myocardial perfusion scans at rest and exercise and comparison with potassium-43. *Radiology* 111: 651–656, 1974

4. ROMHILT DW, ADOLPH RJ, SODD VJ, et al: Cesium-129 myocardial scintigraphy to detect myocardial infarction. *Circulation* 48: 1242–1251, 1973

5. LEBOWITZ E, GREENE MW, FAIRCHILD R, et al: Thallium-201 for medical use. I. *J Nucl Med* 16: 151–155, 1975

6. BRADLEY-MOORE PR, LEBOWITZ E, GREENE MW, et al: Thallium-201 for medical use. II: Biologic behavior. *J Nucl Med* 16: 156–160, 1975

7. NISHIYAMA H, SODD VJ, ADOLPH RJ, et al: Incomparison of myocardial imaging agents. Unpublished

8. ANGER RT, SODD VJ: Dosimetry of ^{129}Cs and ^{131}Cs. *Phys Med Biol* 16: 698–700, 1971

9. CHANDRA R: Dosimetry of ^{129}Cs and ^{131}Cs. *Phys Med Biol* 18: 467–469, 1973

10. FELLER PA, KEREIAKES JG: Dosimetry of ^{129}Cs—further comments. *Phys Med Biol* 19: 220–221, 1974

11. BUDINGER TF, YANO Y, MCRAE J: Rubidium-81 used as a myocardial agent. Lawrence and Berkeley Laboratory Publication 2157, 1973

12. CHANDRA R, BRAUNSTEIN P, STREULI F, et al: ^{134m}Cs, a new myocardial imaging agent. *J Nucl Med* 14: 243–245, 1973

13. DILLMAN LT, VON DER LAGE FC: *Radionuclide Decay Schemes and Nuclear Parameters for Use in Radiation-Dose Estimates.* MIRD Pamphlet No 10, New York, Society of Nuclear Medicine: to be published

14. FELLER PA, SCHOLZ KL: Nuclear parameters and S-factors for ^{201}Tl dosimetry estimates. Unpublished

15. RUNDO J: A survey of the metabolism of caesium in man. *Br J Radiol* 37: 108–114, 1964

16. SNYDER WS, FORD MR, WARNER GG, et al: Estimates of absorbed fractions for monoenergetic photon sources uniformly distributed in various organs of the heterogeneous phantom. MIRD Pamphlet No 5, *J Nucl Med* 10: Suppl No 3, 7–52, 1969

17. SNYDER WS: Personal communication, 1975

18. MOSKALEV YI: Distribution of cesium-137 in the animal organism. AEC-TR-7512: 4–19, 1972

19. SPECTOR WS (ed): *Handbook of Biological Data*, Philadelphia, WB Saunders, 1956, p 163

20. GEHRING PJ, HAMMOND PB: The interrelationship between thallium and potassium in animals. *J Pharmacol Exp Ther* 155: 187–201, 1967

21. FELLER PA: Computer assisted medical internal radiation dosimetry (CAMIRD). *South Med J* 67: 1394, 1974

22. LOEVINGER R, BERMAN M: A schema for absorbed dose calculations for biologically-distributed radionuclides. MIRD Pamphlet No 1, *J Nucl Med* 9: Suppl No 1, 7–14, 1968

23. CLOUTIER RJ, WATSON EE, ROHRER RH, et al: Calculating the radiation dose to an organ. *J Nucl Med* 14: 53–55, 1973

24. BROWNELL GL, ELLETT WH, REDDY AR: Absorbed fractions for photon dosimetry. MIRD Pamphlet No 3, *J Nucl Med* 9: Suppl No 1, 27–39, 1968

25. LOVE WD, BURCH GE: A comparison of potassium^{42}, rubidium^{86} and cesium^{134} as tracers of potassium in the study of cation metabolism of human erythrocytes in vitro. *J Lab Clin Med* 41: 351–362, 1953

THE SOCIETY OF NUCLEAR MEDICINE
23rd ANNUAL MEETING

June 8–11, 1976 **Dallas Convention Center** **Dallas, Texas**

FIRST CALL FOR ABSTRACTS FOR SCIENTIFIC PROGRAM

The Scientific Program Committee solicits the submission of abstracts from members and nonmembers of the Society of Nuclear Medicine for the 23rd Annual Meeting. Original contributions on a variety of topics related to nuclear medicine will be considered, including the following:

Bone/Joint
Cardiovascular
Computer/Data Analysis
Computerized Axial Tomography
Dosimetry
Endocrine/Metabolism
Gastroenterology
Hematology
Instrumentation
In Vitro Assays
Neurology
Oncology
Pediatrics
Pulmonary
Radiopharmaceuticals
Renal/Electrolytes

GUIDELINES FOR SUBMITTING ABSTRACTS

Abstracts accepted for the program will be published in the June issue of the Journal of Nuclear Medicine. Camera-ready copy must be provided by the authors. Therefore, only abstracts prepared on the official abstract form will be considered. These abstract forms must be requested from the Society of Nuclear Medicine, 475 Park Avenue South, New York, N.Y. 10016. Be sure to request enough forms since only original forms can be used for each abstract submitted. The original abstract and six copies with all supporting data attached to each must be submitted. Supporting data is required (three pages maximum—see abstract form).

Abstracts of completed and on-going ("works in progress") projects will be judged together based on scientific merit. The deadline for submitting all abstracts for the scientific program is:

February 1, 1976

Abstracts must be post-marked on or before this date to be considered.

Send the original abstract and six copies with supporting data attached to each *by air mail* to:

John A. Burdine, M.D.
P.O. Box 6598
William Rice Station
Houston, Texas 77005