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Abstract

The half-life of ^{67}Cu was determined through serial gamma-ray spectrometry measurements of the dominant gamma emission (E_γ: 184.6 keV; branching ratio: 48.7%) produced following β- decay. Data were collected consecutively for 1000 s per measurement, with a total of 3063 measurements over the duration of 36 days. The incidence rate for the 184.6 keV gamma-ray was determined from the spectral peak area and duration of each measurement. This rate was then corrected to account for detector dead-time, radioactive decay during each acquisition and drift in the computer clock in comparison to NIST nuclear clock. Least-squares regression analysis was performed to determine the half-life of ^{67}Cu. The result was 61.761 $\pm$ 0.004 h, which is the highest precision measurement to date, and marks a 24-fold precision improvement over the current Nuclear Data Sheets value.

Introduction

Beta-emitting radiopharmaceuticals as an oncologic intervention have expanded in recent years with the development of several new molecular targets [1–4]. Copper-67 has emerged as a promising radionuclide for radiopharmaceutical therapy, thus accurate and precise measurements of the radioactive half-life of ^{67}Cu are necessary for quantitative biomedical implementations [5–10]. A summary of the existing literature and adopted value of the ^{67}Cu half-life is given in table 1, and the work presented here aims to both verify and improve upon these previous measurements.

Methods

Copper-67 was produced at Argonne National Laboratory via the ^{68}Zn(γ,p) nuclear reaction. An isotopically enriched ^{68}Zn metal ingot target was placed proximal to a Bremsstrahlung conversion target (water-cooled tantalum) irradiated by a 40 MeV electron beam with average power of 18.2 kW for a period of 53.5 h. Producing 55.5 g of ^{67}Cu, which was then isolated from the bulk ^{68}Zn matrix by dry sublimation. The copper-rich residue was then digested using HCl and HNO_3. Followed by evaporation to remove HNO_3. Once cooled to room temperature the residue was then re-dissolved using HCl and passed through gravity-fed anion exchange column [12, 16–19].

A high-purity germanium (HPGe, ORTEC GEM20P4-70) gamma detector located at the University of Iowa was calibrated for efficiency and energy response using point sources of NIST-traceable sources of ^{241}Am, ^{57}Co, ^{137}Cs, ^{60}Co and ^{152}Eu (3% Uncertainty, Eckert & Ziegler). Gamma-ray spectra were acquired consecutively for 1000 s per acquisition using a ^{67}Cu sample in an unperturbed geometry for 36 days for a total of 3063 acquisitions. Due to its prominent branching ratio, the primary gamma-ray emission of 184.6 keV (48.7%) for

Table 1. Prior measurements of the half-life of ^{67}Cu, including the result of this work.

References	$T_{1/2} \pm \sigma$ (h)
Reynolds *et al* 1968 [11]	61.88 ± 0.14
Marceau *et al* 1970 [12]	61.00 ± 0.25
Lagoutine *et al* 1972 [13]	61.83 ± 0.07
Rothman *et al* 1974 [14]	62.01 ± 0.14
Junde *et al* 2005 [15] *Current Value*[a]	61.83 ± 0.12
This work	61.761 ± 0.004

[a] Junde *et al* is the currently accepted half-life value which is the weighted average of Reynolds *et al*, Marceau *et al*, Lagoutine *et al* and Rothman *et al*.

^{67}Cu was used. The total peak area was determined by summation of 21 bins, 10 above and below the desired photopeak.

Early time points were associated with up to 9.0% detector dead-time, resulting in ~1099 s elapsing (T_{real}) for a 1000 s live-time (T_{live}) acquisition. To correct for the radioactive decay during each acquisition, the initial incidence rate (I_0) was calculated. If it is assumed that the dead-time does not change significantly during a single acquisition and that the nominal decay constant (λ) is sufficiently close to the true value, then the relationship between the number of counts in the 184.6 keV peak in a spectra (N) and I_0 is described by equation (1)

$$N = \int_0^{T_{real}} \frac{T_{live}}{T_{real}} I_0 e^{-\lambda t} dt \tag{1}$$

Evaluating this integral we obtain

$$I_0 = \left(\frac{N}{T_{live}}\right)\left(\frac{\lambda T_{real}}{1 - e^{-\lambda T_{real}}}\right) \tag{2}$$

It is also useful to make the following definition:

$$C = \left(\frac{\lambda T_{real}}{1 - e^{-\lambda T_{real}}}\right) \tag{3}$$

In this notation, C is the correction factor for the dead-time and radioactive decay. For early time points with the highest level of dead-time (~9%), a correction factor of 1.001 71 was determined. At later time-points (dead-time ~0.4%) this correction factor diminished to 1.001 56. Although the change in C was found to be minimal over the course of counting, its implementation was required for optimal quantitative accuracy. Radionuclidic purity of the produced ^{67}Cu was assessed by summation of the acquired spectra, followed by peak identification (figure 1).

To evaluate for potential drift in the digital acquisition clock during data collection, the CPU clock was compared against the web-based NIST clock before and after the series of measurements. During the 36-day experiment, the total drift was measured to be 19.96 s (0.005 545 h). This shift was assumed to occur linearly over the course of measurements, and a time correction factor was applied to spectral time stamps based on this measurement.

Analysis of the decay curve was performed by least-squares regression using the functional form described by equation (2), where A_0, $T_{1/2}$, and a constant background C were parameters of the fit, as shown in equation (4).

$$f(t) = A_0 e^{\left(\frac{-\ln(2)}{T_{1/2}} * t\right)} + C \tag{4}$$

Initial fitting was performed to obtain fitting residuals. Fitting was repeated with data uncertainty weighting determined from a floating window-derived standard deviation of the initial fitting residuals. Fitting was then performed iteratively until changes in fitting parameters were negligible. The resulting chi-squared per degree of freedom (χ^2/ν) was 0.999, indicating appropriate data uncertainty weighting. All measurement and statistical uncertainty were assumed to be normally distributed. All uncertainties in this work are presented as ± one standard deviation (σ).

Results and discussion

A summed HPGe spectrum is shown in figure 1, and the final decay curve and corresponding fit are shown in figure 2. The half-life value for ^{67}Cu was measured to be 61.761 ± 0.004 h. This result is compared against

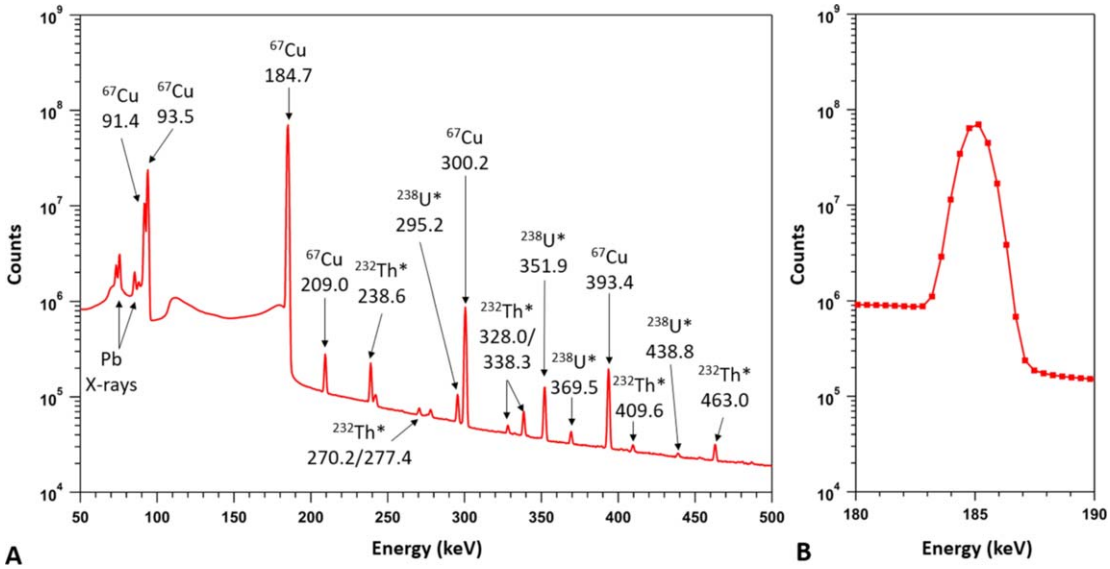

Figure 1. (A) Summed HPGe gamma spectrum. (B) Magnification on the 184.6 keV peak used for half-life determination. *Indicates that this identified peak is the result of this naturally occurring decay scheme.

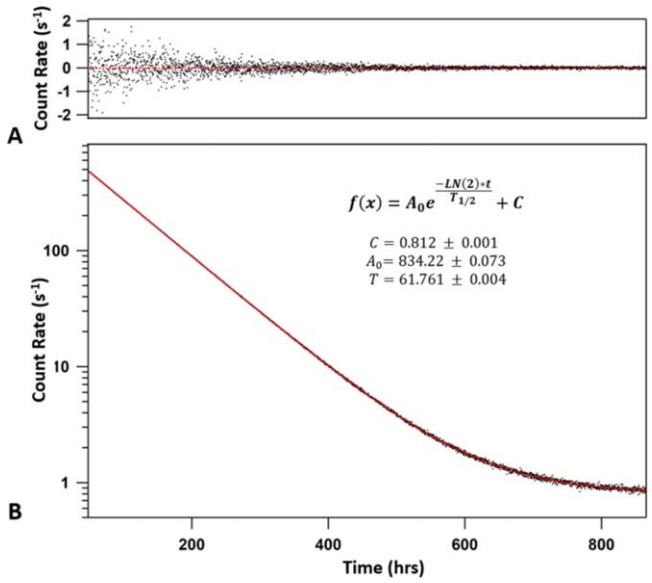

Figure 2. (A) The residual plot acquired during initial fit (B) Decay curve fitting of the summation of all acquisitions (N = 3063) of the primary gamma peak (184.6 keV) and associated fitting residuals. All data were acquired over 866 h of sampling.

literature values in table 1. This result agrees with the currently accepted value (61.83 ± 0.12 h) [15]. Due to the data collection method and duration of sampling, the value determined in this work provides improved precision (0.006%, which is more than 24 times more precise than current Nuclear Data Sheets accepted value).

The absolute difference in half-life specification between this work and the currently accepted value is 0.069 h (4.14 min), which may serve to improve the accuracy of pre-clinical and clinical biomedical studies employing the use of ^{67}Cu.

Conclusion

The half-life of ^{67}Cu has was measured to be 61.761 ± 0.004 h. This is the most precise reported half-life measurement to date for ^{67}Cu, and the measurement agrees with the current Nuclear Data Sheets value. This result may reduce uncertainty associated with several emerging medical applications of ^{67}Cu.

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Data availability statement

The data that support the findings of this study are available upon reasonable request from the authors.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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