CENTER FOR PHYSICAL SCIENCES AND TECHNOLOGY

Vilnius University Hospital SANTAROS KLINIKOS

MEASUREMENTS TRACEABILITY THROUGH COMPARISONS: RESULTS OF FIVE RADIONUCLIDE DOSE CALIBRATORS

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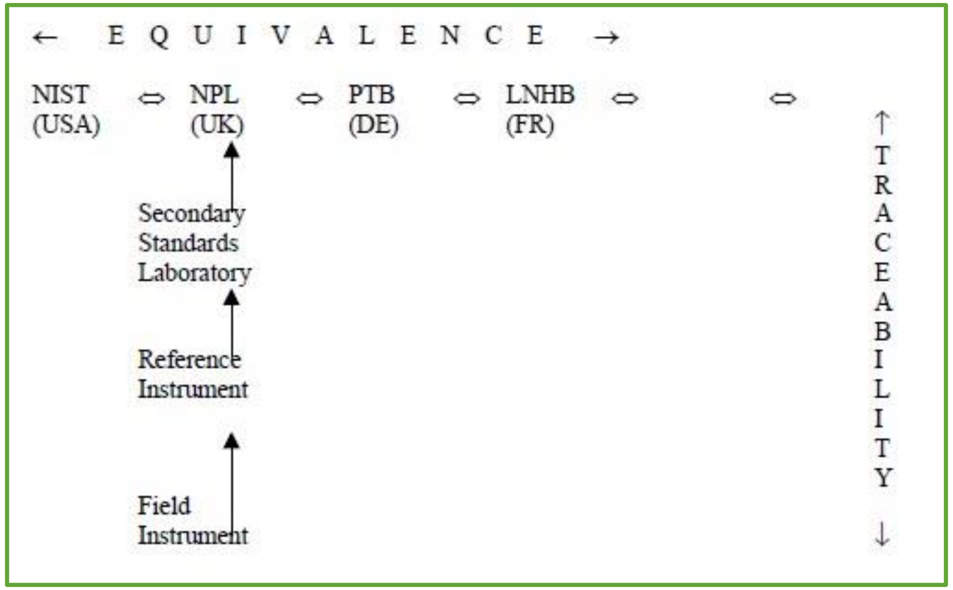
Outline

- Calibration and metrology
- Measurement methods
- Relation to other equipment and procedures
- Results of intercomparison
- International recommendations and experience of other countries

Calibration and metrology



National Physical Laboratory Good Practice Guide No. 93. Protocol for establishing and maintaining the calibration of medicine radionuclide calibrators and their quality control, 2006, NPL.

BIPM

National Metrology Institutes
(National Physical Laboratory and Czech Metrology Institute)

Secondary Standards Laboratory
(Center for Physical Sciences and Technology, Metrology Department, Ionizing Radiation Metrology Laboratory)

Reference Instrument (Capintec CRC-15R and Fidelis)

Field Instrument

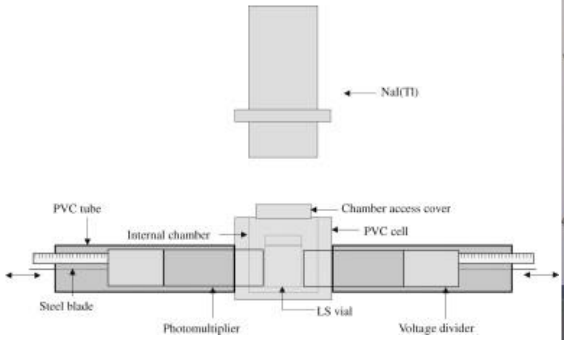
(Veenstra VDC-404, Veenstra VDC-405, COMECER PITAGORA)

Primary measurement methods

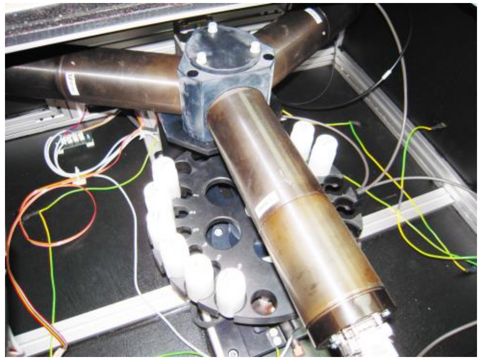
The Triple-to-Double Coincidence Ratio (TDCR)

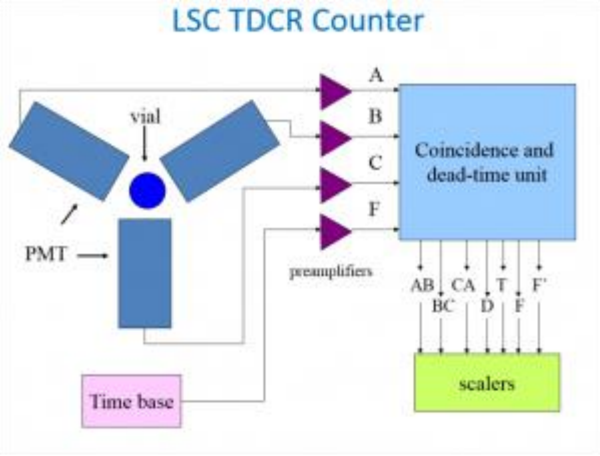
Liquid scintillation counting

The live-timed 4πβ(LS)-γ(NaI(Tl)) anticoincidence counting



- Methods are complementary
- Perform standardization
- Uncertainties are well characterized (<0.5%)





Physical characteristics of radionuclides and calibration coefficients

- A calibration coefficient is the coefficient used to convert the measured ionization chamber current to a nominal activity, form femtoamperes (fA) up to microamperes (µA).
- The magnitude of a calibration coefficient depends upon the radionuclide: ^{22}Na, ^{32}P, ^{57}Co, ^{67}Ga, $^{68}Ge/^{68}Ga$, ^{89}Sr, ^{90}Y, ^{90}Y (glass microspheres), ^{90}Sr, ^{99}Mo, ^{99m}Tc, ^{123}I, ^{125}I, ^{131}I, ^{131}I (capsules), ^{133}Ba, ^{137}Cs, ^{153}Gd, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{201}Tl, ^{223}Ra …
- The physical characteristics (energy, decay scheme, half-life):
- Therapy: α emitters: ^{223}Ra; ^{213}Bi; ^{211}At; ^{225}Ac; ^{227}Ac
- Pure β emitter: ^{32}P; ^{90}Y; ^{89}Sr (For radionuclides emitting only (or mostly) β particles, activity measurement is essentially based on bremsstrahlung X-rays)
- Low-energy: ^{123}I; ^{125}I; ^{201}Tl (For radionuclides emitting a relatively high number of low energy X-rays calibration factors can change significantly with the container)
- PET imaging: ^{11}C; ^{18}F; ^{64}Cu; ^{68}Ga
- The ionization chamber (inner chamber wall thickness, gas pressure, chamber design, and operating voltage)
- The source geometry (container type, container wall thickness, source volume, and position of the container in the chamber)
- Additional components (lead shielding, the sample holder and the removable liner) could influence the measured current

Sealed sources for routine checks

Routine checks of radionuclide activity meters

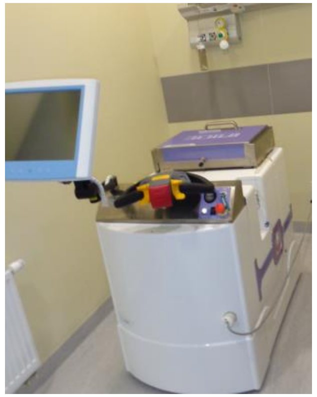
need the use of long lived sources

- Range of photon energies
- Calibrated within 5% or less
- Range of activities

Isotope	$T_{1/2}$	E_γ (keV)
^{137}Cs	30 y	662
^{57}Co	271 d	122, 136
^{60}Co	5.27 y	1173, 1332
^{133}Ba	10.55 y	35, 81, 303, 356

These sources allow for check of stability of the response, but they do not grant accuracy of the reading for isotopes used in clinical practice.

On site measurements



The secondary standard radionuclide calibrator Capintec CRC-15R.

Standard 3 ml syringe and the vial were used for measurement.

Secondary standards

Methods calibrated by primary methods

• Guidance on dial settings

• Complete understanding of different variables that

affect measurement result (Effects of measurement geometry, pure β emitters)

• Provides a method to transfer the standard to the user

Acceptable calibration tolerances for reference and field instruments

Parameter	Reference Instrument	Field Instrument
Repeatability	± 0.5% (1 s.d.)	± 1% (1 s.d.)
Linearity (over range used)	± 1% (1 s.d.)	± 5% (1 s.d.)
Accuracy		
High energy & gamma (> 100 keV)	± 2% (range) to secondary standard	± 5% (range) to reference
Low energy & gamma (< 100 keV)	± 5% (range) to secondary standard	± 10% (range) to reference

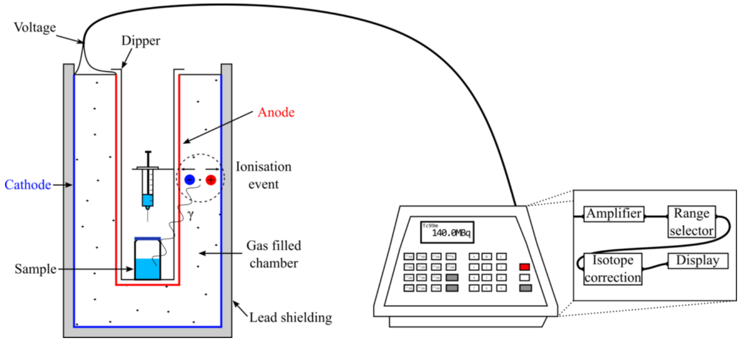
Table 1. Examples of Calibration Coefficients (Vial) from the NPL Secondary Standard Radionuclide Calibrator

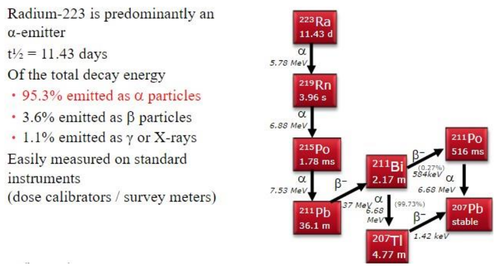
Radionuclide (pA/MBq)	Calibration Coefficient
P-32	0.03518
Y-90	0.0721
Tl-201	0.886
Tc-99m	1.240
Ga-67	1.565
I-123	1.721
I-131	4.073
I-131 (capsule)	4.053
In-111	4.129
F-18	10.39

$$\text{Calibration factor} = \frac{Current\ (pA)}{Activity\ (MBq)}$$

National Physical Laboratory Good Practice Guide No. 93. Protocol for establishing and maintaining the calibration of medicine radionuclide calibrators and their quality control, 2006, NPL

Radionuclide activity calibrator





ACTIVITY CALIBRATOR SHOULD HAVE THE FOLLOWING PHYSICAL CHARACTERISTICS:

Sensitive to energies (X-rays, γ-rays and β particles through bremsstrahlung), from ~ 50 keV and 2 MeV.

- Calibration for each radionuclide
- High count rate (deadtime)
- Linear response, from ~ 100 GBq to 0,1 MBq
- Stability
- Possibility to measure different geometry sourses
- Response time: 2-10 seconds

https://humanhealth.iaea.org/HHW/Radiopharmacy/VirRad/Quality_Control_Procedures/Quality_Control_Module/Radioactivity_concentration/Measurement_tools/Isotope_Calibrator/Principles_of_an_isotope_calibrator/index.html

Source geometry and activity calibrator response

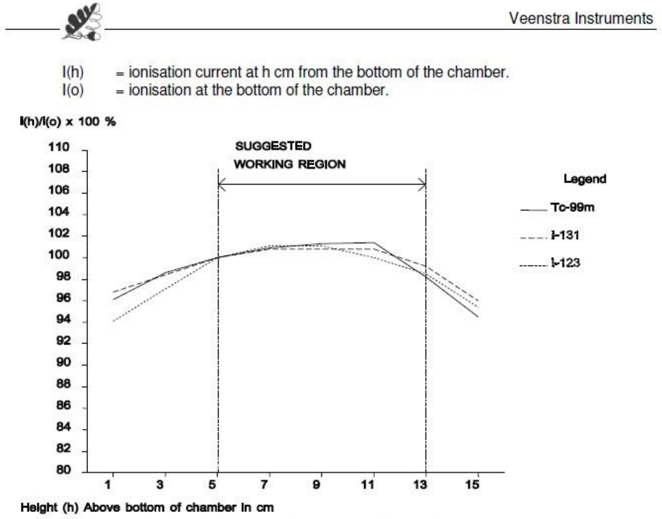
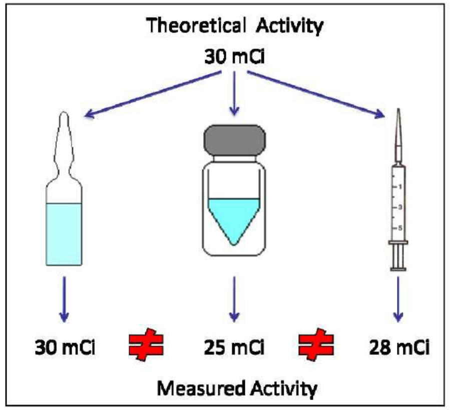
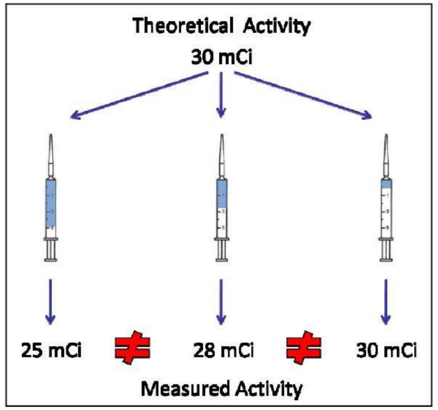
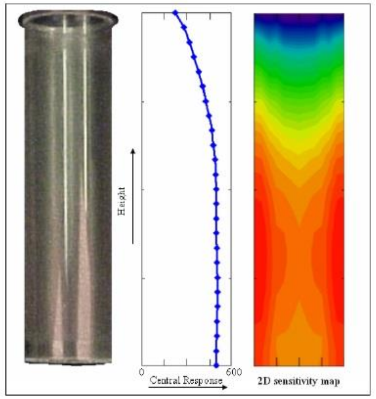
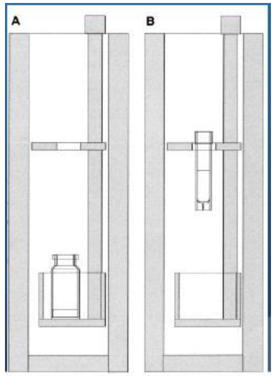


Figure 3 Height-dependence of the ionisation chamber response









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Activity calibrator

- Diagnostic Reference Levels (DRLs)
- Radiopharmaceutical QC
- Standardized Uptake Value (SUV)
- Injected activity (MBq)
- Sensitivity CPS/MBq
- Effective doses (mSv)
- Internal dosimetry
- Staff doses
- Quantification
- SPECT scanning modalities calibration

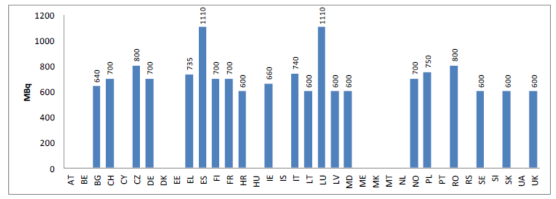
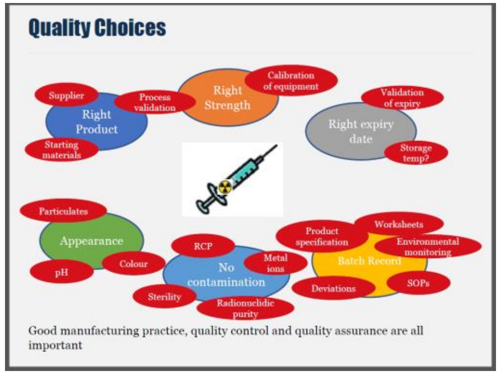


Figure 3.2. Comparison of DRLs for bone imaging, Tc-99m phosphates and phosphonates.

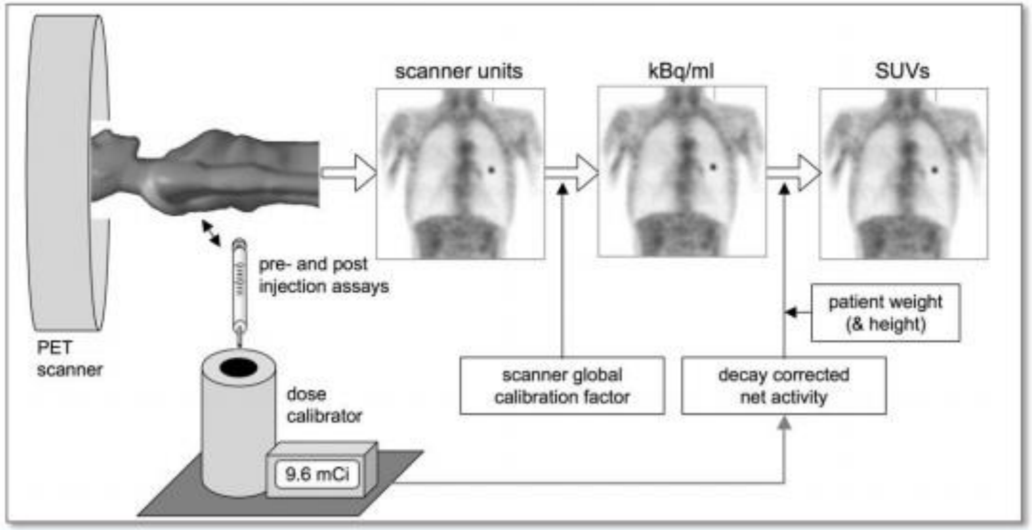
RADIATION PROTECTION N°180, European commission report, 2014



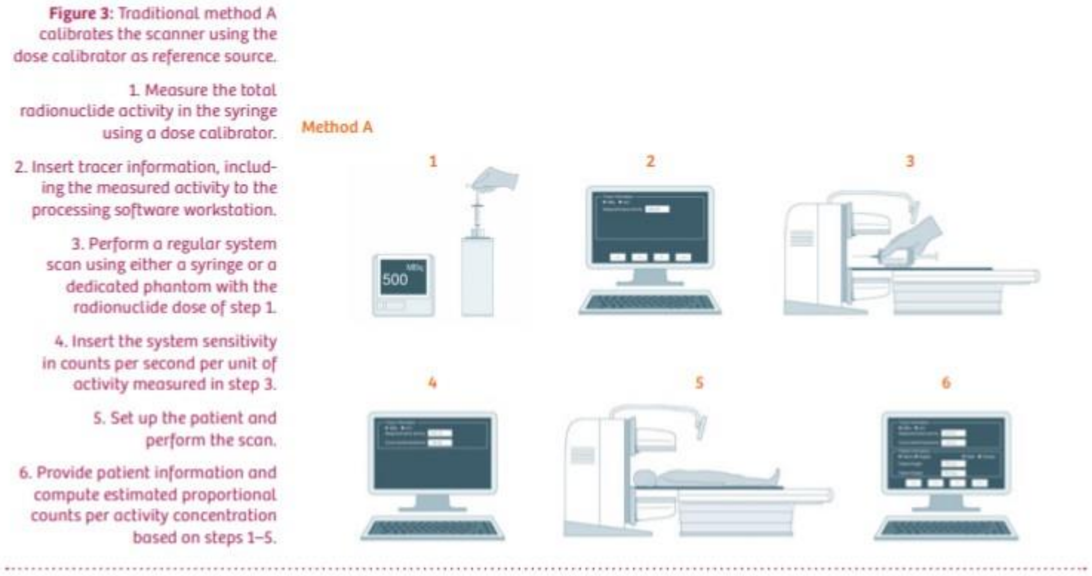
Dr. Maggie Cooper, Radiopharmaceutical chemistry of technetium

Quantification and cross validation

- Cross-validation of radionuclide calibrator with ^{90}Y SIR-Spheres PET/CT's calibration

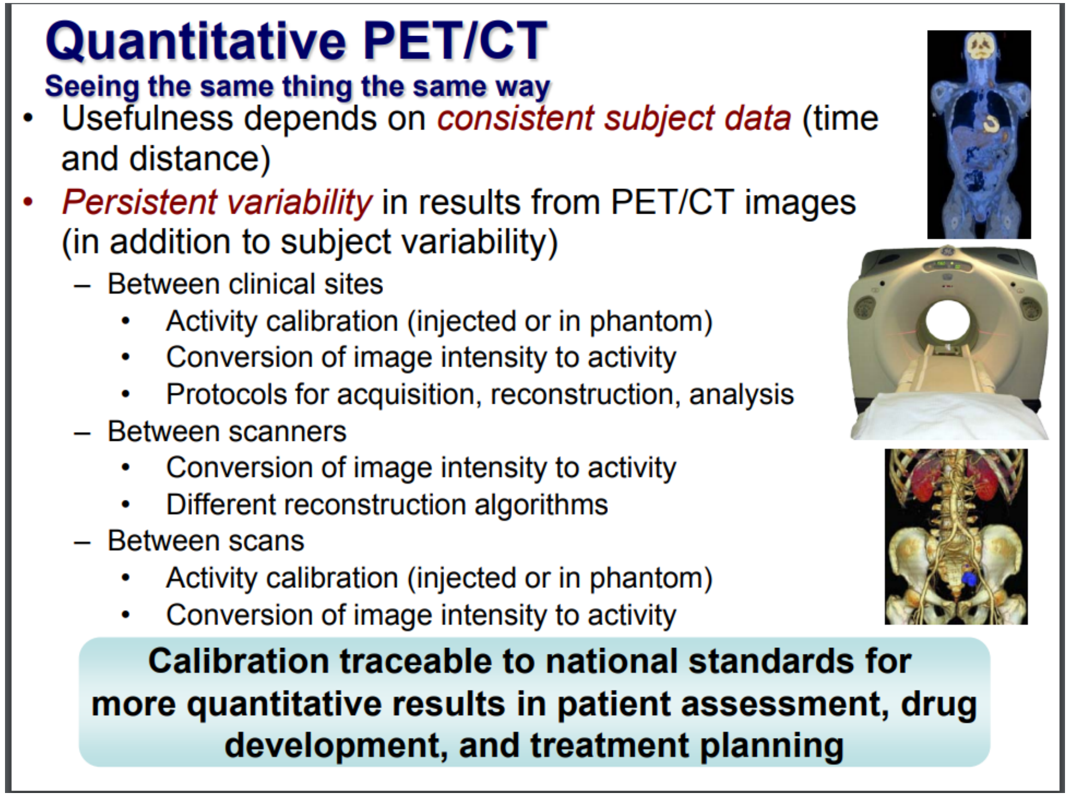


K. Baete, Traceable Quantification for 68Ga based PET/CT



H. Levillain, Precision of pre-SIRT predictive dosimetry

Hormonisation of scanning equipment



Quantitative PET/CT

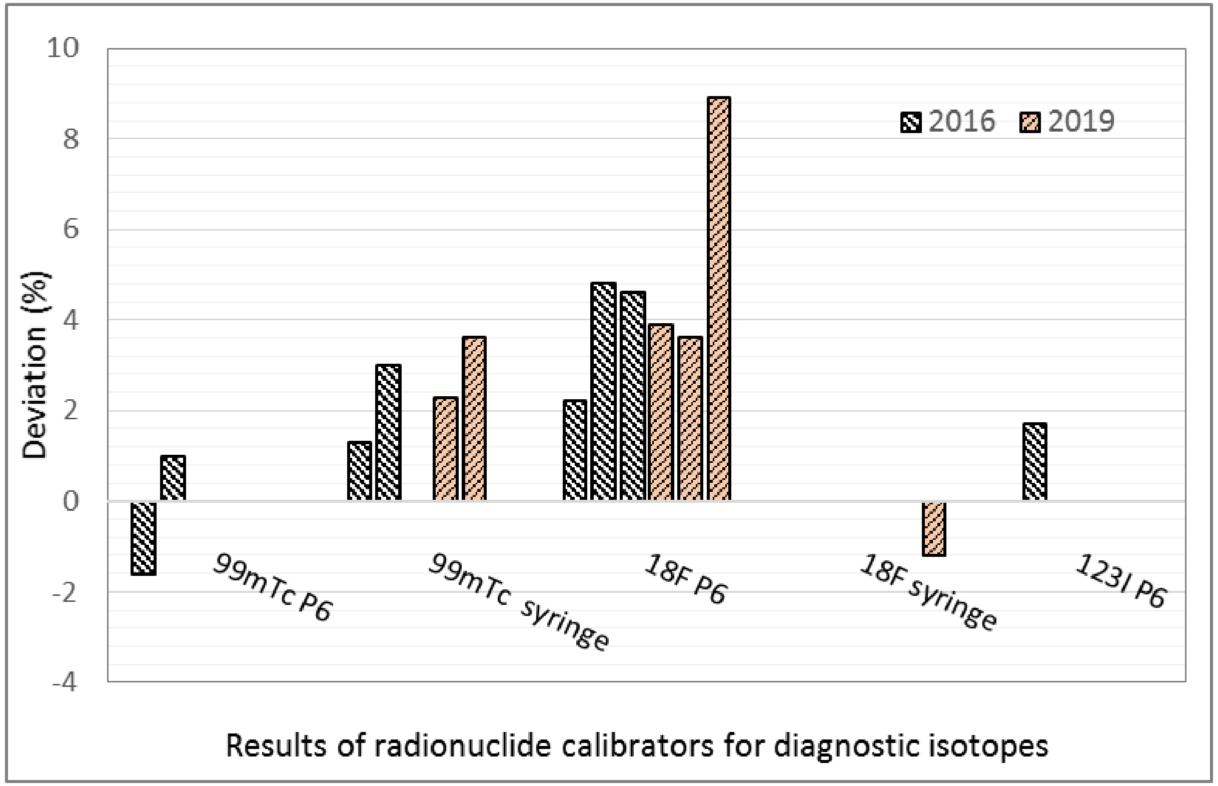
Seeing the same thing the same way

- Usefulness depends on *consistent subject data* (time and distance)
- *Persistent variability* in results from PET/CT images (in addition to subject variability)
  - Between clinical sites
    - Activity calibration (injected or in phantom)
    - Conversion of image intensity to activity
    - Protocols for acquisition, reconstruction, analysis
  - Between scanners
    - Conversion of image intensity to activity
    - Different reconstruction algorithms
  - Between scans
    - Activity calibration (injected or in phantom)
    - Conversion of image intensity to activity

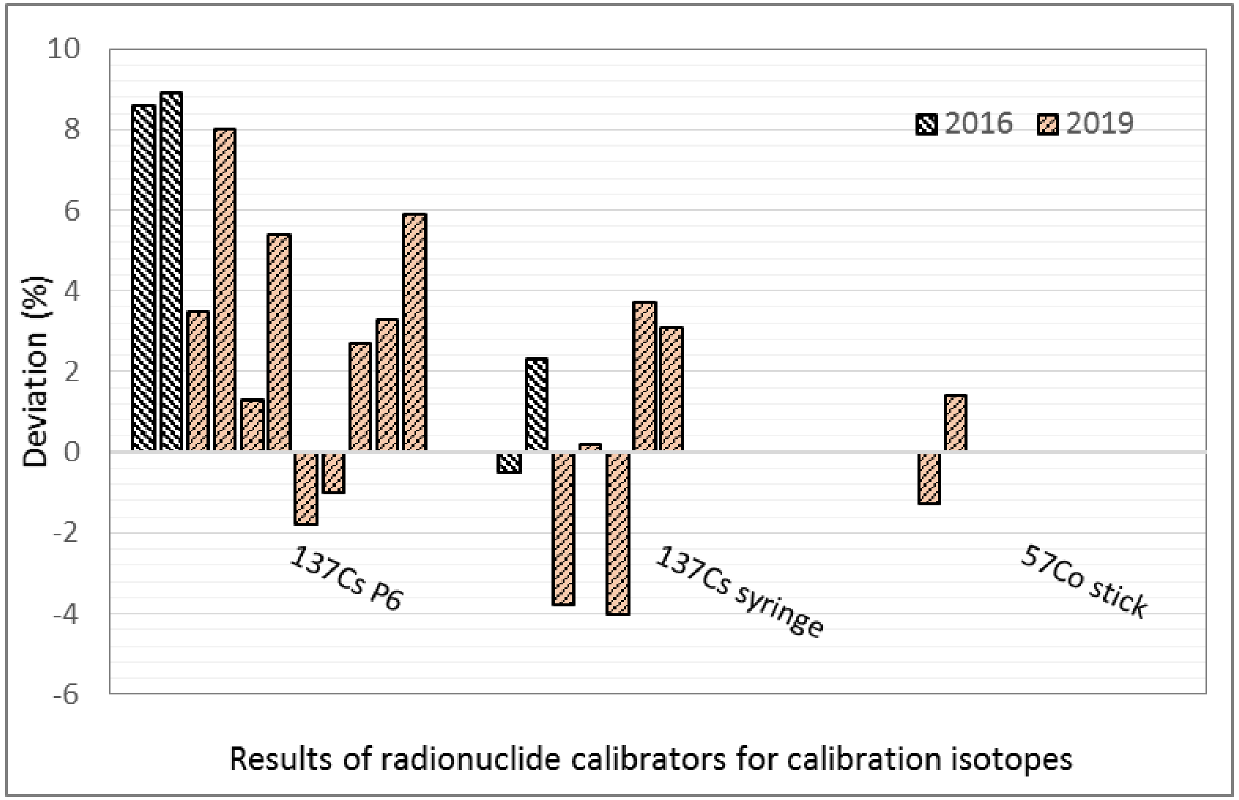
Calibration traceable to national standards for more quantitative results in patient assessment, drug development, and treatment planning

Lisa R. Karam Chief, Ionizing Radiation Division National Institute of Standards and Technology

The results of the intercomparison obtained in 2016 and 2019



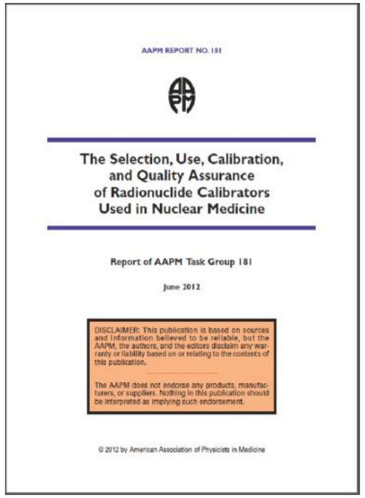
The results of the intercomparison obtained in 2016 and 2019

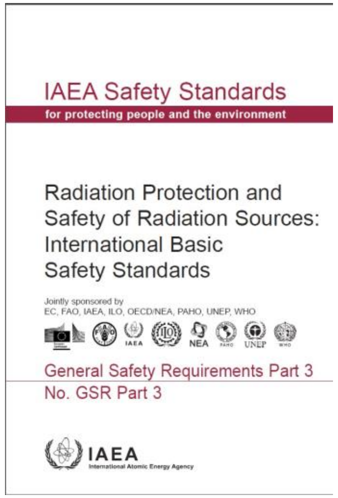


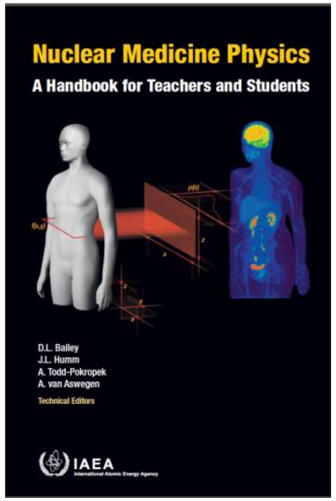
Intercomparison of radionuclide calibrators used in the main Lithuanian hospitals with the secondary standard ionization chamber

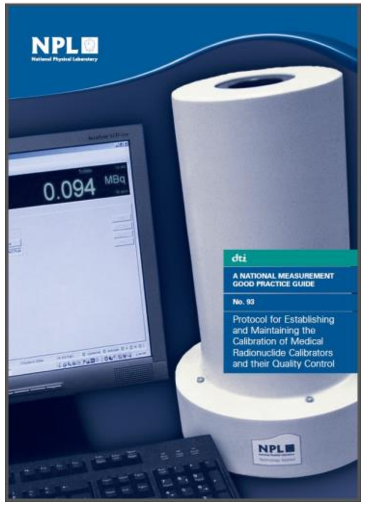
Radionuclide and geometry	**Deviation (%)**
^{137}Cs (P6)	**8,3**
^{123}I (P6)	**3,0**
^{99m}Tc (P6)	**14,8**
^{99m}Tc (syringe)	**12,1**
^{57}Co (Stick)	**1,3**
^{22}Na (Stick)	**4,2**
^{18}F (P6)	**8,9**
^{18}F (syringe)	**4,8**
^{131}I (P6)	**1,9**
^{131}I (capsule)	**5,8**
^{223}Ra (P6)	**1,3**

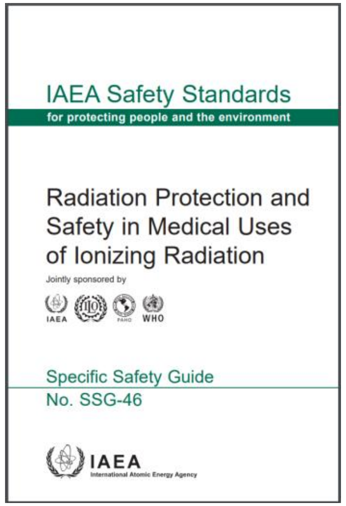
International recommendations











The performance of activity meters must be assured through a quality assurance programme conforming to international, European or national standards (NPL (2006); EC (1997)). The suspension levels are given in Table 3-1 for each critical parameter together with the type of criterion used and a reference to a recommended test method.

3.2.2 Suspension levels for activity meters

Table 3-1 Suspension Levels for Activity Meters

Physical Parameter	Suspension Level	Reference	Type	Notes and Observations
Accuracy	> 5 %	NPL (2006)	A	
Linearity	> 5 %	NPL (2006)	A	
System reproducibility	> 1 %	NPL (2006)	A	

The suspension levels given in Table 3-1 are for instruments used for the measurement of the activity of gamma emitting sources with energies above 100keV. If these instruments are calibrated to measure isotopes emitting low gamma ray energies (below 100 keV) or beta or alpha emitting sources (Siegel et al. (2004)) special measures need to be taken in order to overcome vial and geometry dependent readings. This could be achieved e.g. by measuring a calibrated source in various vials and geometries for setting up individual calibration factors. In these cases the suspension levels in Table 3-1 probably cannot be met. If the instrument is suspected of malfunctioning a test with a relevant source needs to be carried out to confirm the suspicion using the values in Table 3-1 (EANM (2008)).

Equipment shall comply with the set requirements or Criteria for Acceptability of Medical Radiological Equipment used in Diagnostic Radiology, Nuclear Medicine and Radiotherapy (RP162)

4.185. The administered activity should be verified by means of an activity meter (dose calibrator) or other suitable device to ensure that the total activity does not deviate significantly from the prescribed administered activity (e.g. <5% deviation), and the measured value should be recorded. Corrections should be calculated for residual activity in the syringe, cups, tubing, inline filter or other materials used in the administration.

World practice

Physica Medica 45 (2018) 134–142

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Physica Medica

journal homepage: www.elsevier.com/locate/ejmp

Original paper

Intercomparison of ^{99m}Tc, ^{18}F and ^{111}In activity measurements with radionuclide calibrators in Belgian hospitals

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ARTICLE INFO

Keywords:
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Calibration
Traceability
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Radiopharmaceutical
Quality control

ABSTRACT

This study presents current status of performance of radiopharmaceutical activity measurements using radionuclide calibrators in Belgium. An intercomparison exercise was performed among 15 hospitals to test the accuracy of ^{99m}Tc, ^{18}F and ^{111}In activity measurements by means of radionuclide calibrators. Four sessions were held in different geographical regions between December 2013 and February 2015. The data set includes measurements from 38 calibrators, yielding 36 calibrations for ^{99m}Tc and ^{111}In, and 21 calibrations for ^{18}F. For each radionuclide, 3 ml of stock solution was measured in two clinical geometries: a 10 ml glass vial and a 10 ml syringe. The initial activity was typically 100 MBq for ^{99m}Tc, 15 MBq for ^{111}In and 115 MBq for ^{18}F. The reference value for the massic activity of the radioactive solutions was determined by means of primary and secondary standardisation techniques at the radionuclide metrology laboratory of the JRC.

The overall results of the intercomparison were satisfactory for ^{99m}Tc and ^{18}F, since most radionuclide calibrators (> 70%) were accurate within ± 5% of the reference value. Nevertheless, some devices underestimated the activity by 10–20%. Conversely, ^{111}In measurements were strongly affected by source geometry effects and this had a negative impact on the accuracy of the measurements, in particular for the syringe sample. Large overestimations (up to 72%) were observed, even when taking into account the corrections and uncertainties supplied by the manufacturers for container effects. The results of this exercise encourage the hospitals to perform corrective actions to improve the calibration of their devices where needed.

1. Introduction

Nuclear medicine is an invaluable tool for diagnostic and therapeutic purposes. The most widely used radionuclide is ^{99m}Tc, accounting for approximately 80% of all nuclear medicine examinations and about 90% of those used for diagnostic purposes. In 2008, the world total number of procedures performed with ^{99m}Tc was estimated to range between 25 and 30 million annually, with 6–7 million of them taking place in Europe [1]. Other frequently used radionuclides for nuclear medicine in Europe are ^{18}F, ^{201}Tl, ^{123}I, ^{131}I, ^{67}Ga and ^{111}In [2] and the future holds an increasing interest in radionuclides for targeted

to keep the doses "as low as reasonably achievable". Articles 55, 56 and 60 of the European Council Directive 2013/59/EURATOM on the principles of justification and optimization of medical exposures imply proper calibration of all sources giving rise to medical exposure [4]. After all, the use of diagnostic reference levels and the study of dose-effect relationships in therapeutic nuclear medicine procedures depend on the accuracy of the measurement of the activity to be administered. There is also an increased interest in quantification of SPECT and PET images for pre-therapeutic dosimetry of radionuclide therapy. This requires cross-calibration of measurement devices (e.g. gamma cameras, radionuclide calibrator, gamma counter) and a traceability chain.

Contents lists available at ScienceDirect

Physica Medica

journal homepage: www.elsevier.com/locate/ejmp

Original paper

A comparison of four radionuclide dose calibrators using various radionuclides and measurement geometries clinically used in nuclear medicine

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ARTICLE INFO

Keywords:
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Radionuclide
Radionuclide calibrator

ABSTRACT

Purpose: Reliable quantification of radioactivity in nuclear medicine is becoming increasingly important in various therapeutic applications requiring a high accuracy of nuclear medicine measuring equipment, such as radionuclide calibrators. In this study the accuracy of four different radionuclide calibrators was assessed for ^{99m}Tc, ^{111}In, ^{68}Ga and ^{18}F for measurement geometries clinically used.

Methods: Syringes and vials were prepared with a reference activity using a stock solution of which the activity concentration was determined using gamma-ray spectroscopy. The accuracy of four different radionuclide calibrator systems, ISOMED 2000, ISOMED 2010, VIK-202 and Capintec CRC-25R, was assessed by comparing the measured activity to the reference activity.

Results: Deviations in measured activity from reference values were found up to 12.5%, 32.0%, 29.0% and 12.6% for ^{99m}Tc, ^{111}In, ^{68}Ga and ^{18}F, respectively. For ^{68}Ga all radionuclide calibrators systematically overestimated the activity by 10–20%. For ^{111}In, large differences in activity measurements were observed between different source geometries, in particular between syringes and vials. Deviations between radionuclide calibrator systems were found up to 11.8%, 44.4%, 14.4% and 8.7% for ^{99m}Tc, ^{111}In, ^{68}Ga and ^{18}F, respectively. When comparing similar syringe types of different brands filled with identical stock solution volume, deviations up to 1.8%, 5.8%, 10.2% and 3.2% were found for ^{99m}Tc, ^{111}In, ^{68}Ga and ^{18}F.

Conclusion: Substantial deviations in measured activity were found for all radionuclides and radionuclide calibrators, which may result in erroneous activity dosing and image quantification. This underlines the importance of thorough validation of radionuclide calibrators for all measurement geometries and radionuclides clinically used.

DOSE CALIBRATORS QUALITY CONTROLS IN SWITZERLAND: SIX YEARS OF EXPERIENCE

François Bochud [1], Philippe Spring [1], Damian Twerenbold [2], Reto Linder [3], Fritz Leibundgut [4] and Sébastien Baechler [1]

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Abstract

In Switzerland, the legal use of open radioactive sources in nuclear medicine and the general requirements for quality controls are defined in a federal ordinance. The metrological traceability is guaranteed through a directive of the Swiss metrological office (METAS) that requires each instrument to be monitored at least once a year through either a verification or an intercomparison. The verification is performed onsite by an accredited laboratory with a set of three gamma sources (Co-57, Cs-137 and Co-60) and – if applicable – a beta source (Sr-90/Y-90). The intercomparison is made through conventional mail. A source of I-131 or Tc-99m is measured both in the nuclear medicine department and in an accredited laboratory. The maximum tolerated error is 10% for gamma sources and 20% for beta sources. This methodology guarantees that the instruments have a correct response for most of the energy range used in practice. Not all nuclides are systematically probed and manufacturers are ultimately responsible for the calibration factors. The precision of the measurements performed in Switzerland is satisfactory with only about 6% of the measurements out of the tolerances. This monitoring also allowed us to improve the skills of the personnel and update the park of instruments by getting rid of dose calibrators displaying old units.

1. Introduction

Measuring the activity of radiopharmaceuticals before patient injection is an essential monitoring procedure in nuclear medicine [Wastiel 2005]. Together with the producer's surveillance of the radioactive isotope (test for radionuclidic purity) and the labeling (test for radiochemical purity), it guarantees a safe use of radiopharmaceuticals in nuclear medicine. Activity measurement in nuclear medicine departments is therefore part of good laboratory

FIRST RESULTS OF CHECKING THE PERFORMANCE OF DOSE CALIBRATORS IN MEDICAL UNITS IN BULGARIA

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[1]SBALOZ, Sofia, [2]QC consultant GAMMACHECK

Abstract

The dose calibrators are essential instruments in nuclear medicine units to determine the activity of radiopharmaceutical to be administered to the patient. Inappropriate performance of these equipment may compromise the diagnosis. According to the National regulations the following parameters are subject of quality control: background, linearity, reproducibility, accuracy. The aim of this survey was to check the performance of all 26 dose calibrators in the country. The accuracy tests were carried out using one certified reference source ^{137}Cs (662 keV) with trade mark LB 165. The results of the accuracy test show deviations from the expected value in a wide range –20.5 % to +21 %. Only 6 of all 26 dose calibrators meet the requirement of ± 5% deviation of accuracy.

Key words: dose calibrator, quality control, survey

Conclusions

The appropriate quality management programme, traceability of measurements (reference instrument calibrated against standardised reference sources traceable to the National Metrological Institute) are necessary to ensure the accuracy of the administrated patient dose.

Correct measurement of administrated activity is important for imaging, patient dose optimisation, setting the local diagnostic reference levels, administration of beta-ray emitters and for measurement of activity for quantitative imaging in molecular radiotherapy (activity-time integral within the defined volume).

Thank you for your attention,
questions?