

BNL--47949

PRODUCTION OF GALLIUM-66, A POSITRON EMITTING NUCLIDE FOR
RADIOIMMUNOTHERAPY

DE93 000377

Saed Mirzadeh¹ and Yung Yee Chu²

¹Nuclear Medicine Group, Health and Safety Research Division, Oak Ridge
National Laboratory, Oak Ridge, TN 37831-6022

²Chemistry Department, Brookhaven National Laboratory, Upton, NY 11973 USA.

ABSTRACT

Excitation functions for production of ⁶⁶Ga via α -induced nuclear reactions on enriched ⁶⁶Zn have been measured with $E_\alpha \leq 27.3$ MeV and $E_\alpha \leq 43.7$ MeV employing the stack-thin target technique. In addition, the induced activity of ⁶⁷Ga in the same sets of targets allowed an evaluation of the excitation functions of the corresponding nuclear reactions.

INTRODUCTION

Radiolabeled monoclonal antibodies for the purpose of radioimmunotherapy are currently of considerable interest. Several β^- and α -emitting nuclides have been identified for this application (e.g. ⁶⁷Cu¹, ⁹⁰Y², ¹⁸⁸Re³, ²¹¹At⁴ and ²¹²Pb/²¹²Bi⁵). In principle, β^+ -emitting nuclides should also be considered for therapeutic applications; not only is the radiation dose per decay comparable to those of β^- -emitters, but the quantitative imaging ability of positron emission tomography (PET) would enhance dosimetry for β^+ -emitters. Furthermore, β^+ -emitters could be produced in medical cyclotrons. Among possible β^+ -emitters, ⁶⁶Ga is the most interesting. The convenient 9.45 h half-life, the large β^+ branch (51.2%), with high end-point energy (4.15 MeV), and comparable EC branch (44%) with abundant short-range electrons make ⁶⁶Ga an attractive candidate for therapeutic applications.

The production routes of ⁶⁶Ga via peripheral interactions are summarized in Table 1. In this paper we report the preliminary data for production of ⁶⁶Ga via the following reactions:

- I. ⁶⁴Zn[$\alpha,2n$]⁶⁶Ge(2.3 h, EC)→⁶⁶Ga
- II. ⁶⁴Zn[α,np]⁶⁶Ga

The excitation functions were measured with $E_\alpha \leq 27.3$ MeV at the National Institutes of Health (NIH) cyclotron and with $E_\alpha \leq 43.7$ MeV at the 60" cyclotron at Brookhaven National Laboratory (BNL). In addition, the induced activity of ⁶⁷Ga in the same sets of targets allowed an evaluation of the excitation functions of the corresponding [α,n] and [α,p] reactions.

EXPERIMENTAL

For excitation function measurements, thin targets of ⁶⁶Zn (~16 $\mu\text{g}\cdot\text{cm}^{-2}$) were prepared by vacuum evaporating 99.6% enriched ⁶⁶Zn as metal (ORNL) onto 7.664 $\text{mg}\cdot\text{cm}^{-2}$ high-purity Al support foils (99.999%, AESAR/Johnson Matthey, Seabrook, NH). These Al-supported Zn targets were covered with the same Al foils to avoid recoil losses of the product nuclides. The 15.33 $\text{mg}\cdot\text{cm}^{-2}$ Al in each target sample eliminated the need for additional degrader foils. Stacks of sealed targets (between 6-12 target foils in any one experiment) were mounted on water-cooled blocks and irradiated for durations ranging from 10 to 30 minutes with 1.0 μA of 27.3 at the NIH cyclotron or 43.7 MeV at the 60"

cyclotron at BNL. After irradiation, the individual samples were mounted on counting cards for assay by γ -ray spectroscopy. For determination of the 19.0-m ⁶⁷Ge yield, attempts were made to count the samples quickly after irradiation, however, due to high levels of short-lived activities (predominantly 2.3-m ²⁶Al), it was necessary to allow the samples to decay for a period of about an hour before the first measurement. The same sets of samples were used for four independent experiments (three at NIH and one at BNL). Precise determination of the thickness of ⁶⁶Zn in the thin targets will be made at the conclusion of these studies.

A calibrated 50-cm³ high-purity Ge detector, FWHM ~ 1.8 at 1332 KeV, (EG&G ORTEC, Oak Ridge, TN) coupled to a AccuSpec PC-based multichannel analyzer (Nuclear Data/Canberra Inc., Meriden, CT) was used for radioactivity measurements. Typically, samples were counted at a distance of 10 cm from detector surface to eliminate the coincidental summings. The radioactivities in each sample were followed for several half-lives and the decay curve analysis was performed with the CLSQ code⁶. The relevant nuclear decay data, taken from reference 7, are summarized in Table 2. The energy of the cyclotron α -particles were deduced from the operating characteristics of the cyclotrons, and in the case of BNL 60" cyclotron, the beam energy was corrected by 1.5 MeV⁸. The Range Tables of Hubert *et al.*⁹ was used to determined the energy of the degraded incident α -particles.

RESULTS AND DISCUSSION

The excitation function of ⁶⁴Zn[$\alpha,2n$]⁶⁶Ge reaction which was measured in this work and that reported by Porile *et al.*⁹ are shown in Figure 1. Above $E_\alpha = 20.0$ MeV the cross-section increases rapidly and reaches to a maximum of 94 mb at $E_\alpha = 33$ MeV. From the threshold up to 27 MeV (where our two measurements at the BNL and the NIH overlapped) our measured cross-sections agreed well but they were higher than reported values by almost a factor of 10. In the earlier study, quantitation of ⁶⁶Ga activity was made by the measurement of its annihilation radiation in a NaI detector. Activity of ⁶⁶Ga was most likely overcorrected while corrections were made for the contribution from long-lived β^+ emitters. At the higher-energy end of the excitation function, the agreement between our data and that of earlier

MASTER

cross-section values for the production of ^{66}Ga from direct $[\alpha, pn]$ reaction and indirectly from the decay of ^{66}Ge are also shown in Figure 1. The cumulative cross-section reaches to a maximum of 900 mb at $E_\alpha = 32.5$ MeV with a threshold of about 19 MeV. At the maximum region of the excitation function, the agreement between our current and earlier measurements are surprisingly good. The subtraction of the excitation function of reaction I from the cumulative excitation function yields the excitation function for reaction II. The relative probability of reaction II to I, $\sigma_{(\alpha, pn)}/\sigma_{(\alpha, 2n)}$, in the maximum region ($30 \leq E_\alpha \leq 40$) remains rather constant at 6.5 ± 1.0 , indicative of substantially lower binding energy of protons in this mass region. The same set of α -activated targets yielded excitation functions for production of ^{67}Ga via the (α, p) and (α, n) reactions and the results are shown

in Figures 2a and 2b, respectively. In this case, the $\sigma_{(\alpha, p)}/\sigma_{(\alpha, n)}$ is close to unity at the maximum of the excitation functions which occurs at $E_\alpha = 20$ MeV, about 13 MeV lower than that of $(\alpha, 2n)$ or (α, pn) reactions. The peak of the excitation function of (α, n) reaction is larger than of $(\alpha, 2n)$ by almost a factor of 10. However the situation is reversed in the case of (α, p) and (α, pn) reactions, where at the maximum of the excitation functions the ratio of $\sigma_{(\alpha, pn)}$ to $\sigma_{(\alpha, p)}$ is ~ 2.5 . The errors of the cross-sections values are estimated at $\sim 10\%$ at the maximum of the excitation functions and at $\sim 30\%$ near the threshold. The incident α -particle energies are most accurate at the highest energy with a relative error of $\sim 2\%$. This error increases to $\sim 10\%$ below 16 MeV due to straggling process.

Table 1. Gallium Isotopes of Interest in Nuclear Medicine

Isotope	$t_{1/2}$	Mode of Decay	E_β^{max} , MeV	E_γ , MeV (I_γ , %)
^{66}Ga	9.40 h	B^+ (56.5%), EC (44%)	0.367(0.82%)	833.6(6.12%)
			0.747(0.97)	1039.0(38.4%)
			0.935(3.03%)	2190.0(5.74%)
			1.84(0.54%)	2752.1(23.5%)
			4.15(51.2%)	
^{67}Ga	3.26 d	EC (100%)	-	167.0(77.4%)
^{68}Ga	68.3 m	B^+ (90%), EC (10%)	~ 0.8 (~ 2)	1077.4(2.93)
			1.9(89%)	

Table 2. Peripheral Reactions for Production of Carrier-free ^{66}Ga

Nuclear Reaction	References
$^{64}\text{Zn}(\alpha, 2n)^{66}\text{Ge}(2.3 \text{ h}) \rightarrow$	Porile <i>et al.</i> (1959) ¹⁰
$^{64}\text{Zn}(\alpha, pn)$	Porile <i>et al.</i> (1959) ¹⁰
$^{63}\text{Cu}(\alpha, n)$	Porile <i>et al.</i> (1959) ¹¹
$^{65}\text{Cu}(\alpha, 3n)$	Porile <i>et al.</i> (1959) ¹¹
$^{64}\text{Cu}(\alpha, xn)$	Goethals <i>et al.</i> (1990) ¹²
$^{66}\text{Zn}(^3\text{He}, 3n)^{66}\text{Ge}(2.3 \text{ h}) \rightarrow$	
$^{66}\text{Zn}(^3\text{He}, p2n)$	
$^{65}\text{Cu}(^3\text{He}, 3n)$	
$^{66}\text{Zn}(d, 2n)$	
$^{68}\text{Zn}(d, 4n)$	
$^{64}\text{Zn}(p, xn)$	Howe <i>et al.</i> (1958) ¹³
$^{64}\text{Zn}(p, xn)$	Hille <i>et al.</i> (1972) ¹⁴
$^{64}\text{Zn}(p, xn)$	Little, <i>et al.</i> (1983) ¹⁵
$^{64}\text{Zn}(p, xn)$	Kopecky <i>et al.</i> (1989) ¹⁶
$^{66, 67, 68}\text{Zn}(p, xn)$	Tarkanyi <i>et al.</i> (1990) ¹⁷

ACKNOWLEDGMENTS

Research supported by the Office of Health and Environmental Research, U.S. Department of Energy, under contract DE-AC05-84OR21400 with Martin Marietta Energy Systems, Inc.

REFERENCES

- Mirzadeh S., Mausner L. F. and Srivastava S. C., *Appl. Radiat. Isot.*, **37**, 29 (1986).
- Kozak R. W., Raubitschek A., Mirzadeh S. *et al.* *Cancer Research*, **49**, 2639 (1989).
- Mirzadeh S. Rice D. E. and Knapp F. F., Jr., *Appl. Radiat. Isot.* (1991) in press.
- Lambrecht R. M. and Mirzadeh S., *Appl. Radiat. Isot.* **36**, 443 (1985).
- Ruegg C. L., Anderson-Berg W. T., Brechbiel M. W., Mirzadeh S., Gansow O. A. and Strand M., *Cancer Research* **50**, 4221 (1990).
- Cummings J. B., National Academy of Sciences, National Research Council, Nuclear Science Series NAS-NS-3107 (1962).
- Table of Isotopes (Lederer C. M. and Shirley V. S. Eds.) 7th ed. Wiley, New York (1978).

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

END

**DATE
FILMED**

12 / 15 / 92

