Radiopharmacy

An Experimental Dispensing System for Withdrawal, Preparation, and Assay of Tc-99m Radiopharmaceuticals

Juan Trujillo, Sam Krinsky*, Bob Wilson†, Gary Young, Edward Teague, and Karen Kamer

University Hospital Louisville, Louisville, Kentucky

Radiation exposures to the fingertips and hands of technologists were monitored as they prepared radiopharmaceuticals using an experimental dispensing system. Results were compared to those obtained by conventional syringe shields. Our study assessed the overall exposure levels received during each phase of radiopharmaceutical preparation. We describe the speed and ease of our experimental dispensing system; most importantly, we report a reduction in radiation exposure to the fingertips and hands of personnel as measured by thermoluminescent detector chips.

Unnecessary irradiation of the fingertips and hands of personnel preparing radiopharmaceuticals has been an area of concern of several years. The "as low as reasonably achievable" (ALARA) concept (*1*) is a logical outgrowth of this concern. This concept directs nuclear medicine personnel to maintain body and extremity exposures at minimum levels. In the past few years several radiation-reducing devices and techniques have been developed to promote this commitment.

The literature reports several studies to define these techniques and devices (*2,3*). However, many of these did not assess overall exposure levels throughout each stage of radiopharmaceutial preparation—from generator elution to patient injection. An exception to this, a study conducted by Williams et al. (*4*), determined hand exposures during various preparatory steps. This study compared hand exposures received while using an automated dispensing system no longer available.

We evaluated hand exposures received while using an experimental dispensing system (EDS) of unique design. In addition, our measured exposures were compared to hand exposures obtained while using the conventional standard syringe shields. We also compared various methods for ease and speed of operation.

For reprints contact: Juan Trujillo, Dept. of Nuclear Medicine, University Hospital Louisville, 323 E. Chestnut St., Louisville, KY 40202.

*Presently at Allegheny General Hospital, Pittsburgh, PA.

†Presently at University of North Carolina, Chapel Hill, NC.

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Materials and Methods

The generator was eluted into a modified "L-U-8" vial shield (Nuclear Associates, Carle Place, NY) of thickness appropriate to assess Mo-99 breakthrough. This modified shield is designed with a wire handle so that Tc-99m assay may follow Mo-99 breakthrough assay. The shield's base has a velcro pad that will stick to a second piece of velcro, which has been permanently installed in the bottom of the ionization chamber's plastic liner. This allows the shield to be held steady while it is unscrewed and temporarily separated, allowing the glass eluate vial containing Tc-99m to be assayed (Fig. 1).

When using this shield, a correction factor of 1.06 was applied to the Tc-99m assay activity readings, which were consistently lower than those obtained when assaying only the elution vial in the dose calibrator. The shield's base constitutes extra shielding and since it remained in the bottom of the ionization chamber during assay, it created attenuation and scatter conditions that could be experimentally corrected.

After the Tc-99m and Mo-99 assays, an elbow-shaped shield, which has a withdrawing port equipped with a lead glass window, is connected to a shielded and vented three-way needle system. This withdrawing port has a 21-gauge needle that is connected by tygon tubing to one needle of the three-way system used to puncture the rubber septum of the shielded elution vial. In addition, one of these needles leads to a micropore filter vent, which allows the volume of radioactivity in the elution vial to remain essentially under zero pressure as well as eliminating bacteriostatic contamination (Figs. 2 and 3).

The angle of the shielded elbow containing the tygon tubing is such that hydrostatic pressure will not allow Tc-99m to leak out of the 21-gauge needle. Consequently no petcock is required (Figs. 2 and 3).

The EDS is now completely assembled. It is inverted and attached to a ring stand. (Fig. 4) Doses can be withdrawn using a specially designed evacuated syringe. This unique 3-cc syringe, used for dose withdrawal, is sealed airtight with a rub-

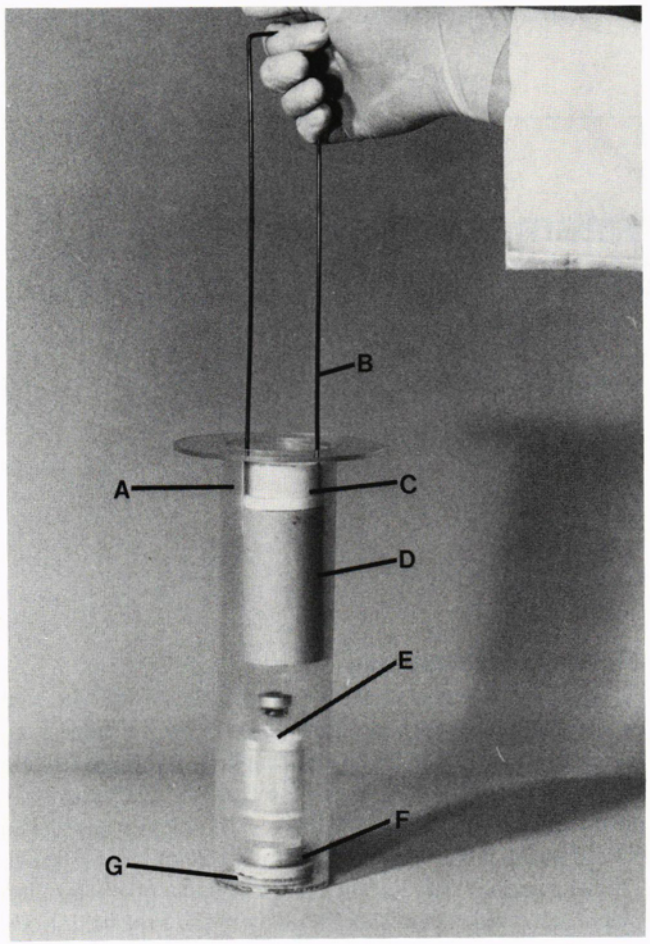

FIG. 1. "L-U-8" vial shield (twisted apart) during Mo-99 and Tc-99m assays in (A) ionization chamber's plastic liner; (B) wire handle; (C) shield top; (D) shield body; (E) eluate vial; (F) shield bottom; and (G) circular velcro strips permanently glued to shield's bottom and to bottom of ionization chamber's plastic liner.

ber septum held into place by a metal luer tipped end (Fig. 5). If the syringe is displaced 1 cc, for example, a vacuum will be created sufficient to allow 1 cc of Tc-99m to be rapidly withdrawn when the syringe's rubber septum is punctured by the needle of the EDS's withdrawing port (Fig. 4). To set a particular volume, the coarsely threaded handle is pulled back so that the tip of the syringe's plunger corresponds to the desired volume, and the spin nut is tightened to that setting. A 3-cc syringe shield is installed and a dose of radioactivity can be withdrawn shielded by the dispensing system.

We determined visually that all syringes filled in this way were filled completely. Since these syringes were not commercially manufactured, however, they were subject to variations in volume capacity. Therefore, the accuracy of dose volume delivery was not quantitatively measured.

Syringe assay can be performed with the syringe shield in place. The shielded syringe is placed in a shielded assay cup (Fig. 6), which has two retractable lateral arms permitting the assay cup to rest on the top of the ionization chamber without being physically held in place. If the syringe has 1 cc of volume in it, for example, its handle will have been displaced by that amount. Since the syringe has no lip, the syringe shield retaining screw must be loosened; then the syringe will drop far enough into the ionization chamber to be assayed (Figs. 6 and 7). When using the shielded assay cup with a syringe shield during the syringe assay procedure, a correction factor of 1.20 must be applied to the Tc-99m activity readings because of the extra shielding associated with previously described components.

A specially designed two-way needle is then installed on the shielded syringe using a needle retaining device (Fig. 8). The shielded syringe's septum is punctured by one end of the two-way needle by pushing straight down, twisting clockwise

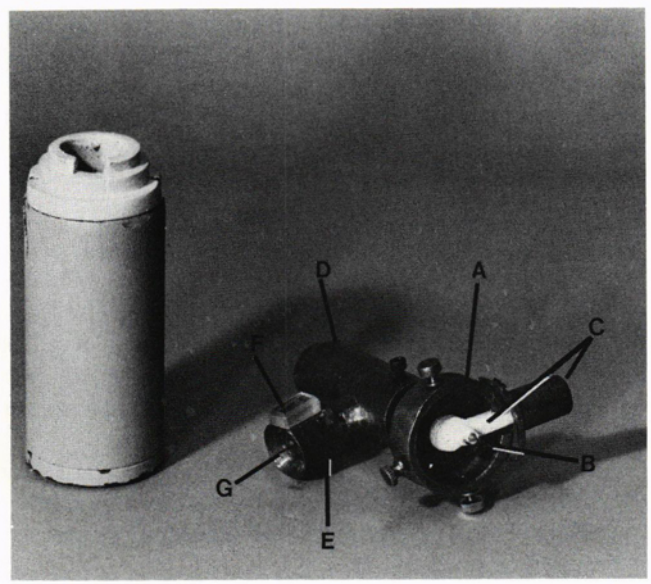

FIG. 2. "L-U-8" vial shield to be connected to (A) shielded three-way needle system that has one of its (B) two needles used to puncture the elution vial leading to (C) shielded micropore filter vent; (D) shielded elbow that has (E) withdrawing port, consisting of (F) lead glass window with (G) 21-gauge needle.

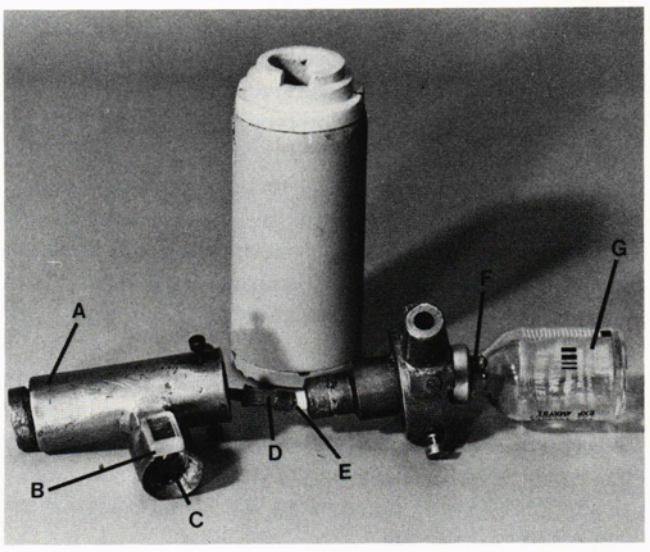

FIG. 3. "L-U-8" vial shield to be connected with (A) shielded elbow component whose (B) lead glass withdrawing port consists of (C) 21-gauge needle connected by (D) tygon tubing to one needle of (E) shielded three-way vented needle system whose remaining (F) two needles will puncture (G) eluate vial when it is in vial shield.

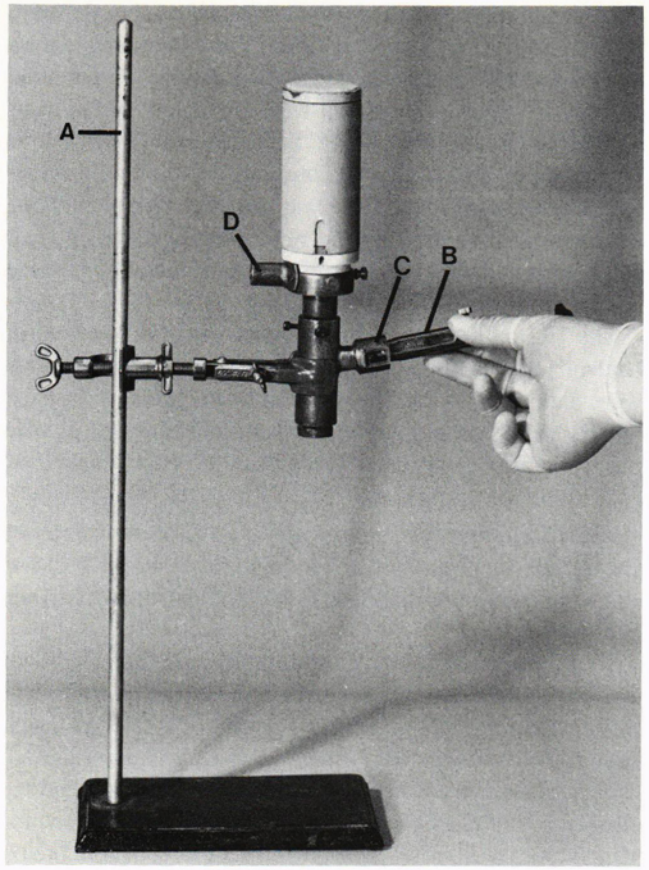

FIG. 4. EDS completely assembled and inverted on (A) ringstand; (B) shielded evacuated syringe being filled as its rubber septum is punctured by 21-gauge needle of (C) shielded elbow's withdrawing port; pressure does not build up within shielded eluate vial because of shielded three-way needle system's (D) micropore filter vent.

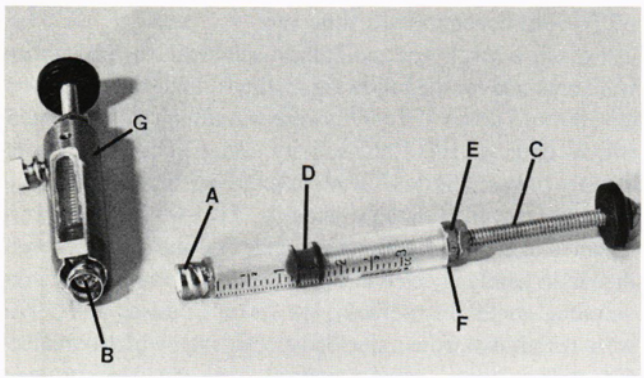

FIG. 5. Specially designed 3-cc syringe whose (A) metal luer tipped end holds (B) rubber septum in place; (C) coarsely threaded handle is pulled back; (D) plunger tip corresponds with desired volume setting; (E) spin nut is tightened; syringe that has no (F) lip is inserted in (G) standard syringe shield; vacuum created within syringe will withdraw desired volume from dispensing system.

to tighten the luer lock, and then pulling the needle and syringe straight up out of the retaining device. The experimental needle retaining device greatly reduces radiation exposure normally received during the conventional method of installing the two-way needle by hand.

After spinning the nut loose on the syringe's handle, the activity in the shielded 3-cc syringe is injected into a shielded kit vial. The shielded kit vial can in turn be connected to another shielded vent system and another elbow system, thereby composing another dispensing system. Multiple dispensing systems could follow in like manner.

Dosimeter Preparation and Assessment: Fifteen pairs of lithium fluoride mini-thermoluminescent detectors (TLDs) were exposed to the 140 keV gamma ray flux of a collimated source of known Tc-99m activity. The TLD chips were analyzed in a model series 2000 TLD (Harshaw Chemical Co., Solon, OH). The TLD's measuring chamber was purged with a constant flow of inert dry nitrogen gas (2–4 l/min) throughout all phases of each read-out cycle. The nitrogen gas reduces the measuring chamber's thermal noise level and thereby increases the sensitivity of the chamber's detection from 5–10 mR minimum to about 1 or 2 mR minimum per TLD (*4*). Extreme care was exercised in establishing correct heating temperature, integration period, and background determination of each read-out cycle to insure reliable data. Likewise, caution was taken in cleaning, annealing, and "zeroing in" the TLD chips prior to each exposure.

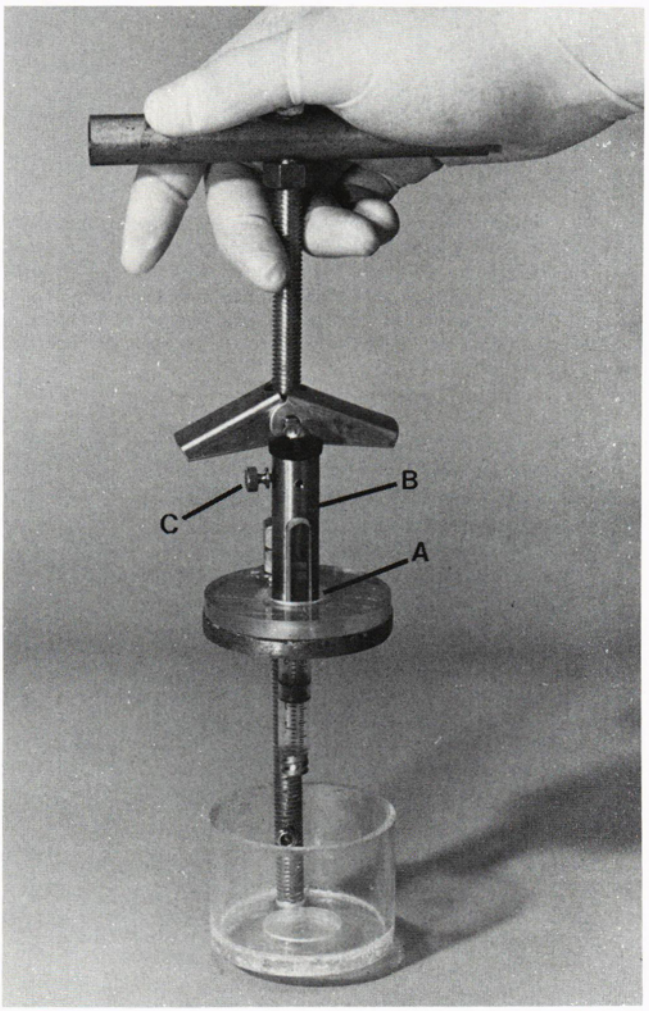

FIG. 6. Assay cup with (A) shielded circular space through which (B) shielded evacuated syringe is inserted for assay; since syringe has no lip, syringe shield's (C) retaining screw is loosened and syringe will fall sufficiently far into assay cup.

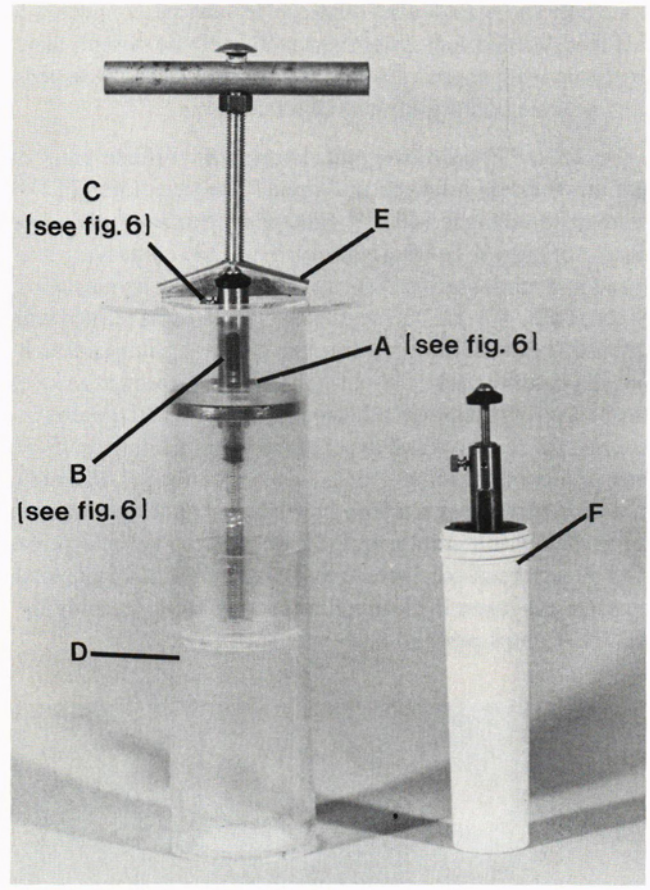

FIG. 7. Assay cup with (A) shielded circular space where (B) shielded evacuated syringe is inserted for assay; since syringe has no lip, (C) syringe shield's retaining screw is loosened and syringe will fall sufficiently far into (D) ionization chamber's plastic liner for assay; (E) retractable lateral arms prevent assay cup from being physically held; before being assayed, all syringes are transported with (F) cylindrical lead syringe shield carrier so that unnecessary exposure is avoided.

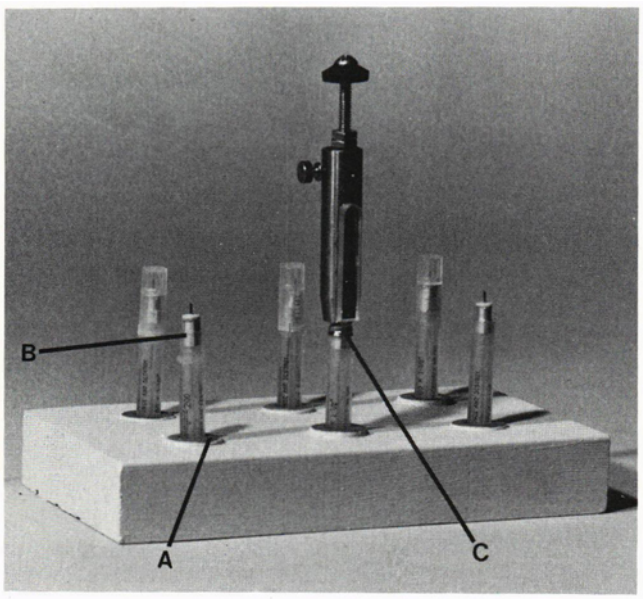

FIG. 8. Syringe needle retaining device with (A) lead tapered holes holding (B) two-way needles; (C) shielded syringe's septum is punctured by one end of two-way needle by pushing straight down, twisting clockwise, tightening luer lock, and then pulling needle and syringe straight up out of retaining device.

Predicted exposure values were mathematically calculated for the distances and exposure times. The values obtained (in nanocoulombs) from the TLD reader's display were plotted on log-log graph paper against the predicted values, thus establishing a calibration curve. Statistical analysis was done for the point values on the calibration curve and a linear regression equation for the line was derived. Using the slope and intercept values from the regression equation, a final equation was developed whereby each nanocoulomb value could be converted to exposure (Fig. 9).

The TLD chips were inserted inside the gauze portion of bandaids that had been cut lengthwise in half. The bandaids were then taped to ten fingertip and hand locations for each hand. Precaution was taken to insure that the TLDs were placed on the various hand locations in the same manner for each exposure comparison (Fig. 10).

Data Collection Methodology: The exposures were obtained during the various phases of radiopharmaceutical preparation with conventional methods (shielded and unshielded) and the EDS.

Exposure levels for generator elution were obtained over a 6-day period and included the installation, elution, and Tc-99m and Mo-99 breakthrough assays of a 2220-mCi generator. The conventional method was used for the test period, which included transferring the eluate vial from its shield to the ionization chamber to assay Tc-99m and then transferring it to a Mo-99 assay shield to check molybdenum breakthrough, and finally transferring it back to its elution shield. Similarly for six days using the EDS, the generator was eluted with a shield thick enough to assess Mo-99 breakthrough. The shield was then inserted in the ionization chamber and Mo-99 breakthrough was assessed. The shield was then temporarily twisted apart in the chamber (as described earlier) and assay of Tc-99m concentration followed.

Exposure levels for radiopharmaceutical kit preparation were obtained for the following methods. In the EDS method, ten 100-mCi doses of Tc-99m were withdrawn from the EDS, which contained 1000-mCi activity, using 3-cc shielded evacuated syringes. The doses were inserted into the shielded assay cup and assayed with the shields on. Two-way needles were installed using the needle retaining device and the doses were then individually injected into ten shielded kit vials. In the conventional method (shielded), six 100-mCi doses of Tc-99m were withdrawn from a shielded elution vial, which contained 600-mCi activity, using standard 3-cc shielded syringes. The doses were individually injected into six shielded kit vials. Each kit vial was transferred from its shield, assayed in the dose calibrator and then transferred back to its shield. This process was repeated with the conventional method (unshielded).

Exposure levels for syringe filling were obtained using the following methods. In the EDS method, 30 25-mCi doses of Tc-99m were withdrawn from the EDS, which contained 1000-mCi activity, using 3-cc shielded evacuated syringes. In the conventional method (shielded), ten 25-mCi doses of Tc-99m were withdrawn from a shielded elution vial, which contained 600-mCi activity, using standard 3-cc shielded sy-

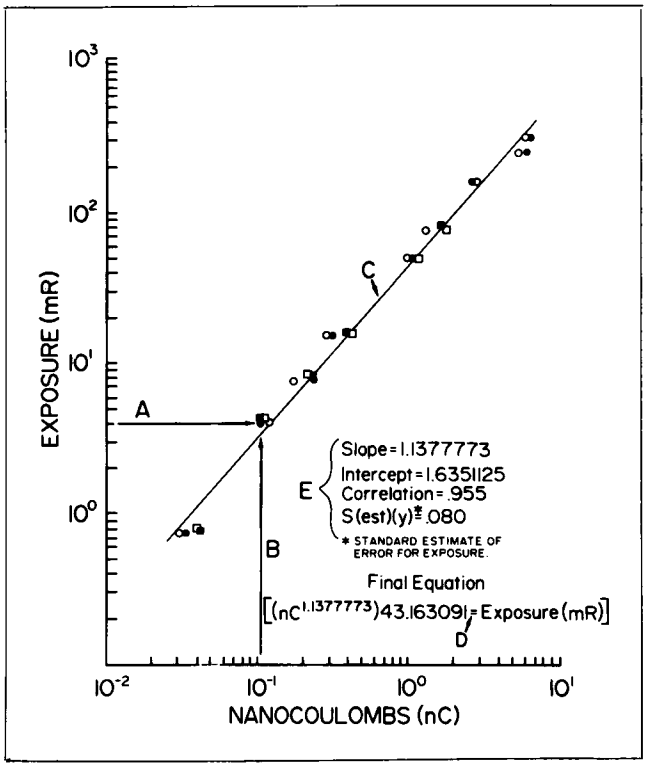

FIG. 9. TLD exposure calibration curve; (A) known exposure values (mR) on y axis; (B) nanocoulomb values on x axis; (C) linear regression equation and line for points; (D) conversion equation for exposure (mR) derived from (E) slope, intercept, correlation, and standard error of estimate.

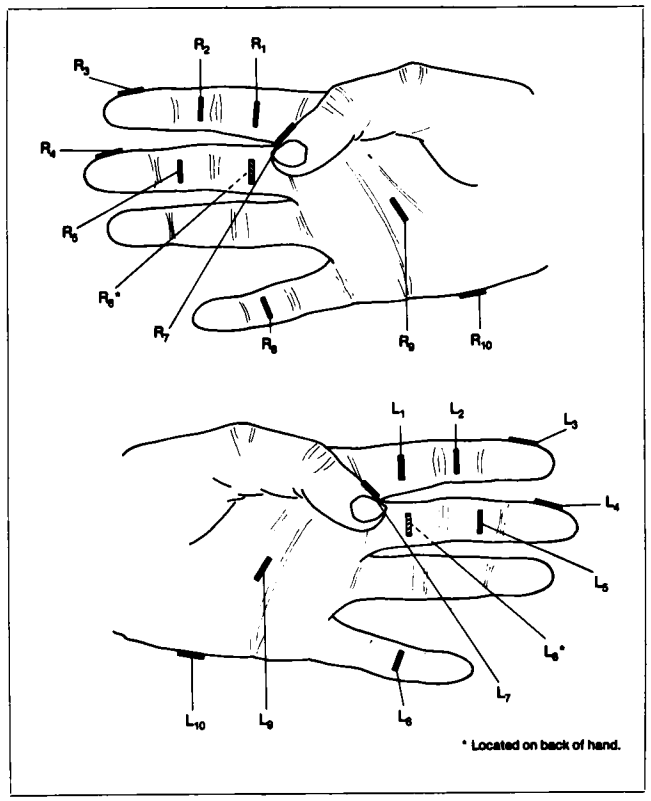

FIG. 10. Location of TLD chips on right and left hands for exposure comparisons; right hand chip locations R_1–R_{10}; left hand chip locations L_1–L_{10}.

ringes. This process was repeated with the conventional method (unshielded). A lead syringe shield carrier was used to transport both shielded and unshielded syringes to the dose calibrator for assay (Fig. 7).

Exposure levels for syringe assay were obtained by repeating the syringe filling part of the experiment. This time the doses were assayed as well. Doses withdrawn from the EDS were assayed with their shields on. Doses filled with conventional syringe shields were removed from their shields, assayed in the dose calibrator, and then returned to their respective syringe shields. Similarly, doses filled without syringe shields were assayed in the dose calibrator following syringe filling conventional method (unshielded). A lead syringe shield carrier was used to transport both shielded and unshielded syringes to the dose calibrator for assay.

Thus, syringe assay exposures were calculated by subtracting exposure levels obtained in the syringe filling phase of the experiment from exposure levels obtained in the syringe filling and assay phase.

Since needle gauge is important in controlling the rate of filling, 21-gauge needles were used consistently. Similarly, the volume of Tc-99m in each syringe was held constant at 0.5 ml.

For a newly designed system to be successfully used on a daily basis, it must not only reduce radiation exposure to laboratory personnel but it must be easy and rapid to use. Therefore, we decided to compare the time required to perform generator elution, kit preparation, syringe filling, and syringe assay with the conventional method (shielded and unshielded) and the EDS, using an electronic digital timer. Minor variations of the previously described stages of radiopharmaceutical preparation were instituted for this phase. Specifically, low activities of Tc-99m were used in order to prevent unnecessary exposure to the technologist performing the timed sequences. Also, the volumes used were altered from 0.5 to 1.0 ml for syringe filling and from 0.5 to 2.0 ml for kit preparation. Finally, syringe filling and syringe assay were made distinctive steps.

Results, Discussion, and Conclusions

The data show that regardless of the technique used, each phase of radiopharmaceutical preparation results in a significant cumulative contribution to weekly exposure. In order to illustrate this finding without being misleading, it was important to establish a representative number of TLD locations for both hands. As Tables 1 through 3 show, whether the TLD chip was placed on the fingertip or midfinger, right hand or left hand, makes a substantial difference in exposure received. Incidentally, the technologists were all right handed and therefore the discussion of exposure data will concern data pertaining to the right hand.

Exposure data (Tables 2 and 3) for the conventional method (shielded versus unshielded) for various phases of radiopharmaceutical preparation reveal an average reduction factor of approximately 2 for weekly exposure when using the conventional method (shielded). Likewise for kit preparation and syringe filling, average exposure reduction factors of approx-

imately 2 and 3, respectively, occur in favor of syringe shields. For assay exposure values, use of conventional syringe shields during assay resulted in an average exposure reduction factor of 2 when compared to unshielded syringes.

Since we obtained our assay exposure values in a slightly unorthodox manner, we feel it is appropriate to explain how these values were derived. One way to establish assay exposure levels would be to have the technologist insert and retrieve a syringe in the dose calibrator (a sufficient number of times using the different methods) to acquire enough exposures for comparison. However, we felt it was important to have two sets of exposure values (one from assay plus filling and one from filling). We correctly predicted that if all variables remained constant, the assay plus filling exposure values should always be measurably higher than the filling values alone. Since we were evaluating an experimental system that produced extremely low exposure levels, this check gave us much more confidence in our overall data.

Tables 1 through 3 show that the EDS had extremely low exposure values for all phases of radiopharmaceutical preparation and greatly outperformed the conventional method (shielded and unshielded).

For the right hand at close distances, the EDS reduced weekly exposure by a factor of better than 25 when compared to the conventional method (unshielded) and by an average factor of 16 when compared to the conventional method (shielded). Further, the data show that the EDS reduces exposure from generator elution by a factor of approximately 75 when compared to the conventional method. Similarly, for kit preparation use of the EDS results in average reduction factors of 18 and 40 when compared to the conventional method, shielded and unshielded, respectively. Likewise for syringe filling the EDS reduces average exposure by a factor of 8 when compared to the conventional method (shielded) and by an average factor of better than 40 when compared to the conventional method (unshielded). Finally, during syringe assay the EDS reduces average right-hand exposure by approximate factors of 2 and 3 when compared to the conventional method, shielded and unshielded, respectively.

Prior to this study one of the predominant doubts among our staff members concerning the EDS's performance was that it appeared cumbersome and that it would be too time-consuming to use on a daily basis. This doubt was silenced somewhat when the exposure data comparing the various techniques were compiled.

A basic and tested principle in reducing radiation exposure consists of three variables: distance, time, and shielding. The EDS and conventional shielded techniques we compared used similar shielding; therefore, the EDS's drastic improvement in radiation reduction over the conventional method (shielded) was probably not due to shielding alone. The EDS probably dominates at least one of the other two variables as well.

In fact Table 4 shows that the EDS produced faster times than the conventional method (shielded) in every phase of radiopharmaceutical preparation. Likewise it produced faster times than the conventional method (unshielded) in every phase of radiopharmaceutical preparation except syringe assay.

During the timing phases of radiopharmaceutical preparation, all technologists using the EDS agreed that although it was a different process, it was faster, more logical, and more expedient. Most significantly, it drastically reduced radiation exposure levels and certainly satisfied the ALARA criterion.

TABLE 1. Average Hand Exposures (mR) Received during Radiopharmaceutical Preparation While Using an Experimental Dispensing System

TLD chip hand locations	Experimental generator elution (1 assembly 6 elutions)	Kit preparation (15, 100-mCi doses)	Syringe filling (50, 25-mCi doses)	Syringe assay (50, 25-mCi doses)*	Total weekly exposure
Right hand fingertip positions R_3, R_4, R_7	1	5	3	6 (67%)	15
Right hand positions R_2, R_5, R_8	1	6	2	3 (60%)	12
Right hand positions R_1, R_6, R_9, R_{10}	1	5	2	2 (50%)	10
Left hand fingertip positions L_3, L_4, L_7	2	4	2	5 (71%)	12
Left hand positions L_2, L_5, L_8	1	3	1	9 (90%)	13
Left hand positions L_1, L_6, L_9, L_{10}	1	2	1	4 (80%)	8

*The percentages in the assay column represent the assay exposure expressed as a percentage of the total exposure in assay and filling.

Appendix

It is routine practice while preparing radiopharmaceuticals to avoid injecting air into the kit vial during preparation or dose withdrawal. The reasoning for this is that air contains oxygen, which has the potential to break down the radiochemical purity.

When one withdraws a dose (2 ml for example) from the EDS, 2-ml of air is allowed to enter the kit vial through the system's micropore vent so

TABLE 2. Average Hand Exposures (mR) Received during Radiopharmaceutical Preparation While Using Conventional 3-cc Syringe Shields

TLD chip hand locations	Conventional generator elution (1 assembly 6 elutions)	Kit preparation 3-cc shielded (15, 100-mCi doses)	Syringe filling 3-cc shielded (50, 25-mCi doses)	Syringe assay 3-cc shielded (50, 25-mCi doses)*	Total weekly exposure
Right hand fingertip positions R_3, R_4, R_7	125	111	16	13 (45%)	264
Right hand positions R_2, R_5, R_8	56	93	16	12 (42%)	177
Right hand positions R_1, R_6, R_9, R_{10}	37	78	19	7 (27%)	140
Left hand fingertip positions L_3, L_4, L_7	6	26	24	9 (27%)	64
Left hand positions L_2, L_5, L_8	6	18	9	10 (53%)	43
Left hand positions L_1, L_6, L_9, L_{10}	6	19	12	6 (33%)	42

*The percentages in the assay column represent the assay exposure expressed as a percentage of the total exposure in assay and filling.

TABLE 3. Average Hand Exposures (mR) Received during Radiopharmaceutical Preparation While Not Using Conventional 3-cc Syringe Shields

TLD chip hand locations	Conventional generator elution (1 assembly 6 elutions)	Kit preparation 3-cc unshielded (15, 100-mCi doses)	Syringe filling 3-cc unshielded (50, 25-mCi doses)	Syringe assay 3-cc unshielded (50, 25-mCi doses)*	Total weekly exposure
Right hand fingertip positions R_3, R_4, R_7	125	300	145	31 (18%)	600
Right hand positions R_2, R_5, R_8	56	174	64	10 (13%)	302
Right hand positions R_1, R_6, R_9, R_{10}	37	138	55	19 (25%)	248
Left hand fingertip positions L_3, L_4, L_7	6	30	20	8 (28%)	63
Left hand positions L_2, L_5, L_8	6	24	12	3 (20%)	45
Left hand positions L_1, L_6, L_9, L_{10}	6	24	18	3 (14%)	50

*The percentages in the assay column represent the assay exposure expressed as a percentage of the total exposure in assay and filling.

that pressure within the vial does not become excessive. Although we did not feel that this would cause excessive oxidation and subsequent deterioration, we did conduct a preliminary test for labeling stability on radiopharmaceutical kits that were attached to the EDS.

On ten occasions a vial of sodium pyrophosphate (PPi/ Mallinckrodt Inc.) was prepared according to the manufacturer's specifications. The amount of Tc-99m added was always approximately 90 mCi and the total volume used was always 2.5 ml. Chromatography was performed on all ten vials of Tc-PPi to establish percent of unbound Tc-99m, percent of bound Tc-99m, and percent of hydrolyzed Tc-99m. ITLC-SG strips (Bionucleonics, Inc., Kenilworth, NJ) were used, as were solvents of acetone and normal saline (0.9%). Care was exercised to insure adequate drying of the chromatography strips, which were subsequently counted in a Q.C. Analyzer (E.R. Squibb, Inc.).

Immediately following the initial labeling procedure, a 0.5 ml dose of Tc-PPi was withdrawn from the EDS every hour for five consecutive hours with shielded evacuated syringes. The dispensing system, and hence the Tc-PPi, was kept in a refrigerator when doses were not being withdrawn.

Five hours after preparation a final chromatographic assessment was performed on all ten vials of Tc-PPi using the same technique as previously described. For all ten vials of Tc-PPi the initial percent of bound Tc-99m was always greater than 94% and the initial percent of hydrolyzed product was always less than 6%. Likewise for all ten vials of Tc-PPi,

TABLE 4. Average Time per Operation for a Particular Phase of Radiopharmaceutical Preparation using Different Methods

Experimental dispensing system	Time (sec)	Conventional unshielded	Time (sec)	Conventional shielded	Time (sec)
Experimental generator elution	34.4	Conventional generator elution	43.1	Conventional generator elution	43.1
Experimental kit preparation	40.5	Kit preparation 3-cc unshielded	44.9	Kit preparation 3-cc shielded	57.0
Experimental syringe filling	11.2	Syringe filling 3-cc unshielded	13.0	Syringe filling 3-cc shielded	20.1
Experimental syringe assay	7.8	Syringe assay 3-cc unshielded	6.4	Syringe assay 3-cc shielded	10.4

the final percent of bound Tc-99m was always greater than 91% and the final percent of hydrolyzed product was always less than 8%.

Acknowledgments

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