Determination of the Efficiency of Commercially Available Dose Calibrators for β-Emitters

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Objectives: The goals of this investigation are to determine whether commercially available dose calibrators can be used to measure the activity of β-emitting radionuclides used in pain palliation and to establish whether manufacturer-supplied calibration factors are appropriate for this purpose.

Methods: Six types of commercially available dose calibrators were studied. Dose calibrator response was controlled for 5 γ-emitters used for calibration or typically encountered in routine use. For the 4 most commonly used β-emitters (^{32}P, ^{90}Sr, ^{90}Y, and ^{169}Er) dose calibrator efficiency was determined in the syringe geometry used for clinical applications. Efficiency of the calibrators was also measured for ^{153}Sm and ^{186}Re, 2 β-emitters with significant γ-contributions. Source activities were traceable to national standards.

Results: All calibrators measured γ-emitters with a precision of ±10%, in compliance with Swiss regulatory requirements. For β-emitters, dose calibrator intrinsic efficiency depends strongly on the maximal energy of the β-spectrum and is notably low for ^{169}Er. Manufacturer-supplied calibration factors give accurate results for β-emitters with maximal β-energy in the middle-energy range (1 MeV) but are not appropriate for use with low-energy (^{169}Er) or high-energy (^{90}Y) β-emitters. β-emitters with significant γ-contributions behave like γ-emitters.

Conclusion: Commercially available dose calibrators have an intrinsic efficiency that is sufficient for the measurement of β-emitters, including β-emitters with a low maximum β-energy. Manufacturer-supplied calibration factors are reliable for γ-emitters and β-emitters in the middle-energy range. For low- and high-energy β-emitters, the use of manufacturer-supplied calibration factors introduces significant measurement inaccuracy.

Key Words: dose calibration; β-emitters; radiation therapy; palliation

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The analgesic radiation therapy of bone metastasis calls for β-emitting radionuclides able to concentrate at the site of bone repair and deliver a dose sufficient for pain palliation for a period of time (*1*). Dosimetry of these radionuclides is difficult because of the complex geometry of bone marrow and the variability of uptake. The aim of this palliative therapy is not to deliver the highest possible dose to the tumor but to obtain a reduction in bone pain. The principal limiting factor for therapy is the depression of bone marrow activity. Doses delivered are much lower than those in conventional radiation therapy, and standardized activities based on clinical experience are used.

Before treatment, the activity to be delivered to the patient must be checked. This measurement is performed in a dose calibrator with the radionuclide in either the manufacturer's glass vial or, preferably, in the syringe to be used for injection. Dose calibrator sensitivity has been studied extensively (*2,3*). Commercially available calibrators are supplied with calibration factors for commonly used γ-emitting radionuclides. However, some problems have been reported in the accuracy of these factors, and Zimmerman and Cessna (*4*) reported errors of about 10% for positron emitters. In addition, the presence of low-energy x- or γ-ray components can introduce a high dependence of dose calibrator sensitivity on measurement geometry because of the high attenuation between the source and the sensitive volume. The use of a copper filter to absorb low-energy radiation and stabilize calibrator response has been proposed (*5*).

Radiopharmaceuticals used for bone palliation are delivered to hospitals in glass vials, and dose calibrator ionization chambers are usually calibrated for measurement in these vials. However, the activity check is best performed in the syringe that will be used for injection. The difference in calibration factor for glass vial and syringe measurements should not be significant for γ-emitters, although differences on the order of 10% for ^{67}Ga and ^{201}Tl have been reported for a Capintec (Capintec, Inc., Pittsburgh, PA) CRC-35 calibrator (*6*).

For β-emitters, dose calibrator activity measurement is mainly based on indirect detection. β-Radiation is absorbed in the radioactive solution itself or in the walls of the recipient vial or syringe, producing bremsstrahlung radia-

TABLE 1
Calibrators Used

Activimeter type	VEENSTRA VDC-405	Atomlab 100	Capintec CRC	Isomed 1000	Centronic* IG12
Gas	Argon	Argon	Argon	Xenon/argon	Argon
Pressure (bars)	12	5	12	10	2
Well dimensions (mm)	69 × 260	64 × 260	61 × 254	47.5 × 220	50 × 315
Shielding (mm lead)	3	6.4	12.7	4	50

*The electronic measurement circuit was developed in our institute.

tion that is measured by the ionization chamber. Because of this mechanism, sensitivity to β-emitters is much less than sensitivity to γ-emitters, since the energy fraction converted to bremsstrahlung is small and attenuation of the low-energy bremsstrahlung is significant. In addition, the amount of the bremsstrahlung produced depends strongly on the atomic number of the material from which it originates.

Problems with the sensitivity of ionization chambers to β-radiation were first discussed in connection with the determination of correction factors for calibrator response to γ-emitters with a nonnegligible β-component (*2*,*3*). The response of commercially available ionization chambers to β-emitters has been studied for different nuclides: ^{89}Sr (*7*), ^{186}Re (*8*), and ^{186}Re and ^{188}Re (*9*). Each of these authors reported variability of response with measurement geometry and stated the necessity of dispensing with calibration factors that are specific to the measurement geometry used in routine practice. For ^{90}Y, an error of 50% in the calibration factor of a commercially available detector has been reported (*10*).

Most commercially available ionization chambers are provided with calibration factors for commonly used β-emitters, but the specific conditions of these calibrations (geometry, recipient type) often are not specified and usually correspond to a measurement in vial geometry. Assuming that ionization chamber response is approximately constant for β-emitters in the middle-energy range (0.7–1.3 MeV), the problem remains that chamber response may differ significantly for low-energy β-emitters because of wall attenuation and for high-energy β-emitters (>2 MeV) in which β-radiation contributes directly to ionization in the chamber's sensitive volume.

The aim of the present work is to investigate the intrinsic efficiency (electrical signal per unit activity) of different commercially available calibrators for β-emitters most commonly used in bone palliation therapy. The appropriateness of the measurements performed to control the activity delivered to patients is considered, and the possible need for a calibration methodology for routine use is discussed.

IONIZATION CHAMBER SENSITIVITY

For measurements with a dose calibrator, the radioactive source to be measured is placed in a well surrounded by a gas volume to which a charge collection voltage is applied. The resultant measured current is directly proportional to the source activity. Stability and robustness of the system are high because of the almost 4π measurement geometry. The system operates in current mode (i.e., not based on the counting of each event), and, as a result, the sensitivity of the system is relatively low. For γ-emitters, sensitivity is of the order of 10 pA/MBq, which corresponds to a mean energy deposition of about 1 keV per disintegration. For β-emitters, the energy fraction converted to bremsstrahlung

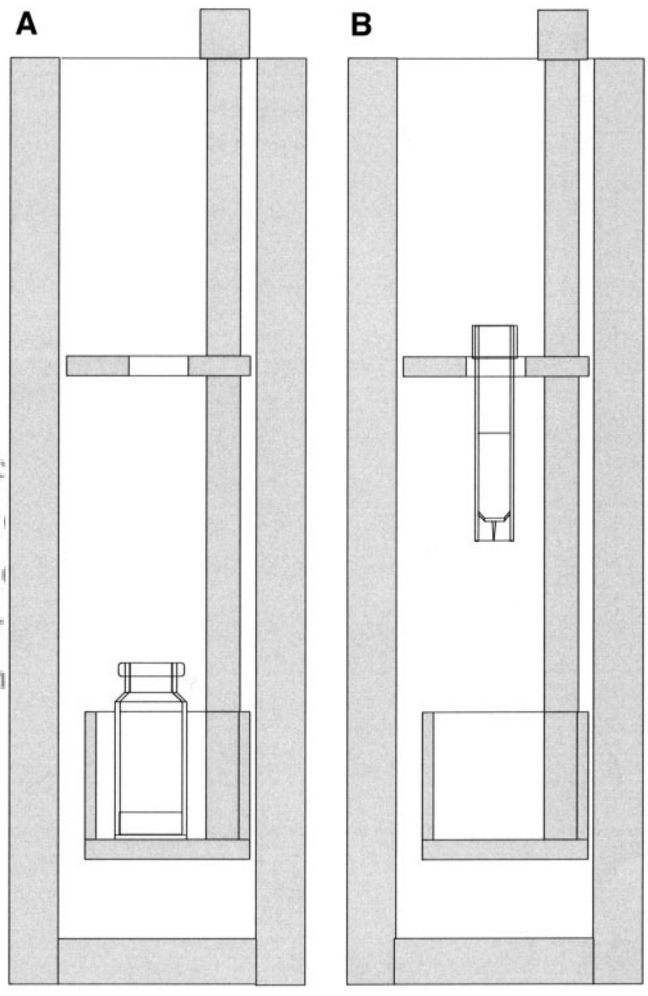

FIGURE 1. Positioning of glass vial and syringe in dose calibrator. (A) Glass vial geometry. (B) Syringe geometry.

TABLE 2
Plastic Tube and Syringe Characteristics

Source container	Material	Maximal volume (mL)	Volume used (mL)	External diameter (mm)	Wall thickness (mm)
Syringe	Polypropylene	2	2	10.65	0.85
Plastic tube	Polypropylene	3.5	2	11.50	0.90

is of the order of about 2% in low-Z material and 5% in glass for a maximal β-energy of about 1 MeV. Energy deposition in the sensitive volume is much smaller than that for γ-emitters, being on the order of 10 eV per disintegration.

According to Schrader (*11*), the sensitivity of an ionization chamber to a nuclide is expressed by the following formula:

$$\varepsilon = \sum_{j} p_{\beta j}\varepsilon_{\beta j}(E_{\beta j}) + \sum_{i} p_{\gamma i}(E_{\gamma i})\cdot\varepsilon_{\gamma i}(E_{\gamma i}),$$

where $p_{\beta j}$ is the emission probability and $\varepsilon_{\beta j}$ the sensitivity of the chamber for a β-particle of maximal energy $E_{\beta j}$, $p_{\gamma i}$ is the emission probability, and $\varepsilon_{\gamma i}$ is the sensitivity of the chamber to a photon of energy $E_{\gamma i}$.

A sophisticated method has been developed to determine experimentally the relation ε_{γ} (E) for about 30 different nuclides, using initially pure monoenergetic γ-emitters and subsequently applying correction factors for multi-γ-emitters and β-contributors. In the case of β-emitters, the β-efficiency has been calculated using some pure β-emitters (*3*).

For commercially available calibrators, efficiency is determined by the manufacturer using calibrated radioactive solutions. Specific calibration factors are derived for use with different nuclides based on these measurements.

MATERIALS AND METHODS

Dose Calibrators

The main characteristics of the calibrators used in this study are given in Table 1.

For the VEENSTRA (VEENSTRA Instrumenten BV, Joure, The Netherlands) and Isomed (MED Nuklear-Medizintechnik, Dresden, Germany) calibrators, measurements were made using 3 different calibrators of the same model. There was excellent reproducibility from one calibrator to another for all nuclides, with maximum difference <1%. This confirms the precise manufacturing of the chamber and the appropriateness of defining generic calibration factors applicable to all chambers of the same type.

For measuring β-emitters, an instrument based on a sodium iodide crystal (Capintec β) was also used.

Measurement Geometry

Different measurement geometries were used for γ- and β-emitters. For γ-emitters, where detection efficiency is not critically influenced by measurement geometry, commercial glass vials (CIS Bio International, Gif-sur-Yvette, France; and Amersham Health, Little Chalfont, Buckinghampshire, U.K.) were placed in a low position in the calibrator well (Fig. 1A). For β-emitters, a polypropylene tube was used to simulate a 2-mL syringe and was positioned in the well in the same position as for a syringe measurement (Fig. 1B). Table 2 compares the characteristics of the tube and the syringe.

Calibrator response was compared for syringe and plastic tube measurements using ^{32}P and ^{169}Er. The observed differences were on the order of 1% for all calibrators.

Radionuclides

In Switzerland, 5 γ-emitters are used to verify the response of systems used in nuclear medicine laboratories: ^{57}Co, ^{60}Co, ^{137}Cs, ^{99m}Tc, and ^{131}I. Calibrator response was checked initially for these radionuclides using glass vial geometry and calibration factors supplied by the manufacturer.

Next, efficiency was measured using syringe geometry for 4 β-emitters with little or no γ-component: ^{32}P, ^{169}Er, ^{90}Y, and ^{89}Sr.

Finally, ^{153}Sm and ^{186}Re, 2 nuclides with nonnegligible γ-components, were measured using syringe geometry.

Radioactive Solutions

Radioactive solutions in ionic form were used so that solutions could be transferred with sufficient accuracy.

TABLE 3
Efficiency of Calibrators for ^{137}Cs

	VEENSTRA VDC-405	Atomlab 100	Isomed 1000/2000	Capintec CRC	Centronic IG12
R (^{137}Cs)	0.93	0.95	0.99	0.98	1.00

TABLE 4
Dose Calibrator Efficiency for γ-Emitters (R_n)

γ-Emitter	VEENSTRA VDC-405	Atomlab 100	Isomed 1000/2000	Capintec CRC	Centronic
^{57}Co	1.01	1.03	1.08	0.99	0.96
^{60}Co	1.03	1.02	0.99	1.00	1.00
^{99m}Tc	1.02	0.94	0.97	0.95	1.00
^{131}I	1.06	0.99	1.02	1.00	1.00

TABLE 5
Intrinsic Efficiency of Dose Calibrators for β-Emitters (R_n)

β-Emitter	VEENSTRA VDC-405	Atomlab 100	Isomed 1000/2000	Capintec CRC	Centronic IG12	Capintec β
^{32}P	0.97	1.05	1.07	1.06	0.97	0.96
^{89}Sr	0.83	0.90	0.89	0.91	0.91	0.85
^{90}Y	1.59	1.73	2.80	1.71	2.01	1.47
^{169}Er	0.068	0.078	0.081	0.078	0.024	0.041

Manufacturer-specified activities were checked using measurements from the national metrology laboratory. For γ-emitters, γ-spectroscopy was used. For β-emitters, liquid scintillation counting was used. Radionuclide purity was checked to make sure that no correction factor was necessary. The uncertainty in the absolute activity of the sources was 2% (1 σ) for γ-emitters and 2% (1 σ) for β-emitters.

Measuring Procedure

Measurement conditions for the study calibrations were carefully controlled by following a rigorous measurement protocol. For each instrument, measurement characteristics, including stability, linearity, and background subtraction, were checked. For background subtraction, in particular, careful attention was necessary because for the ^{169}Er measurements the background signal corresponds to a significant fraction of the measuring signal. For all of the measurements, validation tests were used to confirm the consistency of the results.

RESULTS

Efficiency for ^{137}Cs and Normalization

To ensure that measurements were independent of calibrator sensitivity adjustment, results were all normalized using the ^{137}Cs response. Table 3 gives the results of ^{137}Cs measurements, where R is the ratio of the activity indicated by the instrument using the ^{137}Cs calibration factor (cesium scale) to the absolute activity of the solution.

The results have been normalized by dividing the measured values by R to give efficiencies that are independent of the temporary current intensity amplification setting.

Efficiency for γ-Emitters

Detection efficiency for γ-emitters was measured in glass vial geometry using the manufacturer's calibration factors. Results normalized (Rn) to ^{137}Cs are given in Table 4.

The uncertainty for Rn is about 5% (1 σ), resulting in normalized efficiencies that are all approximately unity. It follows that the manufacturer-supplied calibration factors are accurate.

Intrinsic Efficiency for β-Emitters

To determine the intrinsic efficiency of the calibrators for β-emitters, measurements were first performed using the manufacturer's ^{32}P calibration factor (phosphor scale). Table 5 shows the results normalized to ^{137}Cs measurements.

Check of Calibration Factors

Measurements were made to check the accuracy of the calibration factors supplied by the manufacturer. Results normalized to ^{137}Cs measurements are given in Table 6. For each nuclide, the corresponding scale on the calibrator was used.

To determine the effect of measurement conditions on response, β-emitting solutions were measured in both syringe and glass vial geometries. Table 7 presents the ratio of the glass vial measurement to the syringe measurement for each nuclide/calibrator combination.

Dose Calibrator Efficiency for β-Emitters with a γ-Component

The intrinsic efficiency of dose calibrators for β-emitters with a γ-component (^{153}Sm and ^{186}Re) was measured in syringe geometry using the ^{32}P calibration factor (Table 8).

Calibrator efficiency using the manufacturer's calibration factor for each nuclide is given in Table 9.

DISCUSSION

Efficiency for γ-Emitters

For the efficiency for ^{137}Cs (Table 3), the calibration factors fulfill the accuracy requirement under Swiss law for nuclear medicine calibrators of ±10%. The results for other

TABLE 6
Efficiency of Dose Calibrators for β-Emitters (R_n)

β-Emitter	VEENSTRA VDC-405	Atomlab 100	Isomed 1000/2000	Capintec CRC	Centronic	Capintec β
^{89}Sr	*	0.96	0.72	1.15	0.89	0.93
^{90}Y	1.44	1.31	0.64	1.07	*	0.98
^{169}Er	0.32	*	0.63	*	*	*

*No specific factor available.

TABLE 7
Ratio of Glass Vial Measurements to Syringe Measurements

Emitter	VEENSTRA VDC-405	Atomlab 100	Isomed 1000/2000	Capintec CRC	Centronic IG12	Capintec β
^{32}P	0.97	0.92	1.01	0.92	1.02	1.28
^{89}Sr	0.94	0.89	0.98	0.89	1.01	1.03
^{90}Y	1.08	1.02	0.65	1.02	1.07	1.24
^{169}Er	0.77	0.73	0.86	0.69	0.96	0.96

nuclides have been normalized to this response so that they are independent of the temporary setting of the calibrator. Dose calibrator efficiencies for γ-emitters using the manufacturer's calibration factors are satisfactory (Table 4). The uncertainty of these results is about 5% (1 σ). However, it is worth noting that the manufacturer's calibration conditions are unknown (e.g., vial type) and that a difference between these conditions and the current measurement geometry could cause a difference of some percentages in Rn, which is acceptable.

Efficiency for β-Emitters

For β-emitters, important differences in intrinsic efficiency are related to the maximum energy of the β-spectrum (Table 5).

^{32}P ($E_{\beta max}$ = 1.7 MeV) results are excellent for all calibrators, with the difference between calibrators <10%, indicating that this nuclide could be used as a reference for ionization chamber calibration for β-emitters.

For ^{89}Sr ($E_{\beta max}$ = 1.5 MeV), all commercially available calibrators show efficiency reduced by 16%–20%. For the Centronic and Capintec β instruments, reductions are 7% and 13%, respectively. The small difference in intrinsic sensitivity for ^{32}P and ^{89}Sr is expected because of the small difference in maximum β-energy for the 2 nuclides.

For ^{90}Y ($E_{\beta max}$ = 2.3 MeV), a significant increase in intrinsic efficiency is observed for all calibrators. The enhancement factor of the response is considerably different for different calibrators and varies between 1.5 and 2.8. It is possible that a fraction of the β-particles reaches the sensitive volume of the ionization chamber and that the size of this fraction is strongly related to chamber construction.

Efficiency for ^{169}Er ($E_{\beta max}$ = 0.35 MeV) is very low. For the 4 commercially available calibrators, response compared with ^{32}P is reduced by a factor of about 12. For the Centronic and Capintec β systems the reduction is even more significant.

To summarize, all systems have a good calibration for ^{32}P and a reduction in efficiency for ^{90}Sr of <20%. For high-energy β-emitters (^{90}Y), there is a strong divergence in intrinsic efficiency for different calibrators. For low-energy β-emitters (^{169}Er), intrinsic efficiency is greatly reduced, but commercially available calibrators show approximately the same response reduction.

The results obtained using the calibration factors supplied by the manufacturers (Table 6) show that these factors do not adequately correct the intrinsic efficiencies.

For ^{89}Sr, the results for all calibrators are satisfactory, with the exception of the Isomed instrument. In this case, the calibration factor adjusts the measurement in the wrong direction in relation to ^{32}P. For this instrument, better results would be obtained using the ^{32}P factor.

For ^{90}Y, the sensitivity factors for the VEENSTRA and Atomlab (BIODEX Medical Systems, Inc., New York, NY) are too small compared with the factor for ^{32}P, and the sensitivity factor for the Isomed is too high.

For ^{169}Er, the most critical nuclide, calibration factors are not available for the Atomlab and Capintec CRC calibrators. For the VEENSTRA and Isomed calibrators, activity is underestimated by factors of 3 and 1.5, respectively.

The difference in response between the calibrators is significant and possibly can be attributed to differences in measurement conditions.

The ratios of the glass vial measurement to the syringe measurement (Table 7), with the exceptions of ^{169}Er and the Isomed yttrium measurement are between 0.9 and 1.1. For the Isomed, one could suspect that the reduced efficiency for yttrium in vial geometry is related to the reduced fraction of β-particles reaching the chamber sensitive volume. This result and the strong overestimation in syringe geometry

TABLE 8
Intrinsic Efficiency of Dose Calibrators for β-Emitters with a γ-Component

β-Emitter	VEENSTRA VDC-405	Atomlab 100	Isomed 1000/2000	Capintec CRC	Centronic IG12
^{153}Sm	41.5	42.9	47.7	43.0	*
^{186}Re	6.30	5.93	7.57	6.14	7.27

*No specific factor available.

TABLE 9
Efficiency of Dose Calibrators for β-Emitters with a γ-Contribution

β-Emitter	VEENSTRA VDC-405	Atomlab 100	Isomed 1000/2000	Capintec CRC	Centronic IG12
^{153}Sm	*	1.24	1.09	*	*
^{186}Re	1.00	1.00	0.98	0.96	1.22

*No specific factor available.

could be explained by a manufacturer calibration in vial geometry. However, for ^{169}Er the reduction in efficiency in changing from syringe to glass vial geometry is $<$20%, so this effect alone cannot explain the change in response by a factor of 3.

Efficiency for β-Emitters with a γ-Component

For both ^{153}Sm and ^{186}Re, the intrinsic efficiency is high compared with ^{32}P (Table 8). The relative efficiency between ^{153}Sm and ^{186}Re is proportional to the γ-emission probability of each nuclide, suggesting that efficiency is determined by the γ-contribution. Efficiency is approximately the same for all of the calibrators.

The efficiency obtained using the calibration factors supplied by the manufacturers (Table 9) is in most cases between 0.9 and 1.1.

The syringe geometry used for these measurements may differ from the manufacturers' calibration geometry, but this should not be significant because it is the γ-component that mainly determines response.

CONCLUSION

This work confirms that commercially available dose calibrators are well calibrated for γ-emitting radionuclides (accuracy better than 10%). The calibrators are also generally well calibrated for β-emitting nuclides with a nonnegligible γ-component used for bone palliation (^{153}Sm and ^{186}Re).

Intrinsic efficiency measurements show that although sensitivity to β-radiation is low, it is possible to measure β-activity using these instruments. A calibration factor specific to the measurement conditions should be used.

Manufacturer-supplied calibration factors are unsatisfactory for high-energy β-emitters (^{90}Y) and low-energy β-emitters (^{169}Er). For these nuclides, differences in efficiency observed cannot be attributed to differences in measurement conditions. This is a problem recognized by dose calibrator manufacturers, and new calibration techniques are under investigation.

Our results also show that calibration factors can correctly be applied to all calibrators of the same type. Dose calibrators used in nuclear medicine laboratories could be calibrated by the manufacturers for all β-emitters clinically used and be regularly verified using only 1 β-emitter (e.g., ^{32}P).

It is recommended that users contact the supplier of their calibrator to verify the validity of the calibration factors for β-emitters, in preference to adjusting these factors themselves.

Further investigations using Monte Carlo calculations are in progress to better quantify the effect of measurement conditions on dose calibrator efficiency.

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REFERENCES

1. Atkins HL. Overview of nuclides for bone pain palliation. *Appl Radiat Isot.* 1998;49:277–283.
2. Schrader H. Calibration and consistency of results of an ionization-chamber secondary standard measuring system for activity. *Appl Radiat Isot.* 2000; 52:325–334.
3. Michotte C. Efficiency curve of the ionization chamber of the SIR. *Appl Radiat Isot.* 2002;56:15–20.
4. Zimmerman BE, Cessna JT. The standardization of ^{62}Cu and experimental determinations of dose calibrator settings for generator-produced ^{62}Cu PTSM. *Appl Radiat Isot.* 1999;51:515–526.
5. Kowalsky JR, Johnston RE. Dose calibrator assay of iodine-123 and indium-111 with a copper filter. *J Nucl Med Technol.* 1998;26:94–98.
6. Santry D. The Canadian experience in performing accuracy checks on administered doses of radiopharmaceuticals. *Appl Radiat Isot.* 1998;49: 1453–1458.
7. Coursey BM, Schima FJ, Golas DB, Palabrica OT, Suzuki A, Dell MA. Measurement standards for strontium-89 for use in bone palliation. *Appl Radiat Isot.* 1998;49:335–344.
8. Zimmerman BE, Cessna JT. Experimental determinations of commercial "dose calibrator" settings for nuclides used in nuclear medicine. *Appl Radiat Isot.* 2000;52:615–619.
9. Sahagia M, Razdolescu AC, Grigorescu EL, Luca A, Ivan C. Precise measurement of the activity of ^{186}Re, ^{188}Re radiopharmaceuticals. *Appl Radiat Isot.* 2002;56:349–356.
10. Zimmerman BE, Pipes DW. Experimental determination of dose calibrator settings and study of associated volume dependence in v-vials for rhenium-186 perrhenate solution sources. *J Nucl Med Technol.* 2000;28:264–270.
11. Schrader H. *Activity Measurements with Ionization Chambers*. Monographie BIPM-4. Sèvres, France: Bureau International des Poids et Mesures; 1997.