A Simple Device for Efficient Transfer and Unit Dose Packaging of Xe-127: Concise Communication

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An inexpensive system has been devised for the efficient transfer of Xe-127 gas from the manufacturer's ampule into individual dose vials for patient use. By displacng the gas with an aqueous solution, the initial transfer is made from an ampule of known activity into an evacuated serum vial of predetermined volume with transfer efficiency greater than 99%. A similar principle is used to transfer Xe-127 from the stock serum vial into individual dose vials, with total xenon recovery exceeding 98%. Ability to deliver the desired activity to each vial is within 90–110% of that predicted by calculation. Reproducibility in delivering a given activity was excellent, with all vials falling between 95 and 105% of the mean activity. Stability studies showed that 94% of the Xe-127 activity can be removed from the vials with only 6% absorbed in the rubber stopper after 5 wk of storage. The device costs less than $25.00 and can be constructed easily from common laboratory materials.

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Recently Atkins et al. (1) have shown Xe-127 to be superior to Xe-133 for pulmonary ventilation studies. The 36.4-day Xe-127 decays only 2% per day, making it amenable to unit dose packaging.

Currently Xe-127 is not available from commercial suppliers for routine use in nuclear medicine. Brookhaven National Laboratories supplies it as a radiochemical shipped in an ampule as a concentrated gas, requiring extensive handling to obtain a dose for patient use.

A literature review indicates that many useful devices have been developed to obtain patient doses from multimillicurie ampules of Xe-133. Several of these devices deliver only xenon in saline (*2,3*); others (*4–6*) are designed to deliver xenon in gas or saline, but their complex design precludes easy construction in the hospital laboratory. A commercial device used in our laboratory was not reliable in providing accurate doses of xenon gas because the xenon is diluted with air each time a dose is removed. Veall (*7*) devised a tonometer system whereby water replaced Xe-133 removed through a rubber teat, but he did not report on its efficiency, accuracy, and precision. We have developed a simple, inexpensive device that will efficiently and accurately transfer Xe-127 gas from an ampule of high concentration into unit dose vials for patient use.

MATERIALS AND METHODS

Xenon-127 was purchased in 200-mCi quantities in a 2–3 ml saline-type glass ampule. The ampule contains an inner glass seal retaining the xenon under partial vacuum and an outer rubber seal crimped tightly in place. Figures 1 and 2 show the device in typical setups for xenon ampule-to-vial transfer and unit dose packaging, respectively. Table 1 describes the components used to assemble the device.

The volume of each xenon stock vial is measured

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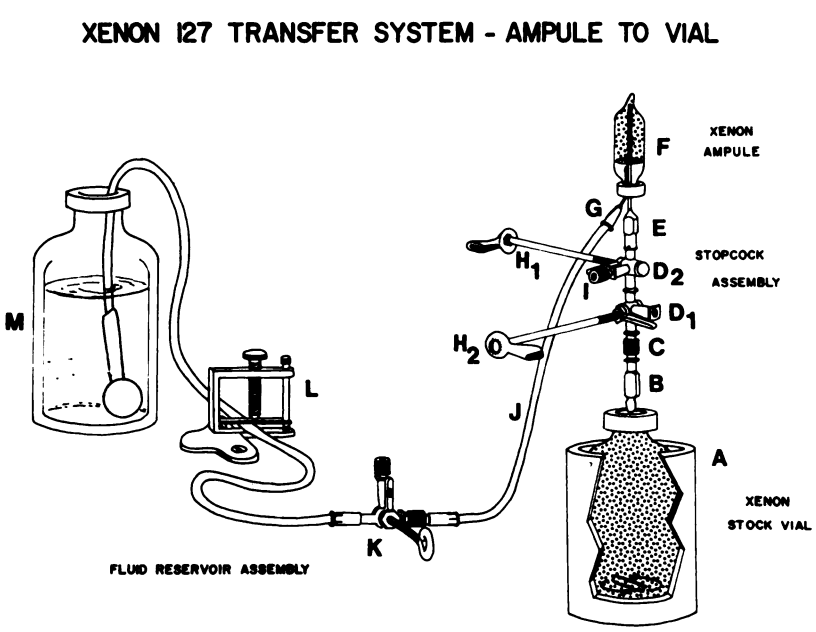

FIG. 1. System for displacing Xe-127 from the manufacturer's ampule to an evacuated stock vial using water or potassium iodide solution.

by displacing the air in the sealed vial with water and noting the volume used.

During xenon transfer, the displacing fluid used was either tap water or potassium iodide solution USP XIX (SSKI).

Unit dose vials were prepared as follows: (a) rubber stoppers (13-mm 1888 gray butyl V-32)* were boiled for 10 minutes in 1% sodium pyrophosphate solution, rinsed in distilled water and dried; (b) 2-ml glass vials were rinsed in distilled water and dried; (c) vials were stoppered, crimp-sealed and 2 ml of air removed using a syringe and 25-gauge needle.

Radioactivity measurements were made using a dose calibrator† set with calibration factor 422.

Procedures for transfer and unit-dose packaging were as follows:

Procedure A—Xenon transfer from ampule to stock vial. The device shown in Figure 1 was assembled and 25 ml of air was removed from the stock vial, creating a partial vacuum. The xenon ampule was attached by thrusting needle (E) through the inner glass seal. The ampule vacuum was relieved by opening stopcocks (D-1) and (D-2) to room air. Screw clamp (L) was closed and the reservoir attached to the ampule. Stopcocks (D-1) and (D-2)

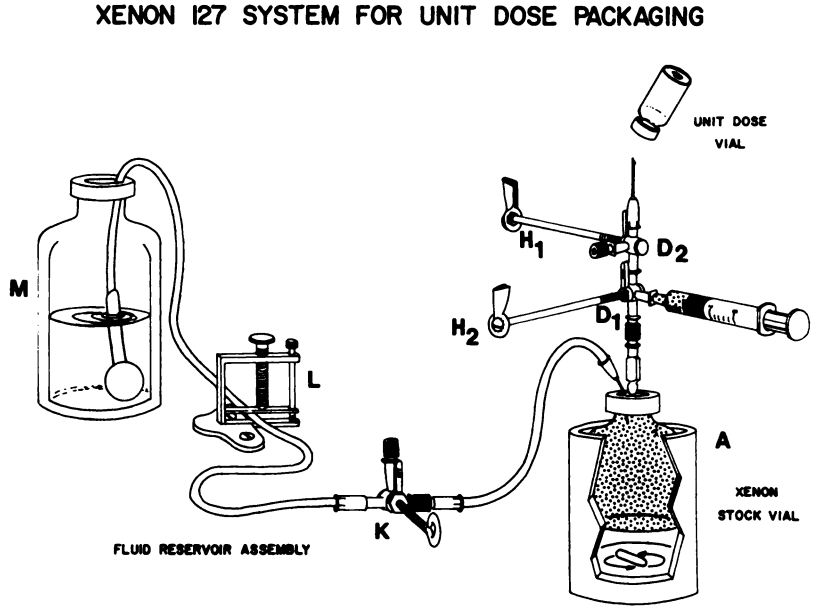

FIG. 2. System for unit dose packaging of xenon-127. An equal volume of fluid displaces the gas removed, maintaining a constant activity concentration.

TABLE 1. DESCRIPTIVE CODE FOR FIGURES 1 AND 2

Letter code	Description
A	Lead-shielded (¾-in.) 20-ml serum vial.
B	Modified stainless steel spinal needle; 17-gauge ⅛-in. blunt end.
C	Male-male Luer slip connector (B-D No. 3113)
D	Three-way plastic disposable stopcock.
E	Modified stainless steel spinal needle; 18-gauge 2-in. blunt end*.
F	Xenon ampule.
G	Disposable hypodermic needle; 21-gauge, 1-in. bent†.
H	Stopcock turn handle; metal turn button attached to 3/16-in. × 4-in. stove bolt screwed into existing hole in stopcock handle, tightened with lock nut.
I	Metal plug (B-D No. 3038).
J	I.V. tubing (Abbott Venotube® 30 No. 4481).
K	Stopcock on-off valve for reservoir assembly; 3/16-in. × 2-in. eye bolt for turn handle.
L	Fixed-position screwclamp (Fisher No. 5-848).
M	Fluid reservoir with metal sinker (B-D No. 3380).

* This needle changed to a 25-gauge ⅜-in. needle for unit-dose packaging (Fig. 2).

† This needle changed to a 17-gauge 1-in. needle for unit-dose packaging (Fig. 2).

were adjusted to allow communication between ampule and stock vial. Screwclamp (L) was released, allowing fluid to displace xenon into the stock vial. The ampule was removed and stopcocks opened to room air nullifying the remaining stock-vial vacuum. Activity transferred was determined as the difference in ampule assay before and after transfer, and this value divided by the stock-vial volume gave the activity concentration in mCi/ml.

Procedure B—Unit-dose packaging of Xe-127. Figure 2 shows the setup for unit dose packaging. The syringe and stopcocks were primed with xenon by drawing 0.5 ml of gas into the syringe and expelling any excess into a unit-dose vial. The volume of xenon needed for a dose was determined by dividing the desired activity (mCi) by the activity concentration (mCi/ml). The dose was obtained after adjusting the reservoir and stock vial stopcocks allowing fluid to displace the gas removed. The stopcocks were then readjusted to expell the dose into a unit-dose vial.

Following each transfer and packaging operation the device was disassembled and radioassayed for residual activity.

Ampule and stock-vial transfer efficiencies were determined by assaying each of them before and after transfer and calculating the percentage yield. Geometry correction for measuring xenon in these containers filled with gas only and finally with liquid was approximated as follows: an empty ampule and 20-ml vial were tightly sealed and evacuated. One mCi of Xe-127 was added and each filled to near capacity with SSKI. The same was done using water. Fluid-to-gas correction factors were determined as the ratio: (activity before fluid addition)/(activity after the addition).

Retention of Xe-127 in unit-dose vials was determined by radioassaying a series of six vials, containing 2 mCi each, at weekly intervals for 5 wk, correcting for decay and comparing measured and theoretical activities. At the end of 5 wk each vial was ventilated and reassayed. Vials were then disassembled and the rubber stoppers assayed separately for residual activity.

Radiation dose to the fingertips during the complete transfer operation was measured using thermoluminescent dosimetry. Dosimeters were attached to the distal pad of the thumb and index finger of each hand.

RESULTS AND DISCUSSION

Transfer efficiencies. Table 2 summarizes xenon transfer efficiencies. Ampule-to-vial transfer efficiency was typically greater than 99% for water or SSKI. Efficiency for stock vial to unit-dose vial transfer was 93 and 99% for water and SSKI, respectively. Initially, water was used due to xenon's low solubility in aqueous fluids (*8*). Alternatively, we chose to use the concentrated salt solution, SSKI, taking advantage of the "salting out" effect to reduce xenon solubility. The use of SSKI increased transfer efficiency by 6%.

Table 3 lists the fluid-to-gas correction factors developed due to the shielding effect of fluid at the end

TABLE 2. XENON-127 TRANSFER EFFICIENCY

	Percentage transfer (mean and range)*	
Transfer fluid	Ampule to stock vial	Stock vial to u.d. vials
Water	99.13 (98.1–99.7)	92.9 (92.4–93.3)
SSKI	99.7 (99.3–99.9)	98.8 (98.6–99.0)

* Mean of 3 separate transfers.

TABLE 3. FLUID-TO-GAS CORRECTION FACTORS

Fluid	Ampule	Serum vial
Water	1.06	1.11
SSKI	1.37	1.45

TABLE 4. UNIT DOSE PACKAGING OF XENON-127

Vial number	Gas volume (ml)	Activity desired (mCi)	Act. conc. (mCi/ml)	Mean values ± s.d. Activity obtained (mCi)	*Dosing accuracy	*Dosing precision
1	0.5	—	8.13†	2.26	Stopcock prime	
2–6	1.0	8.13	8.50	8.50 ± 0.40	104.5 ± 4.9	99.9 ± 4.7
7–11	1.2	10.00	8.44	10.12 ± 0.07	101.2 ± 0.7	100.0 ± 0.7
12–16	1.45	12.00	8.36	12.13 ± 0.08	101.1 ± 0.7	100.0 ± 0.7
17–19	1.7	14.00	8.33	14.16 ± 0.17	101.2 ± 1.2	100.0 ± 1.2
20	1.2	—	8.44	10.00	End of run	

* Accuracy—as percentage desired activity; precision: as percentage mean activity obtained.
† Predicted activity (202 mCi/24.85 ml).

of a xenon transfer operation. Thus, a stock vial filled with SSKI and reading 1 mCi would read 1.45 mCi if only gas were present. The data used to calculate the transfer efficiencies reported in Table 2 were adjusted to correct for this shielding effect.

Our earlier experiments employed a small magnetic stirring bar in the stock vial with the idea of ensuring uniform gas mixing if the device containing xenon were to be stored before packaging. Our latest transfer, however, has been done successfully without this stirring bar, which simplifies the device considerably.

We recently discovered that ampule-to-vial transfer can be made instantaneously by air displacement, eliminating the need for the fluid reservoir in this step. Transfer efficiency was greater than 99% for the two transfers.

Unit-dose packaging. Table 4 shows data from a single unit-dose packaging operation, to illustrate typical results obtained with all operations. Initially, a predicted activity concentration was calculated from the total activity and volume of the stock vial as mentioned in Procedure A. After a few doses were prepared, the true concentration was calculated. The volume of gas needed for subsequent doses was calculated by dividing the desired activity by the true activity concentration. In principle, the activity concentration should remain fairly constant, because gas removed is replaced by an equal volume of fluid in which xenon is poorly soluble. This was supported by data in Table 4, from which the true concentration mean and s.d. was 8.41 ± 0.07 mCi/ml as determined from unit-dose-vial measurements. This value was 3.4% greater than that predicted initially (8.13 mCi/ml), which may be accounted for by the geometry difference between unit-dose serum vials and the xenon ampule whose measurements were used to calculate the total activity initially.

The accuracy and precision of doses 2–6 were less than subsequent doses because of the measurement differences mentioned above and perhaps due to incomplete priming of the stopcock-syringe system initially. The overall dosing accuracy was within 90–110% of that predicted by calculation, and dosing precision was within 95–105% of the mean activity for a dose group.

At the end of a packaging operation, residual xenon activity in the stopcocks and dosing syringe was typically within 1–2% of the original activity.

In preparing unit-dose vials we found that 4 or 5 vials each of 8, 10, 12, and 14 mCi provided sufficient Xe-127 for 20 patients during a 3- to 4-wk period, each receiving between 5 and 8 mCi per dose. The total cost to our hospital is $560.00, including shipping and handling for 200 mCi. This represents an average cost of $28.00 per patient dose.

Retention and removal of xenon. At the end of 5 weeks' storage, the six vials retained an average 95% of the theoretical Xe-127 activity. The range was from 94 to 97%, with an approximate loss of 1% per week. Of the activity remaining in the vials, 94% could be removed by ventilation and 6% remained sorbed to the rubber stopper. Results were identical for all six vials.

Radiation dose. The results of radiation dose measurements appear in Table 5. Assuming the highest dose received and one xenon packaging operation per month, an approximate dose of 1.6 rem (0.54 × 3) to the hands would be received per

TABLE 5. RADIATION DOSE TO THE HANDS

Dosimeter position	Dose in rads ± 10%*
Right thumb	0.44
Right index finger	0.31
Left thumb	0.54
Left index finger	0.36

* Accuracy of measurement method.

quarter year, which is about 1/15 the NCRP limit of 25 rem.

FOOTNOTES

* West Co., Phoenixville, Pa.
† Capintec CRC-4, Montvale, N.J.

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