Photonuclear Production of $^{67}$Cu From Gallium


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Photonuclear Production of $^{67}$Cu From Gallium


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Abstract — Copper-67 is a radioisotope of interest for medical imaging and therapy as well as for understanding stellar and interstellar evolution pertaining to the formation of proton-rich nuclei. Since $^{67}$Cu decays 100% to $^{67}$Zn, understanding this reaction can shed light on the abundance of this and other p-nuclei elements in the universe. Here, the photonuclear production of $^{67}$Cu from $^{71}$Ga and natural gallium is examined as an alternative to its photoproduction from zinc. Two research and development production runs were performed at Thomas Jefferson National Accelerator Facility using an electron linac. During the first run, an 805-W, 30.9-MeV beam was used to irradiate a 1-mm tungsten radiator to create a bremsstrahlung flux. The resulting gamma photons irradiated 30.9 g of natural gallium encased in a graphite crucible for 24.2 h; 7.02 Bq/W·s·kg of $^{67}$Cu activity was produced. During the second run, a 4380-W, 31.5-MeV beam was used for 12.0 h on the same target containing 60 g of natural gallium; 6.41 Bq/W·s·kg of $^{67}$Cu activity was produced. Because of the difficulties in spectroscopically differentiating $^{67}$Cu from $^{67}$Ga, prior to each run, an isotopically pure $^{71}$Ga disk was irradiated using a 100-W beam for 1 h, at the same respective energies. These baseline irradiations allowed for separation of $^{67}$Cu from $^{67}$Ga in the spectroscopic measurements of the natural gallium targets.

Keywords — Photonuclear, copper-67, gallium-71, radioisotope production.

Note — Some figures may be in color only in the electronic version.

I. INTRODUCTION

The $^{67}$Cu radioisotope is a promising nuclide for use in medical imaging and therapy. Furthermore, as photonuclear processes play a role in nucleosynthesis in stars and interstellar regions, and in the natural abundance of elements, better understanding of photonuclear cross sections of elements heavier than iron (requiring p-process synthesis) can only strengthen our comprehension of nuclear astrophysics as well. This paper focuses on the production of $^{67}$Cu via the $^{71}$Ga$(\gamma,\alpha)$ $^{67}$Cu reaction for use in medical applications; however, since many photonuclear reaction cross sections are not well measured, this work also advances a better understanding of these reactions from the standpoint of general nuclear physics.

Copper-67 decays to $^{67}$Zn (100% $\beta^-$) and emits gamma photons with most emissions ranging from 91 to 185 keV, which is in the center of single photon emission computed tomography (SPECT) detection range (20 to 300 keV). This makes it well-suited for SPECT imaging. Copper-67’s therapeutic properties stem from the beta particles emitted (primarily at 392 to 577 keV), which are effective in targeting small tumors up to 5 mm in diameter (Ref. 2). Since $^{67}$Cu emits beta particles used in therapy and gamma photons used for diagnostic purposes, it is labeled a theranostic radioisotope. It is approved for human trials and has been designated as a high-priority

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research isotope\textsuperscript{3} by the U.S. Department of Energy\textsuperscript{4} (DOE). Copper-67 is the longest-lasting radioisotope of copper with a half-life of 61.8 h. This makes it logistically viable for production and transport from an accelerator to a medical facility for use, before it decays to a level no longer active enough for medical application (about 3.5 half-lives, or approximately 9 days).

Historically, \(^{67}\text{Cu}\) has been produced in cyclotrons via \(^{nat}\text{Zn}(p,2p)^{67}\text{Cu}\) and \(^{68}\text{Zn}(p,2p)^{67}\text{Cu}\), via linacs by the same reactions, and in reactors via \(^{nat}\text{Zn}(n,p)^{67}\text{Cu}\) (Ref. 5). Incident proton and neutron beams have a disadvantage compared to photonuclear reactions (via an electron beam converted to bremsstrahlung radiation), both in heat mitigation and scalability. Baryon (light ion) beams primarily interact with the surface of a solid target while high-energy photons can penetrate centimeters deep within a target with little attenuation, promoting the use of larger targets and increasing yield. Photonuclear production can be further scaled-up by simply increasing beam power while holding beam energy fixed. In this case, more photons would be generated at the converter, and thus, more reactions would occur in the target. Increasing power in a proton beam (or a nuclear reactor) has more complications and is a less practical method of increasing yield because of heat dissipation challenges. Liquid and gaseous targets have been used with baryon beam accelerators at high power; however, the heat dissipation difficulties of these targets also include significant technological challenges.

More recently, the DOE Isotope Program has funded several different approaches to the production and is now able to deliver \(^{67}\text{Cu}\) commercially via the \(^{68}\text{Zn}(\gamma,p)^{67}\text{Cu}\) photonuclear production route.\textsuperscript{6} All of these methods use zinc as the target element. After production, it is relatively more difficult to separate \(^{67}\text{Cu}\) from a zinc target due to zinc and copper sharing similar physical and chemical properties. An alternate method, producing \(^{67}\text{Cu}\) from gallium via \(^{71}\text{Ga}(\gamma,\alpha)^{67}\text{Cu}\), should facilitate postproduction separation since gallium is liquid near room temperature (\(~30^\circ\text{C}\) melting point) and is atomically two elements removed from copper. This would lead to a final \(^{67}\text{Cu}\) radioisotope with higher purity, a characteristic required for medical testing and use.

The novel use of \((\gamma,\alpha)\) photonuclear reactions at giant dipole resonance energies (nuclear excitation energies in the 10 to 40 MeV region) was investigated. Historically, photo-production has been discounted due to low specific activity in irradiated targets and difficulties in separating chemically identical species that are made from \((\gamma,n)\) reactions in the original target. Using the \(^{71}\text{Ga}(\gamma,\alpha)^{67}\text{Cu}\) photonuclear reaction creates a daughter with a different atomic number, by two units of charge, from the target. In this case, chemical separation is feasible, and high specific activity can be achieved.

II. METHODS

In September 2020 and January 2021, two \(^{67}\text{Cu}\) production tests (Table I) were performed at the Thomas Jefferson National Accelerator Facility (Jefferson Lab) via the \(^{nat}\text{Ga}(\gamma,\alpha)^{67}\text{Cu}\) photonuclear reaction. These tests were executed using Jefferson Lab’s Low Energy Recirculator Facility (LERF) accelerator (Fig. 1).

LERF provides beam energies up to 40 MeV, with beam currents up to 1.5 mA, depending on the final energy. Because of the high cost of isotopically pure \(^{71}\text{Ga}\), for these test runs, natural gallium (consisting of 60.1% \(^{68}\text{Ga}\) and 39.9% \(^{71}\text{Ga}\)) was used as the target material along with an ~99% pure \(^{71}\text{Ga}\) monitor foil that was simultaneously irradiated to predict the \(^{67}\text{Cu}\) production ratio in the natural gallium target (more on this below).

In order to activate the target for the desired \(^{nat}\text{Ga}(\gamma,\alpha)^{67}\text{Cu}\) reaction, bremsstrahlung flux was generated via an electron beam incident upon a thin (1-mm) tungsten radiator. Actual irradiation conditions were 24.2 h at 30.9 MeV and 805 W average power. This window of time ensured that a sufficient activation in the target was reached.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>List of Experiments</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{71}\text{Ga foil (enriched)}) (^{nat}\text{Ga in crucible})</td>
<td>(^{71}\text{Ga foil (enriched)}) (^{nat}\text{Ga in crucible})</td>
</tr>
<tr>
<td>Irradiation Duration (s)</td>
<td>(3600)</td>
</tr>
<tr>
<td>Beam Energy (MeV)</td>
<td>(30.9)</td>
</tr>
<tr>
<td>Power (W)</td>
<td>(100)</td>
</tr>
<tr>
<td>Target Mass (g)</td>
<td>(0.1)</td>
</tr>
<tr>
<td>Gallium-71 Purity (%)</td>
<td>(98.8)</td>
</tr>
<tr>
<td>Gallium-69 Purity (%)</td>
<td>(1.2)</td>
</tr>
</tbody>
</table>
Average beam energy was selected to minimize undesired byproducts in the monitor foil, such as remaining below the threshold of 35.5 MeV (Ref. 7) for the $^{71}$Ga($\gamma$,4$n$)$^{67}$Ga reaction. Gallium-67 contains overlapping gamma emission lines with those of $^{67}$Cu, causing some difficulty in distinguishing the two during postirradiation spectroscopy. By minimizing unwanted reactions, measurement separation between the desired $^{67}$Cu and the rest of the produced isotopes was optimized.

The target crucible was composed of machined graphite as it served as an electrical and thermal conductor for the gallium during irradiation. The crucible encapsulated 50.9 g of liquid natural gallium within a cylindrical chamber (8-cm length and 1-cm diameter) that was placed in line with the beam axis to maximize immersion in the cone-shaped bremsstrahlung flux. The front face of the crucible was located 8 mm beyond the radiator. Heat was regulated within a copper support structure that included copper plating around the target crucible with cycling water lines enclosed in copper tubing. Postirradiation cooling time was 10 h to ensure minimal doses delivered while handling the crucible.

Prior to production, the graphite block was irradiated empty, for 20 min, to compare thermal simulations to experimental heat buildup. The maximum temperature
was 105°C, well within the safety limits of the graphite. The temperature of the rear of the graphite block increased from 35.7°C to 48.5°C while the temperature of the copper base on the opposite side from the cooling water increased from 37.0°C to 105.1°C. The simulations, which included the block, the water cooling, and the copper support/cooling structure, indicated a maximum temperature of 151.5°C. In addition, the gap between the radiator and the crucible was reduced from 8 to 1 mm to increase the gamma-ray flux within the crucible. COMSOL Multiphysics v4.3b (Ref. 8) was used to determine that a 1-mm gap was optimal to reduce the thermal load on the crucible. Figure 2 shows the temperature distribution for no gap compared to a 1-mm gap. The maximum temperature of the graphite block was reduced to less than 470°C with the 1-mm gap.

Postirradiation, the activities in the crucible and 71Ga monitor foil were measured over several days using a high-purity germanium (HPGe) detector. There is a challenge in spectroscopically differentiating 67Cu from 67Ga, as all gamma spectral lines emitted from 67Cu decays are shared by 67Ga decays (Table II). Since natural gallium comprises 60.1% 68Ga and 39.9% 71Ga, approximately 50 times more 67Ga is produced from the 69Ga(γ,2n)67Ga reaction, which has a larger photon cross section, than 67Cu via the 71Ga(γ,α)67Cu reaction. While 67Ga decay has four additional unique decay lines, the branching intensities of these lines are each less than 0.15%, making them difficult to use in separation.

To overcome these spectroscopic separation challenges, the yield of 67Cu was differentiated from 67Ga by determining the ratio of 67Cu to 67Ga activity produced in the enriched 71Ga monitor foil. The foil contained enough 69Ga impurity (~1%) to allow for measurable 67Ga to be produced via the 69Ga(γ,2n)67Ga reaction channel. The three highest-intensity peaks for 67Cu (91, 93, and 184 keV) were fit using PeakEasy 4.99.4 (Ref. 9) from spectroscopic data acquired during three separate counts over the span of a week following irradiation. Counts were then differentiated between 67Cu and 67Ga decays by weighting their respective line intensities and then calculating the ratio of 67Cu to 67Ga for each line. Finally, the standard deviation of this ratio among the three lines, across the three counts, was numerically minimized via the Generalized Reduced Gradient (GRG) solving method. Monte Carlo simulations were modeled for comparison, using the FLUKA (Ref. 11) v2020.0.9 multi-particle transport code12 (Table III).

### III. RESULTS

The activity results in the natural gallium target were assessed by two different calculations designated as the Enrichment Technique and the Decay Technique. In the Enrichment Technique, the 300.2-keV decay line, which, in the natural gallium target, is more than 98% due to 67Ga, was evaluated to determine the activity stemming predominately from 67Ga decays. The previous foil ratio was then applied to this result to calculate the 67Cu activity in the natural target using the natural ratio generated by Eq. (1):

\[
\text{Natural target} \frac{67\text{Cu}}{67\text{Ga}} \text{ ratio} = \text{Foil} \left( \frac{67\text{Cu}}{67\text{Ga}} \text{ ratio} \times \frac{1.2\% \text{69Ga in foil}}{98.8\% \text{67Ga in foil}} \times \frac{39.9\% \text{67Ga in nat Ga}}{60.1\% \text{69Ga in nat Ga}} \right). \quad (1)
\]
TABLE III
Copper-67/Gallium-67 Photoproduction Ratios with \( \sim 30\)-MeV Bremsstrahlung Beam

<table>
<thead>
<tr>
<th>Copper-67/ Gallium-67 Ratio of Activity</th>
<th>Experimental Ratio</th>
<th>Simulated Ratio (FLUKA 2020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enriched Ga target</td>
<td>3.20 ± 0.05</td>
<td>3.72 ± 0.36</td>
</tr>
<tr>
<td>Natural Ga target</td>
<td>0.026 ± 0.001</td>
<td>0.023 ± 0.003</td>
</tr>
</tbody>
</table>

Via this technique, the \(^{67}\text{Cu}\) productions were determined to be 7.02 Bq/W·s·kg (0.68 μCi/kW·h·g) and 6.41 Bq/W·s·kg (0.62 μCi/kW·h·g) for the lower- and higher-power irradiations, respectively (Table IV). Regarding uncertainty in calculating the ratio of activities, the largest contributor was counting error using the HPGe detector. Other factors such as the effects of beam steering drift and beam intensity drift over the duration of the irradiations are minimized when taking the ratio of \(^{67}\text{Cu}\) to \(^{67}\text{Ga}\) activities. FLUKA simulations with varying beam intensities and with the beam shifted off-axis were performed to verify this. Likewise, error in measured counting time was extremely small relative to the length of the counts (seconds compared to hours) and was also mitigated by taking the ratio of activities. Regarding postirradiation time uncertainty, while \(^{67}\text{Cu}\) and \(^{67}\text{Ga}\) have slightly different half-lives (61.8 and 78.3 h, respectively), they are relatively similar and both long compared to the length of the counts. Uncertainty in the product of fluence and target thickness was negligible because the foils were positioned close enough to the bremsstrahlung converter such that the high-energy portion of the radiation cone was captured nearly entirely by the target. Table V summarizes the causes of uncertainty during the experiments as well as their degree of impact to the calculated ratios.

For the Decay Technique, which was an additional investigational validation, the net peak areas for the 184- and 300-keV lines were used to compute the time-dependent ratio as the \(^{67}\text{Cu}\) and \(^{67}\text{Ga}\) decayed (Fig. 3). A fit to the data was then used to determine the \(^{67}\text{Cu}\) to \(^{67}\text{Ga}\) production ratio in the crucible, irradiated at both powers, and resulted in an estimated ratio for \(^{67}\text{Cu}\) to \(^{67}\text{Ga}\) of 0.023 ± 0.002. Using the measured amount of \(^{67}\text{Ga}\) activity (300-keV line) along with the measured ratio from the fit, the \(^{67}\text{Cu}\) productions were determined to be 6.17 Bq/W·s·kg (0.60 μCi/kW·h·g) and 5.65 Bq/W·s·kg (0.55 μCi/kWh·g) for the lower and higher-power irradiations, respectively.

IV. CONCLUSIONS

The \(^{71}\text{Ga}(\gamma, a)^{67}\text{Cu}\) reaction channel produces less activity at \(\sim 30\) MeV than the \(^{68}\text{Zn}(\gamma, p)^{67}\text{Cu}\) channel by an approximate factor of 20 (Ref. 13), without a commensurate reduction in production cost. However, it may remain a potentially viable alternative production method due to the potential for an easier or cleaner separation and thus a higher-purity end product. To determine this, additional research is needed in separation techniques, which is beyond the scope of this project.

Future work will focus on exploring beam energy for optimization of \(^{67}\text{Cu}\) yield as a medical isotope as well as near-threshold (\(\sim 18\) MeV) production. The lower beam energies could facilitate use of a natural gallium target as the \(^{69}\text{Ga}(\gamma, 2n)^{67}\text{Ga}\) reaction with its threshold of \(\sim 18.6\) MeV would be avoided. If it is determined that an enriched \(^{71}\text{Ga}\) target is required, higher beam energies (up to 40 MeV) could be used, and further research would then be needed to determine the optimal energy to maximize \(^{67}\text{Cu}\) yield while keeping competing radioactive products to a manageable level.

Apart from the medical interest, the lower-energy bremsstrahlung reactions also affect the stellar and interstellar photoproduction of \(^{67}\text{Zn}\) and can address such long-standing questions about the natural abundance of p-nuclei in the universe.

TABLE IV
Summary of Results: Enrichment Technique Versus Decay Technique

<table>
<thead>
<tr>
<th></th>
<th>Power (W)</th>
<th>Beam Energy (MeV)</th>
<th>Activity Ratio (^{67}\text{Cu}:^{67}\text{Ga})</th>
<th>Copper-67 Activity (Bq/W·s·kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrichment technique</td>
<td>805</td>
<td>30.9</td>
<td>0.026</td>
<td>7.02 ± 0.34</td>
</tr>
<tr>
<td></td>
<td>4380</td>
<td>31.5</td>
<td>0.022</td>
<td>6.41 ± 0.16</td>
</tr>
<tr>
<td></td>
<td>805</td>
<td>30.9</td>
<td>0.023</td>
<td>6.17 ± 0.62</td>
</tr>
<tr>
<td></td>
<td>4380</td>
<td>31.5</td>
<td>0.020</td>
<td>5.65 ± 0.72</td>
</tr>
<tr>
<td></td>
<td>805</td>
<td>30.9</td>
<td>0.023</td>
<td>5.04 ± 0.21</td>
</tr>
<tr>
<td>FLUKA 2020</td>
<td>805</td>
<td>31.5</td>
<td>0.024</td>
<td>6.07 ± 0.41</td>
</tr>
</tbody>
</table>
Finally, $^{67}$Cu decays 100% by emitting beta particles (578 keV maximum) and multiple gamma energies while $^{67}$Ga decays 100% by electron capture. Measurement separation of $^{67}$Cu from $^{67}$Ga can unequivocally be made by adding beta-particle coincidence detection to the gamma spectroscopy.

### Acknowledgments

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### Disclosure Statement

No potential conflict of interest was reported by the author(s).

### References


### ORCID

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**TABLE V**

<table>
<thead>
<tr>
<th>Causes of Uncertainty in Ratio of Activities</th>
<th>Minimized by Taking Ratio?</th>
<th>Uncertainty Degree (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counting uncertainty</td>
<td>No</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Efficiency uncertainty</td>
<td>Yes</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Target mass measurement</td>
<td>No</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Target distance from converter</td>
<td>Yes</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Irradiation time (clock)</td>
<td>Yes</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Decay time</td>
<td>Yes</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Beam steering drift</td>
<td>Yes</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Beam intensity drift</td>
<td>Yes</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Counting distance from detector</td>
<td>Yes</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Fig. 3. Ratio of 184-keV ($^{67}$Cu prevalent) to 300-keV ($^{67}$Ga dominant) peak areas over time. The difference in branching intensities in the shared decay lines and half-lives of the two radioisotopes are used to validate the $^{67}$Cu to $^{67}$Ga ratio in the natural gallium target.


