University Research Reactor Production of ^{67}Cu via Long-Term Irradiation

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Service Provided: Penn State Breazeale Reactor, Radiochemistry Research Laboratory, Computational Laboratory

Sponsors: U. S. Department of Energy Office of Science, the Penn State Radiation Science and Engineering Center

Introduction

Medical isotopes are particularly valuable for their widespread use as diagnostic tools, therapeutic agents for disease treatment, and as aids in pharmaceutical research and development [1]. Inconsistent medical isotope supplies limit our ability to develop and implement improved diagnostic and therapeutic procedures [2], and limited domestic isotope production leaves only a small number of scientists and engineers with the expertise to manufacture and purify these elements.

^{67}Cu is a short-lived, radioactive *theranostic* medical isotope in high demand for use as *thera*peutic treatment agents for multiple types of cancer and in medical diag*nostics*. However, it has had a limited and inconsistent supply for several decades [1, 2]. Its 61.83 h half-life and average 141 keV β--particle (100%, 0.61 mm tissue range) provide considerable therapeutic potency for a number of cancers. Its soft gamma-ray emissions (184.6 keV, 48.7%; 93.3 keV, 16.1%; 91.3 keV, 7.0%) allow for single photon emission computed tomography (SPECT) imaging. Copper's biochemistry and biological half-life also make it an ideal theranostic isotope [2,3].

The use of ^{67}Cu for small mammal pharmaceutical research requires approximately 0.15 mCi/subject, while human diagnostic and therapeutic doses are approximately 0.6−14.5 mCi/subject and 3.5−425 mCi/subject, respectively [3]. As of 2008, there was one ^{67}Cu supplier regularly producing ^{67}Cu [1], using a charged particle production method and producing 20−200 mCi of ^{67}Cu per batch [6]. Routine research and clinical use of ^{67}Cu would require a significant increase in the number of suppliers as well as backup production capacity [1].

To contribute to copper isotope availability, we previously performed initial development work to produce both ^{64}Cu and ^{67}Cu via fast neutron (n,p) reactions on enriched ^{64}Cu (99.4%) and ^{67}Zn (94.8%) targets in the Penn State Breazeale Reactor (PSBR). Funded by the Nuclear Physics program in the Department of Energy's Office of Science, we developed a fast neutron flux sample holder to reduce unwanted thermal neutron byproducts, performed scoping experiments with tens of milligrams of target materials (producing a 0.8 mCi ^{67}Cu/g ZnO target), and performed ion exchange separations that reduced zinc content in irradiated samples by a factor of more than 10^3 per pass [3], while at the same time educating and training graduate and undergraduate students in the relevant radiochemical concepts and skills to provide future experts in this important field.

Here, we report the detailed development of the fast flux sample holder, as well as additional calculations and simulations to further optimize experimental parameters for reactor production of ^{67}Cu, so that we may achieve higher production activity per gram of ^{67}ZnO and be able to provide medical researchers with enough activity for radiopharmaceutical research efforts. There is considerable work to be completed in order to complete this effort. This summary describes our efforts so far.

Challenges and Opportunities

Copper-67 and its cousin ^{64}Cu are typically accelerator-produced isotopes. As we proved, these isotopes can be made in a research reactor using fast neutrons [3]. Unfortunately, the fast flux in these reactors is typically too low for commercial-scale production and the thermal flux is too high for the long-term residence required to make higher activities. Figure 1 shows a 3D surface plot of the theoretical maximum activities that can be produced for a given flux and irradiation time.

The data produced at Penn State compares favorably to the previous test irradiations in the literature [3]. In order to go beyond the typical limitations of a university research reactor, the team designed irradiation capsules and a reconfigured irradiation fixture to maximize the ability of a TRIGA reactor to produce and transmit fast neutrons to a target.

The two main challenges in producing fast-neutron reactions in a thermal reactor are delivering enough fast neutrons to the target while reducing the thermal neutrons that will activate target and structural materials and create radiation hazards for the sample processing team. There are also ancillary issues that arise when trying to mitigate the main issues. Severely depressing the thermal flux in the reactor will also reduce the power production in the area of the target, shifting it to other portions of the core. This can create

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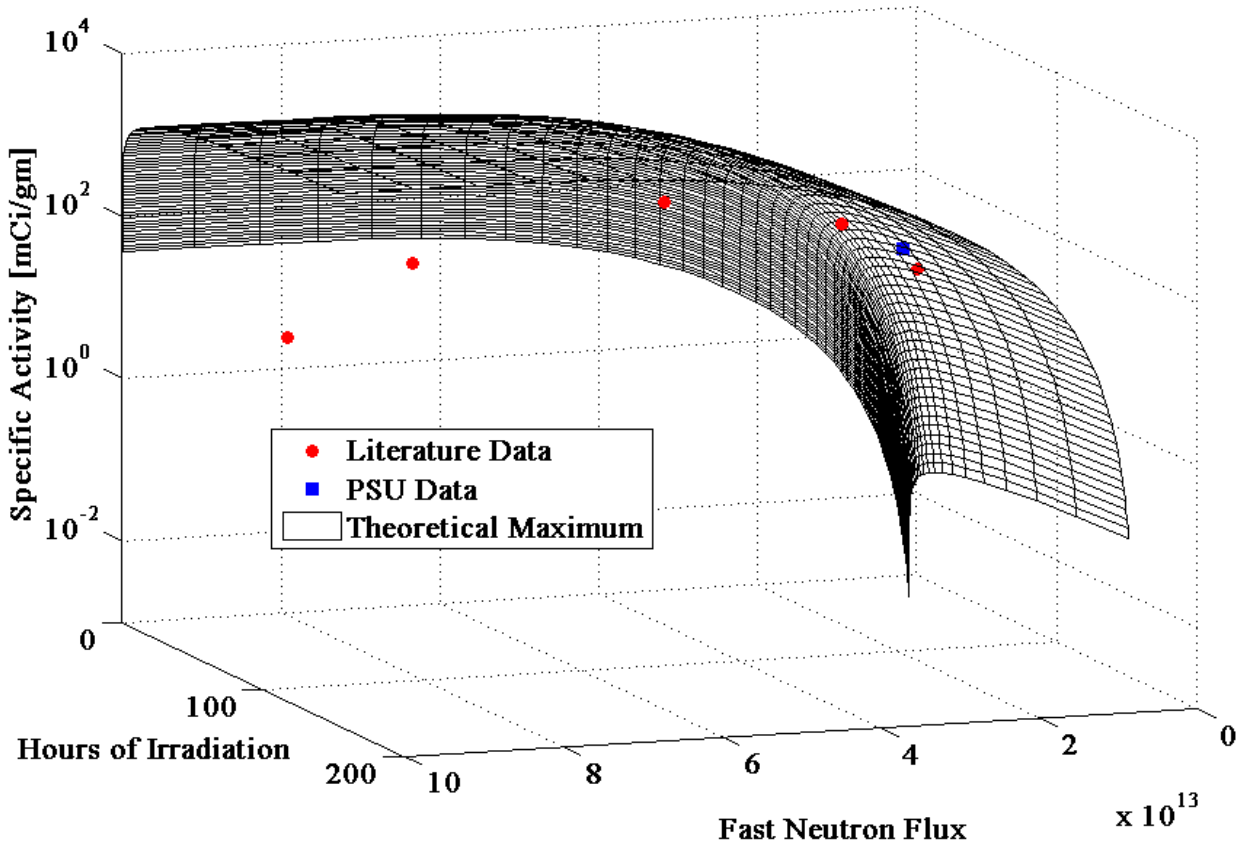

FIGURE 1: Theoretical maximum production for ^{64}Cu and previous irradiation data from the literature and from work at Penn State.

reactor safety issues, including changes in control rod worth and in power detector readings. Insertion and removal of the experiment will cause large shifts in core reactivity, so care must be taken to perform these only while the reactor is shutdown. The other problem is the production of unwanted fast-neutron reactions that can lead to the same handling issues for the processing team. We addressed these issues by using a combination of trial irradiations and extensive computer simulation of the experiment and the core conditions, primarily using MCNP and TRIGSIMS [5, 6].

Figure 2 shows the Penn State TRIGA reactor core loading pattern in 2012, during the initial isotope production efforts. The targets were loaded in either the central thimble (CT) position or at the core periphery in the dry tubes (DT1 or DT2).

The central thimble location has the highest flux in the core and is designed to be a thermal flux trap, so it is flooded with the reactor coolant. There is no readily available alternative for sample irradiations, so the team investigated options for optimizing the central thimble. Figure 3 shows the MCNP predictions for thermal and fast neutron fluxes in the central thimble and the adjacent fuel and coolant channels.

Removing the water from the central thimble increases the fast flux in the target location and reduces the

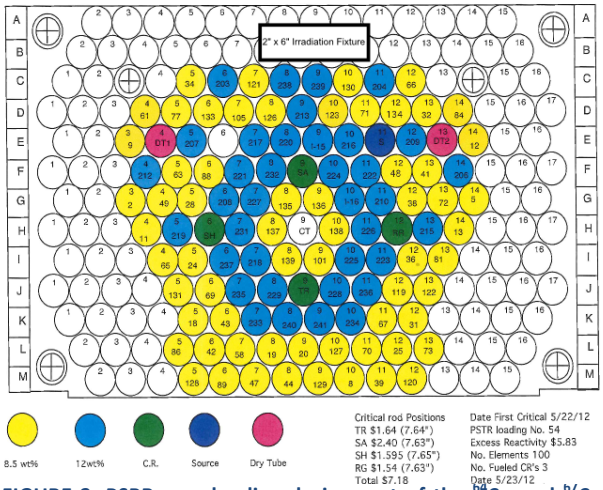

FIGURE 2: PSBR core loading during part of the ^{64}Cu and ^{67}Cu production research and development effort.

thermal flux that serves only to create unwanted radioactivity. The power produced in the adjacent fuel elements decreases by a few percent, due to the lower thermal flux flowing out of the central thimble; but, the overall effect is a higher fast flux and decreased thermal activation.

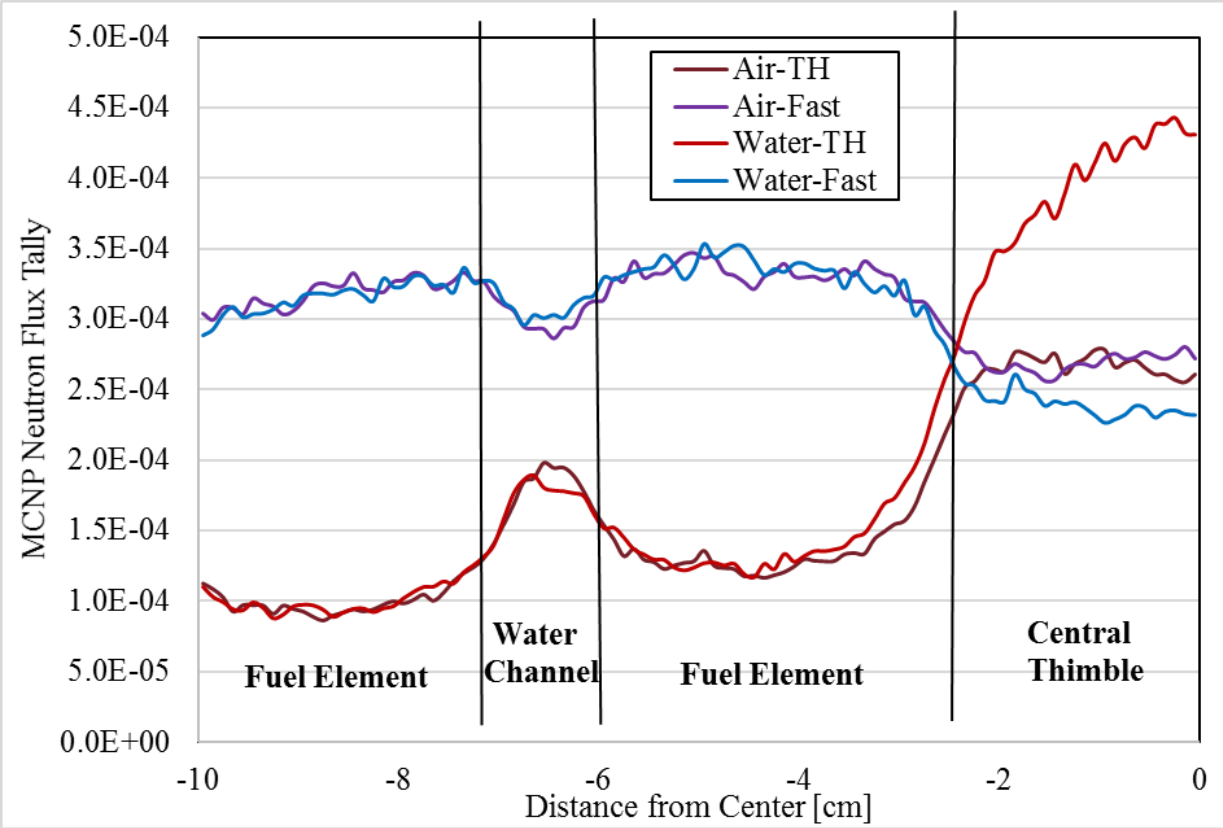

FIGURE 3: Flux profile through PSBR fuel elements, water channels, and the central thimble.

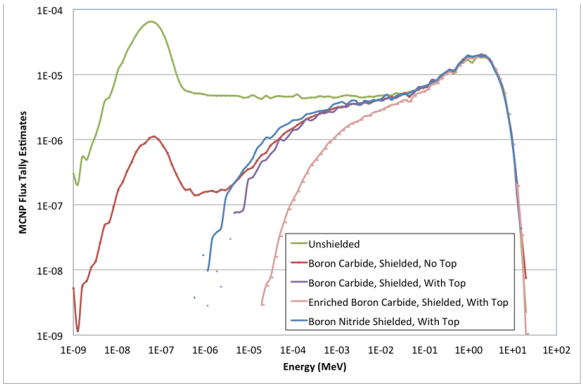

FIGURE 4: MCNP Estimates of the neutron flux spectrum in the sample holder.

Even with this change there was still a relatively high thermal neutron flux reaching the target. The team investigated several sample capsule configurations designed to dramatically reduce the thermal flux reaching the target material. The zinc oxide powder was encapsulated in a high-purity quartz ampule within an outer encapsulation of aluminum (mostly alloy 1100). Various forms and types of neutron absorbing material were simulated as well as built and tested. Figure 4 shows the MCNP simulations of the neutron flux received by the target material inside the outer encapsulation. Because of heating issues with only boron carbide, an outer layer of cadmium metal (0.050 in) will be included in the final design.

The final predicted results are shown in Figure 5. The main radiation component of the final design will be the ^{24}Na produced by fast neutron absorption in the aluminum tubing. The half-life of ^{24}Na is 15.0 hours, so production of ^{64}Cu ($t_{1/2}$=12.7 hours) is not possible with this method. The much longer half-life of ^{67}Cu (61.83 h) allows the irradiation to take place over four weeks of normal operation (Monday–Friday, 8 am–5 pm) during which time, the ^{67}Cu will reach 84% of its saturation activity and then wait over the weekend. By Monday morning, there will still be 50% of the saturation activity of the copper isotope, but less than 15% of the sodium.

Conclusions

While the project has considerable work remaining, the team has shown that there is significant potential to produce research quantities of important radioisotopes at university research reactors.

Acknowledgments

The initial portion of this work was funded by the U.S. Department of Energy – Office of Science grant Development of Innovative Radioactive Isotope Production Techniques at the Penn State University

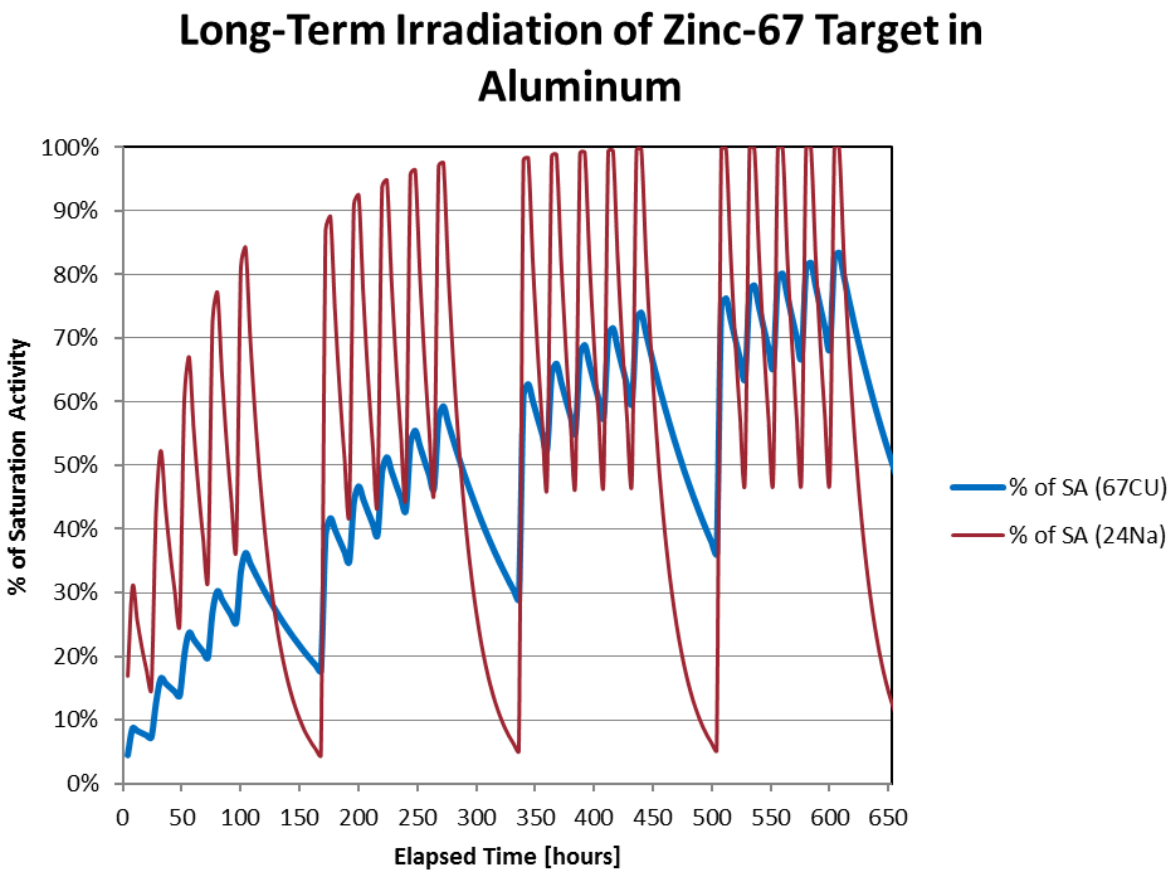

FIGURE 5: Comparison of the induced activity of ^{67}Cu with ^{24}Na during long-term irradiations

Radiation Science and Engineering Center –DE-FG02-10ER41689. Subsequent support was provided through the Penn State Radiation Science and Engineering Center.

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Publications

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