

## Standardization and measurement of gamma-ray probability per decay of $^{177}\text{Lu}$

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### ABSTRACT

The procedure followed by the Nuclear Metrology Laboratory (LMN), at the Nuclear and Energy Research Institute (IPEN), for the primary standardization of  $^{177}\text{Lu}$  is described. This radionuclide is widely used in radiopharmacy due to its convenient half-life and emitted beta ray energies. The  $^{177}\text{Lu}$  solution was supplied during an international comparison sponsored by BIPM in 2009 and the primary standardization has been accomplished by the  $4\pi\beta\text{-}\gamma$  coincidence method using a proportional counter in  $4\pi$  geometry coupled with two NaI(Tl) scintillation counters. The beta efficiency was varied by placing Collodion and aluminum absorbers over and under the radioactive source. The  $^{177}\text{Lu}$  calibrated sources were also measured in a previously calibrated HPGe spectrometer, in order to obtain the emission probability per decay for the selected gamma-ray transitions. The experimental extrapolation curves were also compared with Monte Carlo simulations by means of code ESQUEMA developed at the LMN.

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### 1. Introduction

In Nuclear Metrology, for many years, the  $4\pi\beta\text{-}\gamma$  coincidence technique has been considered a primary standardization method due to its high accuracy and because it can yield the radionuclide activity value depending only on observable quantities (Campion, 1959; Baerg, 1966, 1967, 1973; Kawada, 1972). Usually, this kind of system is composed of a gas-flow or pressurized  $4\pi$  proportional counter, for alpha, beta, electrons or X-ray detection coupled to a gamma-ray spectrometer, composed of a scintillation counter or a semiconductor detector. Alternatively, solid or liquid scintillation counters are used in place of proportional counters in order to allow  $4\pi$  geometry (Garcia et al., 2000; Baccarelli et al., 2003; Dias et al., 2008).

The Nuclear Metrology Laboratory (Laboratório de Metrologia Nuclear—LMN) at the IPEN, in São Paulo, has two  $4\pi\beta\text{-}\gamma$  coincidence systems composed of gas-flow or pressurized  $4\pi$  proportional counters coupled to one or a pair of NaI(Tl) scintillation counters. The latter can be replaced by a HPGe detector. One of the research areas being developed by LMN is the primary standardization of radionuclides applied to Nuclear Medicine.

In this context,  $^{177}\text{Lu}$  became very important recently due to its application in radiotherapy and because it is commercially produced by IPEN. For this reason, it became necessary to develop a primary method for the determination of its activity. In addition, the secondary calibration of this radionuclide by means of gamma

spectrometers also requires the knowledge of the emission probability per decay for its transitions, a parameter which has few values shown in the literature (Firestone et al., 1996; Schötzig et al., 2001; Bé et al., 2004).

The radionuclide  $^{177}\text{Lu}$  decays by  $\beta^-$  emission with a half-life of 6.647(4)d, populating the excited states of  $^{177}\text{Hf}$ , as shown in Fig. 1 (Bé et al., 2004). The most intense gamma-lines are 208.36 keV (10.38%) and 112.94 keV (6.20%). The latter is highly converted with the  $\alpha_T$  coefficient equal to 2.272. The measurements were carried out by LMN during an international comparison sponsored by the BIPM in 2009. The radioactive solution was dispatched to the National Laboratory (LMNRI) in Rio de Janeiro, Brazil, which fractionated the sample and sent a part of it to the LMN, in São Paulo.

For comparison with experimental data, the LMN has developed a methodology for predicting the behavior of extrapolation curves for radionuclide standardization by  $4\pi\beta\text{-}\gamma$  coincidence measurements, using the Monte Carlo technique. This methodology has been applied to  $^{177}\text{Lu}$  in order to obtain reliable values to the extrapolation curve. Updated detector response functions were obtained by means of the code MCNPX (ORNL, 2006) applied to an improved version of the code ESQUEMA (Takeda et al., 2005; Dias et al., 2006).

### 2. Methodology

#### 2.1. Coincidence equations

A full description of the coincidence equations can be found elsewhere (Campion, 1959; Baerg, 1966, 1967, 1973). In the case

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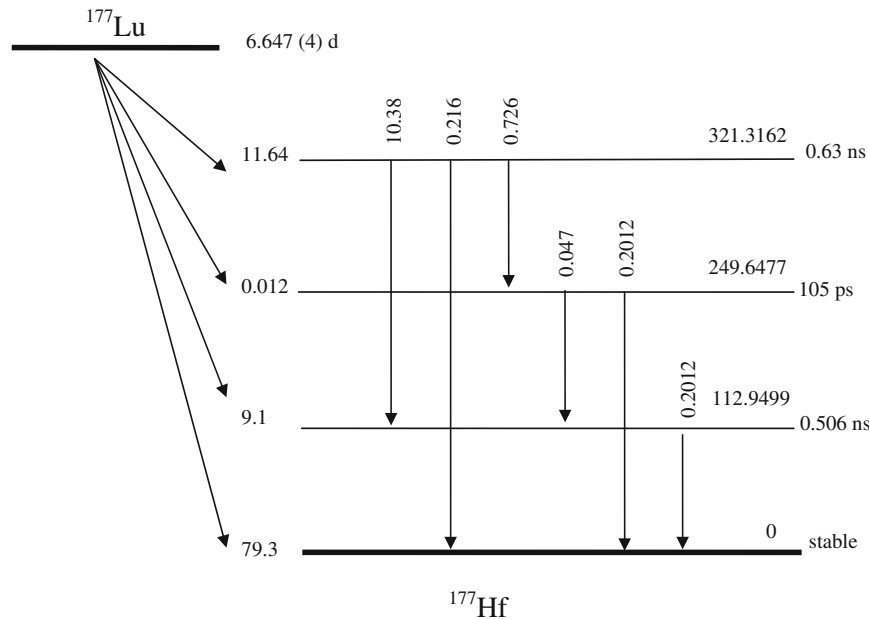


Fig. 1. Decay scheme of  $^{177}\text{Lu}$  (Bé et al., 2004). The energy levels are given in keV, the values above the transitions correspond to intensities in percent.

of  $^{177}\text{Lu}$  the gamma windows were set in two regions, one covering the total energy absorption peak at 113 keV and the other at 208 keV. The equation for each of the selected gamma windows can be given by

$$\frac{N_{\beta}N_{\gamma}}{N_C} = N_0 \left[ 1 + \frac{(1-\varepsilon_{\beta})}{\varepsilon_{\beta}} (\alpha\varepsilon_{ec} + \varepsilon_{\beta\gamma}) \right] \quad (1)$$

where  $N_0$  is the source disintegration rate;  $\varepsilon_{\beta}$  is the total beta efficiency of the proportional counter;  $\alpha$  is the total conversion coefficient;  $\varepsilon_{ec}$  is the internal conversion electron efficiency and  $\varepsilon_{\beta\gamma}$  is the gamma-ray detection probability of the  $4\pi(\text{PC})$ . In the extrapolation limit where  $(1-\varepsilon_{\beta}) \rightarrow 0$ , the activity  $N_0$  can be determined. Corrections for dead time and accidental coincidences were applied according to formulae taken from the literature (Smith, 1978).

Eq. (1) corresponds to the ideal case where the total absorption peaks in the gamma detector can be completely separated. Since the  $\alpha$  values for the two transitions are quite different, the expected slopes for the two extrapolation curves are also quite different. Because of finite energy resolution of NaI(Tl) crystals, the peaks cannot be completely separated and the experimental slopes may reside between these two values. In addition, the beta transition to the ground state, corresponding to the highest energy, has the highest intensity. Since this transition does not contribute with coincidences, the slope of the extrapolation curve has an additional positive component, because the coincident beta rays have lower energies. These effects can be predicted theoretically by the Monte Carlo method, as explained in Section 2.4.

## 2.2. Gamma-ray emission probability per decay

As well as the measurements with the  $4\pi\beta\text{-}\gamma$  coincidence system, a series of measurements were carried out with a gamma-ray spectrometry system consisting of a HPGe detector with 20% relative efficiency and the source positioned in a well defined geometry, approximately 18 cm away from the detector front face. At this distance, the corrections for cascade summing are expected to be small. However, this effect was taken into account

applying a Monte Carlo methodology developed at LMN (Dias et al., 2002). By this method the cascade summing effect can be calculated for all gamma transitions, following the decay scheme from the precursor to the daughter nuclei.

Standard sources of  $^{152}\text{Eu}$ ,  $^{214}\text{Am}$ ,  $^{133}\text{Ba}$ ,  $^{60}\text{Co}$  and  $^{166\text{m}}\text{Ho}$  calibrated in a  $4\pi\beta\text{-}\gamma$  coincidence system were used in order to obtain the gamma-ray efficiency as a function of the energy. A 5th degree polynomial in log-log scale was fitted to the efficiency curve applying the covariance matrix methodology (Smith, 1991). Fig. 2 shows the residues obtained in the HPGe efficiency curve. The points are randomly distributed around the fitted values, showing no bias. The polynomial coefficients together with their covariance matrix are given in Table 1. The overall error in the interpolated detection efficiency ranged from 0.38% to 0.70% and the chi-square value resulted 0.96, indicating a satisfactory fit.

## 2.3. Standardization setup

The  $4\pi\beta\text{-}\gamma$  coincidence system used in this calibration consisted of a proportional counter (PC) in  $4\pi$  geometry coupled to a pair of 76 mm  $\times$  76 mm NaI(Tl) scintillation crystals. The coincidence technique was performed by measuring the electrons in the proportional counter and the gamma-rays in the NaI scintillation counters. The electronic system used the TAC method developed at the LMN for registering of the observed events (Baccarelli et al., 2008).

The radioactive sources were prepared by dropping known aliquots of the radioactive solution on a Collodion substrate  $20 \mu\text{g cm}^{-2}$  thick, previously coated with a  $10 \mu\text{g cm}^{-2}$  gold layer and the sources were dried by a nitrogen jet at  $45^{\circ}\text{C}$  (Wyllie et al., 1970). The mass determination has been performed using the pycnometer technique (Campion, 1975). A total of 10 sources were calibrated in the  $4\pi\beta\text{-}\gamma$  coincidence system. The beta efficiency was varied by means of Collodion absorbers, placed over and under the radioactive sources. All of these sources were measured in the HPGe gamma-ray spectrometer for impurity checks and for gamma-ray emission probability per decay determination.

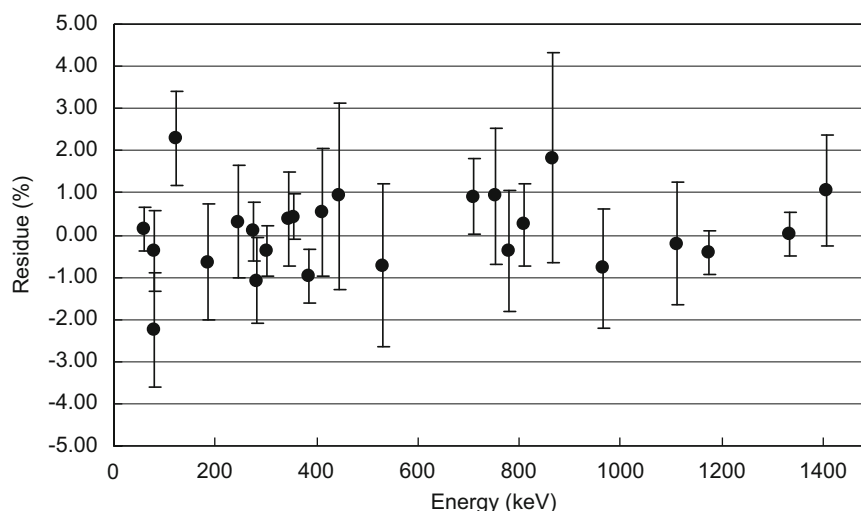


Fig. 2. Percent residues in the HPGe detection efficiency as a function of the gamma-ray energy.

Table 1

Parameters and covariance matrix obtained for the HPGe efficiency curve fitting.

Parameter	Value	Error	Covariance matrix							
$a_0$	2.44E+02	2.5E+01	6.39E+02							
$a_1$	-2.34E+02	2.3E+01	-5.85E+02	5.37E+02						
$a_2$	8.66E+01	8.4E+00	2.12E+02	-1.95E+02	7.06E+01					
$a_3$	-1.57E+01	1.5E+00	-3.80E+01	3.49E+01	-1.27E+01	2.28E+00				
$a_4$	1.40E+00	1.3E-01	3.37E+00	-3.10E+00	1.12E+00	-2.02E-01	1.80E-02			
$a_5$	-4.91E-02	4.7E-03	-1.18E-01	1.09E-01	-3.95E-02	7.11E-03	-6.33E-04	2.23E-05		
Chi-square	0.96									

The function is a 5th degree polynomial, in log-log scale, between efficiency and gamma-ray energy.

#### 2.4. Monte Carlo simulation

The theoretical response functions of each detector have been calculated using the MCNPX Monte Carlo code (ORNL, 2006). A full description of the  $4\pi\beta\text{-}\gamma$  system was developed including details of source substrate and absorbers. An energy range from 1.4 keV up to 4 MeV has been selected for electrons in the 4 $\pi$  detector selecting a total of 298 energy bins in a stepwise scale. For gamma-rays the energy range was from 48 keV to 3.0 MeV in 752 uniform energy bins. The numbers of histories followed were  $5 \times 10^4$  for electrons and  $2 \times 10^6$  for gamma-rays.

The Monte Carlo code ESQUEMA (Takeda et al., 2005; Dias et al., 2006), developed at LMN, has been used for calculating the extrapolation curve in the  $4\pi\beta\text{-}\gamma$  coincidence experiments. This code simulates all transitions from the precursor radionuclide to the ground state of the daughter radionuclide, including all detection processes in the coincidence system. The response tables of all detector system components were calculated previously by the MCNPX code (ORNL, 2006). As a result, the entire coincidence experiment can be simulated. In this way, Eq. (1) could be reproduced theoretically as a function of the beta efficiency, for each of the selected gamma-ray windows.

### 3. Results and discussion

Impurity checks detected 0.030(2)% contribution of  $^{177\text{m}}\text{Lu}$  in the  $^{177}\text{Lu}$  solution, at the reference date. This was corrected by measuring non-coincident gamma-rays from the two radionuclides in the HPGe spectrometer. Because  $^{177\text{m}}\text{Lu}$  has a much larger half life, 160.4(3)d (Table of Radioactive Isotopes, 2009),

and the measurements could only start about one month after the reference date, the impurity correction in the activity amounted to about 0.5% during the measuring time.

Fig. 3 shows the theoretical gamma-ray spectrum calculated by the code ESQUEMA for  $^{177}\text{Lu}$ , in comparison with the experiment, using the pair of NaI(Tl) crystals from the  $4\pi\beta\text{-}\gamma$  system. The two main peaks correspond to 113 and 208 keV total energy absorption peaks, respectively. The small peak to the left corresponds to 83 keV and originates from events where X-rays escaped from the NaI(Tl) crystal. This effect was not simulated in the present version of the Monte Carlo response table, because this would increase considerably the MCNPX processing time. However, since the experimental gamma-ray window was set to include this small peak, this effect can be considered to be accounted for in the simulation.

Fig. 4 shows the experimental extrapolation curve obtained by changing the absorber thickness, for a single radioactive source. From this curve the extrapolation correction was derived for the other nine radioactive sources. The experimental points have an approximately linear trend with positive slope due to the higher efficiency of the beta branch which goes to the ground state, and therefore does not contribute with coincidences. The slope for the 113 keV transition is higher because of the larger internal conversion coefficient.

The final value for the specific activity at the reference date (1 May 2009) was  $3.277(19)\text{MBq g}^{-1}$ . The uncertainty budget of gamma-ray probability determination is presented in Table 2. The main contributions to the overall uncertainty came from the activity value obtained in the  $4\pi\beta\text{-}\gamma$  system and from the HPGe efficiency curve interpolation.

The values obtained for the gamma-ray emission probability per decay are presented in Table 3. Both values for 113 and

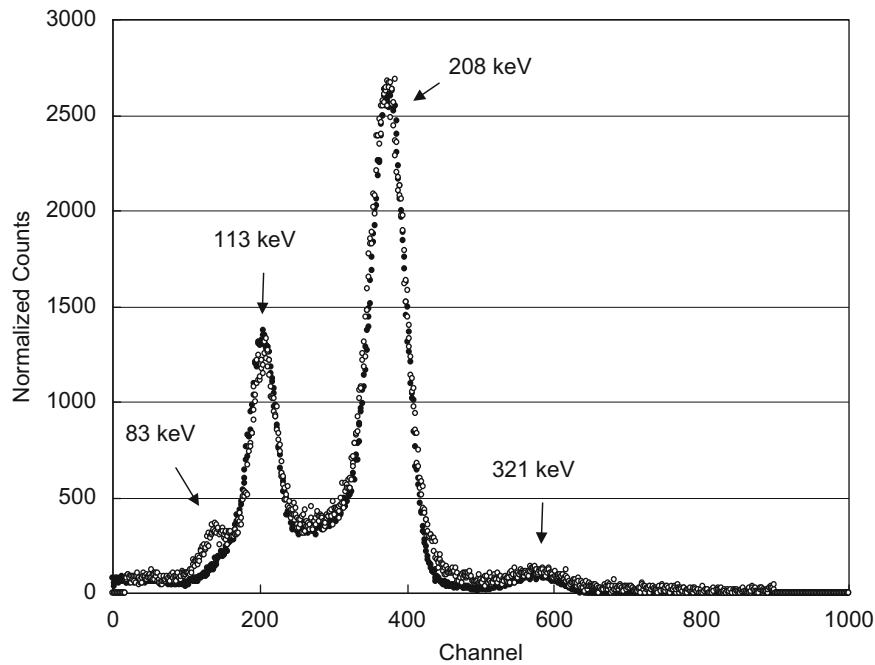


Fig. 3. Gamma-ray spectra obtained for  $^{177}\text{Lu}$  using NaI(Tl) crystals from the  $4\pi\beta\text{-}\gamma$  system. The white marks correspond to experimental data and black marks to the Monte Carlo calculation using code ESQUEMA (Takeda et al., 2005; Dias et al., 2006).

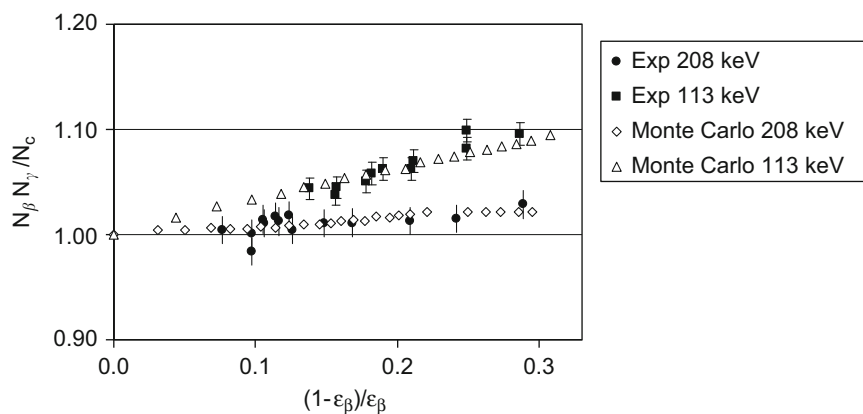


Fig. 4. Normalized extrapolation curves obtained for  $^{177}\text{Lu}$ . The black marks are experimental points and the open marks are the Monte Carlo calculation. The upper curve corresponds to the 113 keV and the lower curve corresponds to the 208 keV gamma windows, respectively. The error bars in the Monte Carlo results are too small to be visible (0.1% statistical error).

**Table 2**  
Uncertainty budget of gamma-ray probability determination, in percent ( $u=1$ ).

Source of error	Error (%)		Correlation factor
	113 keV	208 keV	
HPGe efficiency	0.67	0.55	0.60
Activity	0.58	0.58	1
Cascade summing	0.04	0.04	0
Decay	0.15	0.15	1
Impurity	0.11	0.18	1
Statistics	0.16	0.14	0
Total correlated	0.80	0.75	
Total uncorrelated	0.16	0.15	
Total	0.82	0.77	0.83

The last column shows the correlation factor between the partial errors in the gamma-ray emission probability, corresponding to 113 and 208 keV, respectively.

208 keV are in good agreement with the literature (Firestone et al., 1996; Schötzig et al., 2001; Bé et al., 2004).

#### 4. Conclusion

The experimental results of the  $^{177}\text{Lu}$  extrapolation curves for the two gamma windows agree with the Monte Carlo simulation within the experimental uncertainty, indicating that the theoretical prediction can be used in a reliable way. The specific activity of the  $^{177}\text{Lu}$  radioactive solution has been obtained with good accuracy.

The gamma-ray probabilities per decay for the main transitions agree with recent values from the literature within the experimental uncertainty, which is comparable to that obtained from the other authors. Further measurements are ongoing in

**Table 3**  
Gamma-ray probability per decay of  $^{177}\text{Lu}$ , with corresponding covariance matrix.

Gamma-ray energy (keV)	$I_\gamma$ (this work)	Total error (%)	Correlation matrix ( $\times 1000$ )	$I_\gamma$ (Ref. 1)	$I_\gamma$ (Ref. 2)	$I_\gamma$ (Ref. 3)
112.95	0.0622(5)	0.82	1000	0.0617(4)	0.064(3)	0.0620(7)
208.37	0.1035(8)	0.77	832	0.1036(7)	0.110(6)	0.1038(7)

In the second and last three columns the number inside the parenthesis correspond to the uncertainty in the last digits ( $u=1$ ). Ref. 1 corresponds to (Firestone et al., 1996); Ref. 2 corresponds to (Schötzig et al., 2001) and Ref. 3 corresponds to (Bé et al., 2004).

order to obtain the gamma-ray probability per decay for the weaker gamma lines.

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