Radiation Dosimetry of Two New Tellurium-123m-Labeled Adrenal-Imaging Agents: Concise Communication

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The absorbed radiation doses to humans from 23-(isopropyl[^{123m}Te]telluro)-24-nor-5α-cholan-3β-ol (Te-123m-23-ITC) and 24-(isopropyl[^{123m}Te]telluro)-chol-5-en-3β-ol (Te-123m-24-ITC) have been calculated, based on rat biological data, to assess the relative radiation risks to humans from these two new adrenal-imaging agents. The estimated radiation doses to several critical organs have been compared with dose estimates for a variety of other radiolabeled steroids that have been designed as adrenal-imaging agents. Dose estimates to selected organs from Te-123m-23-ITC are as follows (rad/mCi): adrenals 98; ovaries 8.0; liver 1.6. Similar estimated values for Te-123m-24-ITC are: adrenals 210; ovaries 13; liver 2.0. The radiation dose estimates for these two agents are comparable to the calculated radiation doses from 6β-[(methyl[^{75}Se]seleno)methyl]-19-nor-cholest-5(10)-en-3β-ol (Scintidren) and 19-[^{131}I]iodocholest-5-en-3β-ol (NP-59), two agents currently in clinical use for the diagnosis of adrenal disease.

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Tellurium-123m decays by isomeric transition, with the emission of a single gamma photon in 84% abundance with an optimal energy of 159 keV (Table 1). We have recently demonstrated the pronounced adrenal concentration of 23-(isopropyl[^{123m}Te]telluro)-24-nor-5α-cholan-3β-ol(Te-123m-23-ITC) in rats (*1–3*), and the rat and rabbit adrenals have been successfully imaged with this new agent (*1*). More recently, tissue-distribution studies with a series of structurally modified steroids have defined the various structural features required for improved adrenal uptake of steroids labeled in the side chain with Te-123m (*4*). These studies have shown that 24-(isopropyl[^{123m}Te]telluro)-chol-5-en-3β-ol(Te-123m-24-ITC) is also significantly concentrated by adrenal tissue, and rat adrenals have been imaged with this agent. The marked adrenal concentration of these two Te-123m-labeled steroids, coupled with the superior radiation properties of Te-123m, suggest that these two agents should be considered for preliminary studies in humans. The purpose of this report is to compute the mean absorbed radiation doses to various human organs from these two agents, using recently available nuclear data for Te-123m and biological distribution data from rats.

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RADIOPHARMACEUTICALS

Tellurium-123m was produced in the Oak Ridge High Flux Isotope Reactor by neutron irradiation (10^{15} n/cm^2·sec) of 94.71% enriched ^{122}Te, using the reaction ^{122}Te (n,γ)^{123m}Te. The calculated specific activity of the Te-123m product produced under these conditions is ~40 mCi/mg, but products with maximum specific activities of 2 mCi/mg (254 mCi/millimol) are routinely obtained, indicating significant neutron capture (burn-up) by the Te-123m product. Our calculations, based on data obtained from multiple irradiations, indicate a burn-up cross-section (probability for neutron capture) of approximately 7000 barns for Te-123m. Tellurium-123m-23-ITC and Te-123m-24-ITC (Fig. 1) were prepared and purified by methods previously described (*1,4*).

TABLE 1. NUCLEAR DECAY DATA FOR Te-123m (*5*)

Radiation type	Mean energy per particle (keV)	Mean number per disintegration	Equilibrium dose constant, Δ; (g-rad/μCi-h)
Auger electron-L	3.19	0.885	0.0060
Auger electron-K	22.70	0.070	0.0034
ce-K-1*	56.65	0.427	0.0515
ce-L-1	83.52	0.441	0.0784
ce-M-1	87.45	0.104	0.0194
ce-NOP-1	88.29	0.028	0.0052
ce-K-2	127.19	0.137	0.0372
ce-L-2	154.06	0.018	0.0059
ce-M-2	157.99	0.355	0.0012
x-ray L	3.77	0.093	0.0007
x-ray K_{α_2}	27.20	0.141	0.0081
x-ray K_{α_1}	27.47	0.262	0.0153
x-ray K_{β}	31.00	0.091	0.0060
γ	159.00	0.835	0.285

* ce = conversion electrons.

NUCLEAR DATA

Tellurium-123m has a physical half-life of 119.7 days and decays by isomeric transition with emission of a single primary gamma photon with an energy of 159 keV in 84% abundance. Various internally converted electrons, Auger electrons, and characteristic x-rays of tellurium are also emitted, and the contributions to the overall radiation dose from these emissions have also been included in our calculations. The nuclear decay parameters for Te-123m were prepared by Martin (*5*) and are tabulated in Table 1.

DISTRIBUTION DATA

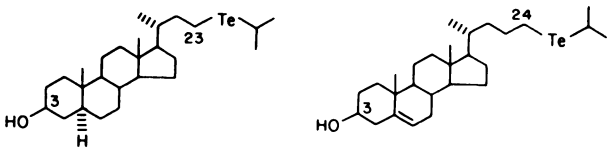
The tissue distribution data in female rats with the Te-123m-labeled adrenal agents were used from previously reported studies (*1,4*). These data were expressed for each tissue as

$$\frac{\%\ \text{kg dose}}{\text{g}} = \frac{\mu\text{Ci in organ/g} \times \text{kg body wt} \times 100}{\mu\text{Ci administered dose}},$$

in order to account for mass variations and to facilitate extrapolation of the data to man. Therefore, the fraction of injected dose in organ h of man (α_h) can be estimated as

$$\alpha_h = \frac{\%\ \text{kg dose/g} \times \text{wt of organ (g)}}{\text{kg body wt of man} \times 100}.$$

The values obtained in this manner (Table 2) presume that the biological distribution and elimination kinetics in man are similar to those observed experimentally in rats. The natural logarithms of the relative mean concentration values, determined at various times after administration of the Te-123m-labeled agents, were then fitted by a least-squares analysis that assumed a single-component first-order exponential. The correlation coefficients calculated in this manner were found to be greater than 0.95, suggesting that the first approximation was sufficient for determining the relative biological elimination constants and intercepts. The relative whole-body elimination constants were determined from urinary and fecal excretion studies in rats; these have been described previously (*1,2*).



24-Nor-23-(isopropyl telluro)-5α-cholane-3β-ol (23-ITC)

24-(isopropyl telluro)-chol-5-en-3β-ol (24-ITC)

FIG. 1. Structures of 23-(isopropyl telluro)-24-nor-5α-cholan-3β-ol (23-ITC) and 24-(isopropyl telluro)-chol-5-en-3β-ol (24-ITC).

TABLE 2. BIOLOGICAL ELIMINATION PARAMETERS CALCULATED FROM THE TISSUE DISTRIBUTION OF THE Te-123m ADRENAL IMAGING AGENTS AFTER SINGLE I.V. ADMINISTRATION IN RATS

	24-ITC		23-ITC	
Tissue	fraction injected dose per organ α_{h1}*	biologic decay constant (h^{-1}) λ_1	fraction injected dose per organ α_{h1}*	biologic decay constant (h^{-1}) λ_1
Liver	0.1049	0.00743	0.0685	0.00640
Spleen	0.0214	0.00840	0.0123	0.01160
Adrenals	0.0237	0.00154	0.0328	0.00507
Kidneys	0.0084	0.00152	0.0094	0.00205
Ovaries	0.0986	0.00411	0.0028	0.00692
Lungs	0.1269	0.01580	0.0657	0.01134
Total body	—	0.00321	—	0.00545

* α_{h1} = instantaneous uptake at t= 0.

TABLE 3. SELECTED S-FACTORS FOR Te-123m (rad/μCi-h)*

Target/source	Mean dose due to nonpenetrating radiation	Mean dose due to penetrating radiation	Total
Liver/liver	118×10^{-6}	35.1×10^{-6}	153×10^{-6}
Spleen/spleen	1180×10^{-6}	191×10^{-6}	1370×10^{-6}
Adrenals/adrenals	15100×10^{-6}	710×10^{-6}	15800×10^{-6}
Kidneys/kidneys	683×10^{-6}	106×10^{-6}	789×10^{-6}
Ovaries/ovaries	19300×10^{-6}	1210×10^{-6}	20400×10^{-6}
Lungs/lungs	212×10^{-6}	23.0×10^{-6}	235×10^{-6}
Total body/total body	3.03×10^{-6}	1.82×10^{-6}	4.85×10^{-6}

* Source and target organ have the same volume. The S factors were calculated according to the MIRD formulism (*6*).

ABSORBED-DOSE ESTIMATES

The calculations used in determining the mean absorbed dose were based on the formulism recommended by the MIRD Committee of the Society of Nuclear Medicine (*6*). The basic relationship is

$$\bar{D}(r_k \leftarrow r_h) = \tilde{A}_h \sum_i \Delta_i \Phi_i (r_k \leftarrow r_h),$$

where $\bar{D}$ is the mean absorbed dose in rad to a given target organ, r_k, from a source organ r_h; $\tilde{A}_h$ is the cumulated activity in μCi-h for source organ r_h; Δ_i is the mean energy emitted by i type radiation per unit cumulated activity in g·rad/μCi-h; and Φ_i is the specific absorbed fraction with units of g^{-1}. Because $\Sigma \Delta\Phi$ is defined for a given radionuclide and source-target combination, Snyder et al. (*7*) developed the S value,

$$S(r_k \leftarrow r_h) = \sum_i \Delta_i \Phi_i (r_k \leftarrow r_h),$$

where S has units of rad/μCi-h. The S factors (Table 3) for Te-123m were calculated using current nuclear data (*5*) and the specific absorbed fractions from MIRD Pamphlet No. 5, Revised (*8*).

The cumulated activity, $\tilde{A}_h$, in the source organs was determined from zero time to infinity; hence the expression

$$\tilde{A}_h = \sum_j \frac{\alpha_{hj} \cdot A_0}{\lambda_j + \lambda} (\mu\text{Ci-h}),$$

where α_{hj} (fraction injected dose/organ) is the instantaneous uptake of Te-123m at zero time for organ h and the jth exponential component; A_0 is the injected activity (μCi); λ_j is the biological elimination constant (h^{-1}) for the jth exponential component; and λ is the physical decay constant (h^{-1}).

The mean dose to a given target organ from Te-123m was then calculated by

$$\bar{D}(r_k \leftarrow r_h) = \tilde{A}_h \cdot S(r_k \leftarrow r_h) \text{ rad}.$$

Decisions regarding the effective biological uptake were not involved in the calculation of $\tilde{A}_h$, since this factor was found to be significantly less than the effective half-life of Te-123m. The resulting error in the absorbed-dose calculation would be no greater than 5%.

RESULTS AND DISCUSSION

For the two Te-123m-labeled agents, Table 4 lists the mean absorbed radiation dose estimates, based on biological data from the female rat, for six human target organs. The estimated dose to the adrenals was calculated to be greater for Te-123m-24-ITC than for Te-123m-23-ITC; this was attributed to the slower biological elimination of the former compound from the adrenal glands. These estimates mainly reflect the predominant influence of nonpenetrating radiation resulting from each nuclear transition of Te-123m to the ground state. Absorbed radiation dose estimates for Te-123m-23-ITC, as computed from biological data from male rats, resulted in a mean dose to the adrenals of only 39 rad/mCi, which is less than half of the absorbed dose calculated for females. The lower mean radiation dose can be attributed to a lower adrenal uptake ($\alpha = 0.0139$) and a relatively short biological half-life (5.3 days) of Te-123m in male rats.

The radiation dose estimates for these two Te-

TABLE 4. MEAN ABSORBED RADIATION DOSE VALUES (rad/mCi) FOR Te-123m-LABELED 23-ITC AND 24-ITC

Tissue	Dose (rad/mCi injected i.v.) 23-ITC	24-ITC
Liver	1.6	2.0
Spleen	1.6	3.4
Adrenals	98.0	210.0
Kidneys	3.2	3.8
Ovaries	8.0	13.0
Lungs	1.3	1.9
Total body	0.8	1.4

TABLE 5. COMPARISON OF ESTIMATED MEAN ABSORBED RADIATION DOSE VALUES TO SELECTED ORGANS FOR THE VARIOUS RADIOLABELED ADRENAL IMAGING AGENTS, CALCULATED FROM FEMALE RAT TISSUE-DISTRIBUTION DATA

Compound	Source of rat tissue-distribution data	Radiation dose*				
		Adrenals	Liver	Kidneys	Ovaries	Spleen
6β-[^{131}I]-Iodomethyl-19-nor-cholest-5(10)-en-3β-ol (NP-59)	Ref. *9*	150(19)	0.12(0.015)	0.55(0.070)	7.3(0.93)	1.7(0.22)
19-(Methyl[^{75}Se]seleno) cholest-5-en-3β-ol	Ref. *10*	61(2.2)	1.0(0.036)	1.1(0.039)	10(0.36)	0.62(0.022)
6β-[(Methyl[^{75}Se]seleno) methyl]-19-norcholest-5(10)-en-3β-ol (Scintidren)	Ref. *14*	93(3.3)	2.1(0.075)	2.0(0.072)	14(0.50)	—
Te-123m-23-ITC	* See footnote	98(3.6)	1.6(0.059)	3.2(0.12)	8.0(0.29)	1.4(0.051)
Te-123m-24-ITC	* See footnote	210(7.7)	2.00(0.074)	3.8(0.14)	13(0.48)	34(0.13)
I-131-23-ITC	†	120(15)	2.1(0.27)	2.5(0.32)	10(1.3)	2.1(0.27)
Se-75-23-ITC	†	24(0.86)	0.96(0.034)	1.4(0.050)	2.3(0.082)	0.60(0.022)

* rad/mCi; values in parentheses are rad/10^6 detectable photons.

† Radiation dose estimates for these hypothetical agents were calculated using the biological data reported for Te-123m-23-ITC.

123m-labeled steroids are comparable to those for several other steroids labeled with I-131 and Se-75 that have been designed for adrenal imaging (Table 5). The estimates were calculated by the same methods for 6β-[^{131}I] iodomethyl-19-norcholest-5(10)-en-3β-ol (NP-59) and 19-(methyl[^{75}Se]seleno)-cholest-5-en-3β-ol, using rat tissue-distribution data reported in the literature (*9,10*). Our calculated dose of 150 rad/mCi for NP-59 (Table 5) agrees with the reported estimate of 150 rad/mCi (*9*). We have not included in Table 5 a dose estimate for I-131-19-iodocholesterol (*11*) since recent reports have indicated that earlier tissue-distribution studies reported for this agent were evidently performed with preparations that contained significant amounts of NP-59 (*12,13*). The dose estimates for 6β-[(methyl[^{75}Se] selenomethyl]-19-nor-cholest-5(10)-en-3β-ol (Scintidren) tabulated in Table 5 were taken from a recent report*, since tissue distribution data were not available to use for calculation of the dose values. The actual dose values in humans from Te-123m-23-ITC and Te-123m-24-ITC may in fact be expected to be considerably lower than the calculated values shown in Table 4 if these two agents behave like NP-59. The results of recent studies with NP-59 indicate that the extrapolation of rat tissue-distribution data gave a very conservative estimate of human adrenal radiation dose (*9*). The calculation of the adrenal radiation dose (using adrenal uptake from patients without adrenal disease) gave values (12–39 rad/mCi) that were considerably less than the dose estimated from rat data (150 rad/mCi) (*9*).

We have also estimated the radiation dose values from I-131-23-ITC and Se-75-23-ITC, assuming the tissue-distribution and excretory properties for these two hypothetical agents to be like those reported for Te-123m-23-ITC. These values have also been included in Table 5, and indicate that the absorbed radiation dose for Se-75-23-ITC would actually be lower than the dose calculated for Te-123m-23-ITC. This difference is a result of the large dose contribution from the conversion electrons emitted from Te-123m (Table 1). The potentially important advantage of using the Te-123m-labeled agents, however, is the superior collimation and detection properties of the abundant 159-keV gamma emitted by Te-123m compared with the multiple gamma emissions from Se-75. In addition, the Te-123m steroids appear to have considerably greater in vivo stability than the radioiodinated agents.

In an attempt to provide a more useful comparison of dose values for the adrenal agents radiolabeled with I-131, Se-75, and Te-123m, we have also included in Table 5 the dose values per million detectable photons. These were calculated using the efficiency factors of a ½-in. sodium iodide crystal detector for the various radionuclides. The abundances of the gamma emissions were also incorporated in our calculation, but other factors, such as tissue attenuation, were not considered. Expressing the radiation dose values in this manner allows a more practical comparison of agents labeled with the different radionuclides. Emitters that are not efficiently detected will require a larger injected dose for adequate adrenal visualization, resulting in a higher radiation dose than would be expected from the traditional method of expressing the dose as rad/mCi. As an example, I-131-NP-59 and I-131-23-ITC show a much higher ra-

diation dose, expressed as rad/10^6 photons, when compared with the other agents.

If human adrenal uptake of Te-123m-23-ITC is similar to that observed in rats, approximately 4% of the injected activity would be expected to concentrate in human adrenals 1 day after i.v. administration. Injection of 200 μCi of this agent would result in the concentration of adequate radioactivity (8 μCi) for scintigraphic visualization of human adrenals. The estimated radiation dose values to the adrenals and ovaries would be 20 rad and 1.6 rad, respectively. Similarly, injection of 200 μCi of Te-123m-24-ITC would deliver an estimated radiation dose of 42 rad to the adrenals and 2.6 rad to the ovaries of female patients. The higher estimated radiation dose from Te-123m-24-ITC is a result of the slower elimination of this agent from the adrenal glands.

FOOTNOTE

* Peacegood JA, Pickett RD, Riley ALM: The development of Se-75-labeled cholesterol analog for adrenal scintigraphy. Read at the British Institute of Radiology Meeting, "In Vivo and In Vitro Radioisotope Investigations of Diseases Involving the Endocrine Organs," London, Feb. 16, 1977.

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