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Excitation function of (p, α) nuclear reaction on enriched ^{67}Zn: possibility of production of ^{64}Cu at low energy cyclotron

Abstract: The potential for production of the medically relevant ^{64}Cu has been investigated by proton irradiation of highly enriched ^{67}Zn targets. The excitation function of the ^{67}Zn(p, α)^{64}Cu a nuclear reaction was measured by the stacked-foil technique up to 30 MeV. The prediction of the TALYS code was also compared to the measured cross section results. Based on the improved database of the ^{67}Zn(p, α)^{64}Cu reaction, thick target yield as a function of energy was also deduced. Production possibility of ^{64}Cu is discussed in detail, employing different energy proton beams and with regards to the ^{61}Cu and ^{67}Cu contamination levels as a function of the target enrichment level. By using 1 μA beam intensity, 6.3505 h irradiation time and enriched ^{67}Zn target (^{64}Zn ≤ 0.5%, ^{66}Zn ≤ 9%, ^{67}Zn ≥ 80%, ^{68}Zn ≤ 10% and ^{70}Zn ≤ 0.5%), the expected EOB (End Of bombardment) yields are 43.66, 88.80 and 156.14 MBq/μA at 12, 15 and 18 MeV proton energies, respectively. Application time-frames were also deduced where the total radio-copper contamination level remains below 1%.

Keywords: Medical radioisotope: ^{64}Cu, Proton induced reaction, Excitation function, Integral yield, ^{61}Cu, ^{67}Cu contamination levels.

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1 Introduction

Among the copper radioisotopes ^{64}Cu is of special interest to nuclear medicine as it can be employed both for medical imaging (*via* Positron Emission Tomography: PET) and for targeted radio-immunotherapy of tumours. Its relative long half-life ($T_{1/2}$ = 12.701 h [1]; decay scheme: EC(43.7%) [1], β^-(38.5%) [1], β^+(17.8%) [2]) not only makes possible performing investigations with ^{64}Cu labelled compounds over several days, but – as an additional benefit – it is short enough to limit the patient's exposure during these studies [3–5].

Several research centres have already investigated its production routes *via* proton (and deuteron) induced nuclear reactions on highly enriched ^{64}Ni (natural isotopic composition of ^{64}Ni: 0.926%) target [6–9]. Nowadays, the ^{64}Ni(p, n)^{64}Cu process is used in practice providing the purest form of ^{64}Cu (both radionuclidic and chemical) in very high yield.

Due to the relative high price of the enriched nickel material, however, alternative ^{64}Cu production methods were also studied worldwide in recent years. As a result of these detailed studies, proton and deuteron induced reactions on highly enriched ^{64}Zn, ^{66}Zn and ^{68}Zn targets have been suggested as candidates for this purpose. The investigated nuclear reactions were as follows: ^{64}Zn(d, $2p$)^{64}Cu, ^{66}Zn(p, $2pn$)^{64}Cu, ^{66}Zn(d, α)^{64}Cu, ^{68}Zn(p, αn)^{64}Cu and ^{68}Zn(d, $\alpha 2n$)^{64}Cu [10–13]. Compilation and evaluation of these other production routes of ^{64}Cu was already the subject of an IAEA's Coordinated Research Project [14]. Furthermore, Aslam *et al.* [15] have also published a comprehensive evaluation of these production related cross section data.

From the point of view of a lower energy 'biomedical' cyclotron (around 12–18 and 6–10 MeV maximum proton and deuteron energy, respectively), the starting energies of ^{66}Zn(p, $2pn$)^{64}Cu (Q = −18.83 MeV), ^{68}Zn(p, αn)^{64}Cu (Q = −7.79 MeV) and ^{68}Zn(d, $\alpha 2n$)^{64}Cu (Q = −10.014 MeV) nuclear reactions are too high to use these processes for practical purposes. Although the above values for the ^{64}Zn(d, $2p$)^{64}Cu (Q = −2.02 MeV)

and ^{66}Zn$(d, \alpha)^{64}$Cu (Q = +7.24 MeV) seems to be acceptable, but unfortunately their reported excitation function curves reach their maximum beyond the available deuteron energy ranges [11, 13]. Additionally, the limited number of higher energy deuteron accelerators in research centres could also limit the widespread application of the 'deuteron ways'.

Surveying the information on cross section data of all ^{64}Cu producing Zn+p and Zn+d reactions, it was found one process that could be useful even at low energies, namely the ^{67}Zn$(p, \alpha)^{64}$Cu (Q = +2.407 MeV) reaction [16]. The excitation function of this reaction was studied by only one author in the past, probably because of the low isotopic composition of ^{67}Zn (4.1%) in natural zinc [17]. It should be noted, however, that in spite of the fact that highly enriched ^{67}Zn material is relative expensive (compared to ^{68}Zn) the ^{67}Zn+p reactions are used for routine ^{67,66}Ga production at low energy cyclotrons [cf. [18, 19]]. Although numerous cross section measurements can be found in the literature for ^{67}Zn+$p$reactions, it is surprising that the database of those processes that produce copper radioisotopes is rather scanty [16].

To evaluate the practical production circumstances of ^{64}Cu (i.e. production energy range, activation time, contamination level(s), time-frame of use etc.) at a biomedical cyclotron *via* the ^{67}Zn$(p, \alpha)^{64}$Cu reaction, it is important to have reliable cross section databases of all Zn+p reactions that form ^{60,61,62,64,67}Cu radioisotopes below 18 MeV. The ^{64}Cu product certainly has radio-copper contamination(s) if a target with lower enrichment level (i.e. < 100% of ^{67}Zn) is activated. From the point of view of ^{64}Cu, the presence of ^{61}Cu($T_{1/2}$ = 3.333 h) and ^{67}Cu($T_{1/2}$ = 61.83 h) [1] at EOB means the major radio-copper contaminations. Although other copper radioisotopes can be also formed below 18 MeV, their half lives are too short (for example: ^{60}Cu($T_{1/2}$ = 23.7 min) or ^{62}Cu($T_{1/2}$ = 9.673 min)) to cause any impurity problem at the time of the practical application. The amount of ^{61}Cu (shorter lived contamination) can prolong the waiting period (cooling time) before the medical applications. Similarly, the presence of ^{67}Cu at EOB may limit the length of the application period of the labelled compounds. Thanks to the available detailed excitation function studies, the cross section database of ^{64}Zn$(p, \alpha)^{61}$Cu (Q = +0.844 MeV), ^{68}Zn$(p, 2p)^{67}$Cu (Q = −9.977 MeV) and ^{70}Zn$(p, \alpha)^{67}$Cu (Q = +0.262 MeV) reactions seem to be well measured and can be used for calculating the thick target yields of the above reactions with the required precision. The only exemption is the ^{67}Zn$(p, \alpha)^{64}$Cu reaction, that – as it was mentioned above – has only one dataset.

To improve the database of the ^{67}Zn$(p, \alpha)^{64}$Cu nuclear reaction, we decided to re-measure its excitation function curve up to 30 MeV and compare the new dataset not only to the available experimental results [17], but also with the predicted ones calculated with the 4th version of TALYS code from the TENDL-2012 online library [20]. Based on the evaluated cross section databases of the contributing reactions, we could calculate the ^{64}Cu EOB yields as function of energy and irradiation time. Additionally, it becomes also possible to estimate the EOB radio-copper contamination levels of the final product as a function of irradiation time and target enrichment level.

We discuss here in detail the actual production possibility of ^{64}Cu *via* irradiations with three different energy proton beams (i.e. 12, 15 and 18 MeV).

2 Experimental

2.1 Targets

Cross sections for ^{64}Cu were measured *via* the activation technique by bombarding the samples in a 'stacked-form' arrangement. Five pieces of highly enriched ^{67}Zn targets (^{64}Zn: 1.44%;^{66}Zn: 2.2%; **^{67}Zn: 91.5 ± 0.5%**; ^{68}Zn: 4.78%; ^{70}Zn: 0.08%; (molar fraction)) were prepared *via* electrodeposition. The preparation method was similar to those given in [18]. The enriched material was supplied by v/o Technabexport, Moscow, Russia. Commercially available thin natural Ni foils (thickness: 8.90 mg/cm^2; Goodfellow Metals, UK) served as target backing material. Other thin metal foils (Ti (9.08 mg/cm^2) and Cu (8.92 mg/cm^2)) which were also used during the experiments (i.e. for energy degradation and beam intensity monitoring) were purchased also from the above source. The diameter of the electroplated ^{67}Zn targets was 10 mm while their thicknesses varied between 7.85 and 12.70 mg/cm^2. The targets and foils used were individually weighed before the activations to evaluate their actual thickness.

2.2 Irradiations and beam current measurement

Two irradiations were done at the AVF-930 isochronous cyclotron of NIRS, Chiba with the same primary proton energy (30.6 ± 0.4 MeV). The energies were determined by magnetic deflection. The same five ^{67}Zn samples were activated in both cases in a special target holder that served also as a Faraday-cup for charge measurement. The time difference between the two activations was almost 6 d.

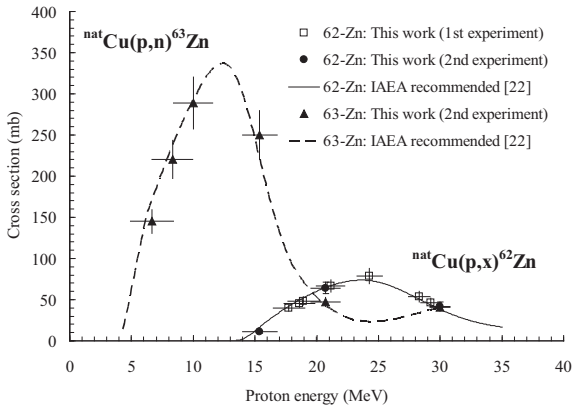

Fig. 1: Excitation functions of ^{nat}Cu+p monitor reactions used in this study for beam monitoring.

This way the ^{64}Cu activity produced during the 1st experiment could decay out until the beginning of the second activation. The ^{67}Zn samples were interspersed with copper energy degrader (and monitor) foils. The number of copper foils was different in the stacks to get ^{64}Cu cross sections at different energies. To prevent the contamination of the targets with cold and radioactive copper isotopes originating from the Cu foils, Ti foils were placed in front of each Zn samples (^{64}Cu is also formed *via* the ^{65}Cu(p, pn) (Q = −9.91 MeV) and ^{65}Cu(p, d) (Q = −7.69 MeV) reactions). Naturally, special care was taken during the assembling and disassembling of the stacks to prevent additional copper contamination of the target samples.

Both activations lasted for 2 h with the same beam current of 100 nA. An Al collimator (thickness: 3 cm) was used to get a well collimated beam ($\varnothing$ = 4 mm) on the surface of the foils. Similar to our previous work on ^{68}Zn+p reaction [21], the values of the accumulated charges were also compared to the calculated ones, obtained *via* the IAEA's recommended ^{nat}Cu+p monitor reaction database [22]. In the case of the first experiment both the ^{nat}Cu(p, xn)^{62}Zn and ^{nat}Cu(p, n)^{63}Zn processes were used, while during the 2nd activation of the foils only the ^{nat}Cu(p, n)^{63}Zn reaction proved useful.

In Figure 1 our measured cross sections of ^{62}Zn and ^{63}Zn, are compared to the recommended values. Beam fluxes determined by direct integration agreed well (within 6%) with the monitor reaction results.

2.3 Activity measurement

The irradiated samples and monitor foils were measured non-destructively using an HPGe detector (EGC15-185-R, 76 cm^3, Eurisys Measures, France) connected to an MCA win2000 data acquisition system. The energy calibration of the detector and the determination of its counting efficiency were done using standard gamma-ray point sources (^{22}Na, ^{54}Mn, ^{57}Co, ^{60}Co and ^{137}Cs) supplied by Isotope Products Laboratories (Burbank, California, USA). The uncertainty of these calibration sources were ±3%. All foils were measured at distances of ≥ 20 cm (from the detector surface), minimizing this way the random pile-ups and summations, and reducing dead-time to less than 3%. Additionally, from this distance the requirement for 'point-like sources' could be also assured. (The activities produced in the samples were concentrated in the center of the foils within a small spot with a diameter of 4 mm.)

Since the enriched ^{67}Zn material was electroplated onto ^{nat}Ni material, ^{64}Cu was produced also *via* the ^{64}Ni(p, n)^{64}Cu reaction in the activated samples. Based on the evaluated database of the ^{64}Ni(p, n)^{64}Cu reaction [22] and taking into account the thickness of the ^{nat}Ni backings, the abundance of ^{64}Ni (0.926%) in ^{nat}Ni, and the irradiation circumstances, we could estimate the amount of ^{64}Cu activity produced in each target backings during the different activations. We compared these estimated activity values with the actual ^{64}Cu ones measured from the samples, and the found them negligible.

The decay characteristics (i.e. dominant gamma-ray energies and their branching ratios) of the measured Ga, Zn and Cu radioisotopes were taken from the Nudat 2.6 database [1].

Since only one γ-ray is emitted in the decay of ^{64}Cu with low intensity, the measurement of the ^{64}Cu activity *via* this line is not so straightforward (1345.8 keV ($I\gamma$ = 0.48%)). There is however, a 'counting window' (between 1.5 and 2.5 half lives after EOB) when ^{64}Cu can be assayed easily [12]. According to the conclusions reported in [23], the possibility to measure the ^{64}Cu activity using the annihilation-peak without chemical separation (decay-curve analysis) was ruled out.

2.4 Calculation of reaction cross sections and their uncertainties

The cross sections were calculated by applying the well-known activation formula. Corrections were made for decay losses during and after bombardment, as well as during counting. No correction was required for the recoil effect as the Ni backings served also as catcher foils. Since ^{67}Zn had only 91.5% abundance in the target material, the obtained cross section values had to be normalized to 100% enrichment level.

The energy degradation along the stacks and the effective particle energy in the middle of each target foil were calculated according to the polynomial approximation of Andersen and Ziegler [24].

Due to the straggling effect and foil thickness uncertainties the initial uncertainty in the proton beam energy increased along the stacks and reached ±1.3 and ±1.7 MeV in the last foils of the 1st and 2nd experiments, respectively,

The estimation of standard uncertainty on the cross section values supposing equal sensitivities for the different parameters was performed as described in [25]. The following individual uncertainties were included in the propagated error: foil thickness or the number of target nuclei, including target non-uniformities (2% but 5% for the electroplated ^{67}Zn); incident particle intensity (4%–6%); detection efficiency (3%–5%), depending on the energy of the gamma-photon; determination of the peak areas, including statistical errors (3%–15%); abundance of the gamma rays analysed (1%–2%). Only the linearly contributing independent uncertainty sources were used and the non-linear sources were omitted in the calculation. The uncertainties of time information (irradiation, cooling and measuring time and half-life) were neglected since their contributions are not significant in this case. The resulting total average uncertainties amount to 10%–12% for monitors and 13%–17% for ^{64}Cu cross sections, obtained as square root of the sum of squares of the contributing sources.

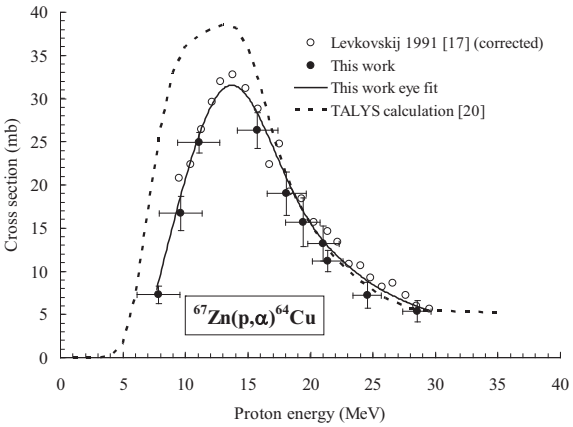

Fig. 2: Excitation function of the ^{67}Zn(p, α)^{64}Cu nuclear reaction.

Table 1: Measured cross sections for the ^{67}Zn(p, α)^{64}Cu nuclear reaction.

Energy (MeV)	Cross section of ^{67}Zn(p, α)^{64}Cu (mb)
7.9 ± 1.7	7.3 ± 1.3
9.6 ± 1.6	16.7 ± 2.2
11.1 ± 1.6	24.9 ± 2.8
15.8 ± 1.4	26.3 ± 2.9
18.1 ± 1.3	19.1 ± 2.4
19.4 ± 1.2	15.7 ± 1.8
21.0 ± 1.2	13.2 ± 1.7
21.4 ± 1.1	11.2 ± 1.5
24.5 ± 1.0	7.3 ± 1.2
28.5 ± 0.9	5.4 ± 1.1

3 Results and discussion

3.1 Cross sections of the ^{67}Zn(p, α)^{64}Cu nuclear reaction

The excitation function for the ^{67}Zn(p, α)^{64}Cu nuclear reaction is shown by closed circles in Figure 2. Table 1 contains the numerical values of the measured cross sections (10 data points) and their uncertainties. To check the reliability of our measurement we have compared the new cross sections to the available theoretical and experimental data. As it was mentioned earlier, only Levkovskij [17] measured this reaction before our study. Unfortunately, the details of his experimental circumstances were not available in the original work. It is supposed that the 1345.8 keV gamma line was employed by him for cross section measurement. Recently, Takács *et al.* [26] have shown that all cross section data for proton induced processes reported by Levkovskij [17] should be decreased by 20% based on the presently accepted value of the monitor reaction (^{nat}Mo(p, x)$^{96\,m}$Tc) that was used by Levkovskij in his original work. Therefore, for comparison we had to re-calculate his values for the ^{67}Zn(p, α)^{64}Cu nuclear reaction. These 'updated' data are reproduced in Figure 2. The predicted excitation function curve calculated *via* the TALYS code [20] is also added to Figure 2 up to 35 MeV.

The two experimental data sets show good agreement with each other not only in the cross section magnitude but they gave the same energy for the position of the peak of the excitation function curve as well (σ_{max} = 30 mb at about 14 MeV). Although the theoretical calculation predicts the same peak position, it overestimates the cross section values over the whole onset part of the excitation function curve. In contrast to this overestimation, the slope part of the curve is in good agreement with the experimental results (beyond 17 MeV).

For thick target yield calculations, therefore, we decided to use the 'eye-fitted' excitation function curve (see Figure 2) of the ^{67}Zn(p, α)^{64}Cu reaction, based on the

data of this work and the values of Levkovskij [17], instead of the predicted values.

3.2 Production possibility of ^{64}Cu *via* the ^{67}Zn(*p*, α)^{64}Cu reaction

The available ^{64}Cu activities as a function of the bombarding energy are reproduced in Figure 3 for enriched ^{67}Zn target. One half of the half-life of ^{64}Cu irradiation time was used during this calculation. The 6.3505 h activation time seems to be acceptable at biomedical cyclotrons having busy production agenda. During this time almost 30% of the saturation activity of ^{64}Cu could be produced. As it can be seen in Figure 3, the yield increases with the increasing energy. It is interesting to mention that the thick target yields of ^{64}Cu calculated *via* the theoretical excitation function curve overestimate the yields based on the experimental data by a factor of 2. As it is expected, the natural zinc target produces the lowest EOB activity (9.25 MBq/μA, (0.25 mCi/μA)) at 20 MeV. It is worth considering that in the case of ^{nat}Zn targets the ^{68}Zn(*p*, *αn*)^{64}Cu reaction also contributes to the formation of ^{64}Cu above 10 MeV. The low yield and the long cooling time due to the co-formed ^{61}Cu (huge amount *via* the ^{64}Zn(*p*, *α*)^{61}Cu reaction) disqualifies the ^{nat}Zn target to use for practical purposes. For example, at 15 MeV more than 56 h cooling time would be necessary to reach < 1% ^{61}Cu/^{64}Cu activity ratio; resulting this way only 370 kBq/μA (0.01 mCi/μA) practical yield. On the other hand, the longer lived radio-copper contaminant, the ^{67}Cu, (*via* the ^{68}Zn(*p*, 2*p*)^{67}Cu and ^{70}Zn(*p*, *α*)^{67}Cu reactions) [22, 27, 28] would decrease the length of the application time (below 11 h; < 1% ^{67}Cu contamination) of the final product. Note, that the presence of ^{61}Cu and ^{67}Cu in the final product has not only influence on the quality of the PET measurement, but also delivers unnecessary dose to the patient. Therefore, the production method selected must keep the contamination levels as low as possible (usually below 1%.)

A zinc target with 100% ^{67}Zn enrichment level provides not only the highest yield (225.59 MBq/μA (6.07 mCi/μA) at 20 MeV)) but the product will be also radio-copper contamination-free as well. Although above 16.37 MeV the formation of ^{62}Cu ($T_{1/2}$ = 9.74 min) becomes possible (*via* the ^{67}Zn(*p*, *α2n*)^{62}Cu reaction) but – as it was discussed earlier – it decays out from the final product during the processing time.

It is obvious that due to high price of 100% enriched ^{67}Zn, target materials with lower ^{67}Zn enrichment levels are the real options for practical purposes.

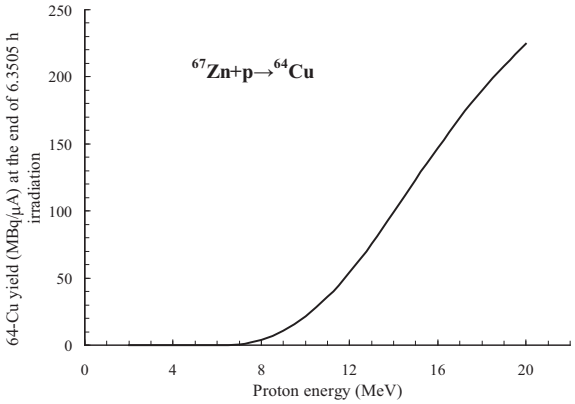

Fig. 3: ^{64}Cu activity as a function of bombarding proton energy.

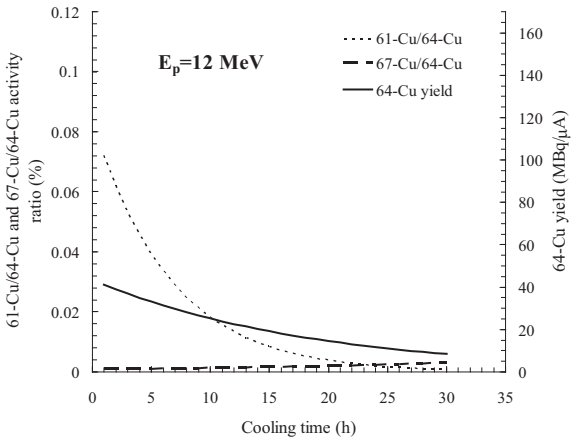

Fig. 4: ^{61}Cu/^{64}Cu and ^{67}Cu/^{64}Cu activity ratio and ^{64}Cu yield as a function cooling time using 12 MeV incident proton energy.

As it can be calculated (Figure 4), acceptable yields (≥ 37 MBq/μA) can be achieved even at 12 MeV using a target containing more than 80% ^{67}Zn. Depending, however on the actual composition of the target, different ^{61}Cu/^{64}Cu and ^{67}Cu/^{64}Cu activity ratios could be observed at EOB. In analyzing the excitation functions of those Zn+*p* reactions that form ^{61}Cu and ^{67}Cu below 18 MeV, the following can be concluded concerning the purity level of the final ^{64}Cu product: a) the amount of ^{64}Zn and ^{70}Zn in the actual target has the major influence on the purity of the final product [14, 27, 28]. b) The amount of ^{66}Zn and ^{67}Zn in the target matrix is indifferent from the point of view of ^{61,67}Cu formation.

Below we discuss in details the available ^{64}Cu yields and the ^{61}Cu/^{64}Cu and ^{67}Cu/^{64}Cu activity ratios as a function of the cooling time at 12, 15 and 18 MeV irradiations (see Figures 4, 5 and 6, respectively). For these calculations an enriched ^{67}Zn target with the following composition (molar fraction) was supposed:

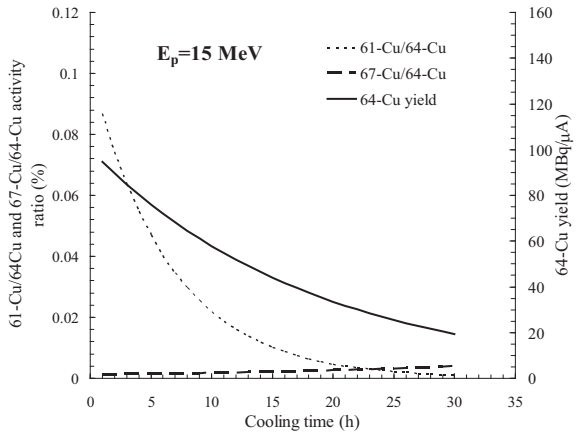

Fig. 5: $^{61}Cu/^{64}Cu$ and $^{67}Cu/^{64}Cu$ activity ratio and ^{64}Cu activity as a function cooling time using 15 MeV incident proton energy.

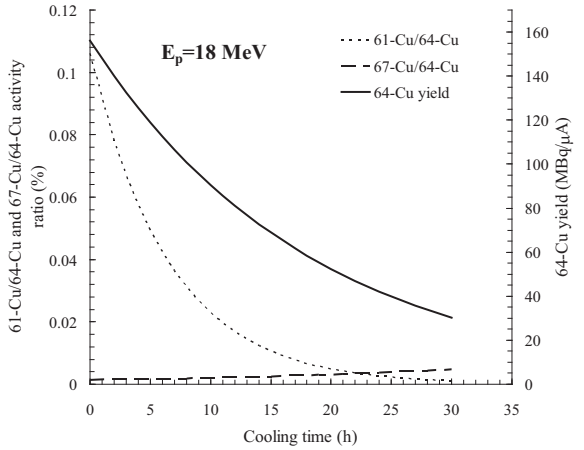

Fig. 6: $^{61}Cu/^{64}Cu$ and $^{67}Cu/^{64}Cu$ activity ratio and ^{64}Cu activity as a function cooling time using 18 MeV incident proton energy.

$^{64}Zn(\leq 0.5\%)$, $^{66}Zn(\geq 9\%)$, $^{67}Zn(\geq 80\%)$, $^{68}Zn(\leq 10\%)$ and $^{70}Zn(\leq 0.5\%)$. The 18→5, 15→5 and 12→5 MeV production energy windows correspond to target thicknesses of 506.8, 362.8 and 226.5 mg/cm^2, respectively.

In the case of the activation with 12 MeV protons, the available EOB yield is 43.66 MBq/μA (1.18 mCi/μA) and the contamination levels are 3.11% ($^{61}Cu/^{64}Cu$) and 0.03% ($^{67}Cu/^{64}Cu$). Figure 4 shows the time dependence (starting from EOB) of the above activity ratios and the practical ^{64}Cu yields. After 7.7 h cooling time, the total contamination level decays below 1%, but it increases above 1% (due to the longer half life of ^{67}Cu) after 81.1 h. The available ^{64}Cu yield (for medical studies) is 28.49 MBq/μA (0.77 mCi/μA) at the beginning of the application time.

15 MeV protons would result 2.3 times higher yield (88.80 MBq/μA (2.70 mCi/μA) than the 12 MeV route. Contamination levels are 3.74% ($^{61}Cu/^{64}Cu$) and 0.04% ($^{67}Cu/^{64}Cu$) (see Figure 5). This process offers a little shorter application window for investigations between 8.9 and 74.4 h after EOB. The useful yield is 61.42 MBq/μA (1.66 mCi/μA).

In every aspect the bombardment with an 18 MeV beam produces the highest ^{64}Cu EOB yield of 156.14 MBq/μA (4.22 mCi/μA) after 6.3505 h irradiation time (see Figure 6). Interestingly, this method offers the shortest time range from 9.4 to 70.4 h (after EOB) for applications. The contamination levels are 3.93% ($^{61}Cu/^{64}Cu$) and 0.05% ($^{67}Cu/^{64}Cu$), while the practical yield is: 93.61 MBq/μA (2.53 mCi/μA) after 9.4 h cooling time.

Longer activation time would result in higher ^{64}Cu yields in all cases with decreasing $^{61}Cu/^{64}Cu$ but with increasing $^{67}Cu/^{64}Cu$ activity ratios at EOB, reducing this way the length of the application time.

There are several chemical separation methods in the literature that can be used for separating the radiocoppers effectively from the zinc matrix and the co-formed other radioactive contaminants [29–31]. The knowledge of the activities of these radioisotopes, especially the Gallium nuclides (^{66}Ga and ^{67}Ga) at EOB are important not only to select the proper separation technique, but to arrange the handling procedure of the radioactive waste. Based on the available cross section databases of the $^{66}Zn(p, 2n)^{66}Ga$, $^{67}Zn(p, n)^{67}Ga$, $^{67}Zn(p, 2n)^{66}Ga$ and $^{68}Zn(p, 2n)^{67}Ga$ nuclear reactions [19, 22], the ^{66}Ga yields after 6.3505 h activation are: 196.1, 341.9 and 544.3 MBq/μA at 12, 15 and 18 MeV, respectively. For ^{67}Ga these data are as follows: 284.5 MBq/μA (12 MeV), 441.4 MBq/μA (15 MeV) and 556.9 MBq/μA (18 MeV). The relative high yields of these radio-gallium isotopes require special care, especially if the recovery of the target material would be necessary within a short time.

4 Conclusions

We have measured the excitation function of the $^{67}Zn(p, \alpha)^{64}Cu$ nuclear reaction up to 28.5 MeV. Our new data showed good agreement with the updated values of the only data set available in the literature. Since the theoretical calculation (*via* the TALYS code) predicted different cross sections for the above process, the ^{64}Cu thick target yields were calculated using the experimental results. Practical production possibilities at three different energies (12, 15 and 18 MeV) were investigated in detail. For all cases highly enriched ^{67}Zn (> 80%) target was suggested with minimum 6.3505 h irradiation time.

It could be concluded that the above reaction can be employed for practical purposes at biomedical cyclotrons, however, it has several drawbacks comparing to the ^{64}Ni(p, n)^{64}Cu process [*c.f.* 6, 14]. The available yields are not only lower (at 15 MeV around 5% of the (p, n) route), but it has very large background of ^{66}Ga and ^{67}Ga at EOB as well. Additionally, it is more difficult to achieve the required chemical purity of ^{64}Cu from a ^{64}Zn target than from a ^{64}Ni. The high amount of the co-produced Gallium radioisotopes has direct influence in the handling of the irradiated target due to the dose and on the chemical processing.

Based on the calculated yields, the 12 MeV production way fits mainly the requirement for an 'in-house' production (43.66 MBq/μA (1.18 mCi/(μ)A) at EOB), while the higher energy irradiations (15 and 18 MeV) could provide enough EOB activities (88.80 MBq/μA (2.70 mCi/μA) and 156.14 MBq/μA (4.22 mCi/μA), respectively) even for transportation to other medical institutions.

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References

1. NuDat 2.6 database. Available from: http://www.nndc.bnl.gov/nudat2.
2. Qaim, S. M., Bisinger, T., Hilgers, K., Nayak, D., Coenen, H. H.: Positron emission intensities in the decay of ^{64}Cu, ^{76}Br and ^{124}I. Radiochim Acta **95**, 67–73 (2009).
3. Szymański, P., Frączek, T., Markowich, M., Mikiciuk-Olasik, E.: Development of copper based drugs, radiopharmaceuticals and medical materials. Biometals **25**, 1089–1112 (2012).
4. Carroll, V., Demoin, D. W., Hoffman, T. J., Jurisson, S. S.: Inorganic chemistry in nuclear imaging and radiotherapy: current and future directions. Radiochim. Acta **100**, 653–667 (2012).
5. Welch, M. J., Redvanly, C. S. (Eds.): Handbook of Radiopharmaceuticals. Wiley & Sons, 2003.
6. Szelecsényi, F., Blessing, G., Qaim, S. M.: Excitation functions of proton induced nuclear reactions on enriched ^{61}Ni and ^{64}Ni: Possibility of production of no-carrier-added ^{61}Cu and ^{64}Cu at a small cyclotron. Appl. Radiat. Isotopes **44**, 575–580 (1993).
7. McCarthy, D. W., Shefer, R. E., Klinkowstein, R. E., Bass, L. A., Margeneau, W. H., Cutler, C. S., Anderson, C. J., Welch, M. J.: Efficient production of high specific activity ^{64}Cu using a biomedical cyclotron. Nucl. Med. Biology **24**, 35–43 (1997).
8. Thieme, S., Walther, M., Pietzsch, H.-J., Henniger, J., Preusche, S., Mäding, P., Steinbach, J.: Module-assisted preparation of ^{64}Cu with high specific activity. Appl. Radiat. Isotopes **70**, 602–608 (2012).
9. Zweit, J., Smith, A. M., Downey, S., Sharma, H. L.: Excitation functions for deuteron induced reactions in natural nickel: Production of no-carrier-added ^{64}Cu from enriched ^{64}Ni targets for positron emission tomography. Appl. Radiat. Isotopes **42**, 193–197 (1991).
10. Kozempel, J., Abbas, K., Siminelli, F., Zampese, M., Holzwart, U., Gibson, N., Lešetický L.: A novel method for n.c.a. ^{64}Cu production by the ^{64}Zn(d,2p)^{64}Cu reaction and dual ion-exchange column chromatography. Radiochim. Acta. **95**, 75–80 (2007).
11. Hilgers, K., Stoll, T., Skakun, Y., Coenen, H. H., Qaim, S. M.: Cross-section measurements of the nuclear reactions ^{nat}Zn(d, x)^{64}Cu, ^{66}Zn(d, α)^{64}Cu and ^{68}Zn(d, $\alpha 2n$)^{64}Cu for production of ^{64}Cu and technical developments for small-scale production of ^{67}Cu *via* the ^{70}Zn(p, α)^{67}Cu process. Appl. Radiat. Isot. **59,** 343–351 (2003).
12. Szelecsényi, F., Steyn, G. F., Kovács, Z., Vermeulen, E., van der Meulen, N. P., Dolley, S. G., van der Walt, T. N., Suzuki, K., Mukai, K.: Investigation of the ^{66}Zn(p, $2pn$)^{64}Cu and ^{68}Zn(p, x)^{64}Cu nuclear processes up to 100 MeV: Production of ^{64}Cu. Nucl. Instrum. Meth. **B240**, 625–637 (2005).
13. Daraban, L., Abbas, K., Simonelli, F., Adam-Rebeles, R., Gibson, N.: Experimental study of excitation functions for the deuteron induced reactions ^{64}Zn(d, $2p$)^{64}Cu and ^{64}Zn(d, αn)^{61}Cu using the stacked-foil technique. Appl. Radiat. Isot. **66**, 261–264 (2008).
14. IAEA Technical Reports Series No. 473.: Nuclear Data for the Production of Therapeutic Radionuclides, (Technical Editors: Qaim, S. M., Tarkanyi, F. , Capote, R.) ISBN 978-92-0-115010-3 (2011).
15. Aslam, M., Sudár, S., Hussain, M., Malik, A. A., Shah, H. A. Qaim, S. M.: Charged particle induced reaction cross section data for production of the emerging medically important positron emitter ^{64}Cu: A comprehensive evaluation. Radiochim. Acta **97**, 669–687 (2009).
16. Experimental Nuclear Reaction Data (EXFOR) (Database Version of February 26, 2013). Available from: www-nds.iaea.org/exfor.
17. Levkovskij, V. N.: Activation cross section nuclides of average masses (A = 40–100) by protons and alpha-particles with average energies (E = 10–50 MeV), Inter Vesi, Moscow, 1991.
18. Tárkányi, F., Szelecsényi, F., Kovács, Z., Sudár, S.: Excitation functions of proton induced nuclear reactions on enriched ^{66}Zn, ^{67}Zn and ^{68}Zn. Production of ^{67}Ga and ^{66}Ga. Radiochim. Acta **50**, 19–26 (1990).
19. Szelecsényi, F., Boothe, T. E, Takács, S., Tárkányi, F., Tavano, E.: Evaluated cross section and thick target yield data bases of Zn+p processes for practical applications. Appl. Radiat. Isot. **49**, 1005–1032 (1998).

20. Koning, A. J., Rochman, D.: Modern nuclear data evaluation with the TALYS code system. Nuclear Data Sheets **113** 2841–2934 (2012) or Koning, A. J., Rochman, D., van der Marck, S., Kopecky, J., Sublet, J. Ch., Pomp, S., Sjostrand, H., Forrest, R., Bauge, E., Henriksson, H.: TENDL-2012: TALYS-based evaluated nuclear data library, www.talys.eu/tendl-2012.html.
21. Szelecsényi, F., Kovács, Z., Nagatsu, K., Fukumura, K., Suzuki, K., Mukai, K.: Investigation of direct production of ^{68}Ga with low energy multiparticle accelerator. Radiochim. Acta **100**, 5–11 (2012).
22. Gul, K., Hermanne, A., Mustafa, M. G. Nortier, F. M., Oblozinsky, P., Qaim, S. M., Scholten, B., Shubin, Yu., Takács, S., Tárkányi, F. T., Zhuang, Z.: Charged particle cross-section database for medical radioisotope production: diagnostic radioisotopes and monitor reactions. IAEA-TECDOC-1211, IAEA, Vienna, May 2001. Available from: http://www-nds.iaea.org/medical/ (last updated 2011).
23. Steyn, G., F., Szelecsényi, F., Kovács, Z., van der Walt, T., N., Dolley, S., G., Vermeulen, C.: Large discrepancies in the excitation function data of the ^{68}Zn$(p, x)^{64}$Cu reaction: a possible explanation. J. Phys. Conf. Series **41**, 561–564 (2006).
24. Anderson, H. H., Ziegler, J. F.: Hydrogen stopping powers and ranges in all elements. In: J. F. Ziegler (Ed.), The stopping and Ranges of Ions in Matter, vol. 3, Pergamon, New York, 1977, p. 1.
25. Guide to the expression of uncertainty in measurements, 1995. International Organization for Standardization, Geneva, ISBN 92-67-10188-9.
26. Takács, S., Tárkányi, F., Sonck, M., Hermanne, A.: Investigation of the ^{nat}Mo$(p, x)^{96\,mg}$Tc nuclear reaction to monitor proton beams: New measurements and consequences on the earlier reported data. Nucl. Instrum. Meth. **B198**, 183–196 (2002).
27. Stoll, T., Kastleiner, S., Shubin, Yu. N., Coenen, H. H., Qaim, S. M.: Excitation functions of proton induced reactions on ^{68}Zn from threshold up to 71 MeV, with specific reference to the production of ^{67}Cu. Radiochim. Acta **90**, 309–313 (2002).
28. Kastleiner, S., Coenen, H. H., Qaim, S. M.: Possibility of production of ^{67}Cu at a small-sized cyclotron *via* the (p, α)-reaction on enriched ^{70}Zn. Radiochim. Acta **84**, 107–100 (1999).
29. Dirks, C., Scholten, B., Happel, S., Zulauf, A., Bombard, A., Jungclas, H.: Characterisation of a Cu selective resin and its application to the production of ^{64}Cu. J. Radioanal. Nucl. Chem. **286**, 671–674 (2010).
30. Al Rayyes, A. H., Ailouti, Y.: Routine simultaneous production of no-carrier-added high purity ^{64}Cu and ^{67}Ga. Nukleonika **56**, 259–262 (2011).
31. Asad, A. H., Smith, S. V., Chan, S., Jeffery, C. M., Morandeau, L., Price, R. I.: Cyclotron production of ^{61}Cu using natural Zn & enriched ^{64}Zn targets. AIP Conf. Proc. **1509**, 91–95 (2012).