Dose Calibrator Performance and Quality Control

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Two different dose calibrators were studied and their performance measured using the following tests: (A) linearity of response over all activity ranges, (B) accuracy when measuring some commonly used radionuclides, (C) the effect of container configuration on the accuracy of measurement, and (D) daily and long-term stability of the instrument. For each instrument tested, a good linear response was observed for activity measurements below 100 mCi, but there was evidence of non-linearity at higher activity levels. The accuracy of each instrument was checked using radionuclide standards from two different sources. The measurements indicated a significant difference between standards that was not possible to resolve. Additionally, assessment of accuracy for a dose calibrator with any standard is difficult unless the manufacturer's calibration procedure is known. The effect of container configuration and photon energy on the accuracy of measuring ^{99m}Tc, ^{131}I, and ^{125}I indicated that large correction factors may be necessary when making measurements of ^{125}I. The measurement of a long-lived standard such as radium, cross calibrated for several radionuclide settings, is an effective means for assurring instrument stability and quality control on a daily and long-term basis.

The radionuclide dose calibrator is used routinely in the clinical nuclear medicine laboratory to make measurements of radiopharmaceutical doses prior to patient administration. Its accuracy and reliability cannot be easily determined by the user unless he understands the instrument's basic structure, method of calibration, and operational pitfalls. A search of the text and research literature indicates that much detailed information is written about ionization chambers per se, with less concern given to dose calibrators *(1-7)*. Several investigators have reported on the accuracy of dose calibrators used in nuclear medicine, Genna et al. *(8)* used commercial standard sources of ^{57}Co, ^{133}Ba, and ^{137}Cs to check the accuracy of four different dose calibrators and noted inaccuracies ranging from -16 to +11%. Payne et al. *(9)* considered the parameters of accuracy, geometry, and linearity and pointed out that accuracy of measurement is influenced by the type of container, especially with low-energy sources like ^{133}Xe. Hare et al. *(10)*, who prepared their own standards and tested dose calibrators in 14 nuclear medicine laboratories, found inaccuracies as high as 15-25%. They also pointed out that simply purchasing a long-lived standard like cesium or radium to check dose calibrator accuracy is not a foolproof method. We agree with these reports since many factors must be considered in making accurate measurements of each radionuclide.

During our present work we found that one dose calibrator manufacturer (Capintec Inc., Mount Vernon, NY) has made significant efforts to update its calibration procedure with major considerations for radionuclide decay schemes, photon energies, and the influence of container configuration on accuracy. Although these efforts are a step in the right direction, the responsibility for making accurate measurements and assurring high-quality operation of the dose calibrator lies with the user.

The rapid growth of imaging procedures at our institution compelled us to buy larger ^{99m}Tc generators. We became suspicious of dose calibrator function when Monday morning eluates from a 500-mCi generator were reading about the same as those from a 400-mCi unit; usually about 740 mCi.

From our investigations *(11)* and those of others, we decided to look more closely at dose calibrator operation and quality control in the nuclear medicine laboratory.

Construction and operation. The functional parts of a dose calibrator include a power supply, ionization chamber, current-to-voltage amplifier, voltage gain amplifier, and output display (Fig. 1). The heart of the dose calibrator is the ionization chamber. The magnitude of current produced in the chamber depends upon the quantity of radioactivity present. Because of differences in the types of radiations emitted and photon energy and abundance, equal activities of different radionuclides will generate different current flow. Thus, 1 mCi of ^{99m}Tc will not generate the same current as 1 mCi of ^{131}I.

In order to read out the correct activity, the circuit includes a voltage gain amplifier that puts out different voltages to drive the output display according to the particular radionuclide being measured. In Fig. 1 the range selection switch consists of electrical resistors to provide different activity ranges. An additional plug-in resistor in the isotope calibration box provides an adjustment in the feedback gain of the voltage amplifier so that equal activities of all radionuclides will readout the same value on the display.

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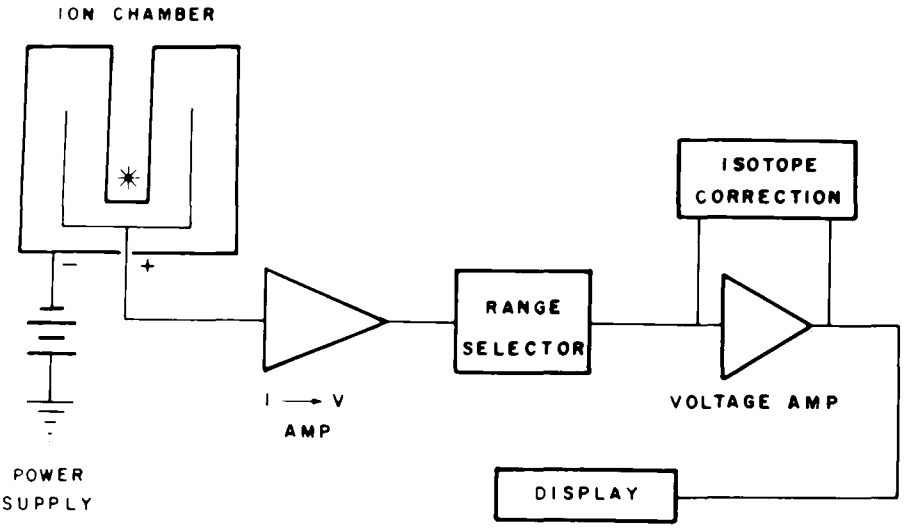

FIG. 1. Block diagram of dose calibrator.

Materials and Methods

RADX Mark V and Squibb CRC-6A dose calibrators were used for all experimental procedures. A linearity check for each instrument was made using ^{99m}Tc-sodium pertechnetate sources contained in 20-ml serum vials. Five sources ranging in strength from 1,000 to 0.1 mCi were used to check the response of each activity range. Slopes of the decay curves were determined using a log-linear least-squares fit of the data and compared to the currently accepted decay constant for ^{99m}Tc.

An assessment of accuracy of each instrument was made using two sets of standard sources. Technetium-99m and ^{131}I sources contained in 3-ml plastic syringes were made and calibrated using the method of Hare et al. *(10)*. Additional sources of ^{99m}Tc, ^{131}I, and ^{125}I were obtained from New England Nuclear Corporation as 5-ml aqueous solutions contained in sealed glass ampules. Each standard was calibrated by measurement in a 4π configuration using a gamma ionization chamber previously calibrated with standards certified by the National Bureau of Standards. Overall error for these sources ranged from $\pm$ 3.9 to $\pm$ 4.2%.

Each dose calibrator was left on at all times and properly zeroed before measurement. Five independent measurements were made for each source and the results averaged and compared to the calibrated values.

Determination of the effect of container configuration on accuracy for measuring radionuclides with widely differing photon energies was studied in both instruments. Solutions of ^{99m}Tc, ^{125}I, and ^{131}I were prepared to contain approximately 40 μCi/ml. Five-milliliter (200 μCi) samples of each solution were pipetted into tared containers which consisted of 5-ml glass ampules, 10-ml glass serum vials, and 5-ml plastic syringes. Three samples of each type container were prepared and reweighed on an analytical balance. Solution weights were determined by subtracting the tare from weights of filled containers. Each sample was measured in the dose calibrator and its specific concentration calculated as microcuries/g of solution. The values for each configuration were averaged and compared.

Daily and long-term stability of each dose calibrator was studied using a 1-mCi radium source contained in a platinum needle. The source was positioned in a plastic holder designed to fit a fixed geometry for each instrument tested. Measurements were made using several radionuclide calibration settings on model CRC-6A and with different plug-in modules for the Mark V. Resistance values for the Mark V isotope modules were determined and adjusted to the manufacturers specifications prior to experimentation. The radium source was positioned into the well of the Mark V and readings were obtained using all plug-in modules, establishing baseline "radium values" for each isotope. For the remainder of the experiment only five modules were used to test instrument stability. In a similar manner the model CRC-6A unit was checked with the radium source at several isotope calibration factor settings ranging from 030 to 778 on the calibration dial. On a daily basis each instrument was checked at the same isotope settings and the respective "radium values" were recorded for comparison.

Results and Discussion

For this experiment a good linear response of the dose calibrator is one which gives a straight-line logarithmic plot of the measured activity on the y axis versus time on the x axis, with the slope of the line equal to the decay constant for ^{99m}Tc. The currently accepted half-life for ^{99m}Tc is 6.03 h *(12)*, from which the decay constant λ is calculated to be 0.1149 h^{-1}. Figure 2 shows a plot of the decay curves for the 100-, 10-, 1-, and 0.1-mCi ^{99m}Tc sources for each dose calibrator. It indicates the experimentally determined decay constant and the deviation from true value expressed as percent error. Each plot is quite linear, with slight deviations from the true slope.

Figures 3 and 4 show the response of each dose calibrator to high activity levels. The Mark V response

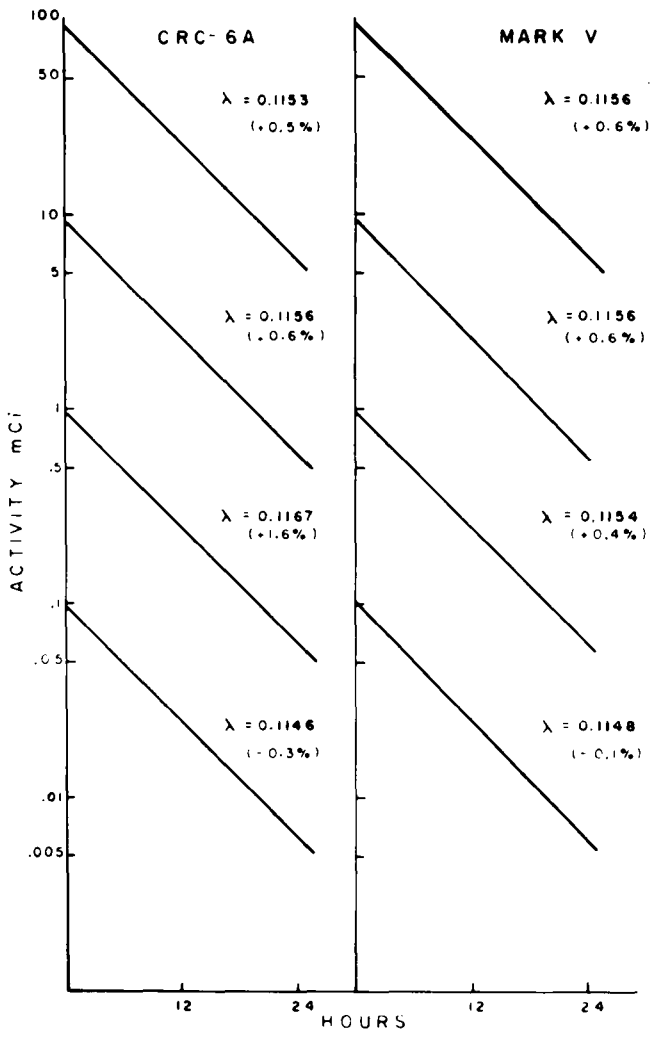

FIG. 2. Squibb CRC-6A and RADX Mark V dose calibrator response to decay of 100-, 10-, 1- and 0.1-mCi ^{99m}Tc sources. Decay curve slopes are expressed as decay constant x in reciprocal hours, with deviation from true slope as percent error.

indicates a "saturation effect" above the 700-mCi activity level (Fig. 3). A check on the linearity of the dose calibrator amplifier using an external current source indicated that the output voltage of the instrument was linearly proportional to current input up to an equivalent current of 1,000 mCi. Therefore, it was concluded that the "saturation effect" was due to the nonlinearity characteristics of the ion chamber rather than saturation of the current amplifier for that amount of current input.

Below the 700-mCi activity level the response was quite linear ($\lambda = 0.1157\ h^{-1}$ between 709- and 79-mCi activity levels).

Some nonlinearity is evident in the model CRC-6A decay curve over the entire activity range between 100 and 1,000 mCi, but most prominently above 400 mCi (Fig. 4).

To quantify the extent of nonlinearity at high activities, decay curves in Figs. 3 and 4 were analyzed by activity segments. Calculated for each segment were the slope (λ), the percent change in slope from that of true ^{99m}Tc decay, and the half-life based upon the experimental slope (Table 1). The response of the Mark V dose calibrator was consistently 732 mCi during the first 4 h of decay (saturation effect), dropping to 709 mCi at the fifth hour. Below 709 mCi each activity segment had a slope that varied by not more than 1% from true ^{99m}Tc decay. Thus, the Mark V was considered to have good linear response for measurements below 700 mCi. When this decay curve was extrapolated back to the y intercept (t=O) the original activity was found to be 1,260 mCi.

For the model CRC-6A decay curve the activity segment between 1,023 and 549 mCi was most nonlinear, having a 10% deviation from true slope. The most linear portion was the 146–74-mCi segment, with only 1.5% deviation. This change to a more positive slope at higher activities is probably from recombination effects in the chamber, owing to high density of ion pairs. This would produce falsely low readings for high-activity sources. To estimate the true initial activity of the source with the model CRC-6A, the three lowest activity values from the decay curve data were used since they occurred in the most accurate segment of the decay curve. Using the expression $A_0 = Ae^{\lambda t}$, zero-time activities (A_0) for each data point were calculated and averaged. The result gave a y intercept at 1,183 mCi, which was 13.5% greater than the 1,023 mCi originally determined with the instrument.

It should be pointed out that such recombination effects at high activities are not very serious from a clinical viewpoint since all patient doses are measured in the lower activity ranges where both dose calibrators

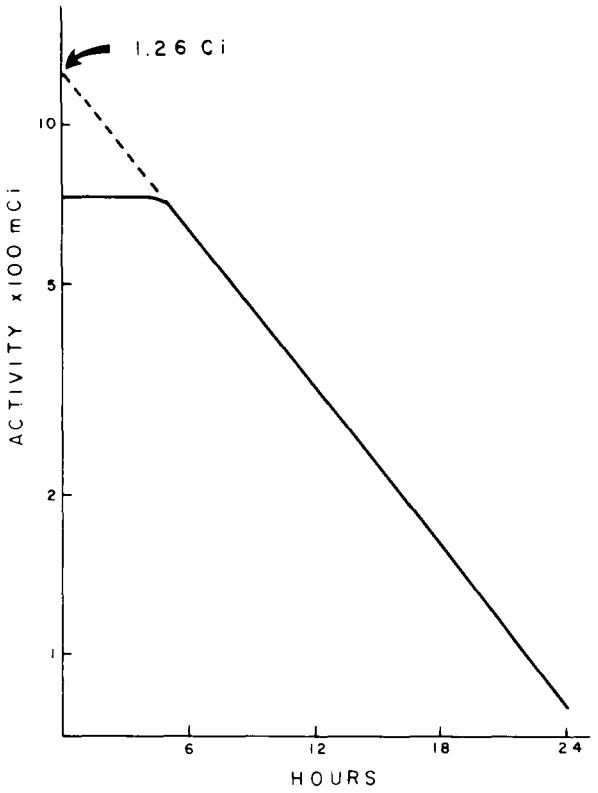

FIG. 3. Decay curve for 1 Ci source ^{99m}Tc measured with RADX Mark V. "Saturation effect" is shown at levels above 700 mCi followed by linear response ($\lambda = 0.1157\ h^{-1}$). Extrapolation (dashed line) indicates source had 1.26 Ci initial activity.

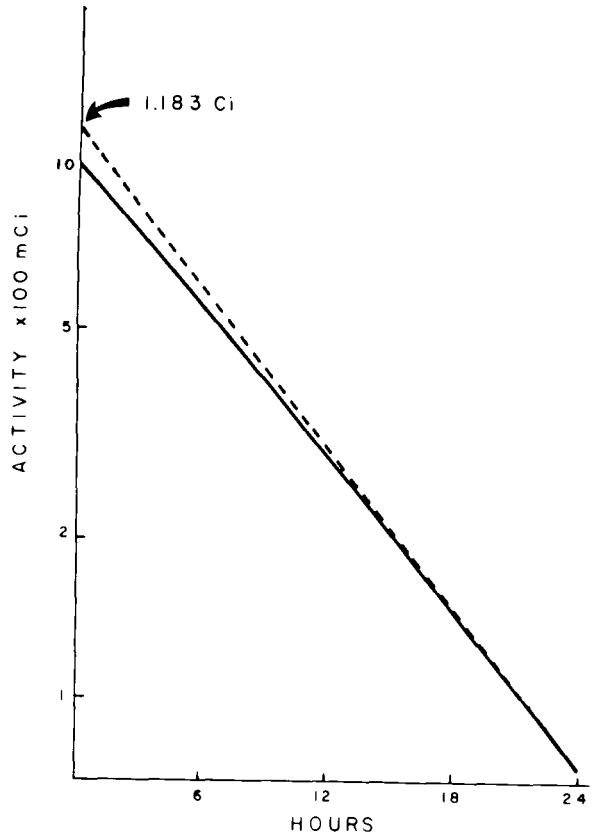

FIG. 4. Decay curve for 1-Ci source of ^{99m}Tc measured with Squibb CRC-6A. Nonlinear response (solid line) is most prominent at high activity levels. Dashed line indicates 1.183 Ci as initial activity.

demonstrated good linear response. However, the extent of such effects should be known if accurate measurement of bulk, high-activity sources such as generator eluates is made.

We have discontinued making bulk assay of generator eluates because of high radiation dose to the hands and fingers. From film exposure measurements Howley et al. *(13)* found the unshielded surface exposure from 600 mCi of ^{99m}Tc in a 10-ml serum vial to be 7.2 R/min. Our alternate method, which gives more accurate results and less radiation exposure, is to measure 1 ml of the eluate in a plastic syringe, returning 1 ml to the elution vial and reassaying the syringe for residual activity in the needle. The difference in the two values is the activity per 1 ml. This value multiplied by the total volume of eluate yields the total activity in the vial.

Container configuration and photon energy. The effect that container configuration had on the accuracy for measuring radionuclides of differing photon energy is shown in Table 2. The average specific concentration for each radionuclide in serum vials and plastic syringes was compared to that in ampules and the percent difference calculated. The results indicated that serum vial and plastic syringe measurements differed from ampule measurements by only a few percent for ^{99m}Tc and ^{131}I, but were significantly different for ^{125}I. These differences are due to the increased thickness of glass in serum vials and lower density of plastic in the syringes. The substantial difference for ^{125}I is due to easy attenuation of its 27- and 35-keV photons by container material.

Standards measurement. Table 3 lists the results of standards measurements made with each dose calibrator. Percent error was calculated as 100 times the difference between measured and calibrated activity divided by the calibrated activity. The spread in percent error between

TABLE 1. Segmental Analysis of High-Activity Decay Curves in Dose Calibrators

Dose calibrator	Activity range segment (mCi)	λ (h^{-1})	Percent difference	T½
Mark V	732-709		Saturation range	
	709-316	0.1159	−0.9	5.98
	316-157-	0.1158	−0.8	5.98
	157- 79	0.1154	−0.4	6.01
CRC-6A	1023-549	0.1034	+10.0	6.70
	549 -285	0.1097	+ 4.5	6.32
	285 -146	0.1107	+ 3.7	6.26
	146 - 74	0.1132	+ 1.5	6.12

TABLE 2. Effect of Container Configuration on Radioassay of ^{99m}Tc, ^{125}I, and ^{131}I

Radionuclide	Dose calibrator*	Specific concentration (μCi/g of solution) Ampule	Serum vial	Plastic syringe
^{99m}Tc	C	44.5	44.0 (−1.1%)	45.2 (+1.4%)
	M	45.2	43.8 (−3.3%)	46.7 (+3.3%)
^{131}I	C	37.1	35.8 (−3.5%)	38.6 (+4.0%)
	M	34.9	34.6 (−0.8%)	35.5 (+2.4%)
^{125}I	C	39.6	20.4 (−48.4%)	57.8 (+45.9%)
	M	25.9	13.5 (−47.8%)	33.7 (+29.0%)

**C = CRC-6A; M = Mark V.*

TABLE 3. Standard Measurements in Dose Calibrators

Isotope standard	Dose calibrator	Container*	Measured activity	Calibrated activity	Percent error
^{99m}Tc (mCi)	M	G.A.	2.36	2.19	+ 7.7
		P.S.	23.5	18.3	+28.4
	C	G.A.	2.13	2.19	− 2.7
		P.S.	21.3	18.1	+17.7
^{131}I (μCi)	M	G.A.	192	207	− 7.3
		P.S.	277	263	+ 5.3
	C	G.A.	213	208	+ 2.4
		P.S.	308	263	+17.1
^{125}I	M	G.A.	127	200	−36.5
		P.S.	—	—	—
	C	G.A.	196	200	− 2.0
		P.S.	—	—	—

**G.A. = glass ampule; P.S. = plastic syringe.*

ampule and syringe measurements was about 20% for ^{99m}Tc and 12% for ^{131}I in both calibrators. This apparent discrepancy between standards could not be explained by differences in plastic and glass causing differential photon absorption since data from the previous experiment (Table 2) indicated such differenes to be small.

Measurements with the model CRC-6A showed good agreement between measured and calibrated activities for standards in ampules but not for plastic syringes. Since this was a new instrument we contacted the manufacturer for details of the calibration procedure. They indicated that radionuclide calibration factors were determined experimentally and their accuracy confirmed using certified standards in 5-ml glass ampules. Because standards in ampules used by us were of similar configuration and traceable to the National Bureau of Standards, we chose to use these standards for our accuracy check.

Details of the calibration procedure for the Mark V instrument were not readily available from the manufacturer. Therefore, it was not known what configuration was used to determine resistence values for isotope plug-in modules. It was evident from the data in Tables 2 and 3 that some adjustment was needed with both dose calibrators to improve accuracy for measurements made in plastic syringes.

Data from these tables were combined to determine the overall error in making measurements of ^{99m}Tc, ^{131}I, and ^{125}I in 5-ml plastic syringes with both dose calibrators (Table 4). The overall percent error is the sum of the percent error in standard ampule measurements (Table 3) and the percent error due to geometric differences between glass ampules and plastic syringes (Table 2). Correction factors are calculated as 100/(100 + percent error). For example, the correction factor for measuring ^{125}I in a 5-ml plastic syringe using the Mark V is calculated as 100/(100 - 6.6), or 1.07.

From this data it is evident that large errors exist when making measurements of ^{125}I in plastic syringes with the model CRC-6A, unless the correction factor is applied. Correct measurements would require dividing the desired activity of ^{125}I by the correction factor and reading the new activity. Thus, if 25 μCi of ^{125}I is desired one would need to measure 36 μCi in a plastic syringe to obtain the correct activity. (The 36 μCi value is obtained by dividing the desired activity, 25 μCi, by the correction factor, 0.69, obtained from Table 4.) If 25 μCi were measured in the syringe without correction, the patient would be underdosed.

TABLE 4. Overall Errors and Correction Factors for ^{99m}Tc, ^{131}I, and ^{125}I in Plastic Syringes

Radionuclide	Dose calibrator *	Overall percent error	Correction factor
^{99m}Tc	C	− 1.3	1.01
	M	+11.0	0.90
^{131}I	C	+ 6.4	0.94
	M	− 4.9	1.05
^{125}I	C	+43.9	0.69
	M	− 6.6	1.07

C = CRC-6A; M = Mark V.

TABLE 5. Dose Calibrator Radium Values for Several Radionuclides

Radionuclide	Radium values (mCi) CRC-6A	Mark V
^{99}Mo	6.60	14.4
^{99m}Tc	4.43	10.3
^{131}I	3.43	3.50
^{125}I	2.01	7.91
^{226}Ra	0.93	1.11

Dose calibrator stability. Table 5 lists activity readings of the ^{226}Ra source for several radionuclide settings with each dose calibrator. These "radium values" for each radionuclide served as a baseline for comparing all subsequent daily readings. The values should not change significantly over a long period of time except to reflect decay of the standard. This is not a problem with radium, but periodic change will be noted if ^{137}Cs or ^{57}Co standards are used.

Over an eight-month period of routine checking we found both instruments to be very stable. The difference between the highest and lowest value recorded for any radionuclide setting never exceeded 3%. Occasionally the contacts for the ^{99m}Tc plug-in module came loose, affecting the reading, but no other problems were noted.

Several radionuclide settings were checked daily in order to identify potential problems that could occur with the dose calibrator. For instance, if the readings for each setting remained the same on a continual basis, one could assume that the instrument was working properly. If all the readings change in the same direction, one might suspect that the unit has drifted from calibration. If only one or two readings change, one could suspect that the isotope calibration factor was incorrect or that the isotope module was not in proper adjustment.

Additionally, if the instrument requires repair or recalibration, the baseline values provide a means of assurring that the unit will make measurements with the same degree of accuracy that it did before repair. This proved valuable to us since the model CRC-6A required replacement of the display module. Subsequent check with the radium source indicated a slight but insignificant rise in readings for all radionuclide settings checked.

Conclusions

The data from this experiment point out that accurate measurements of all radionuclides cannot be made with assurance unless the user knows the calibration

procedure for the dose calibrator. More specifically, he must know the exact container configuration used in establishing radionuclide calibration factors, especially for those radionuclides emitting low-energy photons, where attenuation in container material may be substantial. Recent investigations by Suzuki et al. *(14)* refer to this problem for several radionuclides, most notably ^{133}Xe, ^{125}I, ^{169}Yb, ^{201}Tl, ^{197}Hg, and ^{123}I.

The authors feel that a great benefit would be gained by the nuclear medicine community if all dose calibrator manufacturers would stipulate the exact type container to use for each radionuclide. Since the majority of radiopharmaceutical doses are measured in 1-, 3-, and 5-ml disposable plastic syringes, radionuclide calibration factors for these configurations would be more appropriate.

Another benefit would be gained if the manufacturer would cross calibrate each radionuclide setting with a long-lived source like ^{226}Ra, ^{60}Co, or ^{137}Cs at the time of initial calibrations. Then the source and its cross calibrated values could be supplied with the dose calibrator so that the user has a means of confirming both precision and accuracy as established by the manufacturer. Presently no such system exists and the responsible user must obtain his own standard sources to confirm instrument accuracy.

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