PRODUCTION OF ^{61}CU BY DEUTERON IRRADIATION OF NATURAL NI

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Abstract

^{61}Cu ($T_{½}$=3.33h, 61% β^+) offers several advantages over other Cu radioisotopes for labeling radiopharmaceuticals for positron emission tomography (PET). Production of ^{61}Cu[$CuCl_2$] for distribution to biomedical research facilities has been performed at Cyclotope since 2003. Using the ^{nat}Ni(d,x)^{61}Cu reaction, high purity (99%+) natural nickel plates mounted on the solid target beam line of our TR19/9 cyclotron were irradiated.

In order to significantly increase the production capacity of this radiotracer for future human studies in a cost efficient manner we optimized the existing beam line and solid target station. In addition, a remote chemical processing unit was constructed to dissolve the irradiated plates and separate ^{61}Cu from the Ni matrix and other radionuclide impurities. Target saturation yields, processing method and final product characteristics are described in this presentation.

INTRODUCTION

^{60}Cu, ^{61}Cu, ^{62}Cu and ^{64}Cu are promising nuclides for labeling radiopharmaceuticals for Positron Emission Tomography, PET, (see Table 1). Given their high positron branching ratio, ^{60}Cu ($T_{½}$=23.7 min, 93% β^+) and ^{62}Cu ($T_{½}$=9.7 min, 98% β^+) can render high quality PET images. However, their applications are limited by the short half-lives to uptake times shorter than 1h and their production logistics limits availability to in-hospital accelerators or daily supply of the ^{62}Zn/^{62}Cu generator. ^{64}Cu is an intermediate half-life nuclide ($T_{½}$=12.7 h, 22% β^+) currently used for imaging and therapy [1]. Despite its less than desirable image quality, it is one of the few PET tracers available to study processes with uptake longer than 4h. ^{61}Cu covers the gap between these nuclides offering good quality images and the possibility of commercial distribution from a centralized facility [2].

^{61}Cu can be produced via the following reactions: ^{61}Ni(p,n)^{61}Cu (281 MBq/μA.h at 15 MeV [2], ^{61}Ni natural abundance 1.14%) or ^{60}Ni(d,n)^{61}Cu (90 MBq/μA.h at 8MeV [2], ^{60}Ni natural abundance 26.2%). To take advantage of our existing 9 MeV deuteron beam capability, we developed a method for the production of ^{61}Cu using natural nickel as a target. Based on cross sections values reported in [3], we estimated a thick target yield of 53 MBq/μA.h at 7.9 MeV, for the ^{nat}Ni(d,x)^{61}Cu reaction.

MATERIALS AND METHODS

The original solid target station was designed to accommodate rectangular plates 60 x 125 mm with the beam incident at 9 degrees. It had a tantalum collimator with an opening of 9 mm H x 35 mm W. Beam optics along the beam line consist of one set of permanent quadrupole magnets positioned to maximize beam delivery for 18 MeV protons / 9 MeV deuterons.

Table 1: Cu nuclides for PET [4].

Nuclide	Half-life	Decay modes	Major β^+'s		Major γ's	
			keV	%	keV	%
^{60}Cu	23.7min	93% β+	3772	5.0	1332	88.0
		7% EC	2946	15.0	1791	45.0
			1980	49.0	826	21.7
			1911	11.6		
^{61}Cu	3.33h	61% β+	1215	51.0	283	12.2
		39% EC	932	5.5	656	10.8
^{62}Cu	9.7 min	98% β+	1173	0.34		
		2% EC	876	.15		
^{64}Cu	12.7h	22% β+	579	39.0	1346	0.47
		41%EC	653	17.4		
		38% β-				

To reduce the size of the beam strike on targets, we replaced a tantalum collimator, originally planned for larger electroplated targets, with a water cooled graphite collimator with a rectangular opening of 9 x 15 mm. The transmission efficiency through the new collimator, measured from the cyclotron output to the target, was 51% for 9 MeV deuterons and 46% for 8 MeV deuterons To optimize beam transmission efficiency for 8 MeV deuterons a new location for the quadrupole magnets was calculated using beam transport software [5]. After repositioning the magnets the resulting transmission efficiency was observed to be 85% and 62% for 9 MeV and 7.9 MeV deuterons respectively, close to a 50% improvement from original setting. Figure 1 shows average beam distribution on a solid target projected on the collimator plane for the improved 7.9 MeV deuteron beam.

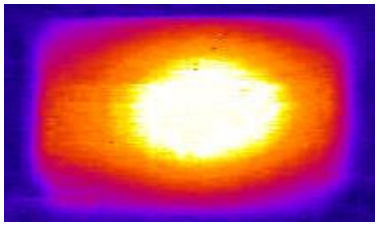


Figure 1. Average beam distribution on a solid target projected on the collimator plane for 7.9 MeV deuteron beam.

Target irradiation

High purity (99%+) natural Nickel plates (1 mm thickness) mounted on the solid target station were irradiated with 7.9 MeV deuterons. Typical activities of 1.8-2.6 GBq were obtained in 90 minutes runs at 25-35μA with average thick target yields of 51.8 MBq/μA.h. Gamma spectroscopy using a HP-Ge detector showed radionuclide impurities, relative to ^{61}Cu (decay corrected at EOB) of 0.11% for ^{58}Co, 0.27% for ^{56}Co for a sample bombarded with 9 MeV deuterons. Other potential impurities like ^{65}Ni were below detectable limits. These results were in good agreement with calculated impurities content using the cross sections published in [3, 6].

^{61}Cu separation

An apparatus for the dissolution of the irradiated area is shown in Figure 2. Through a series of hinges and precision stops, it allows precise target positioning to compensate for different targets thicknesses. The acid bath (8M HCl) is loaded into a pneumatically operated Teflon(PFA) cavity whose open face is pressed against the target irradiated area and sealed with a Viton O-ring. The acid is heated at ~95^{o}C for 1 hour, using a 250 W programmable heater. Typical dissolved mass is between 150-200 mg which corresponds to a target depth of 20-28μm. The dissolved metal/acid solution is then transferred into a column containing an ion exchange resin [7]. At high molarity conditions, Ni(II) is not retained in the resin column and is sent to waste. Several rinses using 8M HCl washes off remaining nickel and cobalt impurities while retaining Cu species. Finally, the ^{61}Cu is eluted with sterile water for injection. Location of product activity through the column is monitored using a PIN diode radiation detector.

The whole process takes between 90-120 min. An average of 740 MBq of ^{61}Cu product with purity >99.9% at EOS and >99.8% at injection time (EOS + 2-4 hours) has been obtained. Typical process efficiency yields are between 25-48% (decay corrected at EOB).

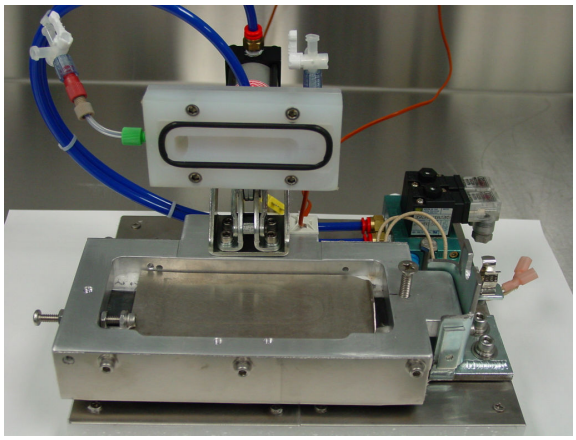


Figure 2. Cu processing apparatus.

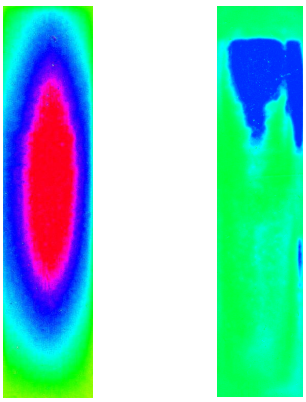
Figure 3 shows the activity distribution on the irradiated Ni plates before and after dissolution. The images were scanned from auto-radiographic films and processed with a fire lookup color spectrum.

The 1 mm thick targets are rinsed with sterile water and cleaned for next run. Target plates can be reused about 20-25 times before significant loss of material.

RESULTS

Bombardment of pure Nickel plates with 7.9 MeV deuterons resulted in ^{61}Cu average thick target yields of 51.8 MBq/μA.h (98% of calculated values at this energy using cross sections published in [3]). A considerable improvement over thick target yields reported by McCarthy [2] of 33.7 MBq/μA.h. Their reduced yields probably due to insufficient target thickness. About 740 MBq of ^{61}Cu are routinely obtained at EOS (99.9% purity).

To further increment our production capacity, improvements on the deuteron beam current output together with installation of an energy degradation foil, to take advantage of higher beam transmission at 9 MeV, are under way.



Before Dissolution After Dissolution

Figure 3. Activity distribution on processed target area, before and after dissolution.

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