Laboraty Equipment

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Dose Calibrator

General

1. Introduction

A dose calibrator is a gas-filled ionisation chamber in the shape of a well, used to determine the intensity of a radioactive source expressed in Becquerels [Bq]. The radioactivity is measured indirectly: X-ray or gamma photons cause ionisation in the gas. A large voltage differential is applied to the electrodes in the chamber. The electrons released by the ionisations are drawn to the anode, which creates a voltage pulse. Using an electronic circuit, this voltage pulse is converted into an electric current. For a given radionuclide, there is a proportional relationship (the "yield") between de activity (Bq) and the strength of the current (μA). For different radionuclides, this relationship depends on the photon energy (keV) and the photon flow (density). The latter is influenced, amongst other things, by the count geometry, such as size and position of the source, and by attenuation. Because of this dependence, the amplification factor of the circuitry must be set separately for each radionuclide. In contrast to gamma cameras, a radionuclide is not measured on a particular peak, but all (X-ray and gamma) photons contribute to the measurement of the activity (and sometimes even the Auger electrons, as with ^{123}I).
Most dose calibrators have pre-programmed selection keys for the proper amplification of certain radionuclides. In addition, an arbitrary setting may be selected. The manufacturer provides a list of radionuclides and their associated settings. The calibration has been performed at the factory for a particular source geometry (syringe) in a certain position.
Apart from the opening of the well, the ionisation chamber is surrounded by lead.
This causes ionisation by background radiation to be kept to a minimum, but there will nevertheless still be some ionisation giving rise to a leakage current. Most dose calibrators have a zero setting which is used to compensate for this leakage current. In older types, the background must first be measured, or first 'zeroed' before a preparation can be measured.
A separate remark must be made about radionuclides which emit many low-energy photons. Owing to differences in composition of the casing (plastic, glass) of the source, it will be precisely these low-energy photons which will make a greater or lesser contribution to the number of ionisations in the ionisation chamber. For these radionuclides, of which ^{123}I and ^{111}In are the most common, a calibration procedure is needed.
When measuring the activity of e.g. ^{123}I one can use a copper tube with a wall thickness of 1 mm. All low-energy (27 to 31 keV) photons will be stopped by this and the measurement will be based solely on the presence of photons with higher energy (159 keV). In reading out the activity, however, account must be taken of a different scale

factor. This can be determined experimentally.
Radionuclides which only emit low-energy photons cannot be measured at all with the copper shielding method. An example of this is ^{125}I, which emits the same low-energy photons (K-shell vacancies) as ^{123}I.
Measuring the activity of a pure beta-emitter such as ^{32}P with a dose calibrator is based on the measurement of Bremsstrahlung. However, the sensitivity is low and heavily dependent on the dimensions and composition of the material in which the source resides. Measurements of the activity of pure beta-emitters are therefore difficult to standardize.

2. Selection of tests and frequency of testing

The tests and frequencies are selected using the principles described in the general Introduction to Equipment. In addition, use has been made of the detailed protocols provided by the IAEA (International Atomic Energy Agency) as described in the document TECDOC-317 for the quality control of dose calibrators.
It is recommended that the background radiation is checked daily. In addition, it is recommended that the constancy of the sensitivity is checked frequently, although the probability that abnormalities will be found here is low. It is essential that the check is integrated into routine activities, for example weekly on Monday morning before work is started, such that execution of the tests is encouraged. Using three solid sources, this check of sensitivity can be carried out quickly including a simple control of the energy dependence and linearity.
The remaining tests are only recommended on (re)acceptance.
If the dose calibrator is used to perform quantitative investigations, e.g. on the PET scanner, additional checks are needed (see PET section).

3. Requirements

The materials required for conducting the tests are

- a balance with a precision of 0,01 g
- ^{99m}Tc and some solid sources (see section protocols)
- loose material such as tweezers, pipettes, syringes and (polystyrene) sample jars.

4. Administration

It is recommended that all test results are registered in a spreadsheet. All faults and all preventive and corrective maintenance should be documented, preferably in a central maintenance management system. This can be used to determine whether certain abnormalities occur regularly or are associated with other abnormalities. When recording repairs, it should be noted what they have entailed.

5. Literature

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- IAEA. Radionuclide 'dose' calibrators. Quality control of nuclear medicine instruments. Technical document (TECDOC-317). 1984:17-34.
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- Wiarda KS. ^{123}I in een dosiskalibrator. [^{123}I in a dose calibrator.] NGB 5 (1);1983:4-7.
- Blok, D, Wie neemt, claimt of heeft de verantwoording voor de radiofarmaca, [Translation of the title: Who takes, claims or has responsibility for the radiopharmaceuticals] Tijdschrift voor Nucleaire Geneeskunde, 2005;27(4):158-60, Calibration and validation equipment.

Background Radiation

1. Introduction and rationale

Although the ionisation chamber is largely shielded with lead, in an empty measuring well, some activity will still be measured. In addition, there will always be a small leakage current through the initial amplification section of the electronics. The summation of these effects is defined as the background radiation. This test examines whether the compensation for this background radiation is functioning adequately.

2. Frequency

It is recommended that, on acceptance, the background radiation is determined in a completely radiation-free environment, and then daily under normal operating conditions (see Pitfalls and remarks).

3. Method

Performing a measurement under controlled conditions with an empty measuring well.

4. Requirements

None

5. Procedure

Ensure that the measuring well is empty.

Acceptance:

Ensure that no activity is present in the surrounding area. Perform a measurement of all radionuclides to be used clinically and for quality control.

Daily:

Perform a measurement for ^{99m}Tc.

Record the date and time of all measurement readings.

6. Analysis and Interpretation

In the event of unexpected deviations, check whether contamination or unexpected activity is present in the vicinity.

7. Action thresholds and actions

For all radionuclides, the background radiation must be less than 50 kBq (see Pitfalls and remarks). If none of the selectable radionuclides produces a sufficiently low reading, then the leakage current compensation must be adjusted. Often, there is an adjustment button for this purpose. After adjustment, the test must be performed again.

If this setting can no longer be further adjusted, the dose calibrator must be checked by the manufacturer.

If an elevated reading occurs with only one or some of the selectable radionuclides, it is likely that the measuring well is contaminated, and must therefore be cleaned.

8. Pitfalls and remarks
In practice, it can happen that at the location of the dose calibrator, there is a permanent low, slowly decaying level of radiation, for example caused by the Technetium generator. The dose calibrator should preferably be shielded to such an extent that this effect is not measurable. If this problem cannot be resolved, the background radiation must be determined and adjusted daily.

Constancy of sensitivity and linearity

1. Introduction and rationale
The amount of radiopharmaceutical administered to a patient is determined by the sensitivity and linearity of the dose calibrator. Alterations to the sensitivity may depend on the energy emitted by the radionuclide. Although in practice the probability of abnormalities in these parameters appears to be very small, the potential consequences are great. Therefore, rather frequent checking is nonetheless recommended, which can, however, be efficiently carried out with a set of three sources.

2. Frequency
It is recommended that the checks be thoroughly incorporated into routine operations so that ongoing performance of the checks is guaranteed (see Pitfalls and remarks): for example weekly, preferably on Monday morning before work is started.

3. Method
The constancy measurement is based on a measurement of the sensitivity using a single solid long-lived source with a photon energy in the region of the radionuclides commonly being used, and measured in a fixed geometry (i.e. in general ^{57}Co).
For checking the energy dependence of the sensitivity, apart from the source of ^{57}Co, a source of ^{133}Ba, ^{137}Cs or ^{60}Co is needed.
Checking the constancy of the linearity is performed using two sources of the same radionuclide which differ so much in activity that they are representative of the range frequently used clinically. Usually ^{57}Co is used, for which, as second source, an old calibration source that has decayed for several years may be utilised)

4. Requirements
See method. For this test, well-calibrated source are needed, with a minimum activity of 1 MBq.

5. Procedure
First check for background radiation. Place each source to be measured in the dose calibrator and measure the intensity. Record the measured value.

6. Analysis and interpretation
Register the result in a spreadsheet and plot the ratio of the result and the expected decay corrected value in a graph.

7. Action thresholds and actions
If the measurement deviates by more than 3% from the expected value, check the measurement set-up and the settings of the dose calibrator, and possibly repeat the measurement. If necessary, repeat the full check of accuracy of the sensitivity and the linearity. If a certain trend becomes visible in the results-graph, contact the manufacturer.

8. Pitfalls and remarks
a. Contamination of the measurement well can lead to deviating measurements.
b. Because the probability of deviations is very low, the biggest risk is that the checks may eventually no longer be performed. Embedding these checks periodically into the routine activities is therefore essential.

Accuracy and precision of sensitivity

1. Introduction and rationale
The sensitivity of the dose calibrator is the basis for the administration of radiopharmaceuticals to the patient. Therefore, this test focuses on the precision and accuracy. Monitoring of the constancy is described separately under "Constancy of sensitivity and linearity".
The precision of a measurement indicates how much an individual measurement can differ from the average of a large number of measurements. The accuracy of a measurement indicates how much the average of such a large number of measurements deviates from the actual value. The constancy (also called the stability) shows how the measurement changes over time. Precision, accuracy and constancy are related to the drift of the high voltage, changes in the gas in the ionisation chamber and in the electronics. The manufacturer often specifies the accuracy and precision based on standard sources. These are well-calibrated radionuclides embedded in perspex. If standard sources are not available, the manufacturer can be asked to perform this test (based on a maintenance contract).

2. Frequency
It is recommended that the accuracy and precision be determined on (re)acceptance.

3.Method
A standard source is placed into the measurement well and measured 10 times. The spread and the average are calculated.

4. Requirements
For this test, well-calibrated sources are needed, of which the activity is at least 1 MBq. The test must be performed using sources that are representative of the clinically used radionuclides. Frequently used standard sources are: ^{57}Co, ^{133}Ba, ^{137}Cs and ^{60}Co.

5. Procedure

For each source, the relevant radionuclide is chosen according to the manufacturer's specification. Check for background radiation. Insert the source into the measurement well using the source holder. Wait until the reading is stable. Remove the source from the measurement well and repeat the measurement after the reading shows zero; carry out a total of 10 measurements.

6. Analysis and interpretation

Correct the measurements for decay.

The accuracy for each source is then calculated by the percentage difference (PV) between the average (A) of the 10 measurements and the actual activity (C):

$$PV = \frac{A - C}{C} \times 100[\%]$$

To obtain the precision for each source, calculate the standard deviation (S) of the difference between each individual measurement (Ai) and the average (A) of the 10 measurements:

$$S = \sqrt{\frac{\sum_{i=1}^{n=10} (A_i - A)^2}{n-1}}$$

The precision is defined by: S/A * 100%

7. Action thresholds and actions

Both the precision and the accuracy are specified by the manufacturer. In general, a precision of 3% and an accuracy of 5% are acceptable. If these values are exceeded, the manufacturer must check the dose calibrator.

8. Pitfalls and remarks

a. Results may vary due to different geometries and radionuclides,
b. With source activities lower than the specified 1 MBq, a good measurement might no longer be possible.
c. The standard sources are often cast in perspex. If this perspex is (partly) damaged, deviations can arise in the measurements because the attenuation of the radiation changes in the perspex.

Linearity

1. Introduction and rationale

Generally, in practice, low to moderate activities are measured. At very high activities, the system will saturate, and less will be measured than is actually present. In other words, the

linear relationship between source intensity and read-out is disturbed. The purpose of this test is to ascertain the extent of this disturbance and at which intensity the saturation starts.

2. Frequency

On acceptance, it is recommended that the linearity is checked over the full activity range. After that, it is recommended that the constancy of the linearity is checked using two activities, which are representative for the range used clinically (see Constancy of sensitivity and linearity).

3. Method

This test can be carried out in two ways:

- Allowing a short-lived radionuclide to decay (decay curve).
- Measurement of a dilution series (logarithmic).

4. Requirements

For both methods a quantity of ^{99m}Tc is necessary (see implementation).

5. Procedure

The linearity must be checked at least over the entire range that is needed in the clinic or for quality checks (typical value of the maximum activity is 10 GBq). Repeat each measurement 3 times and check for background radiation for each measurement. The sample must always be placed in an easily reproducible position inside the source holder.

Decay curve:

Prepare the maximum activity of ^{99m}Tc in a typical clinical volume (5 ml). Measure the activity during ten to thirteen half times, (3 to 4 days) on a regular basis and at least at the beginning and end of the day. Record measurement and time of measurement.

Dilution series:

Prepare a dilution series of ^{99m}Tc from the maximum activity in factors 0,5, 0,2, 0,1, 0,05 down to 0,0001. All the activities must be in equal volumes (see Count geometry). Record measurement and time of measurement.

6. Analysis and interpretation

Collect the measured data in a spreadsheet and plot the measured activity logarithmically against the known decay-corrected activity. The measurements of the lower activities must be at the line of equality. Calculate the relative deviation from the known activity for each measurement. For the higher activities the deviation will increase if the system reaches saturation.

7. Action thresholds and actions

The activity at which the relative deviation exceeds the 5% must be higher than the activities measured in daily practice. Measurements must comply with the manufacturer's specifications.

8. Pitfalls and remarks

Because the source intensity must be measured over a range of 10 GBq to 1 MBq, this means that the decay curve must be measured over 13 half-lives. In so doing, the

ingrowth of any daughter nuclide must be taken into account: when 10 GBq of ^{99m}Tc have decayed to 1 MBq, there is 34 Bq of ^{99}Tc that is ingrown. If ^{195m}Au were to be used, then the ingrowth of ^{195}Au after 13 half-lives would amount to 2,5 kBq, which would yield an inaccuracy of 2,5%.
The disadvantage of the dilution method is that pipetting must be very accurately done and one needs to be cautious for glass wall absorption, and prevent contamination. Furthermore, systematic errors between the different ranges of scale may arise.

Count geometry

1. Introduction and rationale
The measured activity is closely related to the volume and position of the source in the measurement well. Since in practice activities are often measured in different types of syringes, it is important to know how the volume of the sample and the type of syringe used, affect the measurement of the activity. Also the type of needle and cap on the syringe may influence the measurement. The count geometry may have a different effect for each radionuclide. This test must therefore be performed separately for each radionuclide.

2. Frequency
It is recommended that the count geometry is determined on acceptance and when a new type of syringe is introduced.

3. Method
Measurements must be performed in all combinations of isotopes, syringes and volumes used in daily practice. All syringes are filled from the same stock solution with known activity concentration. The exact volumes are measured using a weight measurement of the empty and filled syringe. For each syringe volume, the relative deviation of the standard is calculated. The deviation is a measure of the influence of the count geometry of the dose calibrator. Correction is made for background radiation.

4. Requirements
- The standard volume specified by the manufacturer and all syringes and volumes which are used in clinical practice.
- A balance accurate to 0,01 g.
- Approximately 50 MBq of the radionuclide to be measured in approximately 50 ml of 0,5% HSA (Human Serum Albumin) in saline solution or demineralised water.
- The use of HSA in the preparation of the test solution is preferred in order to prevent the radionuclide binding to the wall of the syringe.

5. Procedure
Example:
- Syringes of 1 ml (3x), 2 ml, 5 ml, 10 ml and 20 ml
- Weigh all syringes (and record).
- Fill the 1 ml syringes to 0,1, 0,5 and 1,0 ml, and fill the remaining syringes completely and weigh again.

- Measure the activity of all syringes.
- Measure the background.

6. Analysis and interpretation

The measurements should be corrected for:

a. The actual contents of the syringes or bottles (by means of weighing);
b. The radioactive decay;
c. The background radiation of the dose calibrator;
d. Any deviation from the linearity of the dose calibrator.

Take account of the counting accuracy of the dose calibrator; if necessary, repeat the measurement several times.

The result identifies the sensitivity of the measurement made with the specific syringe and specific volume relative to the standard. The dose calibrator consists of an ionisation chamber and a measurement well. In practice, the middle of the measurement well appears to be the most sensitive.

7. Action thresholds and actions

Compare with the manufacturer's specifications if available. A deviation of less than 3% is normal, and for the usual syringes, the deviation may not be greater than 5%. For larger deviations, determine a correction table and make sure the user is informed.

8. Pitfalls and remarks

a. When measuring the background radiation, sufficient time must be taken to allow the dose calibrator to return to the resting state.
b. In connection with error propagation during decay corrections, not too much time may elapse between the preparation of the batch and the last measurement.
c. If the dose calibrator is utilized with a lift, it must be checked that the lift is in the correct position.
d. Radionuclides which also have low photon energies, such as ^{123}I, can be measured in a copper sleeve. In so doing, the activity measurement is primarily determined by the higher photon energies and the influence of the count geometry on the measurement can be calculated without interfering factors.
e. To measure the geometric sensitivity, a separate measurement can be performed with a point source at different heights in the measurement well. The measurements will result in a curve with the maximum at the middle of the well. The shape and width of the curve are an indication of the geometry.