Production of ^{64}Cu Radioisotope for PET Radiotracer and Radiotherapy Agent

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1. Introduction

High specific activity Copper-64 radioisotope production employed a cyclotron has been investigated of great interest for PET imaging tracer and targeted radioimmunotherapy agent [1]. The ^{64}Cu radioisotope decays with two distinguished modes: emitting β^+-particle (0.66 MeV, 17.4 %), which allows PET imaging, and emitting β^--particle of 0.579 MeV (39 %) suited for targeted radiotherapy with a half-life of 12.7 h reasonably long enough duration to require for molecule uptake to targeting tumor. The therapeutic potential of ^{64}Cu labeling with tumor targeting molecules like monoclonal antibodies has been demonstrated by achieving therapeutic doses and non-toxicity. Several production methods have been investigated for the production of ^{64}Cu radioisotope, proton beam irradiation of an enriched ^{64}Ni target, or deuteron irradiation to ^{68}Zn target [2]. In this paper, we describe the proposed development process of ^{64}Cu radioisotope with the comparison of theoretical production yields using ^{64}Ni(p,n)^{64}Cu and ^{68}Zn(p,αn)^{64}Cu nuclear reactions.

Also, utilizing a nuclear reactor the production of ^{64}Cu radioisotope had been carried either via the ^{63}Cu(n,r)^{64}Cu or the ^{64}Zn(n,p)^{64}Cu reation. However, the specific activity was rather low and associated radionuclidic impurity was high. Therefore, it is suggested for cyclotron to develope ^{64}Cu radioisotope with the high specific activity and low impurity.

2. Methods and Results

2.1. Target Fabrication

Using a 2π solid target as shown in Figure 1, the production of ^{64}Cu radionuclide will be investigated utilizing MC50 cyclotron [3] at KIRAMS. Target material of ^{64}Ni (or ^{68}Zn) will be electroplated onto an Au-coated Cu plate (see figure 2). The target materials and Au contact condition is critical to increase the proton currents by cooling the layer effectively. The optimized electroplating condition is under investigated and will be presented later. The target surface electroplated Ni is showed at figure 2 (B), while figure 2 (A) indicated the surface of a Cu-plate for the comparison. Heating the Cu plate resistively will carry the thermal stability.

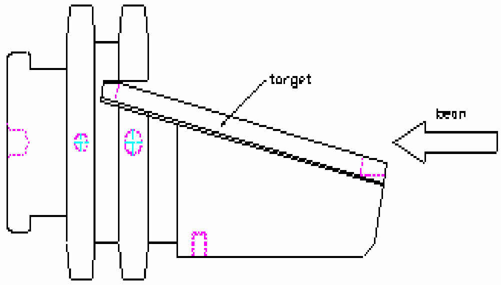

Figure 1. Schematic diagram of a 2π target (not scaled) for the production of ^{64}Cu radionuclide. The target inclined 13 degree with respect to the direction of the incident beam. Cooling water flows a back face of the Cu backing plate.

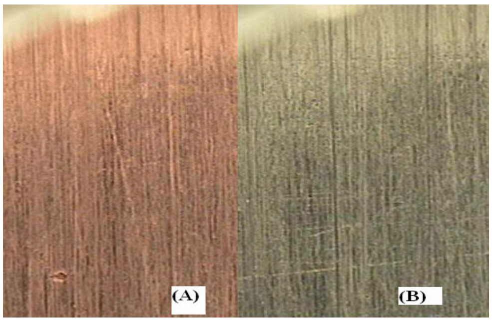

Figure 2. Magnified surface images of Cu-backing plate (A) and Ni electroplated (B) taken by a microscope. Thermal stability was not checked, yet.

2.2. Determination of optimized Ni (and Zn) thickness

To maximize the yield of desired products and minimize the level of radionuclidic impurities, incident energy of proton beam can be optimized by placing Al degrader in front of the target according to the high cross-section ranges in order to take a full benefit of the reaction excitation functions for ^{64}Ni(p,n)^{64}Cu and ^{68}Zn(p,αn)^{64}Cu nuclear reactions, as indicated figure 3. Table 1 makes the list of possible nuclear reactions and suitable proton incident energy range to maximize the production yields. However, ^{67}Cu radioisotope could be another by-product within the energy ranges of above 24 MeV. To avoid the production of ^{67}Cu the incident proton beam energy on ^{68}Zn has to be reduced lower then 24 MeV and the yield also becomes smaller. Employing the target inclined 13 degree with respect to a beam direction, the target material thickness should be optimized within the desired energy ranges of beams passing through the target layer using the SRIM code [4].

Table 1. Possible production routes ^{64}Cu radioisotope

Production route	Energy range (MeV)	Theo. Yield (mCi/uAh)	Ref
^{64}Ni(p,n)^{64}Cu	12 → 9	6.5	1
^{68}Zn(p,αn)^{64}Cu	35 → 20	1.8	5

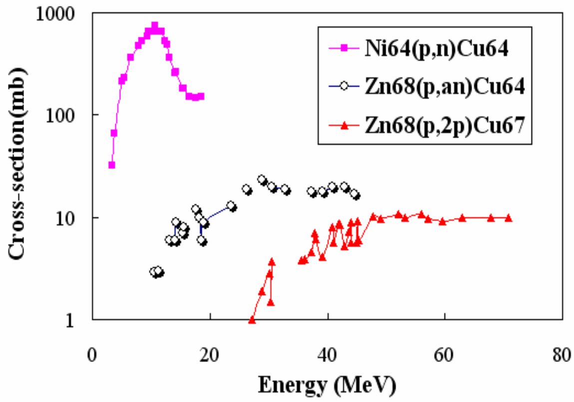

Figure 3. Excitation functions of ^{64}Ni(p,n)^{64}Cu (closed squares) and ^{68}Zn(p,αn)^{64}Cu (open circles) nuclear reactions (taken from refs.[1, 5]). ^{67}Cu could be produced as an impurity.

Figure 4 indicates the way to decide the target thicknesses (5.6 um for Ni and 120 um for Zn) by choosing the optimum energy ranges (E_p = 12 → 9 MeV in Ni, E_p = 35 → 20 MeV in Zn). Using these parameters the theoretical production yields are estimated as 6.5 mCi/uAh and 1.8 mCi/uAh from Ni and Zn target materials, respectively. [1,5]

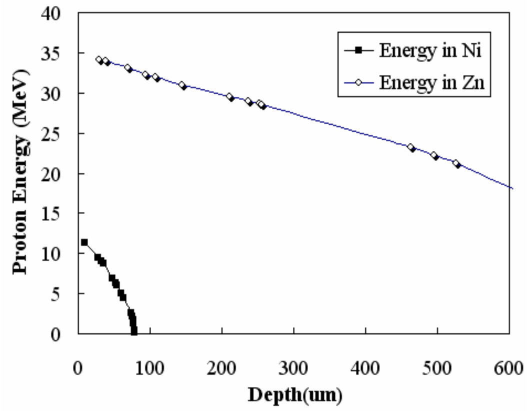

Figure 4. Energy degradation of proton passing through the Ni and Zn target layers, respectively. A x-axis represents an actual traveling distance of proton in target materials. Therefore, the thickness of target is defined as the depth times (sin15).

2.3. Calculation of Expecting Yields

From a given excitation function, the expected yield of a product for a certain energy range (or target thickness) can be calculated using the equation (1):

$$Y = \frac{N_L \cdot H}{M} I(1-e^{-\lambda t})\int_{E1}^{E2}\left(\frac{dE}{d(\rho x)}\right)^{-1}\sigma(E)dE \quad (1)$$

where N_L is the Avogadro number, H the enrichment (or isotope abundance) of the target nuclide, M the mass number of the target element, I projectile current (uA), $(dE/d(\rho x))$ the stopping power, $\sigma(E)$ the cross section at energy E, λ the decay constant of the product and t the time of irradiation.

3. Conclusion

Nuclear data is useful to estimate the production yields of medical radioisotopes, which are used to diagnostic and therapeutic applications. In this paper, we describe developing processes of ^{64}Cu radioisotope with the comparison of theoretical production yields using ^{64}Ni(p,n)^{64}Cu and ^{68}Zn(p,αn)^{64}Cu nuclear reactions.

Acknowledgement

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