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ABSTRACT

Excitation functions for production of ^{66}Ga via α-induced nuclear reactions on enriched ^{66}Zn 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 ^{67}Ga 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 ß$^-$ and α-emitting nuclides have been identified for this application (e.g. ^{67}Cu[1], ^{90}Y[2], ^{188}Re[3], ^{211}At[4] and ^{212}Pb/^{212}Bi[5]). In principle, ß$^+$-emitting nuclides should also be considered for therapeutic applications; not only is the radiation dose per decay comparable to those of ß$^-$-emitters, but the quantitative imaging ability of positron emission tomography (PET) would enhance dosimetry for ß$^+$-emitters. Furthermore, ß$^+$-emitters could be produced in medical cyclotrons. Among possible ß$^+$-emitters, ^{66}Ga is the most interesting. The convenient 9.45 h half-life, the large ß$^+$ branch (51.2%), with high end-point energy (4.15 MeV), and comparable EC branch (44%) with abundant short-range electrons make ^{66}Ga an attractive candidate for therapeutic applications.

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

I. ^{64}Zn[α,2n]^{66}Ge(2.3 h, *EC*)→^{66}Ga
II. ^{64}Zn[α,np]^{66}Ga

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 ^{67}Ga 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 ^{66}Zn (~16 µg.cm^{-2}) were prepared by vacuum evaporating 99.6% enriched ^{66}Zn as metal (ORNL) onto 7.664 mg.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 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 ^{67}Ge yield, attempts were made to count the samples quickly after irradiation, however, due to high levels of short-lived activities (predominantly 2.3-m ^{28}Al), 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 ^{66}Zn in the thin targets will be made at the conclusion of these studies.

A calibrated 50-cm^3 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 code[6]. 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 MeV[8]. 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 ^{64}Zn[α,2n]^{66}Ge reaction which was measured in this work and that reported by Porile *et al.*[9] are shown in Figure 1. Above E_α=20.0 MeV the cross-section increases rapidly and reaches to a maximum of 94 mb at E_α=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

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For excitation function measurements, thin targets of ^{66}Zn (~16 $\mu g.cm^{-2}$) were prepared by vacuum evaporating 99.6% enriched ^{66}Zn as metal (ORNL) onto 7.664 $mg.cm^{-2}$ 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 $mg.cm^{-2}$ 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 ^{67}Ge yield, attempts were made to count the samples quickly after irradiation, however, due to high levels of short-lived activities (predominantly 2.3-m ^{28}Al), 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 ^{66}Zn in the thin targets will be made at the conclusion of these studies.

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cross-section values for the production of ^{67}Ga from direct [α,pn] reaction and indirectly from the decay of ^{67}Ge are also shown in Figure 1. The cumulative cross-section reaches to a maximum of 900 mb at E_α=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 ($30 \le E_\alpha \le 40$) 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_α=20 MeV, about 13 MeV lower than that of (α,2n) or (α,pn) reactions. The peak of the excitation function of (α,n) reaction is larger than of (α,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 ~10% at the maximum of the excitation functions and at ~30% near the threshold. The incident α-particle energies are most accurate at the highest energy with a relative error of ~2%. This error increases to ~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	β^+(56.5%), *EC*(44%)	0.367(0.82%) 0.747(0.97) 0.935(3.03%) 1.84(0.54%) 4.15(51.2%)	833.6(6.12%) 1039.0(38.4%) 2190.0(5.74%) 2752.1(23.5%)
^{67}Ga	3.26 d	*EC*(100%)	-	167.0(77.4%)
^{68}Ga	68.3 m	β^+(90%), *EC*(10%)	~0.8(~2) 1.9(89%)	1077.4(2.93)

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

Nuclear Reaction	References
^{64}Zn(α,2n)^{66}Ge(2.3 h)→	Porile *et al.* (1959)[10]
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^{Nat}Cu(α,xn)	Goethals *et al.* (1990)[12]
^{66}Zn(^{3}He,3n)^{66}Ge(2.3 h)→	
^{66}Zn(^{3}He,p2n)	
^{65}Cu(^{3}He,3n)	
^{66}Zn(d,2n)	
^{68}Zn(d,4n)	
^{Nat}Zn(p,xn)	Howe *et al.* (1958)[13]
^{Nat}Zn(p,xn)	Hille *et al.* (1972)[14]
^{Nat}Zn(p,xn)	Little, *et al.* (1983)[15]
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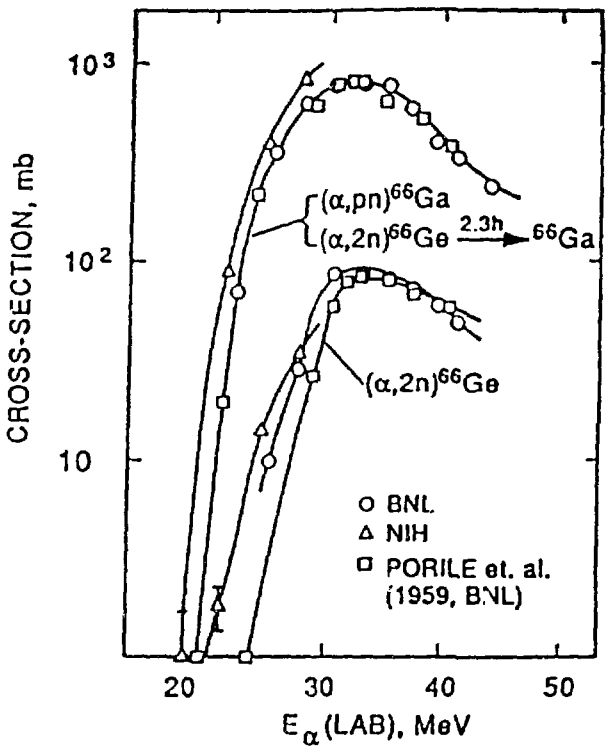

Figure 1. Excitation Functions for Production of ^{66}Ga via α-Induced Reaction on ^{64}Zn.

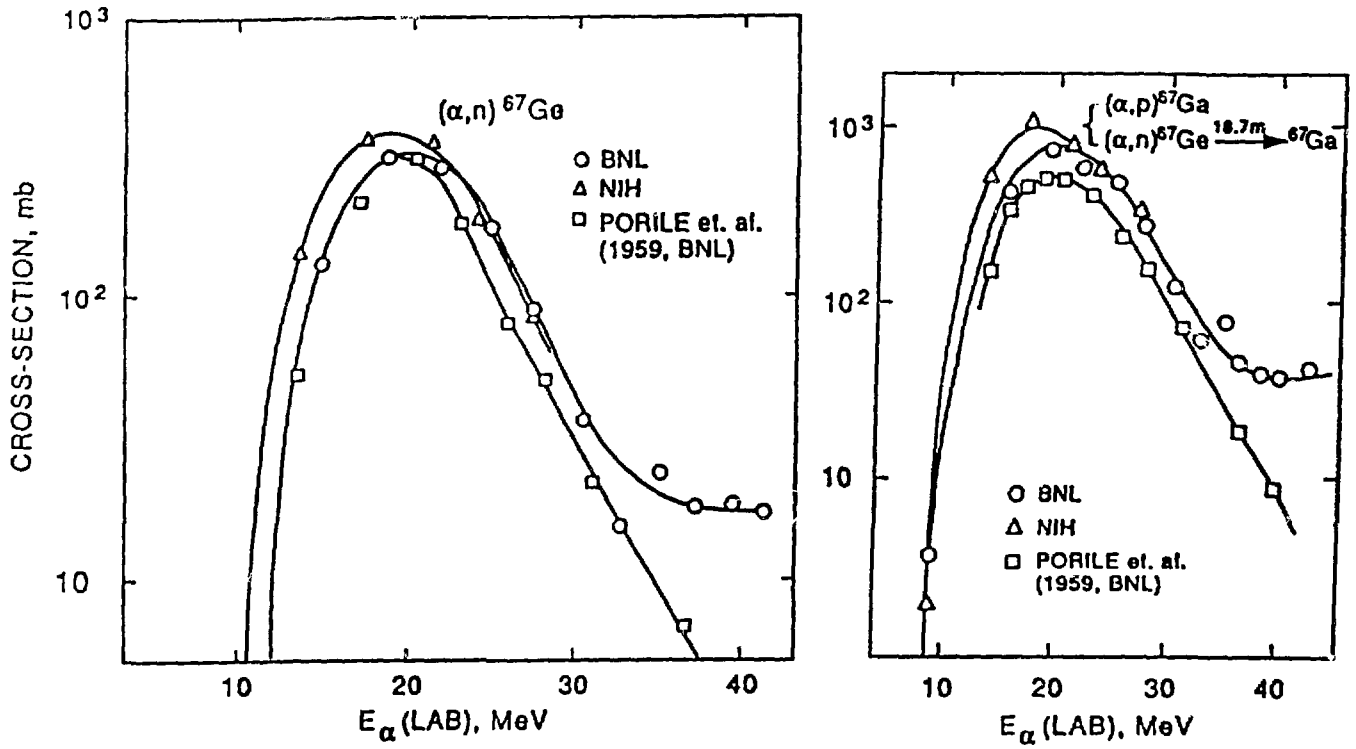

Figure 2a&b. Excitation Functions for Production of ^{67}Ga via α-Induced Reactions on ^{64}Zn