MIRD Dose Estimate Report No. 16: Radiation Absorbed Dose from Technetium-99m-Diethylenetriaminepentaacetic Acid Aerosol

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The estimated absorbed doses from ^{99m}Tc-diethylenetriaminepentaacetic acid (DTPA) administered as an aerosol are given in Table 1. The data and assumptions used for the calculations follow.

RADIOPHARMACEUTICAL

Technetium-99m-DTPA is formed by the addition of ^{99m}Tc as pertechnetate to a lyophilized mixture of $CaNa_3DTPA$ and $SnCl_2$. A ^{99m}Tc-DTPA chelate is formed. This dose estimate report focuses only on ^{99m}Tc-DTPA formed by the above method and not for other formulations that may also contain DTPA. The biological distributions in this report assume a radiochemical purity of 100% and administration by inhalation of the aerosolized radiopharmaceutical.

NUCLEAR DATA

Technetium-99m decays to ^{99}Tc by isomeric transition with a half-life of 6.01 hr. Technetium-99 undergoes beta minus decay with a half-life of 2.11×10^5y. The very small contribution of ^{99}Tc to the radiation absorbed dose has been ignored in these estimates. The nuclear data for ^{99m}Tc and ^{99}Tc are given in Table 2.

BIOLOGICAL DATA

Technetium-99m-DTPA is administered as an aerosol by flowing oxygen or compressed air at about 8–10 liters/min through a nebulizer* containing 1–3 ml of the radiopharmaceutical. The patient inhales the aerosolized product over a period of 3 min. At this flow rate, approximately 125 μl of liquid is inhaled per minute. Most of the radiopharmaceutical is exhaled and trapped in a filter, and 3.1 μl/min are delivered to the alveoli.

Following this initial phase, the patient breathes room air. The ^{99m}Tc-DTPA that has been deposited in the alveoli crosses the alveolar-capillary membrane and enters the

TABLE 1
Estimated Absorbed Dose From the Inhalation of Aerosolized ^{99m}Tc-DTPA

	Absorbed Dose per Unit Administered Activity			
	2.4 hr voiding schedule		4.8 hr voiding schedule	
Organ	rad/mCi	mGy/MBq	rad/mCi	mGy/MBq
		Supine		
Trachea	0.30	0.081	0.30	0.081
Bladder wall*	0.093	0.025	0.18	0.050
Lungs	0.080	0.022	0.080	0.022
Kidneys	0.0095	0.0026	0.0096	0.0026
Ovaries	0.0058	0.0016	0.010	0.0027
Total body	0.0051	0.0014	0.0061	0.0016
Red marrow	0.0041	0.0011	0.0048	0.0013
Testes	0.0039	0.0011	0.0069	0.0019
Thyroid	0.0029	0.00078	0.0029	0.00078
		Erect		
Trachea	0.30	0.081	0.30	0.081
Bladder wall*	0.083	0.022	0.16	0.043
Lungs	0.12	0.032	0.12	0.032
Kidneys	0.0093	0.0025	0.0094	0.0025
Ovaries	0.0052	0.0014	0.0088	0.0024
Total body	0.0063	0.0017	0.0071	0.0019
Red marrow	0.0050	0.0014	0.0056	0.0015
Testes	0.0035	0.00094	0.0060	0.0016
Thyroid	0.0036	0.00098	0.0036	0.00098

* Bladder wall dose is calculated for an assumed constant bladder content of 200 ml.

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* UltraVent (Mallinckrodt Nuclear, St. Louis, MO) has a 0.25 μm mass median aerodynamic diameter with a geometric standard deviation of 2.05. Less than 3% of the aerosol particles exceed 1 μm in diameter. Other nebulizers may produce aerosol size distributions that could have different clearance times from the lungs.

TABLE 2
Nuclear Data (*10*)

Radionuclide	^{99m}Tc				^{99}Tc	
Physical half-life	6.01 h				2.11×10^5 y	
Decay constant	0.115 h^{-1}				3.75×10^{-10} h^{-1}	
Mode of decay	I.T. to ^{99}Tc				Beta minus to ^{99}Ru (stable)	
			Δ_i		Δ_i	
Principal radiation	E_i keV	n_i	rad g/μCi h	Gy kg/Bq s	rad g/μCi h	Gy kg/Bq s
Photon	18-21	0.068	0.0027	2.0E-16		
	140.5	0.89	0.267	2.0E-14		
Nonpenetrating			0.0343	2.58E-15	0.215	1.62E-14

E_i is mean energy per particle or photon.
n_i is mean number of particles or photons per nuclear transition.
Δ_i is mean energy emitted per nuclear transition.
Nonpenetrating radiation from ^{99m}Tc includes conversion and Auger electrons ranging in energy from 1.6 keV to 140 keV.
Nonpenetrating radiation from ^{99}Tc includes beta-minus emissions with a maximum energy of 294 keV and an average energy of 101.3 keV.
Only photons with a mean yield per nuclear transition greater than 0.01 are included.
Note: Complete decay of 1 unit of activity of ^{99m}Tc produces 3.2×10^{-9} units of activity of ^{99}Tc.

bloodstream where it is then filtered by the kidneys and subsequently excreted. The disappearance rate from the lungs has been evaluated by a number of investigators and has been found to be more rapid in various states associated with lung injury (*1,2*). The washout usually follows a monoexponential curve, although a biexponential curve has been noted at times (*2–5*). The biexponential curve is seen frequently in severely ill patients with adult respiratory disease and in coal miners (*4*). In such situations, the washout is more rapid than in normal individuals and therefore the absorbed radiation dose will be lower. This dose estimate is based on the monoexponential washout of the aerosol from normal lungs.

Data used in this estimate are taken from reports of studies performed on 13 subjects at the Brookhaven National Laboratory (*3*) and 25 subjects at the University of Rochester School of Medicine and Dentistry (*6*) with corroborative data from the Harbor-UCLA Medical Center (*7*). Only data from normal subjects are considered. Disappearance from abnormal lungs is more rapid so that the normal situation provides the maximum radiation absorbed dose. Washout from seated subjects is slower than that from supine subjects. Regional variations in lung washout have been ignored. In some patients, especially those with obstructive pulmonary disease, much of the activity may be deposited in major bronchi and eliminated by ciliary motion and either coughed up or swallowed.

Biologic parameters from which this dose estimate is derived are given in Table 3.

TABLE 3
Biologic Parameters for the Distribution of Inhaled ^{99m}Tc-DTPA

	τ_h(h) Supine	τ_h(h) Erect
Lung washin	0.026	0.026
Lung washout	1.58	2.31
Kidneys	0.0394	0.0353
Total body	0.542	0.486
Remainder of body	0.502	0.450
Bladder contents 2.4-hr void	0.606	0.540
Bladder contents 4.8-hr void	1.21	1.05

Residence time (τ_h) for kidneys, total body and remainder of body are derived by the convolution of the biologic parameters α_{h_j} and λ_{h_j} from MIRD Dose Estimate No. 12 (*9*) with those for lung washout.

DOSE ESTIMATE

Assumptions in this estimate are that 37 MBq is delivered to the lung alveoli over a period of 3 min in 9.3 μl of aerosol.† In order to accomplish this, the appropriate concentration of activity is placed in the nebulizer in 3 ml of saline and a total of 375 μl of solution is aerosolized, of which 365.7 μl is trapped in the filter. During the inhalation procedure, the patient breathes normally at 15 breaths per minute, resulting in a deposition of 9.3 μl (37 MBq) of aerosol in the air spaces.

The trachea was modeled as a right circular cylinder with an inside radius of 1.1 cm and a tissue (wall) thickness of 0.2 cm. The radionuclide was assumed to be mixed uniformly with air at a pressure of one atmosphere and filled the inner cylinder. Calculations of the radiation absorbed dose to the wall were accomplished using the computer code EGS4, a coupled photon-electron Monte

† Under usual clinical conditions the concentration of ^{99m}TcDTPA in the nebulizer is approximately 555 MBq/ml, which will result in the delivery of 5.16 MBq to the alveolar space in 3 min at a gas flow of 8 liters/min.

Carlo transport code (*8*). The calculations used the appropriate beta spectrum rather than the average beta energy (provided by G. Akabani, PhD, Battelle Pacific Northwest Laboratories). For 15 breaths per minute and 375 μl distributed in a tidal volume of 500 ml the activity concentration in each breath is 0.0663 MBq/ml.

Uptake in the lungs is considered as a step function with each breath delivering the same amount of activity. The concentration in the trachea and major bronchi is assumed to be constant during the washin and zero during the washout phase.

The alveolar activity leaves the lungs and enters the blood at a rate of 0.53%/min for subjects seated upright and 0.86%/min in supine subjects. Thereafter it is handled by the body as described in MIRD Dose Estimate Report No. 12 (*9*). The lung washout parameters convolved with the biologic parameters from MIRD Dose Estimate Report No. 12 provided the cumulated activity and residence times for the kidneys and total body. The residence times for bladder contents were calculated from the total-body time-activity curve obtained by adding the lung-activity curve to the blood input-activity curve.

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