Technetium-99m DTPA Uptake and Transit in Bone: Effect on Blood Clearance in Rabbits

W.F.D. Sampson

Department of Nuclear Medicine, Royal Naval Hospital, Haslar, Gosport, Hampshire, United Kingdom

The purpose of this study is to explain the initial "plateau" distribution of [^{99m}Tc]DTPA in the forearm found when using serial external counting for kidney clearance measurements. A study by a MIRD task group, McAfee et al. 1979 (*1*), measured the biologic distribution of [^{99m}Tc]DTPA(Sn) in most body tissues but omitted bone, which we believe is a major contributor to this initial "plateau". Using MIRD criteria, measurements were carried out on rabbit humeri and these were compared with results obtained from human subjects. It would appear that initial accumulation of the compound by interstitial bone is the reason for the "plateau" and explains why blood sampling for GFR studies should not be undertaken over the first 2 hr. In addition, the results of this study provide valuable information relevant to bone perfusion studies and the biologic distribution and concentration of i.v. administered drugs during the first 2 hr postinjection.

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The technique of estimating the glomerular filtration rate by serial blood sampling, following a single i.v. injection of technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA)*, is still being used in many departments. Various methods have been published over the past decade by others (*2–5*). All of these methods use plasma-activity curves that can be represented by a two-compartment model (*6*). In our department, an external arm counting technique (*7*) is used that we have compared with serial plasma-activity measurements using a three-compartmental model (*8*) that we believe fits the initial data more accurately. Notwithstanding the method used, no attempt, to our knowledge, has been made to date to explain why plasma equilibrium is not achieved until a variable time following the injection of [^{99m}Tc]DTPA and why a "plateau" effect is observed over this initial period on external counting.

Following the excellent work by McAfee et al. in measuring the distribution of [^{99m}Tc]DTPA in most tissues in dogs, we found the exclusion of bone disappointing because when using our external arm counting to measure renal clearance of [^{99m}Tc]DTPA in human subjects we believed that bone handling of the chelate would provide an explanation of the observed initial plateau lasting 30–90 min.

In order to investigate this phenomenon and rectify the omission of bone in the MIRD study we adopted the technique of McAfee et al. using rabbits instead of dogs and measured the uptake of activity in bone as well as in blood and muscle.

MATERIALS AND METHOD

One nonanesthetized adult New Zealand white rabbit weighing 3.720 kg was given an i.v. injection of 0.5 mCi [^{99m}Tc]DTPA(Sn)* through an ear vein. External monitoring was carried out using a collimated 1-in. NaI crystal placed on the (R) shoulder. Duplicate 10-sec counts were collected every 10 min over a period of 180 min. This was repeated three times over the subsequent 12 days and the counts averaged (Fig. 1). The results were compared with measurements obtained from human subjects using shielded dual 3-in. sodium iodide crystals and counting the lower forearm (*7*) (Fig. 2). Twelve paired healthy adult New Zealand white rabbits, with average weights ranging from 3.221 kg to 3.809 kg and an individual mean weight of 3.636 kg, were then given a single bolus i.v. injection of [^{99m}Tc]DTPA(Sn) adjusted to give 0.5 mCi kg^{-1}. Two animals were killed at 3-, 15-, 30-, 60-, 120-, and 180-min intervals postinjection using an i.v. injection of saturated potassium chloride. Aliquots of blood (heart), muscle (biceps), and bone (humerus) dissolved in nitric acid were subsequently measured for [^{99m}Tc]DTPA content, and the mean concentration of activity in the different organs from

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For reprints contact: W.F.D. Sampson, MPhil, Dept. of Nuclear Medicine, Royal Naval Hospital, Haslar, Gosport, Hampshire, UK P012 2AA.

each group of two animals killed at the times indicated was calculated. Total blood volume for each animal was estimated at 7.0%, skeletal muscle at 32%, and bone at 18% of body weight, respectively. Protein binding of the DTPA compound was measured using Sephadex G50-gel chromatography and was found to be between 2–3% of activity in plasma at 60 min postinjection. All measurements of [^{99m}Tc]DTPA(Sn) distribution were corrected for physical decay. Kidneys from all the animals were examined macroscopically by the pathology department and none showed gross abnormalities.

In a third experiment, a 3.588-kg, white New Zealand rabbit was anesthetized using 1 ml i.m. hymnorm and diazepam 2.5 mg, followed by 50% nitrous oxide oxygen mixture at a flow rate of 2 l/min through a Magill circuit/Hall mask. Surgery was carried out to expose the upper (R) humerus and a skin flap was mobilized. Two CdTe† detectors were placed against the bone and the skin flap and were shielded from background pickup by a wafer of 2 mm lead placed between the muscle and the bone detector and between the skin detector and the underlying tissues.

RESULTS

The results of the measurement of the percentage administered dose of [^{99m}Tc]DTPA per gram of tissue are shown in Table 1. It can be observed that changes in the bone and muscle tissue concentration show an initial decrease followed by an increased uptake up to 60 min in the animals. It can be postulated from this that the cause of the plateau, seen on external monitoring in man, is the accumulation of activity in bone, and to a lesser extent in muscle, over the initial 60 min or so following injection.

The results of the cadmium telluride measurements of blood (skin flap) and bone activity are shown in Fig. 3. From these a similar increase in activity over the initial 60 min is shown in the bone time-activity curve while the blood shows a steady decline.

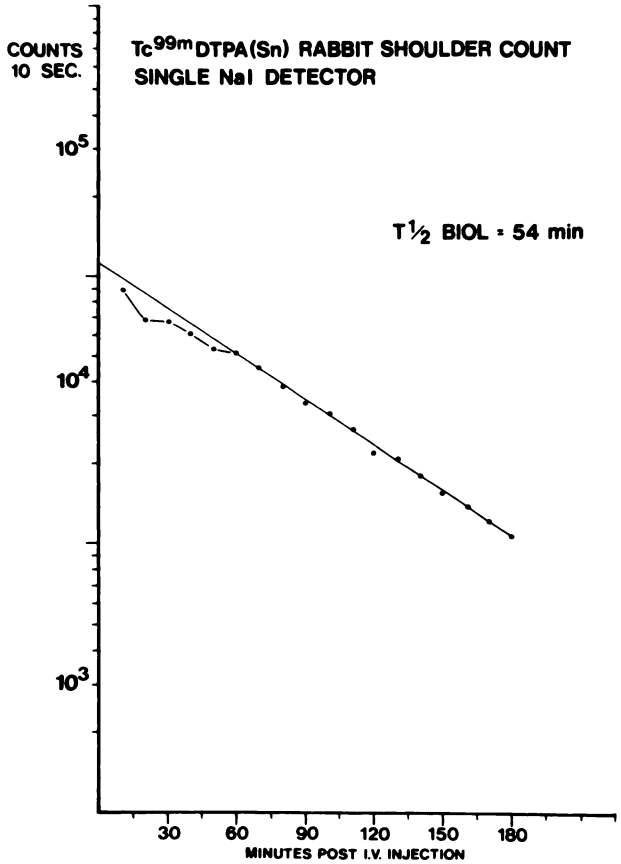

FIGURE 1
External counting time-activity curve for rabbit shoulder.

DISCUSSION

External shoulder counting performed on an individual rabbit (Fig. 1) produces a time-activity curve which does not have the initial pronounced "plateau" seen in the human, shielded, forearm study (Fig. 2). This is probably the result of the ratio of blood to bone/muscle being greater in the rabbit due to thoracic blood back-

TABLE 1
Rabbit-[^{99m}Tc]DTPA(Sn) % Administered Activity per Gram of Tissue*

	3 min	15 min	30 min	60 min	120 min	180 min
Blood						
Animal 1	0.1013	0.0594	0.0412	0.0271	0.0095	0.0056
Animal 2	0.1007	0.0562	0.0406	0.0256	0.0098	0.0065
Muscle						
Animal 1	0.0192	0.0110	0.0074	0.0073	0.0014	0.0009
Animal 2	0.0191	0.0103	0.0072	0.0069	0.0014	0.0010
Bone						
Animal 1	0.0210	0.0180	0.0154	0.0199	0.0042	0.0024
Animal 2	0.0207	0.0170	0.0152	0.0187	0.0044	0.0028

*Total concentration in the organs was estimated for blood at 7%, skeletal muscle at 32%, and bone at 18% of body weight.

ground contribution. Also from Figures 1 and 2 it can be seen that the exponential decay following the "plateau" in the external counting technique does not have the significant change in the curve at 120 min seen in the individual muscle and bone curves in Table 1. The discrepancy in Figures 1 and 2 between the mono exponential nature of the post "plateau" curve, obtained by external counting and the biexponential curves found in bone and muscle is probably due to delayed transit of [^{99m}Tc]DTPA through these tissues followed by wash out by returning plasma which has been proportionately cleared of [^{99m}Tc]DTPA by glomerular filteration. There may also be factors relating to compartments not studied, e.g., tendons and ligaments, that may have an overall effect on equilibrium clearance in the external rabbit shoulder and human forearm measurements (Figs. 1 and 2), but do not apply to specific bone and muscle data collection.

The difference in uptake of chelate between bone and muscle is most probably the result of different dynamics of accumulation of [^{99m}Tc]DTPA(Sn) in the interstitial bone compartment compared to those in the soft-tissue lymphatic system of muscle. In addition,

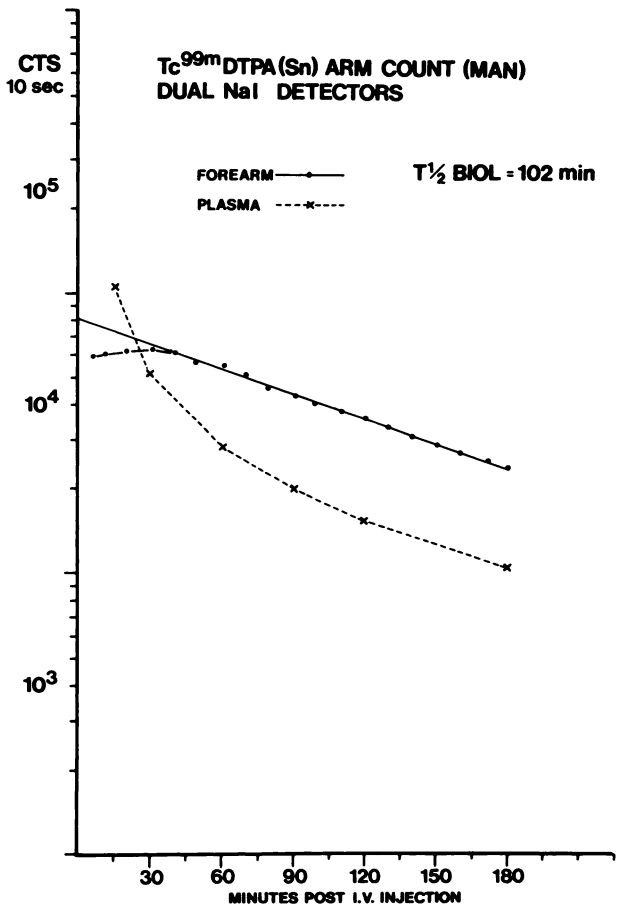

FIGURE 2
External counting time-activity curve for human forearm with concomitant plasma time-activity curve.

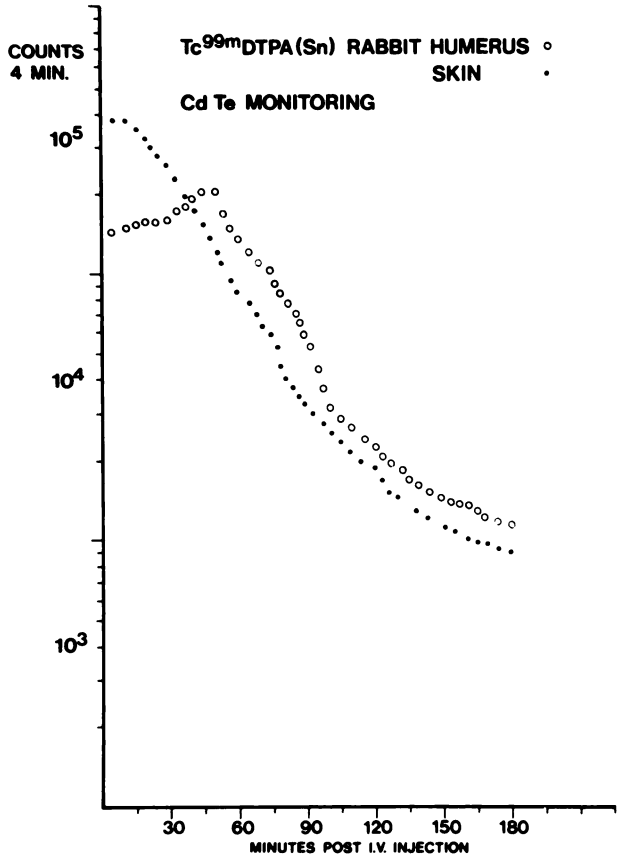

FIGURE 3
Serial external counting of rabbit humerus and skin flap using a cadmium telluride detector.

when we compared the percentage of administered activity in rabbit blood and muscle (Table 1) with the figures of McAfee et al. for dogs they appear to be similar, although the $t_{1/2}$ biol for the chelate is shorter in the smaller mammals.

In conclusion, the differences observed in this paper in bone uptake and clearance of [^{99m}Tc]DTPA(Sn) when compared with other tissues, are factors that must be considered in any dynamic study performed over the initial 2 hr following injection of this compound. Allowances must be made for the ratios of blood, muscle, and bone in any external counting technique employed, for example, the presence of the vertebrae may contribute to error in renal deconvolution techniques (*9*) when posterior imaging is performed and the aorta is used for background subtraction. Again, when external counting is employed to measure synovial clearance of [^{99m}Tc]DTPA(Sn) in joints (*10*) the large ratio of bone to muscle will effect the rate of clearance of chelate.

NOTES

* Diagnostic Isotopes Incorp., NJ.

† Semi-conductor cadmium telluride detectors and Memolog data storage unit. Pharmacia Electronics, Denmark.

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