Dose from Syringe Procedures During Technetium-99m Radiopharmaceutical Preparation

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We examined the dose from ^{99m}Tc contained in syringes and shielded vials to assess in detail the dose burdens in a central pharmacy.

Methods: Absorbed-dose rates at the end of the plunger of a shielded syringe, when ^{99m}Tc is contained either in the syringe or in a shielded vial from which the activity would be drawn, were measured with CaF_2 dosimeters. The dose rates also were calculated with a Monte Carlo model.

Results: When activity was contained in either 3-ml or 10-ml disposable syringes shielded by lead glass, the absorbed-dose rates were 1.35–1.62 mGy hr^{-1} GBq^{-1} (5–6 mrad hr^{-1} mCi^{-1}). When the activity was contained in either a shielded elution or product kit vial, the absorbed-dose rates at the end of the syringe plunger were about 0.40 mGy hr^{-1} GBq^{-1} (1.4–1.5 mrad hr^{-1} mCi^{-1}). These results were reproduced with reasonable accuracy by Monte Carlo simulations.

Conclusion: The dose burden per unit of activity handled from ^{99m}Tc in procedures using syringes is likely to be two to five times larger than the dose burden from calibrating generator eluate. The Monte Carlo simulations suggest that lead K x-rays may be responsible for a significant fraction of the total dose to the fingers and hand of the pharmacist when lead-glass syringe shields are used.

Key Words: extremity exposure; lead-vial shields; lead-glass syringe shields; technetium-99m; procedures using syringes; radiopharmacy

Central radiopharmacies generally dispense radiopharmaceuticals to hospitals and clinics as single-patient doses (unit doses) in disposable syringes for direct patient administration. Although a wide variety of radioisotopes is in use, most of the total radioactivity currently handled is ^{99m}Tc and large commercial radiopharmacies may process 370–740 GBq (10–20 Ci) or more of this isotope each day. Such pharmacies typically serve a large number of remote customers and it is common to fill the majority of prescriptions by reconstituting kits from which multiple unit doses are drawn.

In most cases, two procedures using syringes are needed to prepare a unit dose. The first procedure transfers ^{99m}Tc from the bulk activity eluted from a ^{99}Mo-^{99m}Tc generator to a vial (kit vial) for reconstitution of a particular pharmaceutical. The second is performed when a unit dose is drawn from the kit vial after reconstitution. Unit doses commonly are dispensed in 3-ml disposable syringes while 5-ml or 10-ml syringes are used to withdraw activity from the vials (elution vials) containing the generator eluate.

Syringe manipulations almost always are performed manually, with the elution or kit vial contained in a lead shield and the syringe contained in a lead glass or tungsten shield. Although the design of syringe shields varies in detail, the shields generally provide a high degree of attenuation of the 140.5-keV photon from decay of ^{99m}Tc except for the radiation streaming down the barrel of the syringe. Because of its plastic construction and overall geometry, shielding by the syringe itself is insignificant. As a result, the highest extremity exposure to the pharmacist is found on the fingers used to grasp the end of the syringe plunger and, depending on the actual technique used, on the adjacent region of the palm. The exposure can be considered to arise from two different sources: the activity drawn into the syringe and the activity remaining in the elution or kit vial. The extent to which these two sources contribute to the extremity exposure depends on the total initial activity in the vial, the fraction that is drawn into the syringe, and the geometries presented for radiation streaming through the openings in the vial and syringe shields. For example, the total ^{99m}Tc activity eluted from a new generator at calibration may be as large as 74–592 GBq (2–16 Ci) while the activity needed to reconstitute a kit may lie in the range of 3.7–22.2 GBq (0.1–0.6 Ci). Radiation emanating from the shielded elution vial thus will dominate the absorbed dose initially, while that from the activity drawn into the syringe will dominate as the last of the activity is withdrawn from the vial.

The absorbed dose from procedures using syringes has been addressed in several publications (1) but most reports do not allow assessing the relative importance to the total dose of the different radiation sources encountered, such as bulk activity contained in an elution or kit vial or activity drawn into a syringe. Further, the detailed construction of a vial and syringe

shield and the actual technique used in a syringe procedure can have a significant effect on the total dose received. As an example, Harding et al. (1) measured the dose to the index fingers in a radiopharmacy supplying 11,000 patient doses per year and in a hospital dispensary providing 4500 doses per year. In the radiopharmacy, procedures using syringes included transfer of activity from elution vials to multidose kits and all other radiochemistry performed in the laboratory. Some individual dose preparation also may have been included. In the dispensary, the only procedures performed were the transfer of individual patient doses from multidose vials. Harding et al. (1) compared the absorbed dose received with and without the use of tungsten syringe shields. With syringe shields, they reported maximum dose equivalents of 0.07 mSv GBq^{-1} (259 mrem Ci^{-1}) and 0.18 mSv GBq^{-1} (666 mrem Ci^{-1}) handled in the radiopharmacy and dispensary, respectively. Although not explicitly stated, it is inferred that the principal part of the radioactivity handled was ^{99m}Tc. We note that the modern commercial radiopharmacy in the U.S. generally performs all manipulations required to produce individual patient doses as end products.

More recently, Jansen et al. (2) reported on the radiation doses to radiopharmacy personnel over an 8-yr period. These authors indicate that the personnel monitored were equipped with thermoluminescent dosimeters worn at the base of the middle finger of the right hand and that most of the activity handled was ^{99m}Tc. They reported a mean absorbed dose to the hands, as measured by these dosimeters, of 1.05 ± 0.28 mSv GBq^{-1} (3885 ± 1036 mrem Ci^{-1}), but in this case the dose reported is per unit of activity actually received in the laboratory in the form of ^{99}Mo-^{99m}Tc generators and not per unit of ^{99m}Tc activity actually handled. No syringe shields were used in either the procedures for removing activity from the bulk generator eluate or in preparing individual patient doses. Because the actual quantity of ^{99m}Tc handled was not reported, it is difficult to compare the data reported by these authors with the data reported by Harding et al. (1).

While reports such as those above are useful for broadly assessing radiation safety, they do not provide the basis for a detailed assessment of dose burdens from different activities in a modern central radiopharmacy. With a view toward the latter, we measured absorbed-dose rates at the end of a syringe plunger from ^{99m}Tc contained in a syringe and when the activity was contained in an elution or kit vial under geometries similar to those used by experienced, practicing board-certified nuclear pharmacists. In this paper we report these measurements and discuss Monte Carlo simulations with a physical model that contains the principal features of typical experimental conditions.

MATERIALS AND METHODS

Measurements of Absorbed-Dose Rates

A composite sketch of the overall geometry used in our measurements is shown in Figure 1. The syringes were standard plastic disposable syringes (Becton Dickinson and Co., Franklin Lakes, NJ). The syringe shield was a standard com-
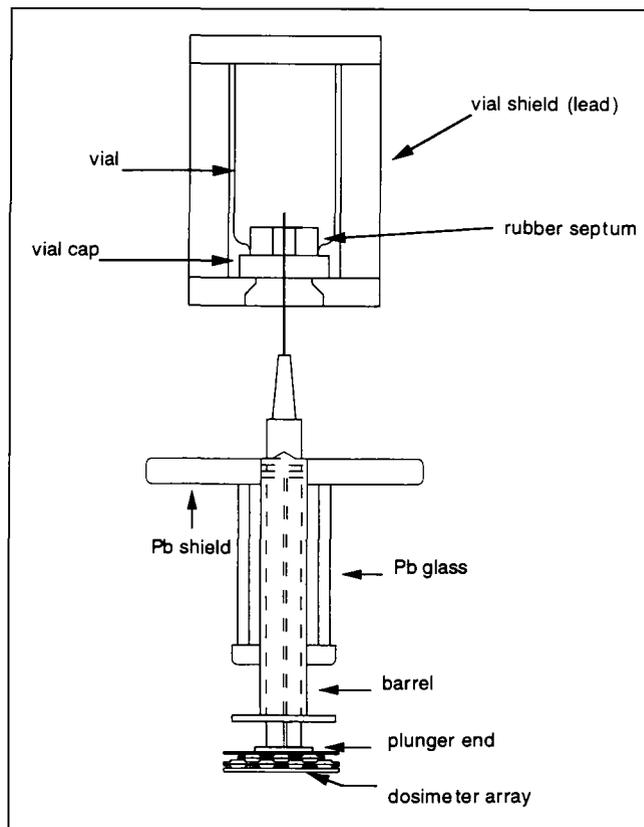
FIGURE 1. Composite schematic diagram of a shielded vial and syringe, and the dosimeter array used for dose rate measurements. When ^{99m}Tc activity was contained in a vial, the dosimeter array was replaced by a single dosimeter package located on the axis of the plunger. When ^{99m}Tc was contained in the syringe, the plunger was withdrawn just enough to accommodate the active solution.

mercial device (Biodex Medical Systems, Inc., Shirley, NY) constructed from a cylindrical lead-glass element and fitted with an annular plate on the end facing the vial shield that contained a 0.32-cm (1/8-inch) lead plate. The vials and vial shields were standard commercial devices (DuPont Merck Pharmaceutical Company, North Billerica, MA) designed to contain either an elution vial or a range of kit vials. Due to design differences, these two vial/vial shield combinations present significantly different geometries for emission of radiation into the opening in the base of the syringe shield. When measuring the absorbed-dose rate from activity contained in a shielded vial, the dimension between the bottom of the syringe shield and the end of the syringe plunger was adjusted to reflect the actual dimension measured during a syringe procedure by an experienced radiopharmacist.

The dosimeter array was centered on the axis of the plunger end and is shown in greater detail in Figure 2. Each dosimeter was a CaF$_2$ chip (0.35 cm × 0.35 cm × 0.097 cm) sealed in two sheets of 0.025-cm thick aluminum to form a square (1.27 cm × 1.27 cm) light-tight package. The array was held together by a thin composite (PC board) and cardboard covers. When the activity was contained in a 10-ml syringe, seven dosimeters were used in the configuration shown in Figure 2. Only five dosimeters were needed for dose measurements when a 3-ml
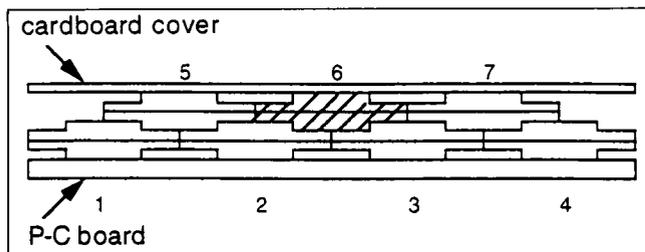
FIGURE 2. Schematic of dosimeter array used to measure exposure from radiation streaming down the barrel of a 10-ml disposable syringe. The numbers in the figure identify individual dosimeter packages, each with the cross section indicated by the cross-hatched area (Dosimeter 6). For measurements with a 3-ml syringe, the dosimeters in Positions 1 and 4 were deleted.

syringe was used and Dosimeters 1 and 4 of Figure 2 were deleted. When activity was contained in a shielded vial, only a single dosimeter was located at the center of the end of the syringe plunger which was in its fully inserted position.

The experiments were conducted behind lead shielding in a fume hood from which all other radioactive sources had been removed. The length of exposure was chosen to ensure that the dosimeter located on the axis of the plunger received an estimated absorbed dose greater than 5 mGy (500 mrad) for which we expected reasonable accuracy in reading the dosimeters. For each experiment, an additional dosimeter was located on the outside of the lead shield and acted as a control to correct for the dose received from extraneous radiation sources between the time of the beginning of an experiment and the time of reading the dosimeters. After an experiment, the dosimeters were removed and placed into a secondary lead shield along with the controls. The activity in the syringe or vial was calibrated with a commercial dose calibrator (Model CRC-12R; Capintec, Ramsey, NJ) to an estimated uncertainty ($\pm$ 1σ) of 5%. The dosimeters were read at the Sandia National Laboratory, Albuquerque, NM. The raw data, reported as total absorbed dose (Gy), were converted into initial absorbed-dose rates (mrad hr^{-1}) after correction for ^{99m}Tc decay during the measurement period. In no case was any absorbed dose reported for a control dosimeter.

Dose rates from activity in a 10-cc syringe were obtained by drawing in 3.0 ml of generator eluate containing ^{99m}Tc with an initial activity of 11.4 $\pm$ 0.6 GBq (308 $\pm$ 15 mCi) and the dosimeters were exposed for 2.40 hr. Dose rates from activity in a 3-cc syringe were obtained by drawing in 1.6 ml of eluate with an initial activity of 2.45 $\pm$ 0.12 GBq (66.3 $\pm$ 3.3 mCi) and the dosimeters were exposed for 2.35 hr.

In order to assess the relative importance of activity contained in elution or kit vials to the absorbed-dose rates to the fingers and hands, ^{99m}Tc eluate was transferred to a shielded vial and the absorbed dose at the end of the syringe plunger was measured in the geometry shown in Figure 1. With the elution vial/10-ml-syringe combination, 20 ml of eluate containing an initial activity of 107 $\pm$ 5 GBq (2883 $\pm$ 144 mCi) was used and the exposure time was 2.18 hr. For the kit vial/3-ml-syringe combination, 8.0 ml of eluate initially containing 26.4 $\pm$
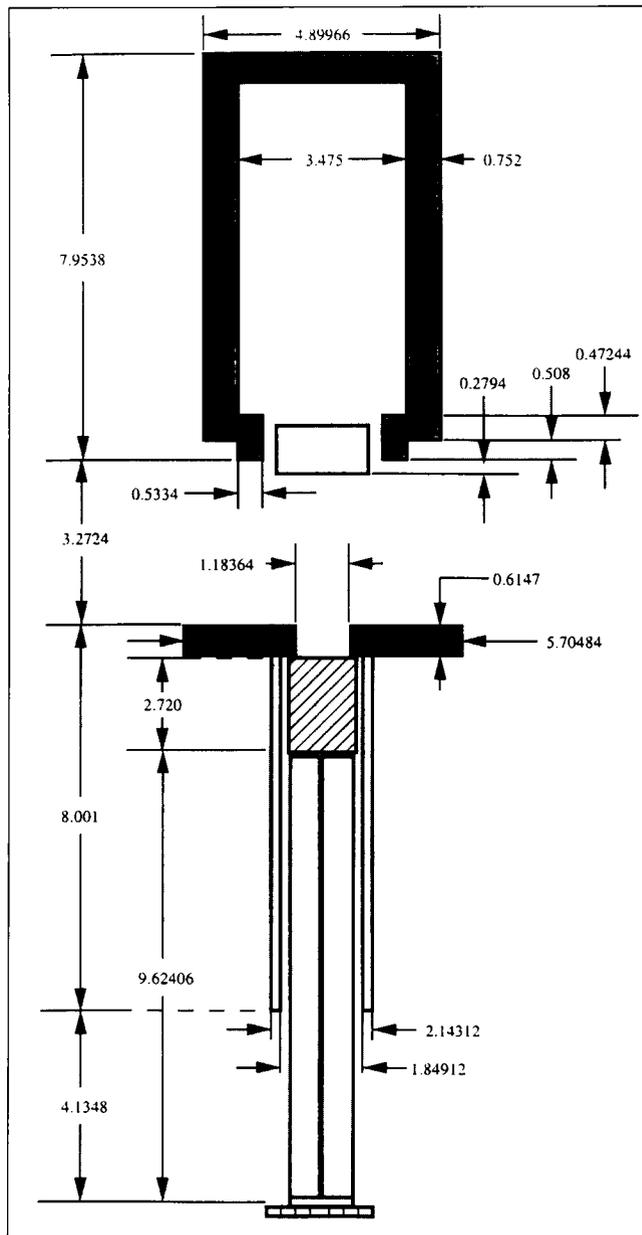
FIGURE 3. Schematic of the Monte Carlo model of vial shield, syringe shield and syringe. The dimensions shown in the figure (cm) are those for the elution vial/10-ml disposable syringe configuration.

1.3 GBq (713 $\pm$ 35 mCi) of activity was used and the exposure time was 2.32 hr.

Monte Carlo Modeling

The four experiments discussed above were modeled in Monte Carlo simulations with the code MCNP (3). For this purpose, the geometry shown schematically in Figure 1 was simplified to that shown in Figure 3. Critical dimensions, such as the source-to-dosimeter distance, the thickness of the lead shields, the diameters of the openings in the vial and syringe shields and so on, were the same as in the experiments. The glass walls of a vial and the plastic syringe barrel were not represented in the model as they cannot account for significant

TABLE 1
Measured Absorbed Dose (Gy) and Calculated Initial Absorbed Dose Rates (mrad hr⁻¹) for Each Dosimeter in the Four Experiments

| TLD no.	Gy × 10^2	$\dot{D}_0$ (exp) (mrad hr^{-1})	$\dot{D}_0$ (MC) (mrad hr^{-1})
	^{99m}Tc in 10-ml disposable syringe		
1	1.59 ± 0.15	751 ± 73	305 ± 5
2	4.42 ± 0.35	2081 ± 164	1971 ± 21
3	4.36 ± 0.34	2057 ± 163	1971 ± 21
4	1.83 ± 0.18	861 ± 83	305 ± 5
5	3.59 ± 0.32	1692 ± 151	1642 ± 13
6	3.61 ± 0.32	1701 ± 151	1665 ± 57
7	3.79 ± 0.34	1786 ± 161	1624 ± 13
	^{99m}Tc in 3-ml disposable syringe		
8	0.598 ± 0.061	291 ± 30	393 ± 3.0
9	0.791 ± 0.095	384 ± 46	556 ± 15
10	0.168 ± 0.027	82.4 ± 1.3	393 ± 3.0
11	0.953 ± 0.097	463 ± 47	608 ± 6.0
12	0.904 ± 0.098	439 ± 47	608 ± 6.0
	^{99m}Tc in elution vial		
14	7.97 ± 0.39	4132 ± 202	4257 ± 247
	^{99m}Tc in product vial		
15	2.17 ± 0.13	1069 ± 64	1156 ± 67

The errors shown (± 1 σ) represent only the uncertainties on reading the dosimeters. Included in the fourth column are initial absorbed dose rates (± 1σ) calculated with Monte Carlo simulations.

attenuation of the ^{99m}Tc photons. The syringe plunger itself was modeled with minor simplifications of its actual geometry. The generator eluate was approximated as pure water and the complex geometries of the solution volume in a vial and the rubber septum of the vial were represented as stacked concentric right circular cylinders. Finally, the dosimeter array was approximated as a continuous sheet of CaF$_2$ covered by two sheets of aluminum. The thickness of each layer was the same as that of the materials in the actual dosimeters. To obtain the radial dependence of the dose rates, the dosimeter was subdivided into concentric annuli centered on the axis of the syringe barrel. The diameter of the central circular area as well as the width of each annulus was taken as 0.63 cm, the center-to-center distance of the CaF$_2$ chips in the dosimeter arrays.

The code output for most runs was the average energy deposited in each annulus per emitted source photon and sufficient histories were followed to ensure reasonably small statistical errors in the final result. The output was then converted into average dose rates for the initial activities used in each of the experiments. In several cases, the code was used to simulate the spectrum of photons penetrating the end of the syringe plunger.

RESULTS AND DISCUSSION

The measured total absorbed doses and calculated initial absorbed-dose rates for the dosimeter arrays used when ^{99m}Tc was contained in the 10-ml and 3-ml syringes are given in Table
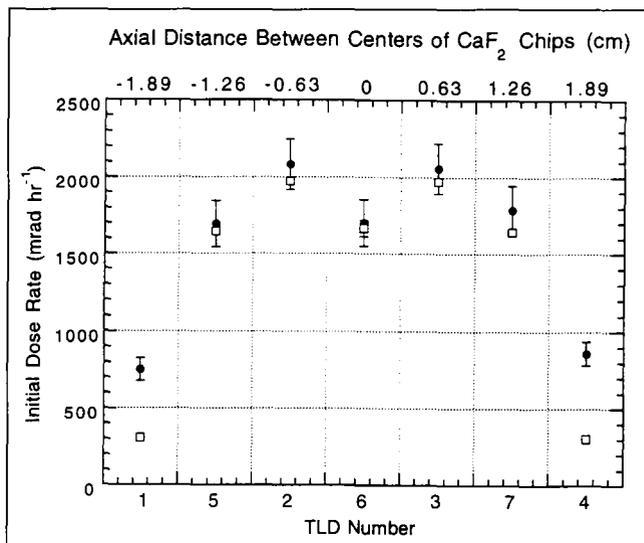
FIGURE 4. Initial dose rates for a 10-ml syringe containing 11.4 ± 0.6 GBq (308 ± 15 mCi) ^{99m}Tc in 3.0 ml saline solution (filled circles). The location of each TLD is shown in the schematic of the dosimeter package. The vertical error bars represent ± 1 σ limits on the measured absorbed dose. Also shown are dose rates calculated with a Monte Carlo simulation (open squares).

1. The initial dose rates also are shown graphically in Figures 4 and 5 and, as expected, the radial dependence of the dose rates is similar in both cases. The dose rate measured for the central dosimeter (Dosimeter 6) is somewhat lower than might be expected in both experiments. Although there is a slightly larger source-to-dosimeter distance for Dosimeters 5, 6 and 7, as compared to the others, it is too small to account for this effect. As shown from the Monte Carlo simulations, the lower dose rate can be traced to the detailed construction of the syringer plungers which causes more attenuation of photons
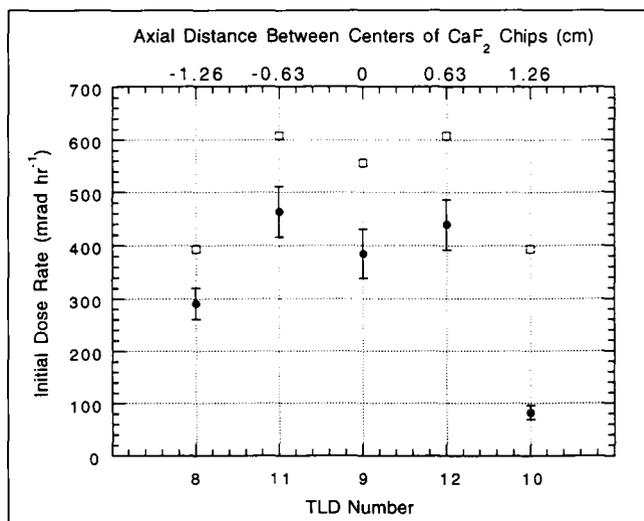

FIGURE 5. Initial dose rates for a 3-ml syringe containing 2.45 ± 0.12 GBq (66.3 ± 3.3 mCi) ^{99m}Tc in 1.6 ml saline solution (filled circles). The vertical error bars represent ± 1 σ limits on the measured absorbed dose. Also shown are the dose rates calculated with a Monte Carlo simulation (open squares).

near the axis of the syringe. The dose rate falls off sharply at large radial distances but not as rapidly as might be expected because of beam spreading as radiation streams down the barrel of the syringe to the end of the syringe plunger. The inner radii of the syringe shields were 0.925 cm and 0.604 cm for the 10-ml and 3-ml syringes, respectively, and it is evident from Figures 4 and 5 that the dose rates do not decrease greatly until a radial distance that is about twice the inner radius of the shield. The asymmetry seen in the dose rates of Dosimeters 8 and 10 of Figure 5 is attributed to a slight error in centering the dosimeter package on the end of the plunger.

Included in both Table 1 and Figures 4 and 5 are the results of the Monte Carlo simulations of these two experimental arrangements. The radial variations of exposure rates are well-reproduced in both cases and the lower exposure rate of the dosimeter centered on the axis of the syringe barrel is due primarily to the design and construction of the syringe plunger. The magnitudes of the experimental initial exposure rates shown in Figure 4 also are reproduced surprisingly well but those in Figure 5 appear to be overestimated in the simulations by 30–40%. The source of this discrepancy is not known with certainty. However, the calibration data for the particular batch from which the dosimeters were drawn did not extend below about 3.5 Gy and thus a considerable systematic error is possible in the extrapolation of the calibration curve to the lower absorbed doses experienced in this measurement (Zarrick TA, *personal communication*, 1997).

Also included in Table 1 are the total doses, initial dose rates derived from them, and the results of the Monte Carlo simulations when ^{99m}Tc activity was contained in the elution and kit vials. Once again the comparison between the experimental and simulated dose rates is excellent and lends support to the capability of the Monte Carlo model to provide good estimates of exposure rates expected with procedures using syringes.

While conditions may vary significantly among syringe manipulations because of varying solution volumes and their geometries, the experimental results reported here provide a measure of the order of absorbed dose from a procedure using a syringe and a measure of the relative importance of bulk activity contained in the vials to the dose commitment. By considering only the dosimeters located on the axis of the syringe, the experimental data imply absorbed-dose rates at the end of a syringe plunger of 1.49 ± 0.15 (5.52 ± 0.56), 1.57 ± 0.20 (5.80 ± 0.75), 0.386 ± 0.027 (1.43 ± 0.10), and 0.405 ± 0.032 (1.50 ± 0.12) mGy hr^{-1} GBq^{-1} (mrad hr^{-1} mCi^{-1}) of ^{99m}Tc handled when the activity is contained in a 10-ml syringe, 3-ml syringe, elution vial and kit vial, respectively. Thus the dose rate from a unit activity in either syringe is larger than the dose rate from a unit activity in the associated vial by a factor of about 3.9. Notwithstanding the greater distance between the bulk activity in a shielded vial from the fingers and hand manipulating the syringe plunger, the dose commitment when first removing activity from fresh generator eluate or a kit vial from which multiple unit doses are to be drawn will be controlled by radiation emitted from the vial shield. For example, with 111 GBq (3 Ci) generator eluate, the absorbed-dose rate at the end of the syringe plunger could be as large as 40 mGy
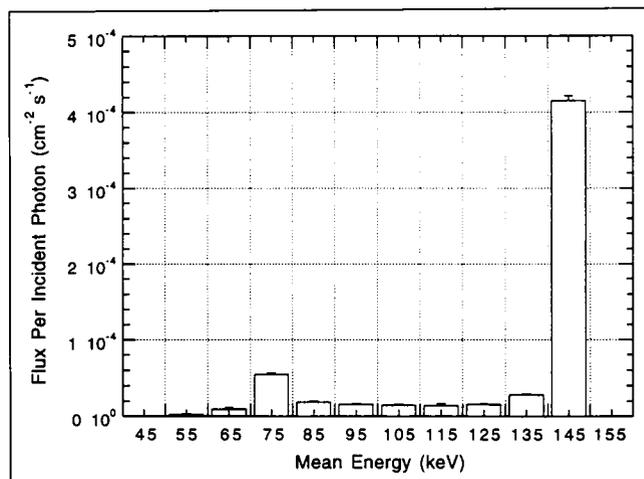
FIGURE 6. Simulated photon spectrum at the end of the plunger of a 10-cc syringe containing 26.4 ± 1.3 GBq (713 ± 35 mCi) ^{99m}Tc. The data have been plotted at the mean energy of the 10-keV-wide energy bins shown.

hr^{-1} (4 rad hr^{-1}) with the personnel shielding common to most radiopharmacies.

The energy spectrum of photons incident on a dosimeter array simulated by the Monte Carlo model under the conditions used to provide the data in Figure 4 is shown in Figure 6. The spectrum is dominated by a peak in the bin centered at 145 keV and is due almost entirely to uncollided source photons at 140.5 keV. An additional peak is seen in the bin centered at 75 keV and is due in large part to K_α x-rays from lead emitted subsequent to photoelectric absorption of source photons in the syringe shield. The less intense K_β x-rays from the same source contribute to the photons in the energy bin centered at 85 keV. The total intensity of the lead K x-rays in the simulated spectrum is about 12% of the intensity of the 140.5-keV photons. However, because the dose rate per incident x-ray is roughly a factor of 3.3 larger than that for source photons, the simulation suggests that the x-rays could contribute as much as 30% to the total absorbed dose at the end of the plunger in this case. A simulation with activity contained in an elution vial under the same geometry used to produce the simulation of exposure to Dosimeter 14 of Table 1 indicated that in this case, the relative contribution of lead K x-rays to the dose is rather small. A careful examination of the two experimental arrangements clearly suggests that the geometry for lead x-ray transport to the end of the syringe plunger is favorable only with activity located within the syringe.

The good agreement between the experimental measurements and the Monte Carlo simulations leads us to have confidence in both the experimental measurements and the ability of the calculations to provide reasonable estimates of dose burdens from procedures using syringes in the radiopharmacy. However, the absorbed-dose rates measured and calculated here are in marked disagreement with those reported by Harding et al. (*1*). Our measurements imply a dose commitment to the fingers of the hand manipulating a syringe of about 5.4 × 10^{-4} mSv GBq^{-1} s^{-1} (2 mrem Ci^{-1} s^{-1}). Assuming that the time to accomplish a manipulation of a syringe lies in the

range of 5–10 sec, the total absorbed-dose commitment would be about $(2.7–5.4) \times 10^{-3}$ mSv GBq^{-1} (10–20 mrem Ci^{-1}). This is roughly a factor of 12–25 times smaller than the value of 0.07 mSv GBq^{-1} (259 mrem Ci^{-1}) reported in Harding et al. The tungsten syringe shields used by Harding et al., provide attenuation factors for ^{99m}Tc γ-rays in the direction normal to the syringe axis of 27–178 depending on the size of the syringe in use. At most, then, the photon attenuation provided by the lead glass of the syringe shields used in this study was a factor of 3 larger. It is certainly possible that the time required to perform a procedure with a syringe is longer than 5–10 sec, but it seems unlikely that an average time approaching 1 min was required.

Because no details are available on the dimensions of the syringes used, the actual construction of the tungsten syringe shields, or of the lead shields in which the elution or kit vials were contained, we can only speculate on possible explanations for the large dose commitment reported by Harding et al. (1). One possible explanation could be the construction of the tungsten syringe shields themselves. In the U.S., most commercial tungsten shields are not fitted with base plates to shield against the principal part of the radiation emanating from the openings of vial shields. If the syringe shields used in the study by Harding et al., were not fitted with such plates and if the openings in the lead vial shields were relatively large, a large dose to the hands could result from the bulk ^{99m}Tc remaining in the elution or kit vial. This is particularly important if, during some portion of a procedure with a syringe, the dosimeters were located at a distance from the axis of the syringe that was larger than the radius of the syringe shield itself.

In a previous publication (4), the dose burden from calibration of eluate from a ^{99}Mo-^{99m}Tc generator was reported to lie in the range $(2.7–10.8) \times 10^{-4}$ mSv GBq^{-1} (1–4 mrem Ci^{-1}) ^{99m}Tc handled. The measurements reported here suggest that the dose commitment from procedures using syringes is likely to be 2–5 times larger. Surprisingly, K x-rays from photoelectric absorption in a lead-glass syringe shield may be a significant contributor to extremity dose from procedures using syringes.

CONCLUSION

Monte Carlo calculations of the type reported here can be used to understand the importance of different radiation source geometries to the total dose commitment from various procedures and the means by which improved radiation safety can be approached. With the large number of diagnostic and therapeutic radiopharmaceuticals now under development, the total quantity of radioactivity used in nuclear medicine can be expected to grow significantly. Coupled with the need to improve laboratory efficiency, which can be limited by radiation safety considerations, the need for cost-effective dose reduction is likely to increase.

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