Half-life of $^{67}\text{Cu}$

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Abstract

The half-life of $^{67}\text{Cu}$ was determined through serial gamma-ray spectrometry measurements of the dominant gamma emission ($E_\gamma$: 184.6 keV; branching ratio: 48.7%) produced following $\beta$-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 $^{67}\text{Cu}$. 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 $^{67}\text{Cu}$ are necessary for quantitative biomedical implementations [5–10]. A summary of the existing literature and adopted value of the $^{67}\text{Cu}$ 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 $^{68}\text{Zn}(\gamma,\text{p})$ nuclear reaction. An isotopically enriched $^{68}\text{Zn}$ 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 $^{67}\text{Cu}$, which was then isolated from the bulk $^{68}\text{Zn}$ 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 $^{241}\text{Am}$, $^{57}\text{Co}$, $^{133}\text{Cs}$, $^{60}\text{Co}$ and $^{152}\text{Eu}$ (3% Uncertainty, Eckert & Ziegler). Gamma-ray spectra were acquired consecutively for 1000 s per acquisition using a $^{67}\text{Cu}$ 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
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
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 67Cu.

**Conclusion**

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

[1] Grozinsky-Glasberg S and Gross D 2012 New drugs in the therapy of neuroendocrine tumors Journal of Endocrinological Investigation 35 930
[2] Forrer F, Valkema R, Kwekkeboom DJ, de Jong M and Krenning EP 2007 Peptide receptor radionuclide therapy Best Practice & Research Clinical Endocrinology & Metabolism 21 111
[3] Kaltsas G, Papadogias D, Makras P and Grossman A 2005 A 2005 Treatment of advanced neuroendocrine tumours with radiolabelled somatostatin analogues Endocrine-Related Cancer 12 683
[4] Mittra ES 2018 Neuroendocrine tumor therapy: 177Lu-DOTATATE American Journal of Roentgenology 211 278
[5] Sun X and Anderson C J 2004 Production and applications of copper-64 radiopharmaceuticals Methods Enzymol. (Amsterdam: Elsevier) pp 237
[6] Moi MK, Meares CF, McCall MJ, Cole WC and DeNardo SJ 1985 Copper chelates as probes of biological systems: stable copper complexes with a macrocyclic bifunctional chelating agent Anal. Biochem. 148 249
[7] Anderson CJ and Ferdani R 2009 Copper-64 radiopharmaceuticals for PET imaging of cancer: advances in preclinical and clinical research Cancer Biotherapy and Radiopharmaceuticals 24 379
[8] Linder MC and Hazegh-Azam M 1996 Copper biochemistry and molecular biology The American Journal of Clinical Nutrition 63 797S
[9] Merrick MJ, Rotsch DA, Tiwari A, Nolen J, Brossard T, Song J, Wadas T, Sunderland J and Graves S 2020 Imaging and dosimetric characteristics of 67 Cu Phys. Med. Biol. 66 035002
[10] Chen J et al 2015 Precise absolute γ-ray and β−-decay branching intensities in the decay of 67Cu Phys. Rev. C 92 044330
[11] Reynolds S, Emery J and Wyatt E 1968 Half-Lives of Radionuclides—III Nucl. Sci. Eng. 32 46
[12] Marceau N, Kruck T, McConnell D and Aspin N 1970 The production of copper 67 from natural zinc using a linear accelerator The International Journal of Applied Radiation and Isotopes 21 667
[13] Lagoutine F, Legrand J, Perrot C, Brethon J and Morel J 1972 Half-lives of a few Radionuclides Int. J. Appl. Radiat. Isotop. 23 (5) 219–224
[14] Rothman S, Peterson N, Chen W, Hines J, Bastar R, Robinson L, Nowicki L and Anderson J 1974 Half-lives of nine radioisotopes Phys. Rev. C 9 2272
[15] Junde H, Xiaolong H and Tuli J 2005 Nuclear Data Sheets for A = 67 Nucl. Data Sheets 106 159
[16] Rotsch DA et al 2017 Production of Medical Isotopes with Electron Linacs NAPAC 2016 (Chicago, IL, October 9–14, 2016) (JACOW) https://accelconf.web.cern.ch/NAPAC2016/talks/thb2602_talk.pdf
[17] Ehst D, Smith N, Bowers D and Makarashvili V 2012 Copper-67 production on electron linacs—Photonuclear technology development AIP Conf. Proc. 150 (American Institute of Physics) 157–61
[18] Ehst DA and Bowers DL 2013 Methods for making and processing metal targets for producing Cu-67 radioisotope for medical applications Google Patents US8526561B2
[19] Ehst DA and Willitt JL 2016 Methods for producing Cu-67 radioisotope with use of a ceramic capsule for medical applications Google Patents US9312037B2