CHAPTER 9

PHYSICS IN THE RADIOPHARMACY

R.C. SMART
Department of Nuclear Medicine,
St. George Hospital,
Sydney, Australia

9.1. THE MODERN RADIONUCLIDE CALIBRATOR

9.1.1. Construction of dose calibrators

Throughout the world, the instrument that is used in nuclear medicine to measure radioactivity is the calibrated re-entrant ionization chamber, commonly known as a radionuclide calibrator or dose calibrator. Commercial systems comprise a cylindrical well ionization chamber connected to a microprocessor-controlled electrometer providing calibrated measurements for a range of common radionuclides (Fig. 9.1). The chamber is usually constructed of aluminium filled with argon under pressure (typically 1–2 MPa or 10–20 atm). Dose calibrators with reduced gas pressure are available for positron emission tomography (PET) production facilities where very large activities may be measured.

FIG. 9.1. A typical dose calibrator (e.g. CRC 25R).

A well liner, made of low atomic number material (e.g. lucite (Perspex)) which can be removed for cleaning, prevents the ionization chamber from becoming accidentally contaminated. A sample holder is provided into which a vial or syringe can be placed to ensure that it is positioned optimally within the chamber. The dose calibrator may include a printer to document the activity measurements or an RS-232 serial communications port or USB port to interface the calibrator to radiopharmacy computerized management systems.

The chamber is typically shielded by the manufacturer with 6 mm of lead to ensure low background readings. Depending on the location of the dose calibrator, the user may require additional shielding, either to reduce background in the chamber or to protect the operator when measuring radionuclides of high energy and activity. However, this will alter the calibration factors due to backscattering of photons together with the emission of Pb K shell X rays arising from interactions within the lead shielding. If additional shielding is used, the dose calibrator should be recalibrated or correction factors determined to ensure that the activity readings remain correct.

As examples of commercial systems, the specifications of two widely used dose calibrators are given in Table 9.1.

TABLE 9.1. SPECIFICATIONS OF TWO COMMERCIAL DOSE CALIBRATORS

Specification	Capintec CRC-25R	Atomlab 200
Ionization chamber dimensions	26 cm deep × 6 cm diameter	26.7 cm deep × 7 cm diameter
Measurement range	Autoranging from 0.001 MBq to 250 GBq	Autoranging from 0.001 MBq to 399.9 GBq
Nuclide selection	8 pre-set, 5 user-defined (80 radionuclide calibrations in memory)	10 pre-set, 3 user-defined (94 radionuclide calibrations in manual)
Display units	Bq or Ci	Bq or Ci
Electrometer accuracy	<±2%	±1%
Response time	Within 2 s	1 s for activities >75 MBq
Repeatability	±1%	±0.3%

9.1.2. Calibration of dose calibrators

A dose calibrator can be calibrated in terms of activity by comparison with an appropriate activity standard that is directly traceable to a national primary standard. National primary standards are maintained by the relevant national metrology institute, such as the National Physical Laboratory (NPL) in the United Kingdom, the National Institute of Standards and Technology in the United States of America and the Australian Nuclear Science and Technology Organisation (ANSTO). Using the activity standard, a calibration factor for the ionization chamber can be determined for the specific radionuclide. The reciprocal of the calibration factor represents the efficiency ε_N of the ionization chamber for the radionuclide *N*.

The nuclide efficiency ε_N can be expressed as the sum of two components:

$$\varepsilon_N = \sum_i p_i(E_i) \cdot \varepsilon_i(E_i) \tag{9.1}$$

where

$p_i(E_i)$ is the emission probability per decay of photons of energy E_i;

and $\varepsilon_i(E_i)$ is the energy dependent photon efficiency of the ionization chamber.

Figure 9.2 illustrates a typical efficiency curve as a function of photon energy. Thin-walled aluminium chambers show a strong peak in efficiency at photon energies around 50 keV. This results from the rapid increase of the probability of photoelectric interactions in the filling gas with decreasing energy and the low energy cut-off with aluminium walls at about 20 keV.

Knowing the energy dependent photon efficiency curve for a specific ionization chamber will enable the nuclide efficiency for any radionuclide to be determined from the photon emission probability for each photon in its decay.

The 511 keV annihilation radiation will be measured when the activity of positron emitting radionuclides is to be assayed. A single calibration factor for all positron emitters cannot be used as the emission probability of the positrons must be taken into account. The probability (branching ratio) of positron emission for ^{11}C is 100% and for ^{18}F is 96.7%.

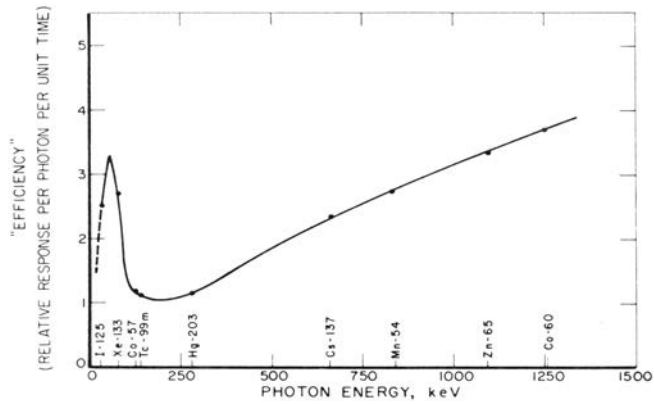


FIG. 9.2. Efficiency curve as a function of photon energy.

9.1.3. Uncertainty of activity measurements

The following sections describe the major sources of uncertainty in dose calibrator measurements.

9.1.3.1. Calibration factor

For medical radionuclides, such as ^{99m}Tc and ^{131}I, the uncertainty of national standards is typically in the range of 1–3%. However, when the standard is used to calibrate a medical dose calibrator, the uncertainty will be larger due to the inherent limit on instrument repeatability. Furthermore, the calibration factor will be for the particular vial size and thickness, and volume of solution, used for the national standard. The calibration factor for a different container (a syringe) and/or a different volume may vary from the established calibration by a significant amount (see Section 9.1.3.6).

9.1.3.2. Electronics

Electrometers measure the current output from the ionization chamber ranging from tens of femtoamperes up to microamperes — a dynamic range of 10^8, corresponding to activity levels from kilobecquerels to hundreds of gigabecquerels. Modern dose calibrators automatically adjust the range while older units required the operator to select the appropriate range. The potential for different linearity characteristics for each range may result in discontinuities when the range is changed. The effects of inherent inaccuracy, linearity and range changing are illustrated in Fig. 9.3. The linearity of the dose calibrator must be

established over the full range of intended use when the unit is commissioned and verified as part of the quality control programme (see Section 9.2.1.2).

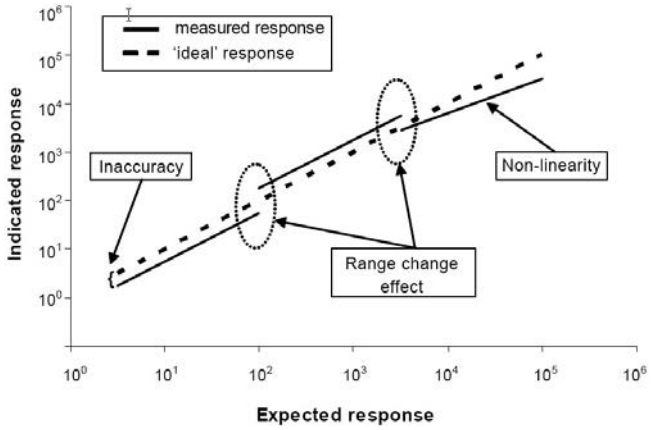


FIG. 9.3. Electrometer inaccuracies (courtesy of the National Physical Laboratory).

9.1.3.3. Statistical considerations

Repeated measurements on a single sample will not be identical because of the random nature of radioactive decay (see Chapter 5). If the measurement period remains constant, the precision of the measured activity will increase as the activity increases. Conversely, the precision will deteriorate for low activity sources. To compensate for this, many calibrators automatically adjust the measurement period depending on the activity level. This may vary from less than one second to tens of seconds for low activities (<1 MBq).

9.1.3.4. Ion recombination

As the activity of the source increases, the probability of recombination of the positive ions with electrons increases. At high source activities, this can become significant and lead to a reduction in the measured current. The effect of recombination is illustrated in Fig. 9.4. For most modern calibrators, the effects of recombination should be less than 1% when measuring 100 GBq of ^{99m}Tc.

9.1.3.5. Background radiation

When the source holder is empty, the dose calibrator will still record a non-zero reading due to background radiation. This will comprise natural background and background from sources within the radiopharmacy. It could

also be due to contamination on either the source holder itself or the well liner. Most dose calibrators provide a background subtraction feature. An accurate measurement of the existing radiation level is made by the calibrator (usually integrating over several minutes to improve precision) which is then automatically subtracted from each subsequent reading. This may lead to erroneous results if the background radiation has changed since it was measured due to the presence of additional nearby sources or contamination. It is, therefore, essential to make regular checks of the background radiation level.

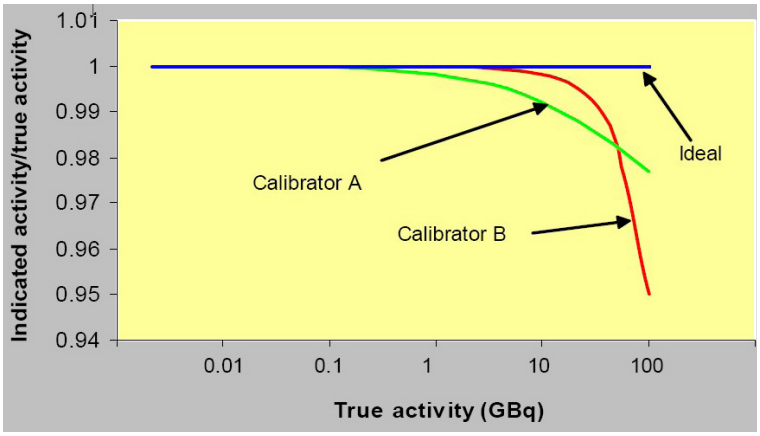


FIG. 9.4. Effects of recombination (courtesy of the National Physical Laboratory).

9.1.3.6. Source container and volume effects

Variations in the composition and thickness of the source container will give rise to corresponding variations in the measured activity. These effects will be most noticeable for low energy photon emitters and pure β emitters. Measurements made at NPL, United Kingdom (Table 9.2) have shown that variations in glass wall thicknesses, which were within the range of the vial manufacturing tolerances, could lead to errors of up to 7% for ^{125}I.

When the activity is drawn into a syringe, the source geometry will be different from that in a vial. Not only will the composition and thickness of the syringe wall be different from that of the vial, but the distribution of the source will also be different depending on the size of syringe used. This is clearly evident in Fig. 9.5, showing measurements at NPL for ^{111}In in three sizes of syringe (1, 2 and 5 mL) from two different manufacturers in comparison to those measured in a laboratory standard P6 vial. Also illustrated in Fig. 9.5 is the effect of changing the source volume without changing the activity. Self-absorption of the emitted

TABLE 9.2. REDUCTION IN DOSE CALIBRATOR RESPONSE DUE TO INCREASES IN GLASS WALL THICKNESS OF 0.08 AND 0.2 mm

Radionuclide	Reduction in response with increase in vial wall thickness of	
	0.08 mm	0.2 mm
^{125}I	3%	7%
^{123}I	0.6%	1.5%
^{111}In	0.2%	0.4%
^{131}I	0.1%	0.25%

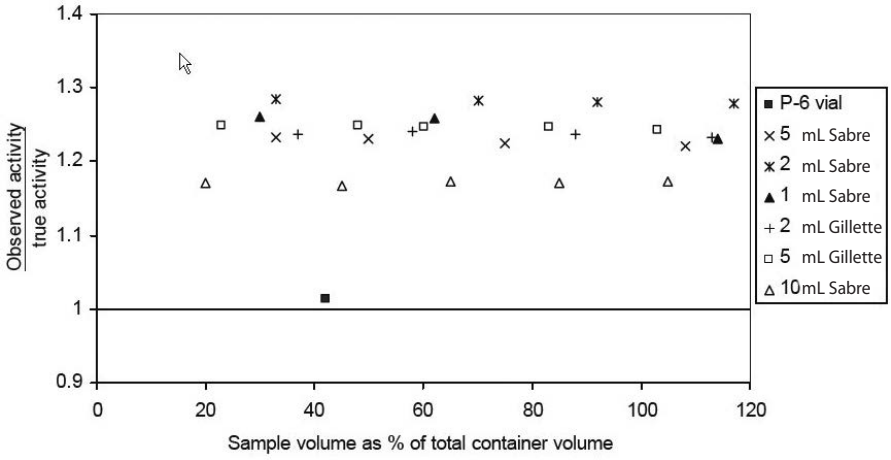


FIG. 9.5. The effects of geometry and sample size on dose calibrator readings, demonstrated for ^{111}In measured in varying syringes (reproduced from Ref. [9.1]).

radiation will change as the source volume changes. This will be particularly important for radionuclides with low energy components such as ^{123}I. For ^{99m}Tc, the correction will usually be less than 1% but should be confirmed for a new dose calibrator or when the supplier of the syringes changes.

9.1.3.7. Source position

The manufacturer's source holder is designed to keep the source at the area of maximum response on the vertical axis of the well. Variations in response due to changes in vertical height or horizontal position of a few millimetres are usually insignificant.

9.1.3.8. Source adsorption

Certain radiopharmaceuticals have been observed to adsorb to the surface of the container. For example, up to 30% of the activity of ^{201}Tl has been found to be adsorbed onto the glass of P6 vials. ^{99m}Tc-tetrofosmin has been shown to adsorb onto the surface of syringes, such that some types of syringe may retain as much as 19% of the activity. Of this, 6% adhered to the rubber plunger with the remainder attached to the plastic syringe barrel. Up to 15% of ^{99m}Tc-macroaggregate of albumin (MAA) may adhere to the syringe, although the amount on the rubber plunger is usually no more than 1%. The possibility of activity adsorption should be considered whenever the facility uses syringes from a different manufacturer.

9.1.4. Measuring pure β emitters

The detection efficiency of ionization chambers for β radiation is low as most, if not all, of the β particles are absorbed in the source solution (self-absorption), in the walls of the container or in the walls of the ionization chamber. The dose calibrator response from β particles will be almost entirely from bremsstrahlung radiation (see Section 1.1.7). In the energy region of interest for ionization chamber measurements, the bremsstrahlung photon spectrum is roughly the same shape as the β particle energy distribution. The average β particle energy is, therefore, a good parameter with which to characterize the ionization chamber response to the bremsstrahlung radiation.

Bremsstrahlung radiation flux is proportional to the square of the atomic number of the absorbing material. Thus, in argon-filled ionization chambers, significant activities are required in order to obtain a precise estimate of the activity. However, as substantial activities of radionuclides are required to be used therapeutically, reliable measurements are possible using pure β emitters used clinically such as ^{90}Y, ^{89}Sr and ^{32}P. However, geometry factors (see Section 9.1.3.6) will be even more important and the system must be calibrated for the specific containers and volumes to be used clinically. Manufacturers are now producing dose calibrators specifically for the measurement of β emitters. These use a sodium iodide detector instead of an ionization chamber, resulting in a significantly increased detection efficiency; however, as the manufacturers state in their product literature, measurements still require exacting attention to the sample container, the sample volume and activity concentration to achieve accurate results.

Most commercially available ionization chambers are provided with calibration factors for commonly used β emitters, although these will usually correspond to the activity within a vial rather than a syringe. The type of vial used in the calibration is often unspecified, so the user should verify the calibration in

the vials normally used in the practice. Similarly, the calibration of the activity within the size of syringe to be used clinically should be established. Published results comparing the intrinsic efficiencies of dose calibrators from five different manufacturers found that all systems had a good calibration for ^{32}P, a reduction in efficiency of approximately 10–20% for ^{89}Sr, and a wide divergence in efficiency for ^{90}Y. For this radionuclide, the results obtained using the calibration factors supplied by the manufacturers ranged from 64 to 144% of the true value, re-emphasizing the need for the calibration to be confirmed within the nuclear medicine department.

Several β emitters used for radionuclide therapy include a γ ray component. These radionuclides include ^{131}I (364 keV, 81.5% abundance) and ^{186}Re (137 keV, 9.5% abundance). For these radionuclides, the ionization chamber efficiency is primarily determined by the γ contribution and the manufacturer's supplied calibrations will usually be accurate to within ±10%.

9.1.5. Problems arising from radionuclide contaminants

Unfortunately, it is often not possible for a solution of a radionuclide to be totally free of other radionuclides. The proportion of the total radioactivity that is present as a specific radionuclide is defined as the radionuclide purity. National and international pharmacopoeia specify the radionuclidic purity of a radiopharmaceutical. For example, the European Pharmacopoeia entry for ^{67}Ga-citrate injection requires that no more than 0.2% of the total radioactivity be due to ^{66}Ga. This requirement must be met at all times up to the expiry time of the product. The US Pharmacopoeia is less stringent, specifying that not less than 99% of the total radioactivity be present as ^{67}Ga at the time of calibration.

The presence of contaminants, even when less than 1% of the total activity, can have a marked effect on the ionization chamber current and, thus, on the measured activity. The British Pharmacopoeia specification for ^{201}Tl-thallous chloride requires that "Not more than 2.0 percent of the total radioactivity is due to thallium-202 and not less than 97.0 percent is due to thallium-201." Thallium-202 has a half-life of 12.2 d and the predominant photon energy is 440 keV. Another possible contaminant is ^{200}Tl which has a half-life of 1.09 d and prominent energies at 368 keV and 1.2 MeV. Both of these radionuclide contaminants will have a high efficiency in a dose calibrator. As the half-life of ^{202}Tl is significantly longer than that of ^{201}Tl, the relative proportion of ^{202}Tl to ^{201}Tl will increase over time. If the accuracy of a dose calibrator is to be checked with a ^{201}Tl source, the apparent accuracy could change depending on when the measurements are taken relative to the stated calibration date. The presence of these high energy contaminants will have an adverse effect on image quality due to increased septal penetration and will also lead to an increased radiation dose to

the patient. The effective dose, in millisieverts per megabecquerel, for ^{200}Tl, ^{201}Tl and ^{202}Tl is 0.238, 0.149 and 0.608, respectively. It should be noted that these problems will be increased if the radiopharmaceutical is administered prior to the nominal calibration date, as the proportion of ^{200}Tl will be higher.

9.2. DOSE CALIBRATOR ACCEPTANCE TESTING AND QUALITY CONTROL

9.2.1. Acceptance tests

Acceptance tests for dose calibrators should include measurements of the accuracy, reproducibility, linearity and geometry response. These are required to ensure that the unit meets the manufacturer's specifications and to give baseline figures for subsequent quality control.

9.2.1.1. Accuracy and reproducibility

The accuracy is determined by comparing activity measurements using a traceable calibrated standard with the supplier's stated activity, corrected for radioactive decay. The accuracy is expressed in per cent deviation from the actual activity and should be measured for all radionuclides to be used routinely. It is recommended that measurements of a long lived source, for example ^{137}Cs, be recorded at the time of initial testing for each radionuclide setting to be used clinically for later quality control.

The reproducibility, or constancy, can be assessed by taking repeated measurements of the same source. If the sample holder is removed from the chamber between each measurement, the measured reproducibility will include any errors associated with possible variations in source position.

9.2.1.2. Linearity

There are several approaches to the measurement of the linearity response of a dose calibrator. Typically, a vial containing a high activity of ^{99m}Tc is measured repeatedly over a period of at least 5 d. During this time, a 100 GBq source will decay to 0.1 MBq. It is essential that the initial activity represents the highest activity that is likely to be used in clinical practice, which will usually be the first elution from a new Mo/Tc generator. A semi-log plot of the measurements, corrected for background, should follow the expected decay of the radionuclide. Any deviation from the expected line at high activities indicates saturation of response of the ionization chamber. Accurate background measurements, at the

time of each assay, are essential as the background will become an increasing component of the reading as the source decays. Deviations from linearity at low activities are likely to be due to radionuclide impurities, such as ^{99}Mo in vials containing ^{99m}Tc.

Another approach that can be used to check the linearity requires a series of radioactive sources that cover the range of activities to be measured. The sources should all be prepared from the same stock solution and the dispensed volumes measured accurately by weighing the vials pre- and post-dispensing. The volume of liquid in each vial should be adjusted with a non-radioactive solution, so that the volume is identical in each vial, to eliminate any geometry dependency in the measurement. The measured activities are corrected for decay to the time of measurement of the first vial and plotted against the dispensed volumes to assess the calibrator linearity. The error in this method will be increased if there are any small variations in the vial wall thickness as the same vial is not used for all measurements.

Finally, linearity can be assessed by repeated measurements on a single vial using a series of graded attenuators appropriate for a specified test source to reduce the measured ionization current. These are typically a series of concentric cylinders that fit over the vial. The attenuation through each cylinder must be accurately known to use this method.

9.2.1.3. Geometry

The measured activity may vary with the position of the source within the ionization chamber, with the composition of the vial or syringe, or with the volume of liquid within the vial or syringe. Appropriate correction factors must be established for the containers and radionuclides to be used clinically, especially if radionuclides that have a substantial component of low energy photons, such as ^{123}I, are to be used. For each vial or syringe to be used clinically, a series of measurements should be undertaken in which the activity remains constant, but the volume is increased from 10 to 90% of the maximum volume by the addition of water or saline. Corrected for decay, a plot of activity against volume should be a straight horizontal line. Any deviations from this can be used to calculate the appropriate correction factor.

Similarly, vial to syringe correction factors can be determined by measuring the activity transferred from the vial to the syringe (original vial activity minus residual activity) and comparing this to the activity measured in the syringe itself.

Geometry dependencies should not change over time; however, if the practitioner changes the manufacturer of the syringes or obtains the radiopharmaceuticals in a different vial size, a new set of calibration factors should be determined.

9.2.2. Quality control

9.2.2.1. Background check

As noted in Section 9.1.3.5, when the source holder is empty, the dose calibrator will still record an 'activity' due to background radiation. This will come from natural background, from sources within the radiopharmacy and/or from contamination present on the source holder or well liner. It is a useful practice to keep a spare source holder and a spare well liner, so that if contamination is detected the contaminated item can be removed from service to be decontaminated, or left until the radioactivity has decayed.

At a minimum, the background should be determined each morning before the dose calibrator is used and recorded. The background subtraction feature, if available, can be used at that time to remove the measured background from subsequent measurements. The technologist should also confirm the absence of any additional background before all activity measurements during the day.

9.2.2.2. Check source reproducibility

A long lived check source should be used on a daily basis to confirm the constancy of the response of the dose calibrator. Sealed radioactive sources of ^{57}Co and ^{137}Cs, shaped to mimic a vial, are available commercially for this purpose. The check source should be measured on all radionuclide settings that are used clinically. Although the recorded activity of a ^{137}Cs source on the ^{99m}Tc setting will not be a correct measurement of its activity, a reading outside of that expected from previous results may indicate a faulty dose calibrator or a change in calibration factor, in this case of ^{99m}Tc.

9.3. STANDARDS APPLYING TO DOSE CALIBRATORS

The International Electrotechnical Commission (IEC) has published two standards [9.2, 9.3] and a technical report [9.4] relating to dose calibrators. IEC standards are often adopted by national standards organizations. Reference [9.3] is for manufacturers to use to ensure that the equipment performance is specified in a standardized way, while Ref. [9.4] is aimed at the users of dose calibrators.

There should also be national standards covering dose calibrators. The American National Standards Institute publication ANSI N42.13-2004 [9.5] is often referenced by US manufacturers. This specifies the minimum requirements in terms of accuracy and reproducibility for dose calibrators:

— "The accuracy of the instruments, at activity levels above 3.7 MBq shall be such that the measured activity of a standard source shall be within ±10% of the stated activity of that source" [9.5];
— "The reproducibility…shall be such that all of the results in a series of ten consecutive measurements on a source of greater than 100 μCi (3.7×10^6 Bq) in the same geometry shall be within ±5% of the average measured activity for that source" [9.5].

9.4. NATIONAL ACTIVITY INTERCOMPARISONS

National metrology institutes are responsible for the development and maintenance of standards, including activity standards. These institutes, often in collaboration with the relevant national professional body, have undertaken national comparisons of the accuracy of the dose calibrators used in clinical practice. Such comparisons have used, where possible, the clinical radionuclides ^{67}Ga, ^{123}I, ^{131}I, ^{99m}Tc and ^{201}Tl, and have been carried out in Argentina, Australia, Brazil, Cuba, the Czech Republic, Germany, India and the United Kingdom. In some countries, such as Cuba and the Czech Republic, participation in the comparison is mandatory, while in many other countries it is voluntary. The surveys can also be used to measure the reproducibility of the calibrators.

As an example, Table 9.3 shows the results from a survey undertaken in Australia in 2007.

TABLE 9.3. SUMMARY OF THE RESULTS OF THE DOSE CALIBRATOR SURVEY UNDERTAKEN IN AUSTRALIA IN 2007

Radionuclide	^{99m}Tc	^{131}I	^{67}Ga	^{201}Tl
No. of calibrators	167	164	116	162
Within ±5% error	86%	80%	84%	73%
Within ±10% error	98%	95%	97%	94%
Within ±10% reproducibility	100%	100%	100%	100%

These surveys also offer the opportunity for the calibration factor to be adjusted if a dose calibrator is found to be operating with an error of >10%.

9.5. DISPENSING RADIOPHARMACEUTICALS FOR INDIVIDUAL PATIENTS

9.5.1. Adjusting the activity for differences in patient size and weight

Protocols used in nuclear medicine practices should specify the usual activity of the radiopharmaceutical to be administered to a standard patient. In most western countries, the standard patient is taken to be one whose weight is in the range 70–80 kg. However, many patients fall outside of this range. If a fixed activity is used for all patients, this will lead to an unnecessarily high radiation exposure to an underweight patient and may lead to images of unacceptable quality or very long imaging times in obese patients.

There have been various approaches to determining the activity to be administered. These are usually designed to provide a constant count density in the image to maintain image quality or to provide a constant effective dose to the patient. For example, it has been shown that for myocardial perfusion scans using ^{99m}Tc-tetrofosmin, the activity should be increased by 150% for a 110 kg patient and by 200% for a 140 kg patient in order to maintain image quality without increasing imaging time.

It has been shown, using the radiation dose tables provided in International Commission on Radiological Protection (ICRP) publications 53, 80 and 106 [9.6–9.8], that the effective dose (mSv/MBq) can be expressed as a simple power function of body weight. Scaling factors for the activity, to give a constant effective dose can, therefore, be derived from the expression $(W/70)^a$, where W represents the weight of the person and the power factor a is specific for the radiopharmaceutical. Again, using ^{99m}Tc-tetrofosmin as an example, a is found to be –0.834. Although the dosimetry models are only available up to 70 kg, this power function can be extrapolated to derive scaling factors for patients whose weight exceeds 70 kg. Using this approach, the activity should be increased by 146% for a 110 kg patient and by 178% for a 140 kg patient. This approach is useful, but should be used with caution. The extrapolated activity would lead to comparable organ and tissue doses for a patient of large body build but not for a patient of similar weight due to large body fat deposits as the biodistribution of the radiopharmaceutical would not be the same in these two cases. Table 9.4 presents the a value for common radiopharmaceuticals.

9.5.2. Paediatric dosage charts

Children are approximately three times more radiosensitive than adults, so determining the appropriate activity to be administered for paediatric procedures is essential. In addition to the scaling factor to be applied to the adult activity, a

TABLE 9.4. THE POWER FACTOR *a* RELATING BODY WEIGHT TO A CONSTANT EFFECTIVE DOSE ACCORDING TO THE EXPRESSION $(W/70)^a$ FOR 14 COMMON RADIOPHARMACEUTICALS

Radiopharmaceutical	*a* value	Radiopharmaceutical	*a* value
^{99m}Tc-DMSA	–0.706	^{99m}Tc-IDA	–0.840
^{99m}Tc-DTPA	–0.801	^{99m}Tc-tetrafosmin	–0.834
^{99m}Tc-MAG3	–0.520	^{99m}Tc-red cells	–0.859
^{99m}Tc-HMPAO	–0.849	^{99m}Tc-white cells	–0.869
^{99m}Tc-MAA	–0.842	^{18}F-FDG	–0.782
^{99m}Tc-sestamibi	–0.871	^{67}Ga-citrate	–0.931
^{99m}Tc-phosphonates	–0.763	^{123}I or ^{131}I iodide	–1.11

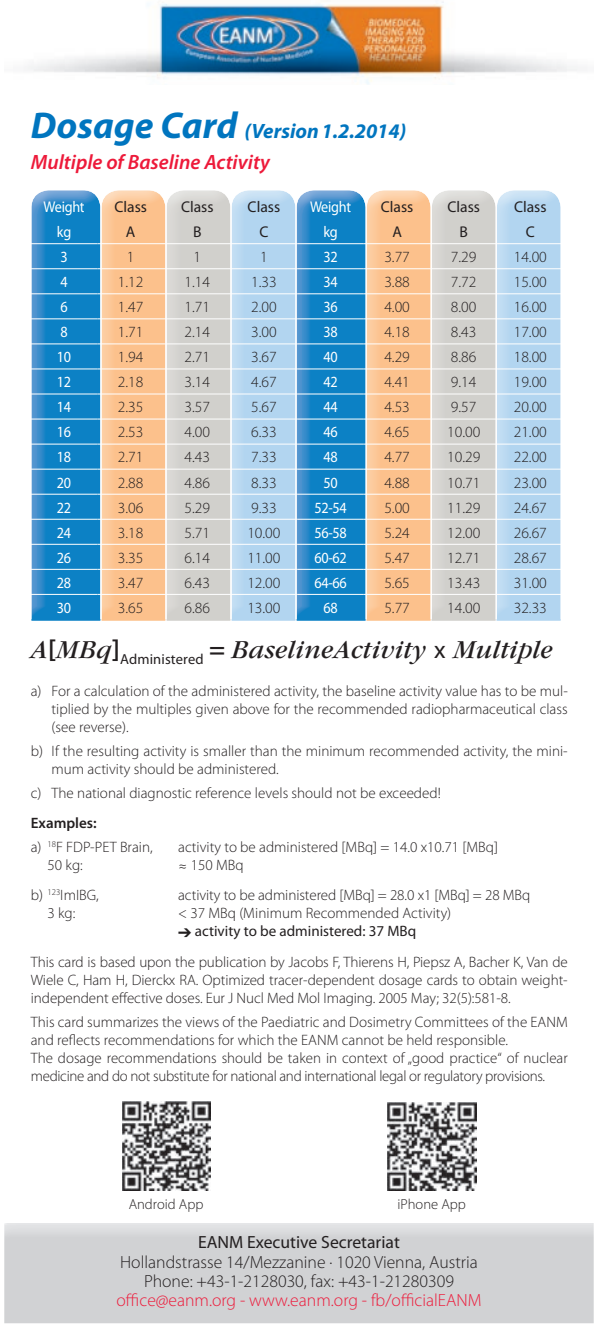
minimum activity must be specified in order to ensure adequate image quality. In the past, the scaling factors were assessed using weight alone or body surface area obtained from both height and weight. These two methods can give rise to quite different scaling factors. For example, the scaling factor for a 20 kg child is 29% of the adult activity using weight alone, but 43% when based on body surface area.

Recently, the European Association of Nuclear Medicine (EANM) Dosimetry and Paediatric Committees have prepared a dosage card which recognizes that a single scaling factor is not optimal for all radiopharmaceuticals. They used the methodology presented in Section 9.5.1 and were able to establish that radiopharmaceuticals could be grouped into three classes (renal, thyroid and others), with different scaling factors for each class. A dosage card is available on the EANM web site that gives the minimum recommended activity and a weight dependent scaling factor for each radiopharmaceutical which was determined to give weight independent effective doses. This dosage card is reproduced here as Fig. 9.6. To assist in these calculations, an on-line dosage calculator is available on the EANM web site[1], in which the user specifies the child's weight and the radiopharmaceutical, and the recommended activity is displayed.

[1] http://www.eanm.org/publications/dosage_calculator.php?navId=285

9.5.3. Diagnostic reference levels in nuclear medicine

The recommendations of the ICRP specifically exclude medical exposures from its system of dose limits, as the patient is directly benefiting from the radiation exposure. However, in Publication 73 (1996) [9.9], the ICRP introduced the term 'diagnostic reference level' (DRL) for patients. DRLs are investigation levels and are based on an easily measured quantity, usually the entrance surface dose in the case of diagnostic radiology, or the administered activity in the case of nuclear medicine. DRLs are referred to by the IAEA as guidance levels in Safety Reports Series No. 40 [9.10], published in 2005. This publication contains a table of guidance levels reflecting the values used in the early 1990s, when single photon emission computed tomography procedures were far less common. A survey of the use of DRLs in eight European countries, published in 2007 [9.11], showed that their introduction in nuclear medicine varied considerably. For example, France had set DRLs for 10 nuclear medicine procedures, Germany for 17 procedures, Italy for 48 procedures, while the United Kingdom listed 96 procedures. In some countries, the DRLs were set at the activities for which marketing approval had been given, while in other countries the DRLs were determined for each procedure by calculating the 75th percentile of the spread of data values collected from a survey of participating practices. The latter approach has been widely used to set DRLs in radiology and has been used in other parts of the world, such as Australia and New Zealand, to establish DRLs in nuclear medicine.



EANM
European Association of Nuclear Medicine
BIOMEDICAL IMAGING AND THERAPY FOR PERSONALIZED HEALTHCARE

Dosage Card (Version 1.2.2014)

Multiple of Baseline Activity

Weight kg	Class A	Class B	Class C	Weight kg	Class A	Class B	Class C
3	1	1	1	32	3.77	7.29	14.00
4	1.12	1.14	1.33	34	3.88	7.72	15.00
6	1.47	1.71	2.00	36	4.00	8.00	16.00
8	1.71	2.14	3.00	38	4.18	8.43	17.00
10	1.94	2.71	3.67	40	4.29	8.86	18.00
12	2.18	3.14	4.67	42	4.41	9.14	19.00
14	2.35	3.57	5.67	44	4.53	9.57	20.00
16	2.53	4.00	6.33	46	4.65	10.00	21.00
18	2.71	4.43	7.33	48	4.77	10.29	22.00
20	2.88	4.86	8.33	50	4.88	10.71	23.00
22	3.06	5.29	9.33	52-54	5.00	11.29	24.67
24	3.18	5.71	10.00	56-58	5.24	12.00	26.67
26	3.35	6.14	11.00	60-62	5.47	12.71	28.67
28	3.47	6.43	12.00	64-66	5.65	13.43	31.00
30	3.65	6.86	13.00	68	5.77	14.00	32.33

$$A[MBq]_{\text{Administered}} = BaselineActivity \times Multiple$$

a) For a calculation of the administered activity, the baseline activity value has to be multiplied by the multiples given above for the recommended radiopharmaceutical class (see reverse).

b) If the resulting activity is smaller than the minimum recommended activity, the minimum activity should be administered.

c) The national diagnostic reference levels should not be exceeded!

Examples:

a) ^{18}F FDP-PET Brain, 50 kg: activity to be administered [MBq] = 14.0 x10.71 [MBq] ≈ 150 MBq

b) ^{123}ImIBG, 3 kg: activity to be administered [MBq] = 28.0 x1 [MBq] = 28 MBq < 37 MBq (Minimum Recommended Activity) → **activity to be administered: 37 MBq**

This card is based upon the publication by Jacobs F, Thierens H, Piepsz A, Bacher K, Van de Wiele C, Ham H, Dierckx RA. Optimized tracer-dependent dosage cards to obtain weight-independent effective doses. Eur J Nucl Med Mol Imaging. 2005 May; 32(5):581-8.

This card summarizes the views of the Paediatric and Dosimetry Committees of the EANM and reflects recommendations for which the EANM cannot be held responsible.
The dosage recommendations should be taken in context of „good practice" of nuclear medicine and do not substitute for national and international legal or regulatory provisions.

Android App

iPhone App

EANM Executive Secretariat
Hollandstrasse 14/Mezzanine · 1020 Vienna, Austria
Phone: +43-1-2128030, fax: +43-1-21280309
office@eanm.org - www.eanm.org - fb/officialEANM

FIG. 9.6. European Association of Nuclear Medicine (EANM) paediatric dosage card (courtesy of EANM).

Recommended Amounts in MBq

Radiopharmaceutical	Class	Baseline Activity (for calculation purposes only) MBq	Minimum Recommended Activity[1] MBq
^{123}I (Thyroid)	C	*0.6*	3
^{123}I Amphetamine (Brain)	B	*13.0*	18
^{123}I HIPPURAN (Abnormal renal function)	B	*5.3*	10
^{123}I HIPPURAN (Normal renal function)	A	*12.8*	10
^{123}I mIBG	B	*28.0*	37
^{131}I mIBG	B	*5.6*	35
^{18}F FDG-PET torso	B	*25.9*	26
^{18}F FDG-PET brain	B	*14.0*	14
^{18}F Sodium fluoride	B	*10.5*	14
^{67}Ga Citrate	B	*5.6*	10
^{99m}Tc ALBUMIN (Cardiac)	B	*56.0*	80
^{99m}Tc COLLOID (Gastric Reflux)	B	*2.8*	10
^{99m}Tc COLLOID (Liver/Spleen)	B	*5.6*	15
^{99m}Tc COLLOID (Marrow)	B	*21.0*	20
^{99m}Tc DMSA	B	*6.8*	18.5
^{99m}Tc DTPA (Abnormal renal function)	B	*14.0*	20
^{99m}Tc DTPA (Normal renal function)	A	*34.0*	20
^{99m}Tc ECD (Brain perfusion)	B	*32.0*	110
^{99m}Tc HMPAO (Brain)	B	*51.8*	100
^{99m}Tc HMPAO (WBC)	B	*35.0*	40
^{99m}Tc IDA (Biliary)	B	*10.5*	20
^{99m}Tc MAA / Microspheres	B	*5.6*	10
^{99m}Tc MAG3	A	*11.9*	15
^{99m}Tc MDP	B	*35.0*	40
^{99m}Tc Pertechnetate (Cystography)	B	*1.4*	20
^{99m}Tc Pertechnetate (Ectopic Gastric Mucosa)	B	*10.5*	20
^{99m}Tc Pertechnetate (Cardiac First Pass)	B	*35.0*	80
^{99m}Tc Pertechnetate (Thyroid)	B	*5.6*	10
^{99m}Tc RBC (Blood Pool)	B	*56.0*	80
^{99m}Tc SestaMIBI/Tetrofosmin (Cancer seeking agent)	B	*63.0*	80
^{99m}Tc SestaMIBI/Tetrofosmin[2] (Cardiac rest scan 2-day protocol min)	B	*42.0*	80
^{99m}Tc SestaMIBI/Tetrofosmin[2] (Cardiac rest scan 2-day protocol max)	B	*63.0*	80
^{99m}Tc SestaMIBI/Tetrofosmin[2] (Cardiac stress scan 2-day protocol min)	B	*42.0*	80
^{99m}Tc SestaMIBI/Tetrofosmin[2] (Cardiac stress scan 2-day protocol max)	B	*63.0*	80
^{99m}Tc SestaMIBI/Tetrofosmin[2] (Cardiac rest scan 1-day protocol)	B	*28.0*	80
^{99m}Tc SestaMIBI/Tetrofosmin[2] (Cardiac stress scan 1-day protocol)	B	*84.0*	80
^{99m}Tc Spleen (Denatured RBC)	B	*2.8*	20
^{99} Tc TECHNEGAS (Lung ventilation)[3]	B	*70.0*	100

[1] The minimum recommended activities are calculated for commonly used gamma cameras or positron emission tomographs. Lower activities could be administered when using systems with higher counting efficiency.

[2] The minimum and maximum values correspond to the recommended administered activities in the EANM/ESC procedural guidelines (Hesse B, Tagil K, Cuocolo A, et al). EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear Cardiology. Eur J Nucl Med Mol Imaging. 2005 Jul;32(7):855-97.

[3] This is the activity load needed to prepare the Technegas device. The amount of inhaled activity will be lower.

FIG. 9.6. European Association of Nuclear Medicine (EANM) paediatric dosage card (courtesy of EANM) (cont.).

9.6. RADIATION SAFETY IN THE RADIOPHARMACY

9.6.1. Surface contamination limits

Surface contamination with radioactivity could lead to contamination of a radiation worker and/or external irradiation of the skin of the worker. Internal contamination could arise from inhalation and/or ingestion of the radionuclide. The surface contamination limits given in Table 9.5 were derived based on a committed effective dose limit of 20 mSv/a and the models for inhalation and ingestion given in ICRP publications 30, 60 and 61 [9.12–9.14]. For each radionuclide, the most restrictive pathway (inhalation, ingestion or external irradiation) was used.

TABLE 9.5. DERIVED LIMITS FOR SURFACE CONTAMINATION

Nuclide	Surfaces in designated areas, including protective clothing (Bq/cm^2)	Interiors of glove boxes and fume cupboards (Bq/cm^2)	Non-designated areas including personal clothing (Bq/cm^2)
^{18}F	100	1 000	5
^{32}P	100	1 000	5
^{51}Cr	1 000	10 000	50
^{67}Ga	1 000	10 000	50
^{89}Sr	100	1 000	5
^{90}Y	100	1 000	5
^{99m}Tc	1 000	10 000	50
^{111}In	1 000	10 000	50
^{123}I	1 000	10 000	50
^{125}I	100	1 000	5
^{131}I	100	1 000	5
^{177}Lu	1 000	10 000	50
^{201}Tl	1 000	10 000	50

9.6.2. Wipe tests and daily surveys

Surveys of the radiopharmacy must be undertaken to ensure that these surface contamination limits are not exceeded and that the operator is not unnecessarily exposed to external radiation. Exposure could result from sources inadvertently left on a bench and from contamination on bench surfaces. Aerosolized droplets from a syringe during dispensing may go unnoticed, so it is essential that all staff are aware that the dispensing area may be contaminated and always wear protective gloves when working in this area. All radiopharmaceutical elution, preparation, assay and administration areas should be surveyed at the end of each working day.

Surveys should initially be undertaken with a survey meter to ensure that no unexpected exposed sources are present in the radiopharmacy. All surfaces should then be checked for contamination using a contamination monitor with a probe appropriate to the radionuclides used. The background radiation levels in the radiopharmacy, particularly in the dispensing area, are often higher than elsewhere in the nuclear medicine department, so quantifying any contamination found using a probe is difficult. If a low energy β emitter is being used, it will prove difficult or impossible to detect with an external probe. In these situations, a wipe test should be used. A minimum area of 100 cm^2 should be wiped and then the activity on the wipe can be assessed using a pancake probe, or more accurately in a well counter. For low energy β emitters, such as ^{3}H or ^{14}C, liquid scintillation counting must be used. When quantifying the surface contamination, it is generally assumed that a wipe test using a dry wipe will remove one tenth of the contamination while a wet wipe will remove one fifth of the contamination.

9.6.3. Monitoring of staff finger doses during dispensing

Systematic studies of the dose to the hands of staff working in radiopharmacies have shown that finger doses may approach or exceed the annual dose limit of 500 mSv to the extremities. The most exposed parts of the hands are likely to be the tips of the index and middle fingers, and the thumb of the dominant hand, with exposure for the index finger being highest. The ICRP has recommended that finger dose monitoring be undertaken for any person handling more than 2 GBq/d and regular monitoring should be carried out if doses to the most exposed part of the hand exceed 6 mSv/month.

Although the dose to the finger tip will be the highest, it is much more practical to wear a ring monitor at the base of the finger. A thermoluminescent dosimeter chip mounted in a plastic ring is usually the most convenient type of monitor. Such monitors are often available in a variety of sizes. The ring should fit tightly, so that it is not inadvertently removed when the gloves are taken off.

The ICRP recommends that the ring monitor be worn on the middle finger with the element positioned on the palm side, and that a factor of three should be applied to derive an estimate of the dose to the tip. If the dosimeter element is worn facing towards the back of the hand, a factor of six should be applied.

The dose to the fingers is critically dependent on the dispensing technique used and the skill of the operator. It is important that staff undertake extensive training in the dispensing technique with non-radioactive solutions prior to dispensing radiopharmaceuticals for the first time. This is particularly important with PET radiopharmaceuticals as the specific dose rate constant is much higher for positron emitters than for radionuclides used for single photon imaging.

9.7. PRODUCT CONTAINMENT ENCLOSURES

9.7.1. Fume cupboards

A fume cupboard is an enclosed workplace designed to prevent the spread of fumes to the operator and other persons. The ‘fumes’ can be in the form of gases, vapours, aerosols or particulate matter. The fume cupboard is designed to provide operator protection rather than protection for the product within the cabinet. A fume cupboard would, therefore, not be suitable as an area for cell labelling procedures as this requires that the blood remain sterile at all times. Fume cupboards usually include a transparent safety screen which can be adjusted either vertically (more commonly) or horizontally to vary the size of the working aperture into the cabinet. Some cupboards are available with a lead glass safety screen to minimize the need for additional radiation shielding. The most common type of fume cupboard is known as a variable exhaust air volume fume cupboard which maintains a constant velocity of air into the cabinet (the face velocity) irrespective of the sash position. Figure 9.7 shows a fume cupboard suitable for use with radioactive materials.

Fume cupboards are available which discharge the exhaust air directly, or after carbon filtration, to the atmosphere, usually above the building. Other cabinets, known as recirculating fume cabinets, rely on filtration or absorption to remove airborne contaminants released in the cabinet, so that the air may be safely discharged back into the laboratory. Recirculating fume cabinets are not normally applicable for use with radioactive materials.

Any installed fume cupboards must meet the requirements of the local appropriate standard and any air discharged to the atmosphere must meet the requirements of the appropriate regulatory authority. The standard will usually specify the minimum face velocity through the working aperture (e.g. 0.5 m/s). This should be checked on a regular basis and should be measured with the

aperture fully open and in its minimum position. At the minimum position, the face velocity may need to be higher to retain a constant exhaust rate from the cabinet.

Before initial use, and as part of a regular quality control schedule, a smoke test should be performed. This is to provide visual evidence of fume containment within, or escape from, the fume cupboard. Smoke is released in and around the fume cupboard and the visual pattern of airflow is observed. The results of the smoke test must be documented and any reverse flows from the confines of the cupboard corrected before subsequent use.

FIG. 9.7. Fume cupboard suitable for use with radioactive materials.

9.7.2. Laminar flow cabinets

Laminar flow cabinets provide a non-turbulent airstream of near constant velocity, which has a substantially uniform flow cross-section and with a variation in velocity of not more than 20%. Laminar flow cabinets provide product protection while a fume cupboard is designed to provide operator protection. The air supplied to the cabinet is usually passed through a high efficiency particulate air filter, which is designed to remove 99.999% of particles greater than 0.3 μm in size. It must be remembered that the laminar flow of air (usually vertical) will be disturbed by the presence of any objects within the cabinet, including shielding

and the arms of the operator. During use, the filtered air may escape from the front of the cabinet, when the airflow is disturbed, so operator protection cannot be ensured.

9.7.3. Isolator cabinets

Isolator cabinets provide both operator and product protection. Figure 9.8 shows an example of a blood cell labelling isolator. The product is manipulated through glove ports so that the interior of the cabinet is maintained totally sterile and full operator protection is provided. Airflow within the isolator is deliberately designed to be turbulent so that there are no dead spaces within the cabinet. The unit illustrated incorporates a centrifuge which can be controlled externally. A dose calibrator can be included within the isolator, so that the cell suspension does not need to be removed from the isolator for the activity to be measured. The isolator incorporates timed interlocks on the vacuum door seals to ensure that the product remains sterile.

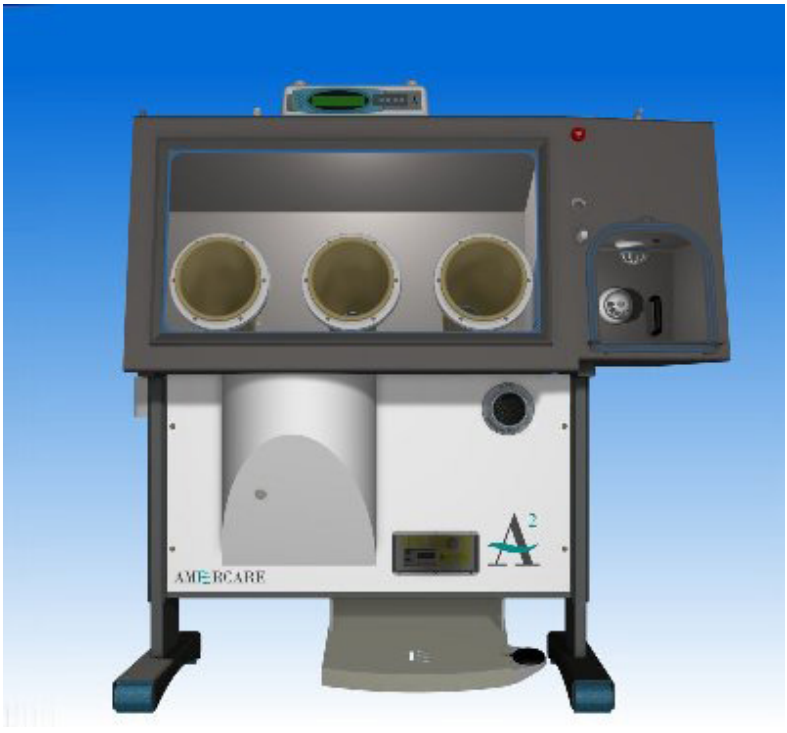


FIG. 9.8. Blood cell labelling isolator (courtesy of Amercare Ltd).

9.8. SHIELDING FOR RADIONUCLIDES

9.8.1. Shielding for γ, β and positron emitters

Shielding will be required in the walls of the radiopharmacy, in any containment enclosures, in a body shield to protect the operator at the dispensing station, and around individual vials and syringes containing radionuclides. Shielding of the walls of the radiopharmacy can be minimized by appropriate local shielding around the sources being handled. Shielding may be constructed from a variety of materials, including lead and concrete in walls, lead or tungsten in local shielding for γ emitting radionuclides, and aluminium or Perspex for pure β emitters. For positron emitters, the shielding will be primarily determined by the 511 keV annihilation photons rather than by the positrons themselves. A low atomic number material, such as aluminium or Perspex, is used for pure β emitters since this minimizes the production of bremsstrahlung radiation. As β radiation has a finite range in materials, determined by the maximum β energy, the thickness of the shielding needs to be greater than this range to ensure that all of the β particles are absorbed. Polymethyl methacrylate (Perspex or lucite) has a density of 1.19 g/cm^3, similar to the density of tissue and water, and is highly suitable for absorbing β particles. Table 9.6 gives the maximum β energy and the range in water for four pure β emitters used in nuclear medicine.

TABLE 9.6. MAXIMUM β ENERGY AND RANGE IN WATER FOR FOUR β EMITTERS USED CLINICALLY IN NUCLEAR MEDICINE. THE ELECTRON RANGE HAS BEEN DETERMINED USING THE CONTINUOUS SLOWING DOWN APPROXIMATION

Radionuclide	E_{max} (MeV)	Range in water (mm)
^{14}C	0.156	0.30
^{32}P	1.709	8.2
^{89}Sr	1.463	6.8
^{90}Y	2.274	11

The highest surface dose rates encountered in the radiopharmacy are likely to be from ^{99}Mo/^{99m}Tc generators which may contain >100 GBq of ^{99}Mo. The primary γ emission from ^{99}Mo has an energy of 740 keV, so requires several centimetres of lead shielding to reduce the dose rates to an acceptable level. The generator, as supplied, will already contain substantial shielding but additional shielding will usually be required. This may be available from the generator

supplier specifically designed for their generator or it may be necessary to construct or purchase an additional shield. Figure 9.9 shows a generator supplied by ANSTO in Australia inside a dedicated lead 'garage'. The body of the radiochemist is shielded by the garage doors while she is attaching the shielded elution vial prior to an elution of the generator. These shields are heavy (>20 kg), so it is important that the bench surfaces are strong enough to support the weight. The generator is itself quite heavy, so mechanical lifting devices may be necessary to prevent back injuries to staff when lifting the generator into position.

FIG. 9.9. Lead garage surrounding a $^{99}Mo/^{99m}Tc$ generator.

Vials of radiopharmaceuticals must be kept shielded. The shields are usually constructed so that only the rubber septum of the vial is accessible, thereby protecting the hands of the operator during dispensing (see Fig. 9.10). The vials themselves should never be held by the fingers once they contain radioactivity, instead long forceps should always be used (see Fig. 9.11).

FIG. 9.10. Shielded vial used to hold reconstituted radiopharmaceuticals.

FIG. 9.11. Using long forceps to handle a vial containing radioactivity.

During radiopharmaceutical preparation, dispensing and administration to the patient, the activity is usually manipulated in syringes. The dose rates at the surface of the syringes may exceed 1 $\mu Sv \cdot s^{-1} \cdot MBq^{-1}$ depending on the volume of liquid and the size of the syringe. The plastic of the syringe provides little absorption of any high energy β particles, and for radionuclides used for therapy, the surface dose rates will be in excess of 10 mSv/s, so that the annual dose limit of 500 mSv to the extremities can easily be exceeded. Syringes should never be more than half filled, so that the syringe can be picked up near the plunger where the fingers are not over the activity. Syringe shields must be used whenever possible. These must be made of Perspex for the pure β emitters and of lead or tungsten for the γ emitters (see Fig. 9.12). A lead glass window is necessary to permit observation of the contents of the syringe. Syringe shields with a spring-loaded catch to hold the syringe in place are preferable to those using a screw, as the screw-thread wears quickly with use.

FIG. 9.12. A tungsten syringe shield for γ emitting radionuclides and a Perspex syringe shield for pure β emitters.

TABLE 9.7. MEASURED TRANSMISION FACTORS FOR LEAD

Thickness of lead (mm)	^{99}Mo	^{99m}Tc	^{67}Ga	^{131}I	^{201}Tl[a]	511 keV
0	1.00	1.00	1.00	1.00	1.00	1.00
1	0.876	0.105	0.455	0.769	0.136	0.891
2	0.776	0.00835	0.280	0.601	0.0709	0.787
3	0.694	6.52×10^{-4}	0.191	0.475	0.0557	0.690
4	0.623	5.09×10^{-5}	0.135	0.379	0.0485	0.602
5	0.561	3.97×10^{-6}	0.0983	0.306	0.0438	0.523
6	0.507	3.10×10^{-7}	0.0730	0.248	0.0430	0.452
7	0.458		0.0551	0.203	0.0422	0.390
8	0.414		0.0420	0.168	0.0415	0.336
9	0.375		0.0324	0.139	0.0408	0.289
10	0.340		0.0253	0.116	0.0291	0.249
12	0.279		0.0157	0.0829	0.0282	0.183
14	0.229		0.0102	0.0605	0.0273	0.135
16	0.188		0.00682	0.0451	0.0193	0.0990
18	0.154		0.00476	0.0342	0.0187	0.0728
20	0.127		0.00345	0.0263	0.0132	0.0535
25	0.0774		0.00177	0.0143	0.00893	0.0247
30	0.0473		0.00104	0.00805	0.00602	0.0114
40	0.0176		4.11×10^{-4}	0.00267	0.00274	0.00240
50	0.00659		1.71×10^{-4}	9.04×10^{-4}	0.00124	5.00×10^{-4}

[a] The transmission data for ^{201}Tl includes a contribution of 1.5% of the contaminant ^{200}Tl, the maximum level likely to be encountered in clinical practice.

9.8.2. Transmission factors for lead and concrete

Section 1.6 indicates that the attenuation of monoenergetic photons through materials such as lead or concrete will be exponential, characterized by the linear attenuation coefficient or the half-value layer (HVL). However, this is only correct for narrow beam geometries, using collimated beams of radiation, which

are rarely encountered in practice. Furthermore, the attenuation of the radiation from radionuclides which emit more than one γ photon, such as ^{67}Ga and ^{131}I, cannot be expressed as a simple HVL.

Tables 9.7 and 9.8 give the measured broad beam transmission factors for lead and concrete for five radionuclides used in nuclear medicine and for 511 keV photons from positron emitters. This information can be used to calculate the required thickness of shielding around vials, for the body protection of the operator and for the walls of the radiopharmacy. The values for ^{201}Tl include a contribution from ^{200}Tl, a common contaminant, which has prominent energies at 368 keV and 1.2 MeV. A contribution of 1.5% of ^{200}Tl has been included which is the maximum likely value at the time of calibration.

TABLE 9.8. MEASURED TRANSMISSION FACTORS FOR CONCRETE (DENSITY: 2.35 g/cm^3)

Thickness of concrete (mm)	^{99}Mo	^{99m}Tc	^{67}Ga	^{131}I	^{201}Tl[a]	511 keV
0	1.00	1.00	1.00	1.00	1.00	1.00
10	0.845	0.779	0.884	0.916	0.759	0.958
20	0.718	0.607	0.769	0.825	0.581	0.909
30	0.614	0.473	0.661	0.735	0.449	0.852
40	0.527	0.368	0.564	0.649	0.349	0.789
50	0.454	0.287	0.477	0.570	0.274	0.722
60	0.393	0.224	0.402	0.498	0.217	0.653
70	0.341	0.174	0.338	0.434	0.173	0.584
80	0.296	0.136	0.282	0.377	0.139	0.518
90	0.258	0.106	0.236	0.327	0.112	0.456
100	0.225	0.0824	0.196	0.284	0.0912	0.399
120	0.172	0.0500	0.135	0.212	0.0612	0.301
140	0.132	0.0304	0.0928	0.158	0.0418	0.224
160	0.101	0.0184	0.0635	0.118	0.0290	0.166
180	0.0777	0.0112	0.0434	0.0879	0.0203	0.123
200	0.0598	0.00679	0.0296	0.0654	0.0143	0.0904
250	0.0312	0.00195	0.0113	0.0312	0.00607	0.0419

TABLE 9.8. MEASURED TRANSMISSION FACTORS FOR CONCRETE (DENSITY: 2.35 g/cm^3) (cont.)

Thickness of concrete (mm)	^{99}Mo	^{99m}Tc	^{67}Ga	^{131}I	^{201}Tl[a]	511 keV
300	0.0163	5.60×10^{-4}	0.00433	0.0149	0.00262	0.0194
400	0.00443	4.61×10^{-5}	6.30×10^{-4}	0.00339	4.95×10^{-4}	0.00417
500	0.00121	3.80×10^{-6}	9.16×10^{-5}	7.70×10^{-4}	9.39×10^{-5}	8.95×10^{-4}

[a] The transmission data for ^{201}Tl includes a contribution of 1.5% of the contaminant ^{200}Tl, the maximum level likely to be encountered in clinical practice.

9.9. DESIGNING A RADIOPHARMACY

Every radiopharmacy is unique and there is no one design that can be used in all situations. The requirements of a single camera practice using only ^{99m}Tc radiopharmaceuticals will be very different from a large teaching hospital with PET facilities and in-patient radionuclide therapy rooms. However, in addition to the general building requirements given in section 3.1.3 of Ref. [9.10], there are some general rules specific to a radiopharmacy that can be applied in most situations:

— The radiopharmacy should be located in an area that is not accessible to members of the public.
— There should be easy access from the radiopharmacy to the injection rooms and imaging rooms to minimize the distance that radioactive materials need to be transported.
— The radiopharmacy should not be adjacent to areas that require a low and constant radiation background such as a counting room.
— There should be an area within the radiopharmacy designated as a non-active area that is used for record keeping and/or computer entry.
— A refrigerator will be required for the storage of lyophilized radiopharmaceutical kits. A laboratory-grade unit is preferred to ensure that the temperature remains constant.
— A dedicated dispensing area with a body shield and lead glass viewing window will be required. This will normally be adjacent to the dose calibrator, so that the dispensed activity can be measured while the operator is still protected by the body shield. The thickness of the shield and window will depend on the radionuclide or radionuclides in use. PET radionuclides

will require substantial thickness and lead glass should be supplied as a single block rather than as a stack of thinner sheets.

— A storage area will be required for reconstituted radiopharmaceuticals, in shielded containers, together with radiopharmaceuticals purchased ready for dispensing such as ^{67}Ga-citrate and ^{201}Tl-chloride.
— The radiopharmacy must contain facilities for radioactive waste disposal. This will normally include separate shielded storage bins for short lived radionuclides such as ^{99m}Tc and for radionuclides with longer half-lives such as ^{131}I. In addition, there must be shielded containers for 'sharps', such as syringes with needles. A separate shielded storage bin may be required if a large number of bulky items, such as aerosol or Technegas kits, need to be stored.
— If a Mo/Tc generator is used, this should be positioned away from the dispensing area to minimize the dose received by the person dispensing the radiopharmaceuticals. Some countries require the generator to be housed inside a laminar flow cabinet. All local regulatory requirements must be taken into account when designing the radiopharmacy.
— If cell labelling procedures are to be performed, a dedicated area with a laminar flow cabinet or isolator will be required to ensure that the product remains sterile during the labelling procedure.
— A fume cupboard, together with an activated charcoal filter on the exhaust, will be required if radioiodination procedures are to be performed.
— Some radiopharmaceuticals require a heating step in their preparation. This is often performed using a temperature controlled heating block. This must be in a dedicated separately shielded area, particularly as several gigabecquerels of ^{99m}Tc are often involved. Similarly, the radiolabelling of blood samples may require local shielding of mixers and centrifuges.
— Wall, floor and ceiling surfaces should be smooth, impervious and durable, and free of externally mounted features such as pipes or ducts to facilitate any radioactive decontamination.
— Bench surfaces should be constructed of plastic laminate or resin composites or stainless steel, and benches must be able to safely withstand the weight of any required lead shielding.
— Hand washing facilities must be available which can be operated without the use of the operator's hands to prevent the spread of any contamination. An eye-wash should also be available.
— A contamination monitor must be available in a readily accessible location. A wall-mounted monitor to check for any hand contamination should be mounted near the exit from the radiopharmacy. A model which can be removed and used as a general contamination monitor is useful.

9.10. SECURITY OF THE RADIOPHARMACY

Until relatively recently, the safety of the staff when handling and storing radioactive materials was the sole concern when designing a radiopharmacy. The security of the radioactivity was often not specifically addressed. Unfortunately, it is now apparent that radioactive materials can be used for malicious purposes and the security of the radiopharmacy must now be considered.

The IAEA has categorized radioactive sources on a scale of 1 to 5, based on activity and nuclide, where category 1 is potentially the most hazardous. Sources categorized as 1, 2 or 3 are known as security enhanced sources. The security measures in place for safety purposes are considered adequate to ensure the physical security of category 4 and 5 sources. Legislation is now, or will be, in place in each jurisdiction to address the security of security enhanced sources. This currently only applies to sealed sources, and no sealed sources used in nuclear medicine are categorized as either 1, 2 or 3. However, the principles can be applied to unsealed sources. A Mo/Tc generator with an activity of greater than 300 GBq is a category 3 source.

Radioactive materials are at most risk of being stolen or lost when they are being transported to and from the facility. They will be in the appropriate transport container and, therefore, can be easily handled by someone with malicious intent. It is essential that all consignments of radioactive materials to the nuclear medicine facility are left in a secure area and not left, for example, on a loading dock. During working hours, all deliveries must be signed for by a designated staff member and the material safely unpacked and stored within the department. Some deliveries may occur outside of working hours. In this case, a dedicated secure area must be provided where the radioactive materials can be left. A key could be provided to the supplier for this area only, so that the radioactivity can be safely and securely delivered, but access to other parts of the facility is prevented. The supplier may need to be accompanied by the facility's security staff when delivering the shipment.

Whether secure access (such as electronic card access) to the radiopharmacy during working hours is required will depend on local requirements and the layout of the nuclear medicine department. It is essential that only trained nuclear medicine staff have access to the radiopharmacy. The need for controlled access needs to be balanced against the possibility of inadvertent contamination of the door or access mechanism by staff returning to the radiopharmacy.

9.11. RECORD KEEPING

The local regulations may specify the minimum records that must be kept at the facility, the form in which these must be kept (paper and/or electronic) and the time for which the records must be kept. Records can be generated as part of the quality assurance (QA) programme, for the receipt and subsequent administration of a radiopharmaceutical to a patient, and for waste disposal.

9.11.1. Quality control records

A key element of any QA programme is proper record keeping, so that any long term trends associated with a particular item of equipment or batch of radiopharmaceuticals can be identified and acted on before image quality and/or patient dose are compromised. Records should, at the very least, include details of:

— Acceptance testing of the dose calibrator;
— All constancy tests;
— Radiopharmaceutical testing.

Failures identified at acceptance or constancy testing and radiopharmaceutical testing, and the actions taken to remedy those failures, should be documented and these records kept for the lifetime of the equipment.

The following records should be kept for all generator elutions:

— Time of elution;
— Volume of eluate;
— Technetium-99m activity;
— Molybdenum-99 activity;
— Radionuclidic purity.

9.11.2. Records of receipt of radioactive materials

Complete records of the radionuclide, activity, chemical form, supplier, supplier's batch number and purchase date should be kept. On arrival, if a package containing radioactive material is suspected of being damaged, the package should be:

— Monitored for leakage with a wipe test;
— Checked with a survey meter for unexpectedly high external radiation levels.

If a package is damaged or suspected of being damaged, the supplier should be contacted immediately, and the details recorded.

9.11.3. Records of radiopharmaceutical preparation and dispensing

The preparation of radiopharmaceuticals needs to be performed in accordance with the manufacturer's requirements as specified in the product documentation, including any quality control such as thin-layer chromatography.

Records of each preparation should include the:

— Name of the radiopharmaceutical;
— Cold kit batch number;
— Date of manufacture;
— Batch number of final product;
— Radiochemical purity results;
— Expiry date.

A record for each patient dose dispensed must be kept with the:

— Name of the patient;
— Name of the radiopharmaceutical;
— Measured radioactivity;
— Time and date of measurement.

All unit patient doses (syringes, capsules or vials) supplied by a central radiopharmacy should identify the patient's name and the radionuclide and radiopharmaceutical form. These should be verified on arrival and the activity should be confirmed in a dose calibrator prior to administration to the patient, and recorded as above.

9.11.4. Radioactive waste records

Radioactive waste generated within a nuclear medicine facility usually consists of radionuclides with half-lives of less than one month. This waste will normally be stored on-site, be allowed to decay to background radiation levels and then be disposed of as normal waste or biologically contaminated waste (see Section 3.4.7). It is, therefore, not normally necessary to keep records of radioactive waste disposal from the facility, but it will be necessary to keep records of the waste in storage while it decays. In some circumstances, the waste will contain a single known radionuclide, such as ^{131}I from patients receiving radioiodine ablation therapy. In many cases, the waste will contain a mixture of

short lived radionuclides. Each package of waste (bag, sharps container, wheeled bin) must be marked with the:

— Radionuclide, if known;
— Maximum dose rate at the surface of the container or at a fixed distance (e.g. 1 m);
— Date of storage.

The above information should be recorded, together with information identifying the location of the container within the store, and the likely release date (e.g. ten half-lives of the longest lived radionuclide in the container).

When the package is finally released for disposal, the record should be updated to record the dose rate at that time, which should be at background levels, the date of disposal, and the identification of the person authorizing its disposal.

Old sealed sources previously used for quality control or transmission scans, such as ^{137}Cs, ^{57}Co, ^{153}Gd and ^{68}Ge, should be kept in a secure store until the activity has decayed to a level permitted for disposal, or the source can be disposed of by a method approved by the regulatory authority.

REFERENCES

[9.1] TYLER, D.K., WOODS, M.J., Syringe calibration factors for the NPL Secondary Standard Radionuclide calibrator for selected medical radionuclides, Appl. Radiat. Isot. **59** (2003) 367–372.

[9.2] INTERNATIONAL ELECTROTECHNICAL COMMISSION, Calibration and Usage of Ionization Chamber Systems for Assay of Radionuclides, IEC 61145:1992, IEC (1992).

[9.3] INTERNATIONAL ELECTROTECHNICAL COMMISSION, Medical Electrical Equipment — Radionuclide Calibrators — Particular Methods for Describing Performance, IEC 61303:1994, IEC (1994).

[9.4] INTERNATIONAL ELECTROTECHNICAL COMMISSION, Nuclear Medicine Instrumentation — Routine Tests — Part 4: Radionuclide Calibrators, IEC/TR 61948-4:2006, IEC (2006).

[9.5] American National Standards Institute, Calibration and Usage of "Dose Calibrator" Ionization Chambers for the Assay of Radionuclides, ANSI N42.13-2004, ANSI (2004).

[9.6] INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, Radiation Dose to Patients from Radiopharmaceuticals, Publication 53, Pergamon Press, Oxford and New York (1988).

[9.7] INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, Radiation Dose to Patients from Radiopharmaceuticals (Addendum to ICRP Publication 53), Publication 80, Pergamon Press, Oxford and New York (1998).

[9.8] INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, Radiation Dose to Patients from Radiopharmaceuticals — Addendum 3 to ICRP Publication 53, Publication 106, Elsevier (2008).

[9.9] INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, Radiological Protection and Safety in Medicine, Publication 73, Pergamon Press, Oxford and New York (1996).

[9.10] INTERNATIONAL ATOMIC ENERGY, Applying Radiation Safety Standards in Nuclear Medicine, Safety Reports Series No. 40, IAEA, Vienna (2005).

[9.11] EUROPEAN ALARA NETWORK (2007), http://www.eu-alara.net/index.php?option=com_content&task=view&id=156&Itemid=53

[9.12] INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, Limits for Intakes of Radionuclides by Workers, Publication 30, Pergamon Press, Oxford and New York (1979).

[9.13] INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, 1990 Recommendations of the International Commission on Radiological Protection, Publication 60, Pergamon Press, Oxford and New York (1991).

[9.14] INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, Annual Limits on Intake of Radionuclides by Workers Based on the 1990 Recommendations, Publication 61, Pergamon Press, Oxford and New York (1991).

BIBLIOGRAPHY

GADD, R., et al., Protocol for Establishing and Maintaining the Calibration of Medical Radionuclide Calibrators and their Quality Control, Measurement Good Practice Guide No. 93, National Physical Laboratory, UK (2006).

GROTH, M.J., Empirical dose rate and attenuation data for radionuclides in nuclear medicine, Australas. Phys. Eng. Sci. Med. **19** (1996) 160–167.

NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL (Australia), Recommended Limits on Radioactive Contamination on Surfaces in Laboratories, Radiation Health Series No. 38, NHMRC (1995).

SCHRADER, H., Activity Measurements with Ionization Chambers, Monographie Bureau International des Poids et Mesures No. 4 (1997).