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Abstract

The present paper addresses the calibration of well-type ionization chambers (ICs) used at LNE-LNHB as standard transfer instruments to calibrate hospitals in the case of ^{90}Y-labelled resin microspheres SIR-Spheres (Sirtex, Australia). Developed for interventional oncology, this radiopharmaceutical is directly injected in the liver for cancer treatment by radioembolization also known as selective internal radiation therapy. The present work was carried out in the framework of the European project MetroMRT (Metrology for molecular radiation therapy, HLT11). As commonly performed in radionuclide metrology for radiopharmaceuticals, the objective is to ensure the metrological traceability of SIR-Spheres to nuclear medicine services. The first studies were focused on primary measurements of SIR-Spheres based on the Triple to Double Coincidence Ratio method (using both liquid scintillation and Cerenkov counting), applied after the chemical dissolution of the ^{90}Y-labelled resin microspheres. Because ^{90}Y is a high-energy β^--emitter, the IC response strongly depends on the transport of electrons in the radioactive solution and the surroundings (vial,

chamber liners and materials). The variability of IC-responses due to the geometry dependence is investigated by means of measurements and Monte Carlo simulations (Geant4 code) in the case of a Vinten IC. The aim of the present study was also to propose a reliable uncertainty for IC calibration for the standard transfer of SIR-Spheres to end-users.

Keywords: Radionuclide metrology, SIR-Spheres standardization, ^{90}Y-labelled resin microspheres, Calibration of ionization chambers, Monte Carlo simulation.

1. Introduction

The collaborative project "Metrology for molecular radiation therapy" (MetroMRT, HLT11) initiated within the European Metrology Research Programme aimed at providing metrological support in the field of targeted radionuclide therapy (D'Arienzo et al., 2014). Molecular radiation therapy (MRT) refers to therapeutic techniques where a high-radiation dose is internally delivered to a specific target such as tumors. During the 3-year MetroMRT project (2012-2015), the participation of the Laboratoire national Henri Becquerel (LNE-LNHB) was chiefly focused on the standardization of ^{90}Y-labelled resin microspheres SIR-Spheres (Sirtex, Sydney, Australia) used for Selective Internal Radiation Therapy (SIRT) in the case of the treatment of malignant liver disease by radioembolization (Dezarn et al., 2011). As conventionally performed in NMIs (National Metrology Institutes) for radiopharmaceuticals (Zimmerman and Judge, 2007), the aim is to provide a reliable metrological traceability between primary standards and nuclear medicine services. The interest of this study is also to respond to the need of MRT quantitative imaging applied to monitor biodistribution of ^{90}Y-labelled microspheres in tissues after therapeutic injection (Bagni et al., 2012). The purpose is to ultimately develop specific-patient dosimetry based on quantitative tomographic imaging in the case of SIRT treatments (Pasciak et al., 2014).

The ^{90}Y-microsphere product supplied by Sirtex in a specific vial contains a nominal activity of 3 GBq (at the reference date) in a 5 mL solution of sterile, pyrogen-free water for injection to patients. The procedure developed at LNE-LNHB for primary measurements of SIR-Spheres (Lourenço et al., 2015) based on the TDCR (Triple to Double Coincidence Ratio) method, differs from the techniques already described in Mo et al. (2005) and Selwyn et al. (2007). Indeed, the standardization of SIR-Spheres was carried out after a complete chemical digestion of the 5-mL solution of microspheres in the original vial delivered by Sirtex. The reproducibility of this procedure was also verified. The present article deals with the calibration with the Sirtex vial of the ionization chambers (ICs) used for metrological traceability at LNE-LNHB. Due to the fact that ^{90}Y is a high-energy β^--emitter (E_{max} = 2279 keV), the variability of calibration factors resulting from the sensitivity of the vial geometry is investigated (Coursey et al., 1993; Fenwick et al., 2014). This geometry dependence is also studied by means of Monte Carlo (MC) simulations of the Vinten IC using Geant4, a general-purpose toolkit for the simulation of the transport of particles in matter (Agostinelli et al., 2003). The problem of systematic deviations between experimental and calculated calibration factors observed in the case of high-energy β^--emitters is discussed. The objective is to assess a reliable uncertainty of IC calibrations for the transfer of SIR-Spheres standard to hospitals.

2. Primary measurements of SIR-Spheres and calibration of ionization chambers

2.1 Primary measurements of ^{90}Y-labelled resin microspheres

Primary measurements were carried out using the TDCR method after complete chemical digestion of the ^{90}Y-labelled resin microspheres in the original Sirtex vial (Lourenço et al., 2015) in order to optimize the sample aliquoting and to obtain measurement conditions for TDCR counting close to aqueous solutions. The dissolution protocol based on the Fenton reaction was developed to achieve the complete solubilization of the 5 mL volume SIR-

Spheres by direct addition of reagents in the Sirtex vial (iron, hydrogen peroxide and nitric acid). For source preparation, the dissolved resin-microspheres were subsequently 100-fold diluted in order to minimize color quenching for Cerenkov counting (Bobin et al., 2010). A good agreement on activity concentrations was obtained between TDCR measurements using liquid scintillation and Cerenkov emission. For subsequent IC calibration, the activity of SIR-Spheres in the Sirtex vial was assessed from these primary measurements with a relative standard uncertainty of about 1.5 %.

2.2 Calibration of ionization chambers

2.2.1 Technical description

For the transfer of the SIR-Spheres standard, measurements were performed with two different well-type ICs commonly used at LNE-LNHB as secondary instruments: the Vinten 671 IC manufactured by Centronic (Amiot, 2004) and the Normandy IC manufactured by Rib Technologie.

The Vinten IC has a cylindrical aluminium chamber with a 10.5 L effective volume (filled with N_2 gas at a pressure of 1 MPa) including a coaxial re-entrant well (73-mm diameter, 374-mm height) made of aluminum (2-mm thick) with a polyvinyl liner placed on top (0.5-mm thick). The IC is equipped with a central aluminum-alloy electrode (2-mm thick) and it is housed in a Bakelite support (1-mm thick) surrounded by a 50-mm thick layer of lead shielding in order to reduce the background.

The Normandy IC has also an aluminum chamber with an effective volume of about 8 L (75-mm re-entrant well diameter, 1.5-mm thick) filled with Ar gas (0.2-MPa pressure) equipped with an aluminum alloy electrode. This chamber is surrounded by a shielding composed of a 5-mm-thick layer of lead and outer 2.5-mm-thick layer of steel. The source

holders for both ICs have different shapes: one is made of Teflon® for the Normandy IC and the other of polymethyl methacrylate (PMMA) for the Vinten IC.

At LNE-LNHB, the calibration of the Vinten IC is generally carried out with specific LNHB ampoules (wall thickness of 0.61 (1) mm) filled with 5 mL of radioactive solution (HCl 0.1 mol L^{-1} usually). The Normandy IC is especially dedicated to the transfer of standards to nuclear medicine services. For that purpose, it is calibrated for about twenty radiopharmaceuticals in different source geometries (e.g. vials, syringes). The Vinten IC is employed as a reference for the follow-up of calibrations for all radionuclides.

2.2.2 Calibration factors for SIR-Spheres

SIR-Spheres are manufactured by Sirtex in a specific glass vial filled with 5 mL of a solution containing a mixture of sterile water and ^{90}Y-labelled resin microspheres settled down at the bottom of the vial because of their higher density. In order to homogenize the activity distribution for the measurements with dose calibrators, it advised by the manufacturer to proceed with the microspheres fully suspended in the 5-mL volume after vial shaking. At LNE-LNHB, the calibrations of the two ICs were carried out without vial shaking (after the microspheres sedimentation). The calibration factors for both ICs were previously given in Lourenço et al., (2015) with associated uncertainties mainly due to primary measurements (about 1.5 %).

2.2.3 Variability of the IC response with vial geometry

The vial-dimension measured at LNE-LNHB from a batch provided by Sirtex gave the following averaged values: wall thickness of about 2.0 (2) mm and bottom thickness of 2.8 (4) mm. In order to estimate the influence of the geometry variability on the IC calibration, ten vials with different masses (comprised between 18.6 g and 20.6 g) were filled with 5 mL

of ^{90}Y aqueous solution (25 μg/g of Y in 0.04 M HCl). Some of these vials provided by Sirtex were previously measured with active SIR-Spheres (Lourenço et al., 2015). The plot in Fig. 1 displays the mass current (pA per g) obtained with the ten vials in the Vinten IC. Only statistical uncertainties are attached to the results. A decrease of the mass current as a function of the vial mass is clearly observed. This correlation between the IC response and the empty-vial mass yields to a difference of about 14 % between the minimum and maximum values. It can be observed in Fig. 1 that the variability of the mass currents (relative standard deviation ~ 5 %) is much higher than the associated uncertainties. The same measurements were also performed with the Normandy IC; an analogous correlation is also observed (Fig. 2) but with a lower maximum difference of about 5 %. The variability of the results is also lower (relative standard deviation ~ 1.5 %).

The same measurements were carried out with a copper attenuator (0.5-mm thick tube); a significant downward shift of about 40 % for the Normandy IC (see Fig 2) and about 26 % for the Vinten IC (see Fig. 1) was observed. The mass currents depending on the measurement configurations are reported in Table 1. In the case of the Vinten IC, the correlation is strongly reduced with a significant decrease of the variability (relative standard deviation ~ 0.6 %). On the contrary, the correlation and the variability remain almost identical in the case of the Normandy IC.

For all the measurement configurations (with and without attenuator), the higher mass current was obtained with the vial at 18.69 g. The same behavior was also observed in both ICs when some of the Sirtex vials of the batch (18.69 g, 18.7 g and 18.93 g) were previously measured with active SIR-Spheres. The lowest difference between the IC responses with these three vials was obtained also with the Normandy IC (~ 2 %) without the copper attenuator. This effect could be due to the fact that the bottom thickness of the vial at 18.69 g is the lowest of the vial batch.

The measurements carried out with the batch of ten vials with increasing masses can help to assess a reliable uncertainty for IC calibration with SIR-Spheres. It was observed that the IC response depends on the detector design and the mass of the vial as well as its geometry. Because the Normandy IC calibration for SIR-Spheres is more robust with regards to the obtained results, it is now used at LNE-LNHB for secondary measurements of SIR-Spheres with a conservative relative uncertainty equal to 5 % in order to consider the variability due to the Sirtex vial. In the case of the Vinten IC, the relative uncertainty should be higher than 10 %. It can be also drawn from the study that this value can be significantly reduced by the use of a copper attenuator (0.5-mm thick).

3. Monte Carlo calculations of the calibration factor

The response of pressurized ICs is based on the measurement of the total charge generated in the gaseous region due to electron/ion pairs created with the transport of ionizing radiation. As a result, the IC calibration factor is sensitive to the chamber design (e.g. chamber liners, type of filling gas, shielding), the nature of solutions (e.g. volume and composition), the vial dimensions, the source holder and also the radionuclide decay scheme. MC simulations of radiation-matter interactions are very useful to study the resulting effects of those properties or the addition of other elements such as liners (Ceccatelli et al., 2007; Kryeziu et al., 2007; de Vismes and Amiot 2003). In this framework, several investigations based on the use of MC calculations to estimate calibration factors have already been implemented at LNE-LNHB. The IC response for many radionuclides decaying through photon cascades such as ^{60}Co, ^{22}Na, ^{18}F or ^{99m}Tc in LNHB ampoules were calculated using the Penelope code (Salvat et al., 2009). These investigations have shown the ability of MC simulations to estimate adequately the IC response in the case of photon-emitter radionuclides for which an excellent agreement with experimental values (lower than 1 %) were obtained

(Amiot, 2004; Amiot et al., 2012). This work was extended for the present study in the case of pure β^--emitters such as ^{90}Y.

3.1. Methods

In this study, the Geant4.10.0 version was used to simulate the mean energy deposited in the effective volume of the Vinten IC. The geometry modelling (including source-detector arrangement and surroundings) was implemented using detailed drawings provided by the manufacturer and x-ray of the chamber and a filling gas pressure determined in de Vismes and Amiot (2003). The Sirtex vial was modelled as a pure glass material (SiO_2, density of 1.32 g/cm^3) filled with 5 mL of a mixture of the resin microspheres settled down and pure water (70 % of the total volume). The resin microspheres were simulated in the hydrated form with a mass per unit volume of 1.06 g/cm^3 measured at LNE-LNHB. The following chemical composition was used (Dias and Shapka, 2001): carbon (31.9 %), hydrogen (7.7 %), oxygen (50 %) and sulphur (10.3 %)

The emission of β^--particles is randomly generated as a uniform distribution in the whole radioactive volume (corresponding to the resin microspheres in the case of SIR-Spheres) and uniformly in all possible random directions with initial electron energies drawn from a calculated β^--spectrum. These source specifications are implemented *via* a specific module based on the General Particle Source (GPS) available in Geant4. Particles are tracked throughout various regions of the detector until their energy becomes smaller than the prescribed value of the threshold cut-off energy (250 eV). After running a large number of particles (10^8 events for a statistical precision better than 1 %), the calibration factor in term of pA/MBq is calculated using the total mean energy E (eV) deposited in the gaseous region according to the following expression: $C = e.\frac{E}{W}.10^{18}$, assuming that the charge collection in the gas is 100 %; e (coulomb) is the electron charge and W (eV) the mean energy required to

produce electron/ion pair (34.8 (2) eV for N_2 with regards to the Vinten IC as given in ICRU report 31 (1993).

3.2 Calculation of calibration factors in the case of pure β^--emitters

Depending on β^--emitter maximum energies, the total energy deposited in the IC gas region can mainly be due to the production of bremsstrahlung photons along the track of electrons in matter. To test the physics models, simulations were performed with three sets of electromagnetic (EM) models available in Geant4 and which are able to run adequately the EM processes. The theoretical model 'G4EmStandard' based on the Seltzer-Berger model and both low-energy models: 'G4EmLivermore' (Ivanchenko et al., 2011) and 'G4EmPenelope' based on the Penelope code (Salvat et al., 2009).

As described in the Geant4 user-guide, the cross sections of the bremsstrahlung process used in the 'G4EmStandard' model are obtained by interpolating the published tables containing energy-differential cross sections from 1 keV to 10 GeV, with an associated uncertainty of 10 % (Seltzer and Berger 1986). The angular distribution and the sampling of radiated energy are calculated according to an analytical model well validated for high energies (Agostinelli et al., 2003). Regarding the model 'G4Livermore', the total cross section of the bremsstrahlung process and the shape of the photon energy spectra are released from the interpolation of the evaluated cross section and data reported from the EEDL Livermore library (Perkins et al., 1991).

The model 'G4EmPenelope' corresponds to a re-engineering in Geant4 of the bremsstrahlung model from the Penelope code, which nevertheless uses the reported EEDL data but differs slightly in terms of implementation. Many papers in the recent literature have shown that the proposed models are able to predict in a fairly good way the simulation of the transport of photons and electrons in matter, even if the Penelope model seem slightly

preferable over the other two in the range of energy from few eV to few MeV (Pandola et al., 2015; Ivanchenko et al., 2011).

The response of the Vinten IC was simulated here using the specific LNHB ampoules (filled with 5 mL of aqueous solution) in the case of three pure β^--emitters: ^{90}Y (E_{max} = 2279 keV, 1st forbidden unique transition), ^{89}Sr (E_{max} = 1495 keV, 1st forbidden unique transition) and ^{32}P (E_{max} = 1710 keV, allowed transition). The respective spectra were computed with the homemade BetaShape program, described in much detail by Mougeot, (2015), using experimental shape factors and decay-scheme parameters from the Table of radionuclides (Bé et al., 2006). This program takes precisely into account the energy dependence of the theoretical shape factor in the case of forbidden unique transitions.

Table 2 presents the ICs calibration factors obtained for the three β^--emitters decays and for the EM physics models tested. Table 3 shows the typical uncertainty components of the MC calculation in the case of ^{90}Y decay. Regarding these results, significant underestimations compared to the experimental IC responses were obtained: ^{90}Y (30 %), ^{32}P (40 %) and ^{89}Sr (41 %). It should be noted that the implementation of other EM physics models does not reduce the large discrepancies between experimental and simulated values. The maximum difference between the three EM models remains lower than 8 %. This underestimation was already observed with MC calculations performed at LNE-LNHB for the Vinten IC and another which is the Vacutec IC filled with an Ar-Xe gas mixture (Amiot, 2014).

The sensitivity to the calculated ^{90}Y β-spectrum was tested by using three experimental shape factors depending on the term W representing the β particle energy: 1, $1-0.0064\times W$ and $1-0.0114\times W$ (Mougeot, 2015); the result shows only a 1 % variation of the IC response.

It should be mentioned that for the three β^- decays tested, the effective contribution of the bremsstrahlung process to the total mean energy deposited in the gas region was estimated to about 5 % for ^{90}Y, 90 % for ^{32}P and close to 100 % for ^{89}Sr. In the case of the ^{90}Y, the major part of the total energy deposited in the gas region is due to the initial electrons from the β-spectrum. Besides, additional simulations were performed by varying the interpolated cross section of the bremsstrahlung at the boundaries of the associated uncertainties (±10 %). These fluctuations have finally led to a small variation of the total energy deposited (2 % maximum difference). To conclude regarding these investigations, it seems that the IC response of the Vinten IC cannot be adequately reproduced by MC calculations for calibrations whereas they do for photons emitters. Despite the use of different chambers, the kind of spectrum and energy range or the models of EM physics implemented, the large discrepancies between experimental and simulated IC responses are not reduced.

Up to now this problem remains unsolved and requires advanced investigations to understand these discrepancies. For that reason, MC simulations were performed in the following only to assess the variability of IC response due to the vial geometry dependence for secondary measurements of SIR-Spheres.

3.3 Vinten IC response variability due to Sirtex vial by means of MC calculations

The variability of the Vinten IC response for Sirtex vials was also investigated by means of MC simulations. The calculations were first performed for two representative Sirtex vials among the ten measured (dimensions implemented in manner to be close to both representative vials weighing 20.4 g and 18.93 g) filled with 5 mL of ^{90}Y aqueous solution. A relative difference of 6 % between both vials was obtained on calculated calibration factors. This result is coherent with the difference of 8 % obtained with measurements. The impact of the copper attenuator (0.5-mm thick) was also simulated. As observed experimentally, the MC calculations yield a decrease of the IC response (about 20 %). Furthermore, as expected,

the relative difference between both modeled vials is strongly reduced with the usage of copper attenuator (0.5 % with simulated model compared with 0.6 % for experiment).

The IC responses were also calculated for the two representative Sirtex vials (20.4 g and 18.93 g) filled with resin microspheres (as described in section 3.1) in order to check for potential differences with the behavior observed with ^{90}Y aqueous solution. The simulations performed by varying the wall thickness from 1.8 mm to 2.0 mm lead to a difference on the Vinten IC response of about 3.5 %. The same MC calculations carried out by varying the bottom thickness from 2.2 mm to 3.2 mm yield to a difference of about 1 %. The influence of the density of glass was also tested. It appears that the variation of the density (1.32 g/cm^3 to 1.33 g/cm^3 entails an increase of the IC response of about 4 %. On the contrary to the case of aqueous solution, the MC calculations with SIR-Spheres underestimate the effect of the variation of the vial geometry compared with experiments. These deviations could be due to the composition of the resin microspheres used for the simulation.

4. Discussion

The standardization of SIR-Spheres was investigated at LNE-LNHB to establish a metrological traceability to hospitals in order to respond to the need for MRT quantitative imaging and the development of specific-patient dosimetry (D'Arienzo et al., 2014). At LNE-LNHB, two ICs were calibrated with primary measurements based on TDCR measurements after complete dissolution of the active microspheres in the original Sirtex vial (Lourenço et al., 2015). The problem of the uncertainty of the IC calibration factors due the variability of the Sirtex vial was investigated by means of experimental studies and MC calculations.

Experimental results were obtained with vials of different masses (filled with 5 mL of ^{90}Y aqueous solution) provided by Sirtex. A correlation between the IC response and empty-vial mass was observed with both calibrated ICs: Vinten 671 IC (filled with N_2 gas at 1 MPa)

and Normandy IC (filled with Ar gas at 0.2 MPa). The differences of the IC responses between the Sirtex vials were higher with the Vinten IC (14 %) than with the Normandy IC (5 %). Additional measurements performed with a copper attenuator (0.5-mm thick) showed that these differences between the Sirtex vials are significantly reduced in the case of the Vinten IC (about 2 %).

The variability of the Vinten IC response with the vial geometry (wall and bottom thickness) was also studied by means of MC calculations using the Geant4 code. The problem of the underestimation of the IC response (in term of energy deposited in the gas volume) was addressed but it has been possible to give a definitive explanation on its origin. More investigations are on-going to improve MC calculations of IC calibration factors. Regarding relative variations, the simulation results were more coherent with experiments for the study of the IC response variability with the variation of Sirtex vial geometry filled with aqueous solution. The extension of the MC calculations to the modelling of SIR-Spheres led to a slight underestimation of the influence of the Sirtex vials on the Vinten IC response. This problem could be due to the composition of the resin microspheres used for the modelling or due to the fact that the β^--emission is considered as uniform in the whole volume of SIR-Spheres.

Finally, it can be drawn from the present study that the Normandy IC calibration for SIR-Spheres is more robust with regards to the variability of the Sirtex vials. In consequence, this transfer instrument is now used at LNE-LNHB for secondary measurements of the ^{90}Y-labelled resin microspheres with a relative uncertainty equal to 5 %. In the case of the Vinten IC, the relative uncertainty (higher than 10 %) can be significantly reduced by the use of a copper attenuator. A specific design of the source-holder could also be studied in order to improve the robustness of IC calibrations of SIR-Spheres.

Acknowledgements

This work was supported by the EMRP joint research project “Metrology for Molecular Radiotherapy” (MetroMRT, HLT11) which has received funding from the European Union on the basis of Decision No 912/2009/EC. The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union.

The authors wish to thank Sirtex for providing SIR-Spheres and vials.

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Figure captions:

Fig. 1: Mass current as a function of mass of ten Sirtex vials (filled with 5-mL of ^{90}Y aqueous solution) in the Vinten IC (with and without copper attenuator). Only statistical uncertainties are considered (~ 0.2 %).

Fig. 2: Mass current as a function of mass of ten Sirtex vials (filled with 5-mL of ^{90}Y aqueous solution) in the Normandy IC (with and without copper attenuator). Only statistical uncertainties are considered (~ 0.3 %).

Table captions:

Table 1: Mass current as a function of mass of ten Sirtex vials (filled with 5-mL of ^{90}Y aqueous solution) in both ICs (with and without copper attenuator).

Table 2: Calibration factors of β^--emitters calculated with a Geant4 modelling of the Vinten IC in case of the LNHB ampoule filled with ^{90}Y aqueous solution. Three different Bremsstrahlung models available in Geant4 were tested.

Table 3: Typical uncertainty components of the MC calculation of the Vinten IC response in the case of ^{90}Y decay.

Fig. 1

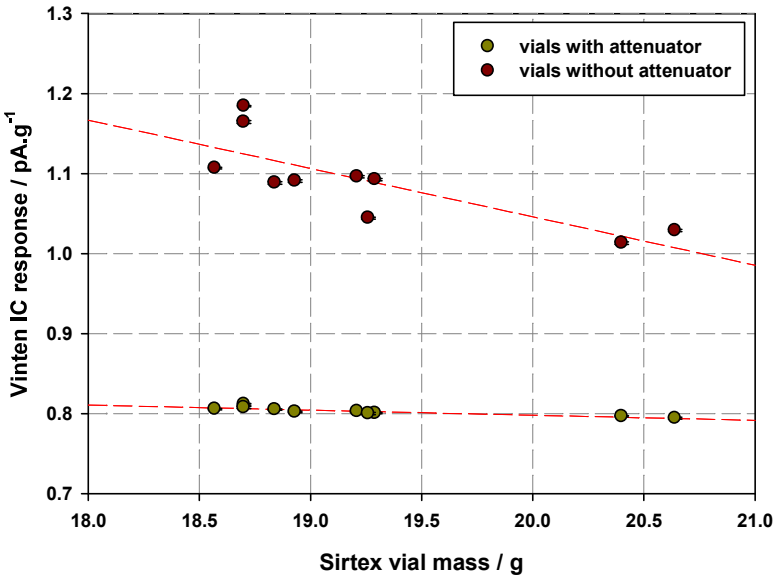
vials with attenuator
vials without attenuator
Vinten IC response / pA.g-1
Sirtex vial mass / g
1.3
1.2
1.1
1.0
0.9
0.8
0.7
18.0
18.5
19.0
19.5
20.0
20.5
21.0

Fig. 2

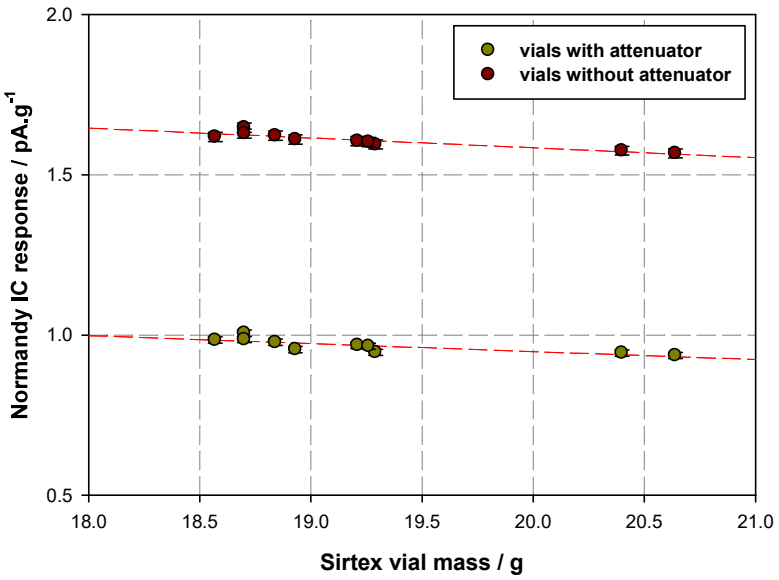
vials with attenuator
vials without attenuator
Normandy IC response / pA.g-1
Sirtex vial mass / g
2.0
1.5
1.0
0.5
18.0
18.5
19.0
19.5
20.0
20.5
21.0

Table 1

Sirtex vial mass (g)	**Normandy IC response (pA/g)**		**Vinten IC response (pA/g)**	
	Without attenuator	With attenuator	Without attenuator	With attenuator
18.57	1.618 (5)	0.984 (3)	1.107 (2)	0.806 (2)
18.69	1.647 (5)	1.006 (3)	1.184 (2)	0.812 (2)
18.70	1.629 (5)	0.986 (3)	1.165 (2)	0.808 (2)
18.84	1.622 (5)	0.977 (3)	1.088 (2)	0.805 (2)
18.93	1.610 (5)	0.955 (3)	1.091 (2)	0.802 (2)
19.20	1.605 (5)	0.968 (3)	1.096 (2)	0.803 (2)
19.26	1.602 (5)	0.965 (3)	1.044 (2)	0.800 (2)
19.30	1.594 (5)	0.946 (3)	1.093 (2)	0.801 (2)
20.40	1.575 (5)	0.944 (3)	1.013 (2)	0.797 (2)
20.64	1.567 (5)	0.936 (3)	1.029 (2)	0.794 (2)
Relative standard deviation	**1.5 %**	**2.3 %**	**5 %**	**0.6 %**

Table 2

β-emitters	**Experimental calibration factor (pA/MBq)**	**Calculated calibration factor (pA/MBq)**		
		G4EmPenelope	G4EmLimermore	G4EmStandard
^{90}Y	5.06 (7) $x10^{-1}$	3.50 (5) $x10^{-1}$	3.31 (5) $x10^{-1}$	3.25 (5) $x10^{-1}$
^{32}P	3.46 (2) $x10^{-2}$	2.10 (3) $x10^{-2}$	2.05 (3) $x10^{-2}$	1.99 (3) $x10^{-2}$
^{89}Sr	2.45 (1) $x10^{-2}$	1.44 (2) $x10^{-2}$	1.44 (2) $x10^{-2}$	1.43 (2) $x10^{-2}$

Table 3

Uncertainty components	**%**
^{90}Y decay scheme	0.4
Shape factor of beta spectrum	0.35
computed mean-energy deposited	0.8
physics models	0.5
W-value required for e^-/ion pair creation	0.57
combined relative uncertainty	1.5

Highlights:

- Ionization chambers (ICs) used at LNE-LNHB for metrological traceability were calibrated for SIR-Spheres ^{90}Y-labelled resin microspheres.
- The variability of IC-response due to the Sirtex vial geometry was investigated by means of measurements and Monte Carlo simulations.
- A correlation between the IC response and the mass of Sirtex empty-vial was observed.
- A reliable uncertainty for IC calibration with SIR-Spheres at LNE-LNHB is proposed.