Kinetics and Dosimetry of Thallium-201 in Human Testes

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Thallous chloride (^{201}Tl) is a well-known imaging agent. It has been shown to accumulate in the testes. In view of this, the testicular kinetics of ^{201}Tl is investigated in humans and the absorbed dose to the organ calculated. **Methods:** Thallous chloride ^{201}Tl was injected intravenously into four patients for myocardial perfusion studies. After clinical evaluation, the testicular uptake and clearance of ^{201}Tl were monitored for about 1 wk using a gamma camera. **Results:** Testicular uptake of ^{201}Tl was rapid with a mean biological uptake half-time of 0.67 hr and mean biological clearance half-time of 280 hr. The mean maximum testicular uptake of ^{201}Tl was about 0.4% of the injected activity. These data were utilized to calculate the average absorbed dose to the testes. The absorbed dose to the testes was calculated to be 3.5×10^{-4} Gy/MBq (1.3 rad/mCi) of injected activity. **Conclusion:** When the relative biological effectiveness of the Auger emitter ^{201}Tl is taken into account, the equivalent dose to the testes is 9.5×10^{-4} Sv/MBq (3.5 rem/mCi).

Key Words: thallium-201; human testes; dosimetry; myocardial perfusion

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Thallous chloride (^{201}Tl) has been widely used for a variety of nuclear medicine imaging procedures. Thallium-201 decays by electron capture, resulting in the creation of a vacancy in an inner atomic shell. The series of atomic transitions that follow results in the emission of numerous (~37) low-energy Auger electrons (*1*). The highly localized energy deposition by these electrons can cause biological damage similar to that imparted by alpha particles of high linear energy transfer (*2*). In fact, it has been shown that ^{201}Tl is about three times more effective than its beta-emitting counterpart, ^{204}Tl, in killing spermatogonial cells in mouse testes (*3*).

Human testes are highly radiosensitive (*4*). Accordingly, the ICRP assigned the testes as the highest tissue weighting factor ($w_T = 0.20$) (*5*). It has been shown in humans (*6–8*) and animals (*6,9*) that a substantial amount of ^{201}Tl is taken up by the testes following intravenous administration. Because of this, the high radiosensitivity and the large tissue weighting factor, it is essential to carefully determine the absorbed dose and equivalent dose delivered to the testes by this imaging agent. In this study, the testicular uptake of ^{201}Tl is measured in four patients and the average absorbed dose to the organ determined (Fig. 1).

METHODS

Four patients between the ages of 40–50 undergoing myocardial perfusion studies at rest (no exercise) were injected with about 59 MBq (1.6 mCi) of ^{201}Tl. Testicular phantoms were prepared for each patient by filling two balloons with 20 ml of water containing a precalibrated amount of ^{201}Tl (about 230 kBq, 6.2 μCi, each). Following clinical evaluation of myocardial perfusion, the testicular uptake and clearance of ^{201}Tl were monitored for a period of about 1 wk using a gamma camera fitted with a 12-in. NaI crystal, high-resolution parallel-hole collimator and a 70 keV ± 20% window using the following methods. The patient was completely covered (including the penis) with lead aprons (2 mm Pb equivalent) to attenuate the ^{201}Tl photons, and the testes were pulled from between the aprons so that only the testes were unshielded. Counts in the entire field of view of the gamma camera were recorded with a collimator-to-object distance of 4.8 cm and acquisition time of 5 min. The combined scatter and background counts (entire body including testes covered with lead aprons) were collected for each time point and the testicular counts corrected accordingly. The counts in the balloon standards were obtained at each time point with the two phantoms arranged in the same manner as the patient's testes. These standard counts were corrected by the background counts obtained in the absence of the phantoms. Representative data for a single patient are shown in Table 1. The percent of injected activity in the testis was calculated using the following equation:

$$\%IA = 100 \times \left(\frac{\text{Testicular counts} - \text{Scatter and background counts}}{\text{Phantom counts} - \text{Background counts}}\right) \times \left(\frac{\text{Phantom activity}}{\text{Injected activity}}\right). \quad \text{Eq. 1}$$

RESULTS

The percent of injected activity in the testes as a function of time postinjection is given in Table 2 and Figure 1 for all

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TABLE 1
Representative Data (Patient 3)*

Time (hr)	Testes counts†	Scatter and background counts‡	Phantom counts§	Background counts¶
1	12018	3970	23286	1993
27.5	11398	3988	18283	1920
52	12613	5858	17838	4750
76	8876	3633	12808	2105
98	6486	3394	10342	1950
189	3854	2427	5705	1780

*Patient was injected with 58.8 MBq (1.59 mCi); the two balloon standards contained a total of 0.448 MBq (12.1 μCi). All data are for a 5-min acquisition time.
†Only testes protrude through lead aprons.
‡Entire body covered by lead aprons.
§Two balloon phantoms.
¶Background in absence of phantoms and patient.

four patients. A least squares fit to the pooled patient data is performed using the biexponential function:

$$\%IA = a_o (e^{-0.693t/T_{bc}} - e^{-0.693t/T_{bu}}), \quad \text{Eq. 2}$$

where T_{bc} and T_{bu} are the biological clearance half-life and uptake half-time in the organ, respectively. The fitted values of a_o, T_{bc} and T_{bu} are 0.46%, 280 hr and 0.67 hr, respectively, for the pooled data. Given the physical half-life of 73.1 hr for ^{201}Tl, the corresponding effective clearance half-life T_{ec} is 58 hr and the effective uptake half-time T_{eu} is 0.66 hr (Fig. 1).

The total absorbed dose to the testes D_t can be calculated by summing the contribution from decays occurring within the organ itself with the contribution from decays occurring in the body B:

$$D_t = \tilde{A}_B S_{t \leftarrow B} + \tilde{A}_t S_{t \leftarrow t}. \quad \text{Eq. 3}$$

The quantities $\tilde{A}_B$ and $\tilde{A}_t$ are the cumulated activities in the body and testes, respectively. The S values $S_{t \leftarrow B}$ and $S_{t \leftarrow t}$ are the dose to the testes per unit cumulated activity in the body and testes with values of 1.73×10^{-16} Gy/Bq-s (2.3×10^{-6} rad/μCi-hr) and 2.25×10^{-13} Gy/Bq-s (3×10^{-3} rad/μCi-hr), respectively (*10*). Replacing T_{bc} and T_{bu} with T_{ec} and T_{eu} in Equation 2, one obtains $\tilde{A}_t = 1.37 \times 10^9$ Bq-s per MBq (381 μCi-hr per mCi) of injected activity. Hence, the testicular self-dose $D_{t \leftarrow t}$ is about 3.0×10^{-4} Gy/MBq (1.1 rad/mCi) injected. Atkins et al. (*6*) and Krahwinkel et al. (*8*) have reported whole-body effective clearance half-lives of 57 and 58.8 hr, respectively. Taking the average of these values, one obtains the cumulated activity in the whole body to be 3.0×10^{11} Bq-s per MBq (83,400 μCi-hr per mCi) of injected activity. Hence, the testicular dose from activity in the whole body is about 5.4×10^{-5} Gy/MBq (0.2 rad/mCi) injected. Therefore, the total testicular dose is about 3.5×10^{-4} Gy/MBq (1.3 rad/mCi).

DISCUSSION

The testicular dose of 3.5×10^{-4} Gy/MBq (1.3 rad/mCi) is substantially higher than the values of 1.6×10^{-4} Gy/MBq (0.59 rad/mCi) and 9.2×10^{-5} Gy/MBq (0.34 rad/mCi) reported by Atkins et al. (*6*) and Krahwinkel et al. (*8*), respectively. However, data from Gupta et al. (*7*) for five patients show an even higher testicular uptake than observed in the present work, thereby suggesting doses even higher than those reported here. The testicular absorbed dose of 5.6×10^{-4} Gy/MBq given in ICRP 53 (*11*) is consistent with the testicular kinetics reported by Gupta et al. (*7*). It should also be noted that Hosain and Hosain have calculated a dose of 3.8×10^{-4} Gy/MBq (1.4 rad/mCi) based on an extrapolation of animal data to humans (*9*). This is in close agreement with the present calculations based on human data.

TABLE 2
Percent Injected Activity in the Testes at Times Postadministration of ^{201}Tl

Patient 1		Patient 2		Patient 3		Patient 4	
t (hr)	%IA	t (hr)	%IA	t (hr)	%IA	t (hr)	%IA
4	0.19	3	0.675	1	0.29	0.75	0.25
24	0.41	23	0.57	27	0.34	1.00	0.26
47	0.48	46	0.59	52	0.39	24.00	0.38
71	0.47	168	0.39	76	0.37	49.00	0.30
94	0.35			98	0.28	144.00	0.24
				189	0.28		

Thallium-201 decays by electron capture and internal conversion and as a consequence emits numerous Auger electrons (*1,3*). When such radionuclides localize in the cell nucleus, the biological effects imparted by the Auger electrons can be much greater than expected (*2,3,12,13*). Using the mouse testes as an experimental model, it has been shown that the prolific Auger emitter ^{201}Tl is about three times more effective per unit dose than the beta emitter ^{204}Tl in causing spermatogonial cell killing (i.e., RBE ~3) (*3*). Inasmuch as this model is relevant to humans (*4*), this suggests that calculation of the equivalent dose to the testes H_t from ^{201}Tl should reflect the enhanced biological effectiveness of this radiopharmaceutical. Considering that the testicular self-dose $D_{t\leftarrow t}$ is about 3.0×10^{-4} Gy/MBq (1.1 rad/mCi), and the RBE for ^{201}Tl is about three (*3*), then $H_{t\leftarrow t} = 9.0 \times 10^{-4}$ Sv/MBq (3.3 rem/mCi). The total equivalent dose to the testes is then $H_{t\leftarrow t} + H_{t\leftarrow B} = 3.3 + 0.2 = 3.5$ rem/mCi (9.5×10^{-4} Sv/MBq). Since the highest tissue weighting factor is presently assigned to the testes ($w_T = 0.20$) (*5*), and up to 167 MBq (4.5 mCi) of ^{201}Tl is administered to patients for imaging, careful assessment of the testicular dose and biological effectiveness of the radiations is of critical importance in risk assessment considerations for this radiopharmaceutical (*14*).

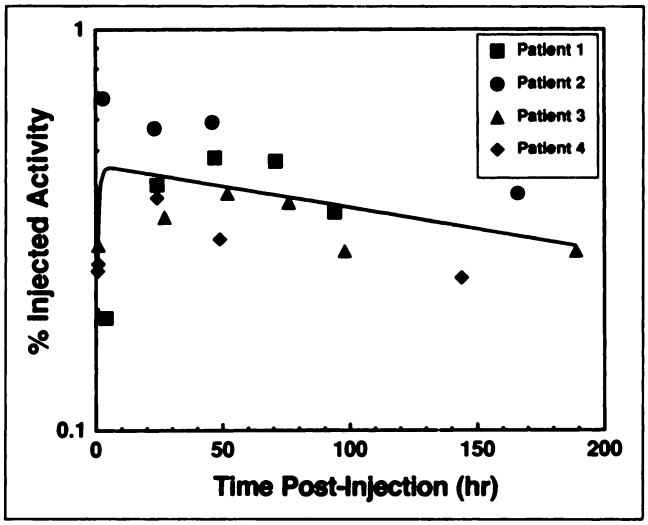

FIGURE 1. Testicular uptake and clearance of ^{201}Tl in humans following intravenous administration. The percent injected activity in the organ is plotted as a function of time postadministration for four patients. The solid line is a least squares fit to the pooled data.

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