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Is $^{70}\text{Zn}(d,x)^{67}\text{Cu}$ the best way to produce ^{67}Cu for medical applications?

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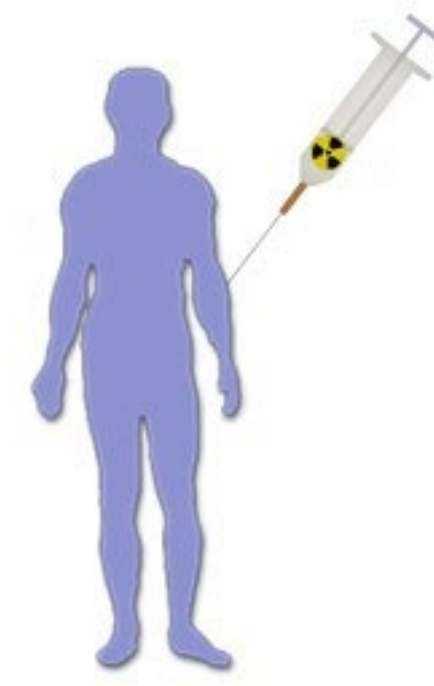
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^{67}Cu medical interest

- Therapeutic use in internal radiotherapy.
- β -emitter with a maximum energy of 561 keV (3 mm in water) [1].
- Comparable to ^{177}Lu currently used in internal vectorised radiotherapy [2].
- SPECT imaging possible with the 184.6 keV (48.7%) γ emission.
- Personalised treatment for patients with the theranostic approach : ^{64}Cu (12.7 h) and ^{67}Cu .
- ^{64}Cu production route is well defined (a biomedical cyclotron delivering protons on a ^{64}Ni target). [4]
- Production route for ^{67}Cu are not well defined.



^{67}Cu «ID card»

^{67}Cu decays to ^{67}Zn (stable) at 100%.
 $T_{1/2} = 61.83$ h.
 β and γ emitter:
 $E_{\beta\text{moy}(1)} = 121$ keV, $E_{\beta\text{max}(1)} = 377.1$ keV (57%),
 $E_{\beta\text{moy}(2)} = 154$ keV, $E_{\beta\text{max}(2)} = 468.4$ keV (22.0%).
 $E_{\beta\text{moy}(3)} = 189$ keV, $E_{\beta\text{max}(3)} = 561.7$ keV (20.0%).
 $E_{\gamma(1)} = 93.3$ keV (16.1%), $E_{\gamma(2)} = 184.6$ keV (48.7%). [3]

Motivation Identify the best route to produce ^{67}Cu with the highest yield and purity.

^{67}Cu production route

Why the $^{70}\text{Zn}(d,x)$ reaction?

- The target allows the separation of Cu.
- High purity ^{67}Cu is achievable.
- ^{64}Cu production can be avoided.
- ^{70}Zn exists and is available in metal form.
- Possibility to make thick targets.
- The yield seems promising but needs to be refined → complete the production cross section. [5]



Energy threshold for Cu isotopes (MeV)

Reaction	^{63}Cu	^{64}Cu	^{65}Cu	^{67}Cu
$^{67}\text{Zn}(d,x)$	7.9	0	0	2.1
$^{68}\text{Zn}(d,x)$	18.5	10.3	0.1	4.6
$^{70}\text{Zn}(d,x)$	34.6	26.4	16.2	0

^{70}Zn Targets

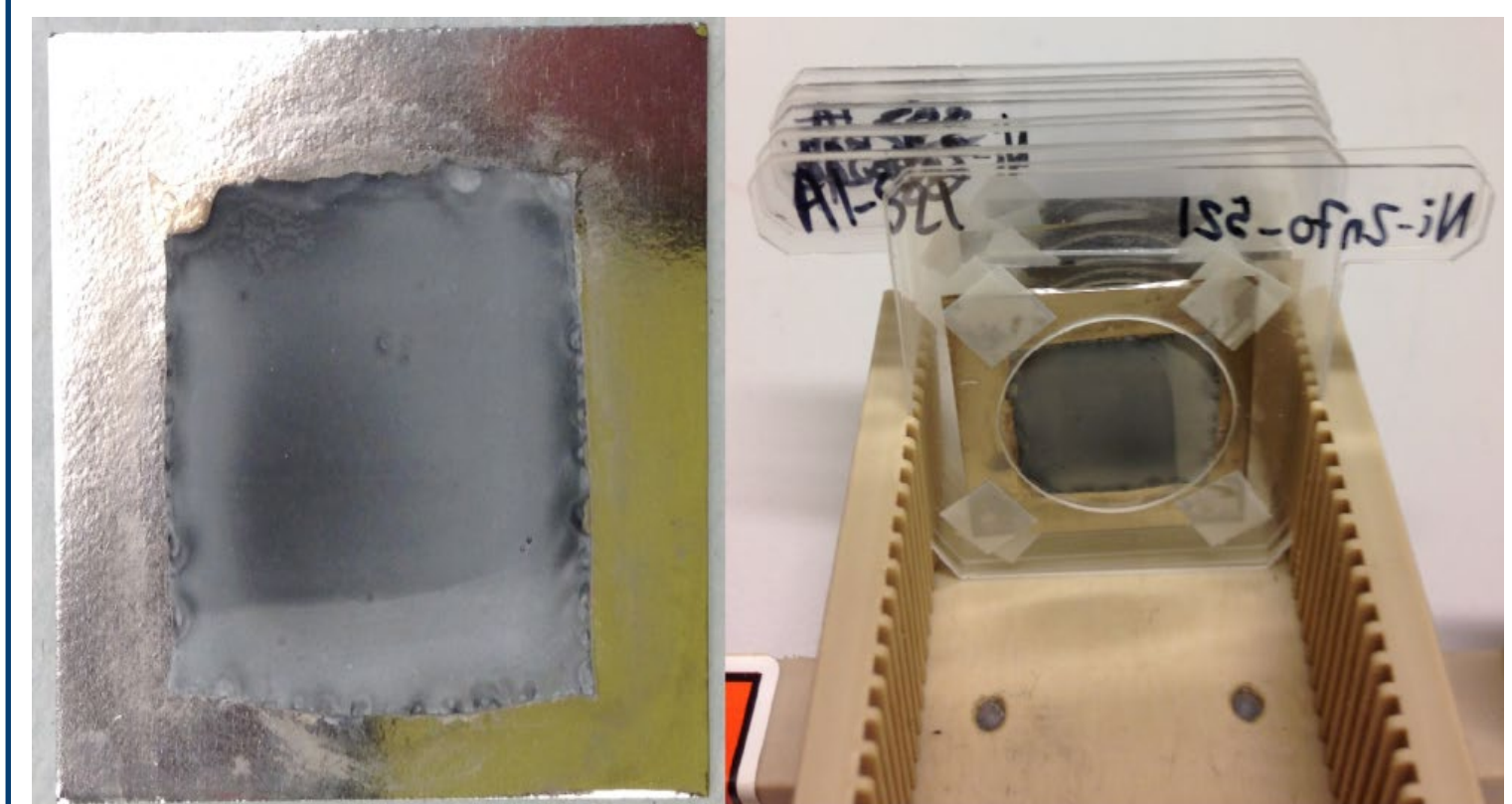
High purity (97.5%) ^{70}Zn metal powder was used to prepare targets by electrodeposition as done in previous work using ^{68}Zn [5].

- The selected backing is natural nickel, ^{nat}Ni .
- 30 min of electrodeposition to achieve ca. 10 μm of thickness.
- Thickness was measured before irradiation.



Electrodeposition device

^{70}Zn deposit on ^{nat}Ni



Stacked-foils

The stacked-foils method

- Stacked thin foils to make multiple cross section measurements in a single irradiation.
- The beam intensity was measured in two ways:
 - Trough the monitor cross section $^{nat}\text{Ti}(d,x)^{48}\text{V}$ (uncertainty ~8%).
 - Using an instrumented faraday cup placed in vacuum (uncertainty ~2%).
- Obtained values are in agreement reinforcing confidence that the experience was under control.
- Measurement of the activity produced after irradiation performed by gamma spectrometry with HPGe.

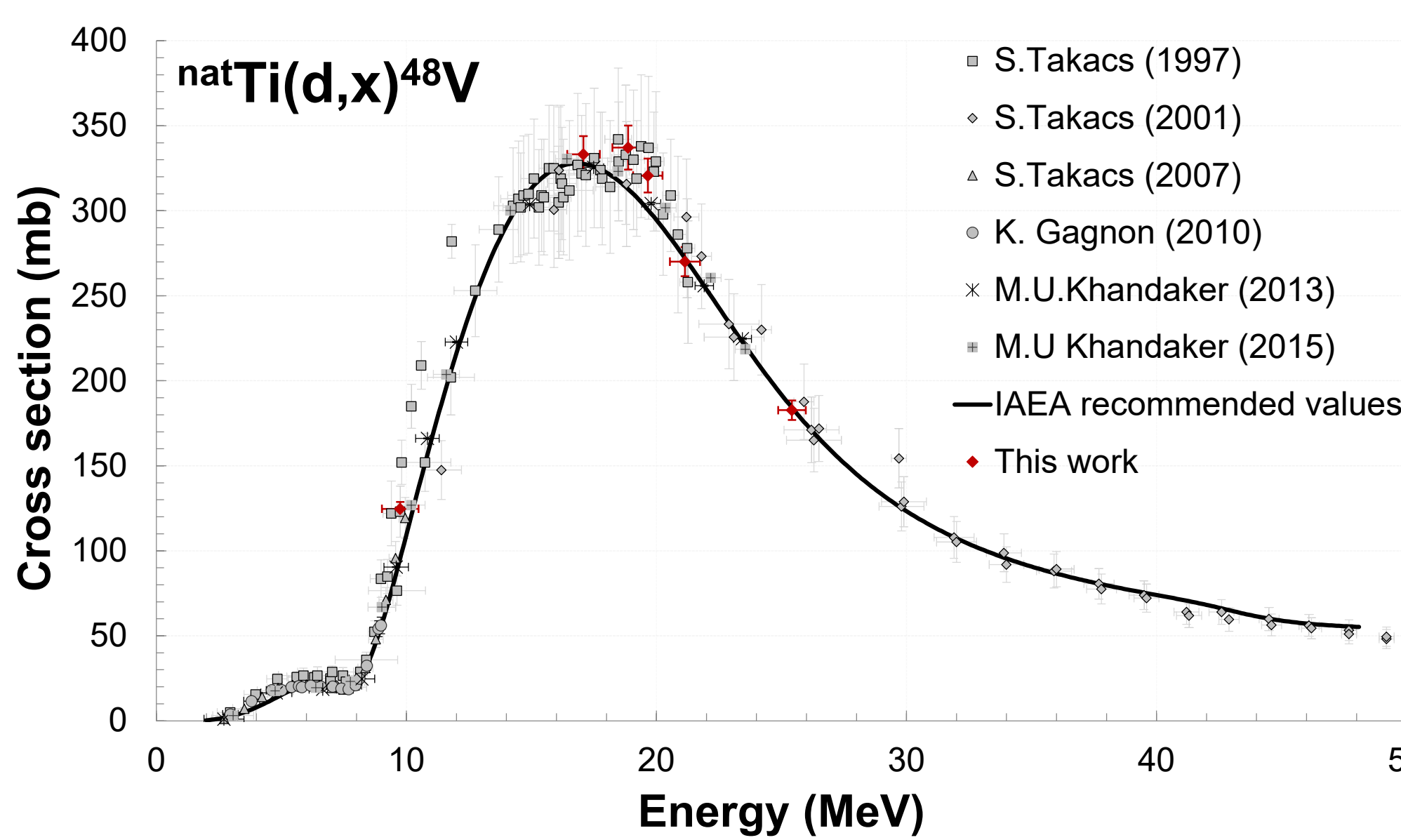


Fig. 1 - Cross section of the monitor reaction measured with the Faraday cup under vacuum. [6-12]

$^{70}\text{Zn}(d,x)^{67}\text{Cu}$ cross section

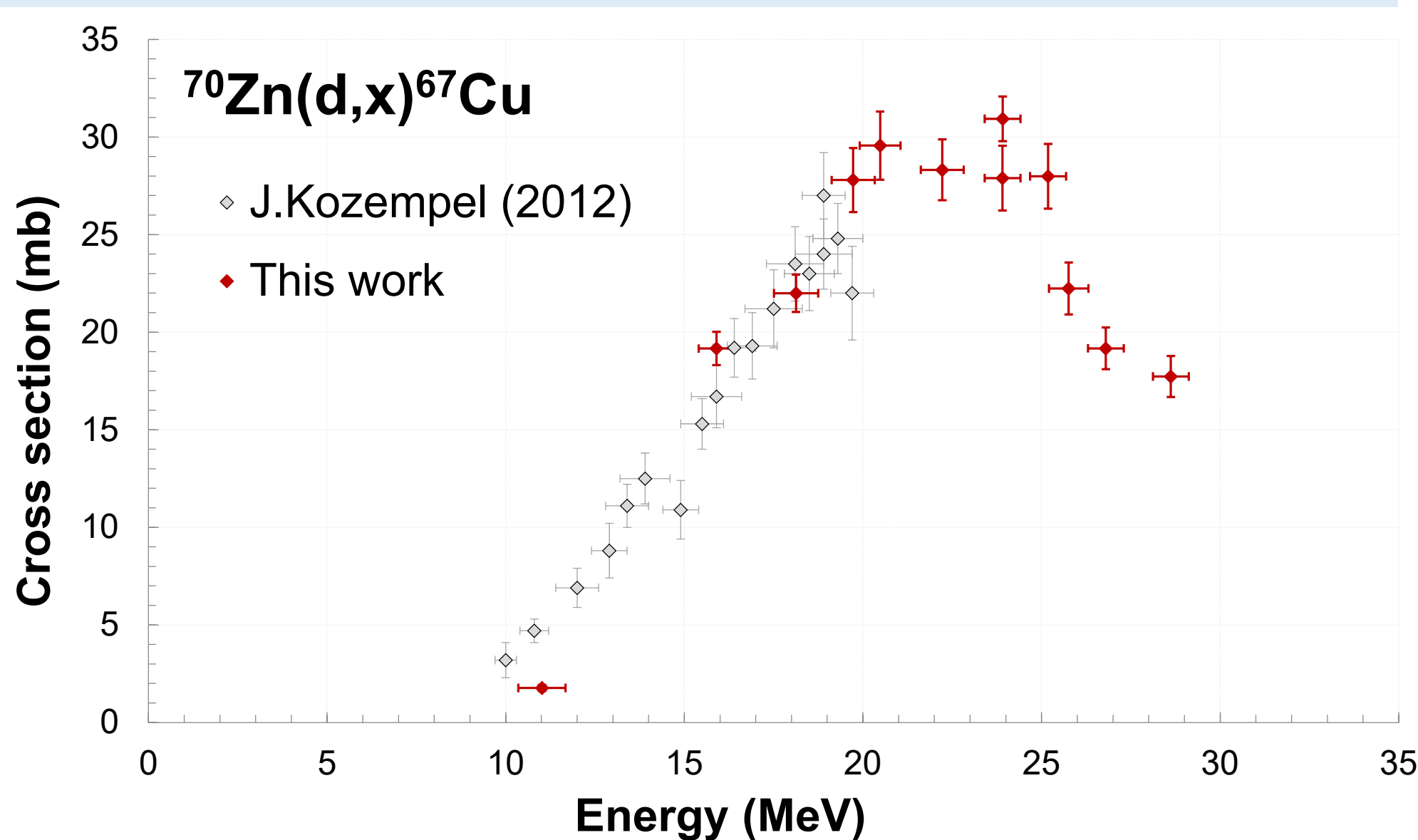


Fig. 2 - Cross sections of reaction $^{70}\text{Zn}(d,x)^{67}\text{Cu}$. [13]

- Additional $^{70}\text{Zn}(d,x)^{67}\text{Cu}$ cross section data points up to 28.7 MeV.
- The maximum cross section was determined.
- Our values are in agreement with the data shown by Kozempel (2012) [13].
- The yield of the $^{70}\text{Zn}(d,x)^{67}\text{Cu}$ reaction can be calculated up to the threshold energy of the reaction producing ^{64}Cu (26.4 MeV).

Yield and Purity

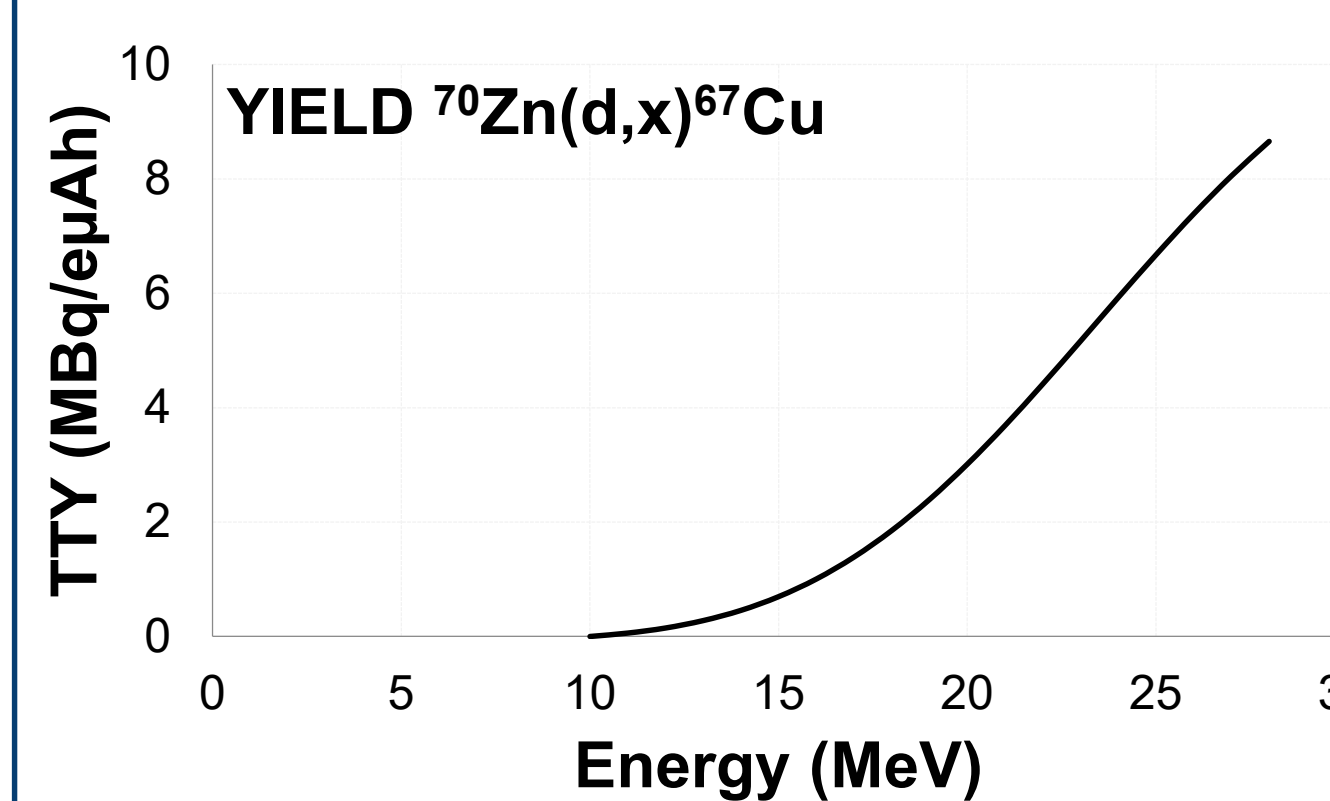


Fig. 3 - Thick Target Yield curve for the $^{70}\text{Zn}(d,x)^{67}\text{Cu}$ reaction.

- Considering the ^{64}Cu threshold production at 26.4 MeV and the ^{70}Zn price, the preferred energy range is 16-26 MeV → 576 μm thickness of ^{70}Zn .
- To reduce the short-lived $^{66,68,69}\text{Cu}$ ($T_{1/2}$: 5.1 min ; 0.52 min ; 2.8 min) in final product → wait 70 min to achieve 99.99% ^{67}Cu activity.
- The calculated specific activity is 1.87 GBq/nmol or 27.9 TBq/mg for theoretical maximum value which equals 28.0 TBq/mg.

Conclusions

- In our stacked foils experiments, the beam intensity has been obtained using an instrumented Faraday cup and monitor reaction $^{nat}\text{Ti}(d,x)^{48}\text{V}$, $^{nat}\text{Ni}(d,x)^{56}\text{Co}$, $^{nat}\text{Ni}(d,x)^{56}\text{Co}$ and $^{nat}\text{Ni}(d,x)^{61}\text{Cu}$. These values are in agreement indicating that the experiment was well controlled.
- Our new data on $^{70}\text{Zn}(d,x)^{67}\text{Cu}$ allows to clearly identifying the maximum of the cross section around 30 mb for an incident energy of 23 MeV.
- This production route is of great interest as it limits strongly the production of ^{64}Cu that is directly linked to the level of ^{68}Zn impurity in the target.
- With a 26 MeV deuteron beam and a target of 576 μm , the production yield is estimated to be 6.4 MBq/ $\mu\text{A}/\text{h}$ and allowing the production of 16.4 GBq with a specific activity of 27.9 TBq/mg for an irradiation of 40 h with an intensity of 80 μA followed by a decay period of 70 min and with a 100% enriched ^{70}Zn target.
- This amount of ^{67}Cu activity produced with high specific activity and without ^{64}Cu is suitable for clinical studies.

References

[1] NIST (National Institute of Standards and Technology), Software online, "Stopping Powers and Ranges for Electrons (estar)".
 [2] C. Bailly, A. Vidal, C. Bonnemaire, F. Krarber-Bodéré, M. Chérel, A. Pallardy, C. Rousseau, E. Garcion, F. Lacoëuille, F. Hindré, S. Valable, M. Bernaudin, C. Bodet-Hindré, M. Bourgeois, « Potential for Nuclear Medicine Therapy for Glioblastoma Treatment », Front. Pharmacol. vol. 10 p772, 2019.
 [3] "Chart of Nuclides from National Nuclear Data Center (NNDC)." [Online]. Database NuDat 2.8
 [4] A. Hermanne, F. Tárkányi, S. Takács, S. F. Kovalev, and A. Ignatyuk, "Activation cross sections of the $^{64}\text{Ni}(d,2n)$ reaction for the production of the medical radionuclide ^{64}Cu ," Nucl. Insts Meth Phys. Res. Sect. B Beam Interact. with Mater. Atoms, vol. 258, no. 2, pp. 308–312, 2007.
 [5] G. Pupillo, T. Sounalet, N. Michel, L. Mou, J. Esposito, and F. Haddad, "New production cross sections for the theranostic radionuclide ^{67}Cu ," Nucl. Instruments Methods Phys. Res. Sect. B Beam Interact. with Mater. Atoms, vol. 415, no. October 2017, pp. 41–47, 2018.
 [6] A. Hermanne et al., "Reference Cross Sections for Charged-particle Monitor Reactions," Nucl. Data Sheets, vol. 148, pp. 338–382, 2018.
 [7] S. Takács, M. Sonck, B. Scholten, A. Hermanne, and F. Tárkányi, "Excitation functions of deuteron induced nuclear reactions on (^{nat}Ti) up to 20 MeV for monitoring deuteron beams," Appl. Radiat. Isot., vol. 48, no. 5, pp. 657–665, 1997.
 [8] S. Takács et al., "New cross-sections and intercomparison of deuteron monitor reactions on Al, Ti, Fe, Ni and Cu," Nucl. Instruments Methods Phys. Res. Sect. B Beam Interact. with Mater. Atoms, vol. 174, no. 3, pp. 235–258, 2001.
 [9] S. Takács, F. Tárkányi, B. Király, A. Hermanne, and M. Sonck, "Evaluated activation cross sections of longer-lived radionuclides produced by deuteron induced reactions on ^{nat}Ni ," Nucl. Insts Meth Phys. Res. Sect. B Beam Interact. with Mater. Atoms, vol. 260, no. 2, pp. 495–507, 2007.
 [10] K. Gagnon, M. A. Avila-Rodriguez, J. Wilson, S. A. McQuarrie, "Experimental deuteron cross section measurements using single ^{nat}Ti foils from 3 to 9 MeV with special reference to the prod. of ^{47}V and ^{51}Ti ," Nucl. Inst Meth Phys. Res. Sect. B Beam Int. Mater. Atoms, vol. 268, no. 9, pp. 1392–1398, 2010.
 [11] M. U. Khandaker, H. Haba, J. Kanaya, and N. Otuka, "Excitation functions of (d,x) nuclear reactions on natural titanium up to 24 MeV," Nucl. Instruments Methods Phys. Res. Sect. B Beam Interact. with Mater. Atoms, vol. 296, pp. 14–21, 2013.
 [12] M. U. Khandaker, H. Haba, M. Murakami, and N. Otuka, "Production cross-sections of long-lived radionuclides in deuteron-induced reactions on natural zinc up to 23 MeV," Nucl. Insts Meth Phys. Res. Sect. B Beam Interact. with Mater. Atoms, vol. 346, pp. 8–16, 2015.
 [13] J. Kozempel, K. Abbas, F. Simonelli, A. Bulgheroni, U. Holzwarth, and N. Gibson, "Preparation of ^{67}Cu via deuteron irradiation of ^{70}Zn ," Radiochim. Acta, vol. 100, no. 7, pp. 419–423, 2012.

