

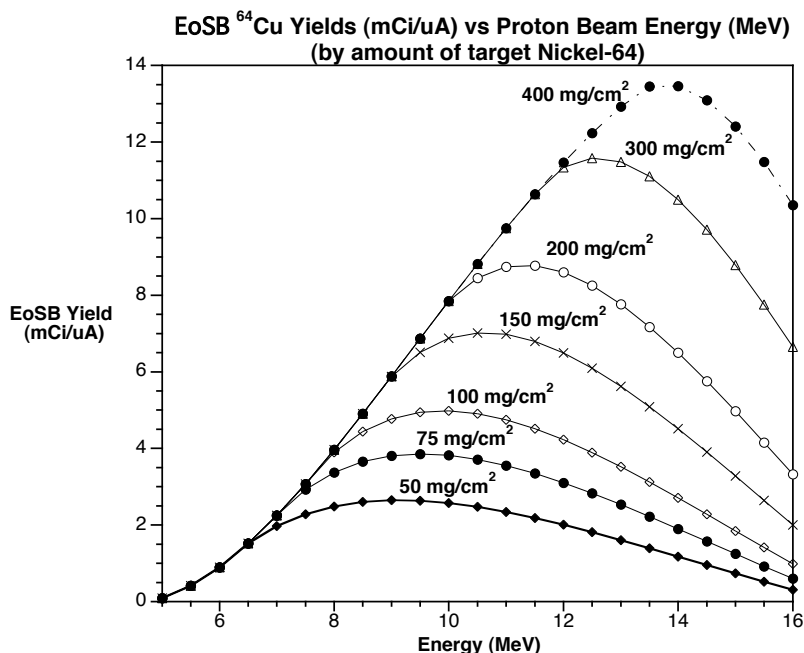
Routine Production of Cu-61 and Cu-64 at the University of Wisconsin

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The application of copper isotopes in PET research has undergone a dramatic rise, driven by their versatile chelation chemistry, favourable decay characteristics, and national distribution potential. The (p,n) reaction has long been used to produce ^{61}Cu and ^{64}Cu from ^{61}Ni and ^{64}Ni with reported yields of 21.4 ± 2.2 mCi/uA/hr and 8.7 ± 0.4 mCi/uA/hr at 11 MeV, respectively.¹ The $^{64}\text{Ni}(p,n)^{64}\text{Cu}$ reaction in particular necessitates careful consideration of incident particle energy. Electrodeposition of enriched ^{61}Ni and ^{64}Ni target material onto high purity gold or silver blanks has been described previously and appears to be limited to approximately 80-120 mg/cm², by time and cost concerns.

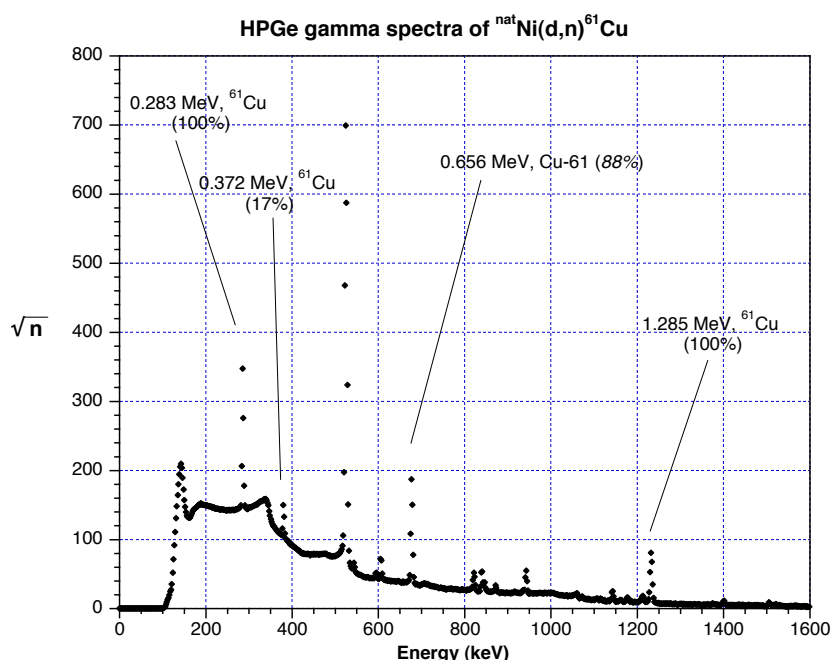
Using the pooled cross section data $\sigma(E)$ for the $^{64}\text{Ni}(p,n)^{64}\text{Cu}$ reaction,² the end of saturated (EoS) yield of ^{64}Cu can be predicted as a function of ^{64}Ni thickness and incident beam energy, shown below. This family of yield curves strongly suggests that very thick targets ($\approx \frac{1}{2}$ gram/cm²; $\approx \$10,000$ in ^{64}Ni inventory) are needed to take advantage of proton energies above 11 MeV, being prohibitive both in cost and plating time. We have degraded the 16 MeV incident proton energy of the PETtrace to approximately 12 MeV with a 0.23 mm tantalum foil to improve the efficiency of our production runs. However, it is apparent that our legacy CTI RDS 112 is still far better suited for the weekly production of ^{64}Cu at the 0.5 Ci level for our own needs, as well as national distribution of the excess.



Copper-61 offers several advantages over ^{64}Cu for PET imaging, namely 61% vs 20% β^+ branching and a 3.4 hr vs 12.7 hr half-life, which combine to result in a three-fold greater useful β^+ flux to absorbed radiation dose ratio for trapped agents. Three reactions present themselves for cyclotron facilities without alpha beams: $^{61}\text{Ni}(p,n)^{61}\text{Cu}$, $^{60}\text{Ni}(d,n)^{61}\text{Cu}$, and $^{64}\text{Zn}(p,\alpha)^{61}\text{Cu}$. With the

recent three-fold price increase of enriched ^{61}Ni , we have reverted to the $^{60}\text{Ni}(d,n)^{61}\text{Cu}$ reaction for protocols needing Cu-ATSM for hypoxia imaging in human and veterinary patients.³ Human studies use enriched ^{60}Ni plated on gold discs. Animal studies, with more relaxed specific activity requirements (>300 mCi/ μmole), can utilize the deuteron irradiation of ^{nat}Ni targets, obviating the need for recycling of enriched target stock. The HPGe spectrum below testifies to the radionuclidic purity of the ^{61}Cu . Electroplated and foil targets are dissolved in HCl at 100°C , accelerated with H_2O_2 . Alternatively, biasing the Ni foil (10 volts, 1 amp) in unheated concentrated HCl removes approximately 40 mg of the foil and $>90\%$ of the activity in 3 minutes.⁴ The dissolution apparatus is identical to the electroplating setup. These platers have been recently improved, adding flow, temperature control, pulsed voltage and current regulation under LabView control.

As more subtle targeting strategies develop, the chelation of copper radionuclides to molecular imaging candidates will permit PET to determine the best lead compound, significantly shortening the time to achieve diagnostic utility. Any improvements in the supply of ^{61}Cu and ^{64}Cu will greatly serve that end.



¹ Avila-Rodriguez M A (2007). Low energy cyclotron production of multivalent transition metals for PET imaging and therapy. Ph.D. Dissertation University of Wisconsin Press, Madison, WI.

² Cyclotron Produced Radionuclides: Physical Characteristics and Production Methods (2009). IAEA Technical Reports Series No. 468. IAEA Press, Vienna, Austria.

³ Tolmachev V, Lundqvist H, Einarsson L (1998). Production of ^{61}Cu from a natural nickel target. Applied Radiation Isotopes, 49(1-2), 79-81.

⁴ Martin C C, Oakes T R, Nickles R J (1990). Small Cyclotron Production of Cu-60 PTSM for PET Blood Flow Measurements. J Nucl Med 31, p815.