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Measurements of the absolute gamma-ray emission intensities from the decay of ^{166}Ho

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ABSTRACT

^{166}Ho ($T_{1/2} \approx 26.8$ h) is an emerging theragnostic radionuclide of interest in nuclear medicine due to its peculiar decay scheme, featuring high-energy β^- emission (≈ 1.8 MeV) coupled with the main gamma-ray emission (≈ 80.6 keV). Using the new ^{166}Ho activity standard and the well-calibrated, high-energy resolution HPGe detector, both available at ENEA-INMRI, a new determination of several ^{166}Ho gamma-ray emission intensities, I_γ, was performed with low uncertainty. The new I_γ values contributed to the Decay Data Evaluation Project.

1. Introduction

The radionuclide ^{166}Ho ($T_{1/2} = 26.795$ (29) h) decays through β^- emissions to the excited states of ^{166}Er. The two main β^- transitions, with energy 1773.9 keV and 1854.5 keV, are directed to the first excited state and the ground state of ^{166}Er, with emission probability, I_β, of 50.5% and 48.2%, respectively; the first one is associated to the emission of a gamma ray with energy 80.5725 (13) keV and emission intensity $I_\gamma = 6.55$ (8) %. The decay scheme of ^{166}Ho is shown in Fig. 1 (Bé et al., 2004). Holmium belongs to the group of the 15 rare earth elements, known as lanthanides, which are the focus of interest in nuclear medicine for applications in cancer therapy. In particular, ^{166}Ho possesses the ideal characteristics for use in diagnostic applications with the Single Photon Emission Computed Tomography (SPECT) technique, thanks to its short half-life, appropriate gamma-ray emission, and high-energy β^- emission beneficial for therapeutic tumour treatment. For this reason, in recent years, a wide range of applications for ^{166}Ho as a medical radionuclide has been studied in order to prepare drugs for the treatment of hepatocellular carcinoma (HCC) and bone metastases, including the use of selective internal radiation therapy (SIRT or radioembolization). The very short half-life of holmium, when compared to other high-energy pure β^- emitters used in nuclear medicine for therapeutic purposes, such as ^{32}P ($T_{1/2} \approx 14.3$ d) and ^{90}Y ($T_{1/2} \approx 2.7$ d), or to other theragnostic radionuclides with similar physical properties, such as ^{177}Lu ($T_{1/2} \approx 6.7$ d), combined with its other physical and chemical properties, makes this radionuclide appealing for therapeutic applications. In fact, over 90% of the radiation transported by the particles emitted in its decay process is deposited in the organ under treatment in a short time period, or in other words, with a relatively high-dose rate. Additionally, holmium also displays paramagnetic properties, making it suitable for potential use in magnetic resonance imaging (MRI) combined with other diagnostic techniques (Klaassen et al., 2019).

Due to the growing interest in ^{166}Ho for nuclear medicine and the significant expansion of its clinical applications, there is a strong need for a new accurate standard of this radionuclide in the metrology community. This is essential to support its medical uses, especially for the calibration of tools routinely used in clinical practice for activity measurements or quantitative imaging.

For these purposes and within the framework of the EMPIR MRTDosimetry project (MRTDosimetry, 2016), a study was initiated at several National Metrology Institutes (NMIs), which were partners of the research project. The aim was to develop a new ^{166}Ho standard and to also perform a new determination of ^{166}Ho nuclear data for the submission of the achieved results to the Decay Data Evaluation Project (DDEP) (Bobin et al., 2019).

The two main intense β^- branches, associated with the low-intensity γ ray at ≈ 80.6 keV, make ^{166}Ho suitable for primary activity measurements using the Triple-to-Double-Coincidence Ratio (TDCR) technique in liquid scintillation mode (Broda et al., 2007). This is due to the high detection efficiency achieved with this technique for this radionuclide.

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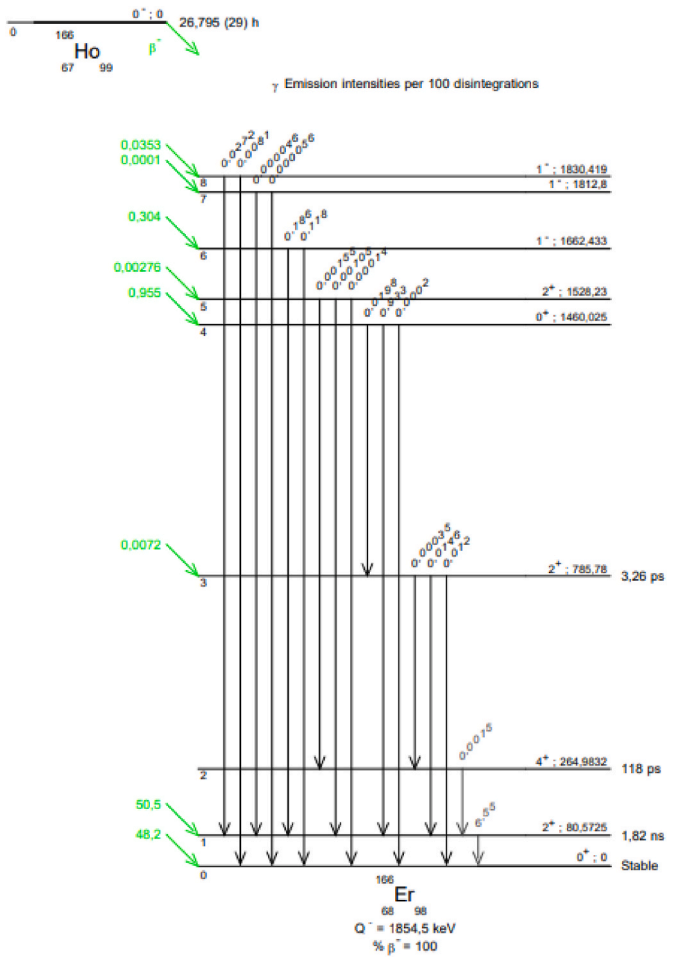


Fig. 1. Decay scheme of ^{166}Ho (Bé et al., 2004).

In particular, the two TDCR counters owned by ENEA-INMRI, namely the Hidex 300 SL "Metro" version (Kossert et al., 2014) and the home-made portable one (Capogni and De Felice, 2014), were utilized in this study to standardize a^{166}Ho liquid solution produced at TRIGA MARKII reactor operating at LENA Laboratories in Pavia, Italy (LENA). This collaboration took place within a scientific partnership with the Gemelli Hospital in Rome (Vaccaro et al., 2023). The new standard was used to calibrate two well-type Ionization Chambers (ICs) at ENEA-INMRI for ^{166}Ho, namely the fixed IG11-A20 Centronic IC and the NPL-CRC portable one. A gamma-ray emitting impurity check of the ^{166}Ho master liquid solution, produced at TRIGA MARKII reactor in Pavia, was performed using the ENEA-INMRI well-calibrated and high-energy resolution HPGe detector, hereinafter referred to as the ENEA-INMRI HPGe detector.

The paper will focus on the primary activity measurements of ^{166}Ho carried out by the two TDCR counters, using the same set of sources prepared in the Ultima Gold (UG) liquid scintillation (LS) cocktail from the aforementioned master liquid solution. Furthermore, this work will highlight the results obtained at ENEA-INMRI regarding the new determination, with low uncertainty, of the several gamma-ray emission intensities, I_γ, of ^{166}Ho by using the ENEA-INMRI HPGe detector, mainly calibrated with long-lived gamma-ray emitting standard sources available in the laboratory.

2. Basic considerations for ^{166}Ho measurements

The ^{166}Ho master liquid solution, standardised at ENEA-INMRI, was obtained through the (n,γ) reaction by irradiating a small metallic filament (mass less than 1 g) of ^{165}Ho with the thermal neutron spectrum of the TRIGA reactor at LENA in Pavia. Due to the very high purity of the irradiated sample of ^{165}Ho, the presence of unknown gamma-ray emitting impurities in the aforementioned liquid solution was not expected. The only expected by-product of the ^{165}Ho(n,γ)^{166}Ho reaction is the long-lived ($T_{1/2} \approx 1.1\ 10^3$ years) metastable ^{166m}Ho with a factor of about 7 part per million (ppm) respect to ^{166}Ho (Klaassen et al., 2019). The presence of ^{166m}Ho in the master liquid solution and, more generally, the degree of purity of this solution, were checked using the ENEA-INMRI HPGe detector. In contrast, the standardization of the ^{166}Ho master liquid solution was carried out at ENEA-INMRI using the Tiple-to-Double Coincidence Ratio (TDCR) absolute method in liquid scintillation (LS) mode.

Performing measurements with an HPGe detector means taking into account all the recommendations described in (Debertin and Helmer, 1988) for accurate and precise gamma-ray spectrum analysis. In particular, absolute measurements of gamma-ray emission intensities, I_γ, of a specific gamma-ray emitting radionuclide with an HPGe detector involves identifying, through the recorded spectrum, the main full-energy peaks (FEPs) of the radionuclide under study. Quantifying the I_γ (E) for each emitted gamma-ray of energy E is then achieved by analysing its FEPs and by knowing its activity A, according to the following formula:

$$I_\gamma(E) = \frac{N(E)}{L.T.\ \varepsilon(E)\, A} \prod_k C_k \tag{1}$$

where $N(E)$ is the net area under the FEP of energy E, $L.T.$ is the live time of the measurement (expressed in seconds), $\varepsilon(E)$ is the FEP efficiency for each gamma-ray, obtained through a calibration procedure with long-lived gamma-ray emitting standard sources, and C_k are the correction factors applied to the measurement. In this particular work, three correction factors were applied, i.e.: source decay during the measurement; source activity decay to a reference time; correction for coincidence summing effect in the efficiency determination.

The activity A of the radioactive source was determined using the absolute TDCR method by performing measurements of the same LS sources at different time in the 4πβ integral counting geometry. To analyse the TDCR data, the following equation (Capogni et al., 2012) was considered:

$$\rho(t) = \sum_{k=0}^{n-1} A_k \varepsilon_k f_k e^{-\lambda_k t} \tag{2}$$

where, in a radioactive sample containing n different radionuclides: $\rho(t)$ is the background-corrected integral count rate; t is the time elapsed from the reference time; A_k, ε_k, $f_k = \frac{1-e^{-\lambda_k T}}{\lambda_k T}$, and λ_k are the activity at the reference time, the counting efficiency, the correction factor for decay during a counting time T and the decay constant λ_k of the kth radionuclide, respectively.

In the case of a radioactive sample containing two radionuclides with significantly different half-lives, such as the ^{166}Ho and ^{166m}Ho, the unknown A_0 and A_1 values can be obtained by considering the analytical method developed in (Capogni et al., 2012), and references therein. This method involves taking repeated count rate readings at different times during the nuclide decay. These different readings allow the construction of linear systems comprising two equations, and their solutions provide a set of data for the two unknown activities. The mean values of the two sets of data, which, for a significant number of data points, will be distributed in a Gaussian manner, represent the sought A_0 and A_1 activity values.

The application of this integral counting method requires a preliminary analysis based on high-energy resolution γ-ray spectrometry to identify potential gamma-ray emitting impurities which could be present in the radioactive sample.

3. Materials and methods

This section provides the details of the experimental part of the work carried out at ENEA-INMRI to determine the new ^{166}Ho gamma-ray emission intensities, I_γ, starting from the sources preparation for primary and secondary activity measurements systems, continuing with the absolute measurements carried out with the two ENEA-INMRI TDCR counters, to then finish with the analysis performed on the data recorded for ^{166}Ho with the ENEA-INMRI HPGe detector available in the laboratory.

3.1. Sources preparation

A closed glass ampoule containing 4 mL roughly of ^{166}Ho in liquid solution of 1 M HNO_3, nominally having roughly 15 MBq·g^{-1} of activity concentration, A_c, at the start of measurements time (SMT), was handled at the Radiochemistry Laboratory of ENEA-INMRI for the preparation of the different sources to be measured by the primary and secondary activity systems available at the Radioactivity Laboratory of the Institute.

A liquid source was prepared directly from the above liquid solution in a P6-geometry glass vial filled with 4 cc of the radioactive solution. This vial was promptly placed at the bottom of the well of the ENEA-INMRI ionization chamber (IC), model NPL-CRC, for the calibration of the chamber. A sequence of IC readings was recorded at various starting-measuring times.

From the P6 vial were then prepared the following sources:

1) n. 1 liquid source in ENEA-INMRI flame-sealed glass vial (height 50 mm, diameter 15 mm) containing 3.6 mL of radioactive solution, and used to calibrate the IC Centronic IG11-A20;
2) n. 3 solid point-like sources with mass of 0.010395 g, 0.010445 g and 0.021469 g (relative uncertainty of 0.05%), and used for measurements with the ENEA-INMRI HPGe detector.

From the same P6 vial, a diluted ^{166}Ho solution of about 500 kBq·g^{-1} was prepared, using 1M HNO_3 as diluent, in order to make n. 2 liquid scintillation (LS) counting sources for ^{166}Ho primary standardization with the TDCR method. These sources were prepared in two 20 mL high-performance glass vials with low potassium content, filled with 10 mL of ULTIMA GOLD™ (UG) liquid scintillator. The UG was selected for its high stability and because it is usually used by ENEA-INMRI laboratory for liquid scintillation counting (LSC) applications. In particular, about 20 mg of ^{166}Ho diluted solution, roughly equivalent to 10 kBq at the start measurement time (SMT), was added to the 2 above vials by gravimetric deposition with a polyethylene pycnometer.

The point-like sources for measurements with the ENEA-INMRI HPGe detector were prepared by quantitatively depositing one (approximately 10 mg) and two drops (approximately 20 mg), corresponding to activities of about 150 kBq ad 300 kBq, respectively, of the ^{166}Ho mother solution onto three disc-shaped plastic holders and using a pycnometer. These point-like sources were dried under infrared lamp and covered by a thin adhesive plastic tape. This preparation technique for point-like sources was used for any type of point sources measured by the ENEA-INMRI HPGe detector.

One blank LSC source was prepared with the same reagents and procedures described above, replacing radioactive solutions with doubly distilled water. The same procedure was applied for preparing blank γ-ray spectrometry and ICs sources.

The procedure for calibrating the two IC chambers was the same as described in sections 3.1 and 3.2 of the reference (Capogni et al., 2016).

3.2. Counting systems used for ^{166}Ho direct activity measurements

The two ENEA-INMRI TDCR counters mentioned above were used for the ^{166}Ho primary standardisation. For the setup of the Hidex TDCR counter, extensive studies conducted in (Kossert et al., 2014) allowed

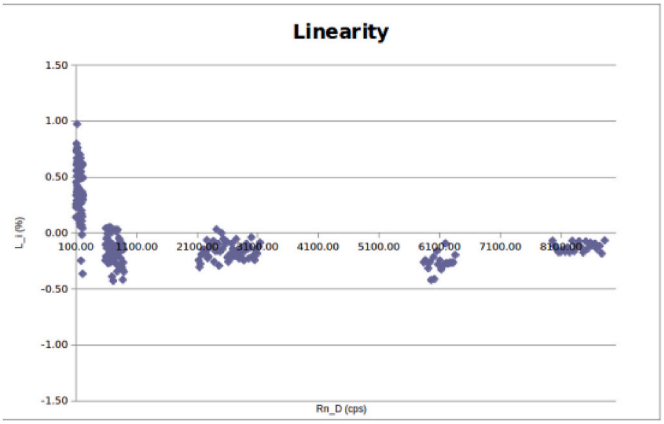


Fig. 2. Linearity (%) as function of the count rate (cps) of the ENEA-INMRI TDCR Hidex 300 SL (Metro version) counter.

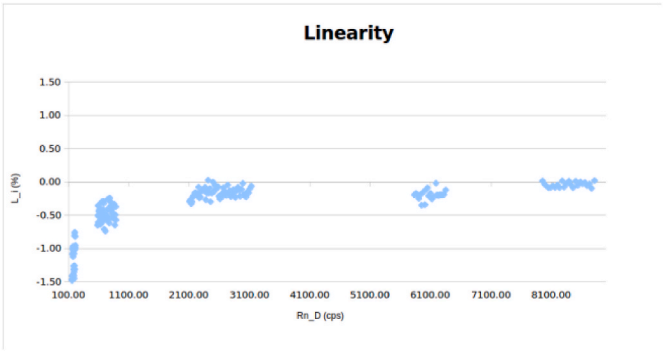


Fig. 3. Linearity (%) as function of the count rate (cps) of the ENEA-INMRI TDCR portable counter.

the selection of a coincidence resolving time, t_c, of 40 ns for ^{166}Ho activity measurements. Differently, considering the results obtained in (Capogni and De Felice, 2014) for the ENEA-INMRI TDCR portable counter, a dead time, t_{dead}, of 50 μs and a coincidence resolving time, t_c, of 140 ns were applied on the raw data. The data were recorded in list-mode by the deadtime-less Desktop CAEN DT5720 digitizer (250 MSample/s, 12 bit ADC, 4 channels) and analyzed by two custom software programs, one written in C++ by CAEN and the other in the CERN ROOT environment by ENEA-INMRI (Mini et al., 2014 and references therein).

Both of the LSC sources were measured repeatedly in the range of (100–9000) counts per second (cps) in both TDCR counters. This also allowed for the verification of the linearity of the two instruments, as depicted in Figs. 2 and 3. The counting time, T, selected to obtain a good counting statistics, was 1200 s in both counters. In particular, the linearity L_i (%) was defined as:

$$L_i = 100\,\frac{R_{n,D} - R_0}{R_0} \tag{3}$$

where: $R_{n,D}$ is the net reading (cps) of the logical sum of double

Table 1
Main characteristics of the ENEA-INMRI HPGe detector.

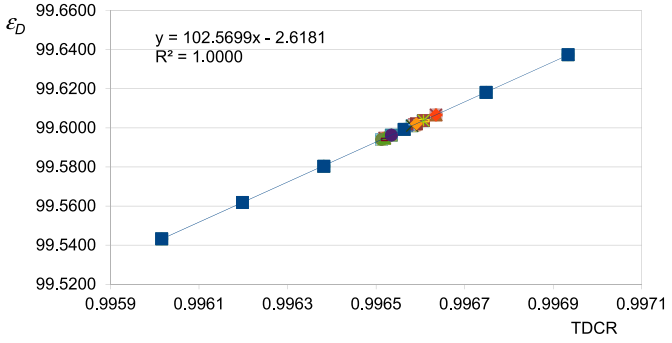
Type	p
Geometry	coaxial
Diameter of the crystal	65.9 mm
Height of the crystal	55.5 mm
Energy resolution at 122.0 keV	0.91 keV (FWHM)
Energy resolution at 1332.5 keV	1.79 keV (FWHM)
Energy threshold	15 keV

Table 2
Main gamma-ray emitting impurities detected in the ^{166}Ho master solution.

Radionuclide	A_c (Bq·g^{-1})	u(A_c) ($k = 1$) (%)
^{166m}Ho	14.4	2.5
^{177}Lu	1849.0	4.4
^{140}La	142.0	6.4
^{160}Tb	10.0	4.2

Table 3
Gamma-ray energies and emission intensities used to compute the data reported in Table 2; data from (Nucleide-LARA).

Radionuclide	E_γ (keV)	I_γ (%)
^{166m}Ho	280.4630 (23)	29.54 (25)
	711.697 (3)	54.9 (9)
	810.286 (4)	57.3 (11)
^{177}Lu	112.9498 (4)	6.20 (7)
	208.3662 (4)	10.38 (7)
^{140}La	487.022 (6)	46.1 (5)
	1596.203 (13)	95.40 (5)
^{160}Tb	879.378 (2)	30.1 (6)
	966.166 (2)	25.1 (5)

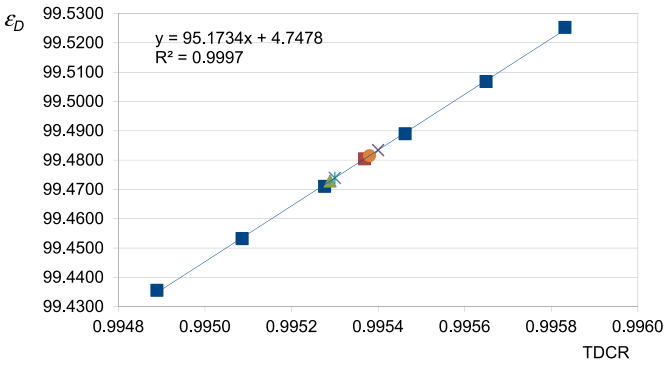


Figs. 4. ^{166}Ho logical sum of double coincidences efficiency (%), ε_D, as function of TDCR parameter. The blue square points are the theoretical values. The different coloured points are the ε_D values computed for TDCR experimental values obtained in the Hidex TDCR counter. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

coincidences, D, corrected for dead-time, background and decay to the SMT; R_0 is the arithmetic mean (cps) of all readings.

From Figs. 2 and 3, it can be observed that the absolute value of L_i is lower than or equal to 1.5% in the range of (100–9000) counts per second (cps) in both TDCR counters. The background rate, in terms of D readings, was 1 cps for the Hidex counter and 10 cps for the portable TDCR.

The impurity check was carried out using the ENEA-INMRI HPGe detector, and its main characteristics are detailed in Table 1. The three solid point-like sources, specifically prepared for this kind of measurements, were positioned at a distance of 10.06 cm from the top of the detector. The typical count rate within the measurements range and at ≈ 80.6 keV line was of (30–300) s^{-1}, while the typical background rate was less than 0.001 s^{-1}. The counting time was set at 80000 s to ensure high counting statistics. Table 2 presents the main impurities of the ^{166}Ho master solution, as detected by the ENEA-INMRI HPGe detector, along with their activity concentrations, A_c (Bq·g^{-1}), referenced to the SMT. Table 3 presents the data, from reference (Nucleide-LARA), of gamma-ray energies, E_γ *(keV)*, and emission intensities, I_γ *(%)*, of each detected impurity, used to compute the data reported in Table 2.



Figs. 5. ^{166}Ho logical sum of double coincidences efficiency (%), ε_D, as function of TDCR parameter. The blue square points are the theoretical values. The different coloured points are the ε_D values computed for TDCR experimental values obtained in the portable counter. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

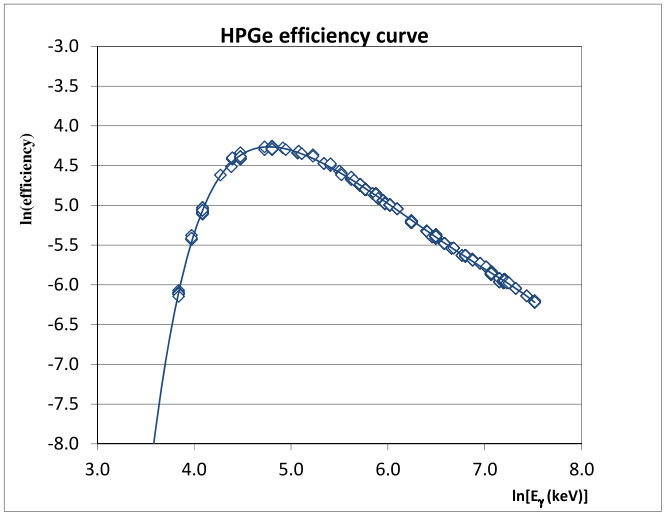


Fig. 6. Efficiency (%) as function of the gamma-ray energy (keV), represented in double natural-logarithmic scale, of the ENEA-INMRI HPGe detector for the measurement geometry used.

3.3. *Efficiency calculation*

The TDCR method requires knowledge of the counting efficiency for the Logical Sum of the Double Coincidences, D, and the Triple Coincidences, T, for the activity calculation. The MICELLE2 code (Kossert and Grau Carles, 2010), kindly provided by PTB, was used to compute the D efficiency, ε_D, and the T efficiency, ε_T, for ^{166}Ho in the two ENEA-INMRI TDCR counters as function of the TDCR parameter. A value of the Birks constant, kB, of 0.0100 cm MeV^{-1} was assumed. Linear interpolation of the theoretical values of ε_D and ε_T, calculated with the MICELLE2 program over a range of TDCR parameter values that overlap with the experimental TDCR values measured by the two TDCR counters, was employed.

In particular, the ^{166}Ho counting efficiencies ε_D*(TDCR)*, computed for the Hidex counter and the portable one, are shown (in square blue colour) in Figs. 4 and 5, respectively. The different coloured points reported in both figures are the ^{166}Ho counting efficiencies ε_D obtained by the experimental TDCR values measured in the Hidex and the portable counter and using the following linear interpolation formula:

$$\varepsilon_D = m\ TDCR + q \tag{4}$$

Table 4
Radionuclides and respective gamma-ray energies used for the HPGe efficiency calibration; data from (Nucleide-LARA).

Radionuclide	E_γ (keV)
^{210}Pb	46.539 (1)
^{241}Am	59.5409 (1)
^{177}Lu	71.6418 (6)
	112.9498 (4)
	208.3662 (4)
	249.6742 (6)
^{133}Ba	80.9979 (11)
	160.6121(16)
	223.2368 (13)
	276.3989 (12)
	302.8508 (5)
	356.0129 (7)
	383.8485 (12)
^{109}Cd	88.0341 (10)
^{152}Eu	121.7818 (3)
	244.6976 (8)
	344.2789 (12)
	411.1165 (12)
	443.965 (3)
	778.9045 (24)
	867.380 (3)
	964.079 (18)
	1408.013 (3)
^{57}Co	122.06079 (42)
	136.47374 (29)
^{99m}Tc	140.511 (1)
^{123m}Te	158.99 (5)
^{139}Ce	165.8576 (11)
^{226}Ra	186.211 (13)
^{131}I	284.305 (5)
	364.490 (4)
	636.989 (4)
	722.911 (5)
^{51}Cr	320.0835 (4)
^{113}Sn	391.698 (3)
^{198}Au	411.80250 (17)
^{85}Sr	514.007 (3)
^{124}I	602.7255 (21)
	968.1939 (38)
	1045.1252 (39)
	1376.089 (30)
	1509.375 (20)
	1690.9716 (37)
^{134}Cs	604.720 (3)
	795.86 (1)
^{137}Cs	661.6553 (30)
^{88}Y	898.042 (11)
	1836.070 (8)
^{60}Co	1173.228 (3)
	1332.492 (4)
^{22}Na	1274.537 (7)
^{64}Cu	1345.77 (6)

where m and q are the straight line parameters obtained by the linear interpolation of the ε_D theoretical values computed with the MICELLE2 code, and reported in both figures.

In this work, at the same time, the ENEA-INMRI HPGe detector was used for two purposes: to conduct an accurate and precise examination of gamma-ray emitting impurities in the master solution, as mentioned earlier, and to perform a new determination of several ^{166}Ho gamma-rays intensities, I_γ. Specifically, a robust efficiency curve of the ENEA-INMRI HPGe detector (displayed in a double natural-logarithmic scale in Fig. 6) was employed, as standard procedures followed in the gamma-ray spectrometry laboratory of the Institute. This curve was established by measuring mainly long-lived gamma-ray emitting standard point-like sources available in the laboratory, with additional values obtained by short-lived gamma-ray emitting sources directly standardized in the laboratory. A list of radionuclides with the corresponding energies used for the efficiency calibration of the ENEA-INMRI HPGe detector is provided in Table 4.

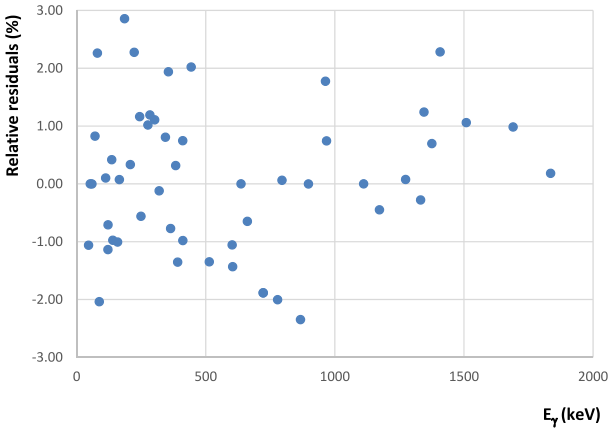


Fig. 7. Distribution of the relative residuals (%) as function of the gamma-ray energy (keV) associated to the fitting of the HPGe efficiency curve (Fig. 6) of the ENEA-INMRI HPGe detector.

Subsequently, the experimental points of ENEA-INMRI HPGe efficiency curve were fitted using two type of functions: a 6th-degree polynomial curve for energies lower than 250 keV roughly, and a straight line for energy greater than or equal to this value; the two parameters, slope coefficient and intercept of y-axis, of the linear fit are: −0.810081 (3) and −0.126251 (2), respectively, with a coefficient of determination $R^2 = 0.9988$. The distribution of the relative residuals (%) of the fit as function of the gamma-ray energies (keV) is shown in Fig. 7.

The new I_γ values of ^{166}Ho were determined by knowing: a) the net count rate at the FEP of the selected gamma-ray lines of holmium; b) the corresponding efficiencies, computed using only the efficiency curve above of the ENEA-INMRI HPGe detector; c) the activity of the ^{166}Ho point-like sources measured with this detector in the same geometry in which the efficiency curve above was obtained, and prepared from the ^{166}Ho master solution, this latter activity standardized by the TDCR technique as explained later.

4. Activity concentrations results by the primary method

The primary activity measurements of the ^{166}Ho solution were performed using the two ENEA-INMRI TDCR counters, mentioned above. The two LSC sources were measured in both counters repeatedly over time, as discussed in section 3.2. For the activity determination 10 measurements in the Hidex detector and 5 in the portable one were considered. A typical count rate of the logical sum of double coincidences, recorded in both TDCR detectors, was about $5{\cdot}10^3$ cps. Because the files produced by the CAEN digitizer, which contain the events recorded by the portable TDCR in list-mode format, are very large (about 1 GB, both in binary and txt format), the number of measurements made in the portable TDCR for determining the activity of the radioactive sources was lower than that considered for the Hidex counter. The activity concentration, A_c, of the master solution was obtained by the net count rate of the logical sum of double coincidences, $R_{n,D}$, divided by the related counting efficiency, ε_D, and the radioactive mass, m, of the source measured; at the same time A_c can be calculated by knowing the net count rate of the triples coincidences, $R_{n,T}$, divided by the related counting efficiency, ε_T, and m, i.e.:

$$A_c = \frac{R_{n,D}}{\varepsilon_D\, m} = \frac{R_{n,T}}{\varepsilon_T\, m} \tag{5}$$

The net count rate for D and T coincidences were corrected also for the decay of the ^{166}Ho source during the real measurement time, t_r, using the correction factor f_k as expressed in section 2 above.

Table 5
Uncertainty budget for ^{166}Ho primary standardisation.

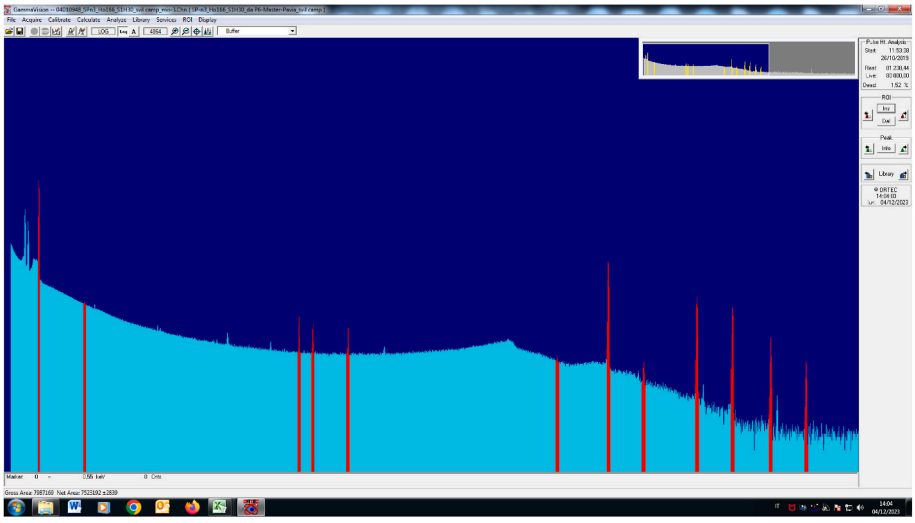
Source of uncertainty	Relative standard uncertainty (%)	Type (A/B)
counting statistics	0.25	A
Weighing	0.01	A
dead time	0.20	B
Background	0.01	A
counting time	0.01	B
interpolation of efficiency curve	0.30	B
decay scheme parameter	0.30	B
input parameter and statistical models	0.20	B
half-life	0.25	B
main gamma-ray emitting impurities	negligible	A
variability from different counters	0.68	B
Combined standard uncertainty ($k = 1$)	0.92	

The purity check performed on the master solution using the ENEA-INMRI HPGe detector and reported in Table 2 was also taken into account for the activity computation. The deviation between the results obtained for A_c considering the logical sum of double coincidences and the triple coincidences is lower than 0.1% for both counters. The ^{166}Ho A_c value obtained as final result is (150.17 ± 1.38) 10^5 Bq · g^{-1} at the SMT considered as reference time for all the measurements. The ^{166}Ho A_c value was computed as arithmetic mean of the two results obtained, separately, by the two sets of measurements performed with the two TDCR counters. In Table 5 is reported the uncertainty budget of the primary activity measurements. The component "variability from different counters" takes into account the different measurement settings (dead time, coincidence resolving time) of the two different types of TDCR detectors used and requires further investigation. The relative radionuclidic purity of the master solution is confirmed to be 99.99%, indicating a high-level of purity based on the ratio of the ^{166}Ho activity concentration, A_c, to the total activity concentration of ^{166}Ho and all the impurities listed in Table 2.

5. ^{166}Ho gamma-ray emission intensities, I_γ, by HPGe measurements

The ^{166}Ho spectrum recorded by the ENEA-INMRI HPGe detector, for one of the three point-like sources prepared for the HPGe measurements, is shown in Fig. 8. The spectrum was measured and analyzed using the ORTEC GammaVision 5.2 software. In Fig. 8 the main 12 gamma-ray lines of ^{166}Ho are highlighted in red colour. The counts are reported in the y-axis of the spectrum; the energy of each gamma-ray line is reported in Table 6, as in the reference (Bé et al., 2004). To compute the new I_γ for ^{166}Ho, only 8 out of 12 gamma-ray lines were selected both to avoid interferences with ^{166m}Ho gamma-ray emissions and to have better counting statistics for the corresponding FEP net area. The eight selected ^{166}Ho gamma-ray lines are numbered as: 3, 4, 5, 7, 9, 10, 11 and 12, as reported in Table 6. The efficiencies for these eight gamma-ray lines were estimated by the efficiency curve depicted in Fig. 6, with the values as follows: 0.0045062, 0.0043451, 0.0039804, 0.0025225, 0.0022575, 0.0021684, 0.0020802, 0.0020051, respectively. The uncertainties (less than or equal to 3%) on these efficiency values were computed taking into account the relative residuals (shown in Fig. 7) of the fit of the efficiency curve (shown in Fig. 6). The coincidence summing correction (CSC) factors used for each gamma-ray line are: 1.014755, 1.012668, 1.007536, 1.002768, 1.002858, 0.997307, 1.002878, 1.00. The uncertainties on these CSC factors range in a typical interval between 0.10 and 0.20%. The CSC factors have been computed using the version 4.2 of the GESPECOR tool (Arnold and Sima, 2004), by simulating a ^{166}Ho point-like source at a distance of 10.06 cm from the top of the ENEA-INMRI HPGe detector, i.e. in the same geometry of measurements of the real ^{166}Ho point-like sources prepared from the master solution. By knowing, for each gamma-ray line, the net count rate in the FEP area (corrected for background, subtracted in automatic mode with the GammaVision software mentioned above), the related efficiency $\varepsilon(E_\gamma)$, and the activity of the standardized ^{166}Ho source, the gamma-ray intensities, $I_\gamma(E)$, were then determined for each of the eight gamma-ray lines above using equation (1) of section 2. In Table 6 the new $I_\gamma(E)$ for the eight ^{166}Ho-selected gamma-ray lines are reported and compared with the same quantities published by DDEP in reference (Bé et al., 2004), and other ^{166}Ho I_γ data, available in literature, as reported in (Bobin et al., 2019).

In Table 7 the uncertainty budget for the 1379.5 keV gamma-ray



Figs. 8. ^{166}Ho spectrum recorded, for a single solid point-like source measured at a distance of 10.06 cm from the top of the ENEA-INMRI HPGe detector. The main 12 gamma-ray lines of ^{166}Ho are highlighted in red colour. The counts are reported in the y-axis; the numbers in the x-axis are associated to energy of each gamma-ray line reported in Table 6. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 6
New ^{166}Ho I_γ measured at ENEA-INMRI compared with data available in literature. The energy values (and their uncertainty) come from (Bé et al., 2004).

Crt. No.	Energy (keV)	ENEA-INMRI	I_γ photons per 100 disintegrations			
			LNHB	CMI	NPL	DDEP (Bé et al., 2004)
1	80.5725 (13)	–	6.61(7)	6.636 (49)	6.618 (51)	6.55(8)
2	184.4107 (11)	–	–	–	–	
3	674.24 (7)	0.0202 (8)	0.0193 (8)	–	0.02142 (68)	0.0198 (17)
4	705.21 (7)	0.0143 (6)	0.0134 (6)	–	0.01474 (65)	0.0146 (12)
5	785.78 (7)	0.0123 (6)	0.0118 (6)	–	0.01306 (58)	0.0120(3)
6	1263.24 (15)	–	–	–	–	
7	1379.446 (10)	0.902 (29)	0.896 (13)	0.904 (20)	0.9051 (69)	0.933(35)
8	1447.66 (15)	–	–	–	–	
9	1581.852 (15)	0.179 (6)	0.180 (4)	0.180 (6)	0.1792 (24)	0.186(4)
10	1662.424 (15)	0.116 (4)	0.114 (3)	0.1164 (41)	0.1157 (13)	0.118(5)
11	1749.837 (14)	0.0258 (9)	0.0259 (7)	–	0.02590 (48)	0.0272 (10)
12	1830.408 (24)	0.0078 (5)	0.0080 (3)	–	0.00807 (26)	0.0081(2)

Table 7
Uncertainty budget for 1379.5 keV gamma-ray emission intensity.

Source of uncertainty	Relative standard uncertainty (%)	Type (A/B)
counting statistics	0.40	A
Activity	0.92	A/B
FEP detection efficiency	2.99	A
FEP area	0.50	A
live time	0.15	B
background	0.15	A
counting time	0.01	B
decay correction (reference + during counting)	0.05	B
dilution factor	0.20	B
coincidence summing	0.25	B
Combined standard uncertainty ($k = 1$)	3.22	

emission intensity of ^{166}Ho is reported, as an example.

All the uncertainty values reported in the text of the manuscript and in all the Tables are given for a coverage factor $k = 1$.

6. Conclusions

A new ^{166}Ho primary activity standard was developed at ENEA-INMRI, in the framework of the EMPIR 15HLT06 MRTDosimetry project, using the absolute Triple-to-Double Coincidence Ratio (TDCR) technique. By the new ^{166}Ho activity standard and by using the ENEA-INMRI HPGe detector, new precise and accurate measurements of several gamma-ray emission intensities, I_γ, for eight gamma-ray lines of ^{166}Ho were performed. The new data set of ^{166}Ho gamma-ray emission intensities was communicated to the Decay Data Evaluation Project (DDEP), that is carried out by an international collaboration to produce recommended data for the nuclear and metrology community working in the field of ionizing radiations and nuclear measurements. The accurate and precise knowledge of the gamma-ray emission intensities of a radionuclide, such as the ^{166}Ho, is strongly recommended for the applications of such radionuclide in the field of nuclear medicine where it can be used for quantitative diagnostic imaging and/or therapy.

CRediT authorship contribution statement

M. Capogni: Writing – original draft, Supervision, Methodology, Investigation, Funding acquisition. **A. Fazio:** Methodology, Investigation. **M. Vaccaro:** Methodology, Investigation. **P. De Felice:** Supervision, Resources, Methodology, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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