A novel approach to medical radioisotope production using inverse kinematics: a successful production test of the theranostic radionuclide $^{67}$Cu

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Abstract

A novel method for the production of important medical radioisotopes has been developed. The approach is based on performing the nuclear reaction in inverse kinematics, namely sending a heavy-ion beam of appropriate energy on a light target (e.g. H, d, He) and collecting the isotope of interest. In this work, as a proof-of-concept, we studied the production of the theranostic radionuclide $^{67}$Cu ($T_{1/2}=62$ h) via the reaction of a $^{70}$Zn beam at 15 MeV/nucleon with a hydrogen gas target. The $^{67}$Cu radionuclide, alongside other coproduced isotopes, was collected after the gas target on an Al catcher foil and their radioactivity was measured by offline γ-ray analysis. After 36 h from the end of the irradiation, apart from the product of interest $^{67}$Cu, the main radioimpurity coming from the $^{70}$Zn+p reaction was $^{69}$Zn ($T_{1/2}=13.8$ h) that can be reduced by further radio-cooling. Moreover, along with the radionuclide of interest produced in inverse kinematics, the production of additional radioisotopes is possible by making use of the forward-focused neutrons from the reaction and letting them interact with a secondary target. A preliminary successful test of this concept was realized in the present study. The main requirement to obtain activities appropriate for preclinical studies is the development of high-intensity heavy-ion primary beams.

Keywords:

1. Introduction

Medical radionuclides play a central role in nuclear medicine in the fields of diagnostic imaging and radioimmunotherapy (RIT) (Qaim (2017); Srivastava (2014); Stocklin (1995)). Radionuclides emitting low-range highly ionizing radiation ($\beta^-$ or $\alpha$ particles, Auger or conversion electrons) are essential for RIT approaches. Apart from a number of standard radionuclides, currently the $\beta^-$ emitters $^{47}$Sc ($T_{1/2}=3.4$ d), $^{67}$Cu ($T_{1/2}=2.6$ d), $^{109}$Rh ($T_{1/2}=1.5$ d), $^{161}$Tb ($T_{1/2}=6.9$ d) and $^{186}$Re ($T_{1/2}=3.7$ d) (Champion (2014); Qaim (2017)) are increasingly interesting. Specifically, $^{67}$Cu, the longest-lived radioisotope of copper, is ideally suited for both radioimmunotherapy and imaging for several reasons (Asabella (2014)). First, from a chemical perspective, copper is an essential trace element for most organisms and specifically for humans as it takes part in important biochemical processes (Linder (1991)). The coordination chemistry of Cu has been well established (Price (2014)). Copper can be linked to antibodies, proteins and other biologically important molecules (Follacchio (2018); Ting (2009); Schubiger (1996); Sugi (2017)). The nuclide $^{67}$Cu can be combined with the same type of radiopharmaceuticals as $^{64}$Cu ($T_{1/2}=12.7$ h) or $^{61}$Cu ($T_{1/2}=3.3$ h) leading to efficient theranostic pairs (Zimmerman (2003)).

The half-life of $^{67}$Cu (62 h) is appropriate to deliver a high dose rate to the tumor. Furthermore, its $\beta^-$ decay ($E_{\gamma_{\text{ave}}}=141$ keV) is followed by the emission of soft $\gamma$ radiation of 185 keV (48.7%), 93 keV (16%) and 91 keV (7%). This makes $^{67}$Cu suitable for imaging the radiotracer distribution by single-photon emission computed tomography (SPECT) using the cameras widely developed for the 140 keV $\gamma$ rays of $^{99m}$Tc. Compared to the standard RIT radioisotope $^{90}$Y ($T_{1/2}=64$ h, $E_{\gamma_{\text{ave}}}=2.28$ MeV), which is a pure $\beta^-$ emitter, $^{67}$Cu offers the possibility of SPECT imaging and treatment of smaller size tumors (up to 4 mm, compared to 12 mm in the case of $^{90}$Y). In addition, $^{67}$Cu compares favorably with another standard radioisotope, $^{111}$In ($T_{1/2}=8.0$ d, $E_{\gamma_{\text{ave}}}=0.61$ MeV), which has a longer half-life and emits higher energy $\gamma$ rays (0.364 MeV, 82%) and thus, may increase the undesired dose to the patient and the medical personnel.

It is noteworthy that while the other radioisotopes of copper, especially $^{64}$Cu, have already been used in radiopharmaceuticals for a wide range of preclinical and clinical studies (Follacchio (2018); Peng (2006)), $^{67}$Cu has been used in a rather
limited number of studies, albeit with very promising results (Jin (2017); Katz (1990); Knogler (2007); Novak (2002)). The main factor limiting the wider preclinical and clinical use is its limited availability (Smith (2012)).

The production of $^{67}\text{Cu}$ in nuclear reactors started about 50 years ago (O’Brien (1969)) and continues until present in several reactor facilities (e.g. Johansen (2015); Uddin (2014); Mirzadeh (1986)). Recently, however, the main focus has shifted to methods based on particle accelerators (Smith (2012)). Presently, the main production route is via the reaction $^{68}\text{Zn}(p,2p)^{67}\text{Cu}$ (Katabuchi (2008); Medvedev (2008); Pupillo (2018); Stoll (2002)). This approach is based on the use of intense medium-energy ($E_p=70–100$ MeV) proton beams that are available by several particle accelerators, including medium-energy cyclotrons. However, these multipurpose facilities cannot dedicate all their beam time to radioisotope production.

Other production routes based on lower-energy charged particle reactions are $^{70}\text{Zn}(p,\alpha)^{67}\text{Cu}$ (Hilgers (1993); Jamriska (1999); Kastleiner (1999)); $^{70}\text{Zn}(d,n)^{67}\text{Cu}$ (Kozempel (2012)) and $^{64}\text{Ni}(p,p)^{67}\text{Cu}$ (Hosseini (2017)); $^{64}\text{Ni}(n,p)^{67}\text{Cu}$ (Ohya (2018); Sakurn (2004)). Moreover, production routes based on reactions induced by accelerator-produced neutrons have been applied (Kawabata (2013); Kim (2013); Sato (2014); Spahn (2004)). In addition, $^{67}\text{Cu}$ has been produced in photofragment nuclear reactions using bremsstrahlung photons from high-intensity electron linacs (Gopalakrishna (2018); Starovoitova (2014, 2015); Yagi (1978)).

Finally, isotope harvesting in projectile fragmentation facilities has been suggested as an alternative source of medical isotopes. A proof-of-concept was presented in the recent work by Mastren et al. (Mastren (2014, 2015)) at the NSCL. This work involved harvesting and separation of $^{67}\text{Cu}$ from a mixture of projectile fragments stopped in an aqueous beam-collection system. The $^{67}\text{Cu}$ radionuclide separation was followed by radiolabelling and biodistribution studies.

A general characteristic of all the previous production methods is the fact that the desired radioisotope of $^{67}\text{Cu}$ is produced inside the target material which can be moderately or highly expensive, depending on the setup and approach. In regard to the production of $^{67}\text{Cu}$, the natural abundance of $^{68}\text{Zn}$ is 18.45%, $^{70}\text{Zn}$ is 0.61% and $^{64}\text{Ni}$ is 0.93%. Thus, in these cases, an efficient analysis scheme is necessary for the collection of the desired $^{67}\text{Cu}$ isotope and the recovery of the target material for subsequent re-use in the production scheme (Smith (2012)).

Along with this traditional scheme, in the isotope-harvesting route, the isotope of interest has to be separated from a very broad range of radioisotopes of other elements that are abundantly coproduced in a projectile fragmentation reaction. Thus, an appropriate multistep separation process is necessary (Mastren (2015)).

In this paper, we present an innovative approach for the production of medical radioisotopes based on inverse-kinematics nuclear reactions, that is, sending a heavy-ion beam on a light target and collecting the radioisotope after the target. The main advantage of using an inverse kinematics reaction is that the products are strongly focused along the beam direction and, thus, can be easily collected for immediate use.

Proof-of-principle of the aforementioned approach is presented for the production of $^{67}\text{Cu}$ via the reaction of $^{70}\text{Zn}$ beam at 15 MeV/nucleon with a hydrogen gas target. This work demonstrates that important non-standard medical radioisotopes with high radionuclide purity can be produced, provided that low-energy and high-intensity primary beams are available. Our method has some similarity with the isotope-harvesting approach from fragmentation facilities, in the sense that, in the latter, the fragmentation reactions also occur in inverse kinematics, albeit at high energies (above 100 MeV/nucleon) producing a very broad range of isotopes. The inverse kinematics approach, however, takes place at low energy. By choosing the appropriate reaction channel, the radionuclide of interest can be selectively produced with minimal radioimpurities and implanted in an appropriate catcher material for subsequent use (after minimal radiochemical processing if necessary). In parallel, the forward-focused neutrons from the primary reaction can be sent to a secondary target for additional radioisotope production.

The structure of the paper is as follows: in section 2, we present the experimental setup and the measurements; in section 3, we continue with the data analysis and the results. In section 4, we discuss improvements of the present method and further plans. Finally, in section 5, we provide a summary and conclusions.

![Figure 1: (Color online) The cryogenic gas target cell used in the present work (Brinkley (2003)).](Image)

2. Experimental Setup and Measurements

The experimental work took place at the Cyclotron Institute of Texas A&M University (TAMU). A primary beam of $^{70}\text{Zn}^{15+}$ from the ECR source was accelerated by the K500 superconducting cyclotron to an energy of 15 MeV/nucleon and transported to the target chamber of the MARS recoil separator.
Figure 2: (Color online) Schematic diagram of the irradiation setup. A $^{70}$Zn beam at 15 MeV/nucleon enters the gas cell and interacts with the hydrogen gas. The heavy reaction products, including $^{67}$Cu, after exiting the gas cell are implanted in the Al catcher. The energies of the beam are listed as it passes through the entrance window, the gas and the exit window (thick red arrows). The dashed (green) arrows represent the neutrons produced via the interactions of the $^{70}$Zn beam with the hydrogen gas and the Al catcher. For details, see sections 2, 3.2 and 3.3.

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The beam impinging on a cryogenic gas cell filled with H$_2$ gas held at a pressure of 2.7 atm in contact with a liquid nitrogen reservoir (Brinkley (2003)). The cryogenic gas cell (figure 1) has a length of 10 cm with 4 µm Havar entrance and exit windows of 19.0 mm diameter. The experimental setup is schematically shown in figure 2. An aluminum foil, mounted on an aluminum target frame (with a hole of 12.7 mm) placed after the hydrogen gas cell, was used to collect the produced $^{67}$Cu nuclei from the reaction of the $^{70}$Zn beam with the proton target. The irradiation lasted 6.5 h with a beam current of 0.31 pA (particle nA) (2.0×10$^9$ particles s$^{-1}$). The current was periodically monitored and was nearly constant (within 15%). The measurement of the current was performed by inserting a Faraday cup mounted on the same target ladder as the Al catcher frame. The measurement of the beam current at this location (i.e. after the gas cell) was 8.0 nA of $^{70}$Zn (7.0 MeV/nucleon) at an average charge state of 26+. This equilibrium charge state value was calculated with the parametrization of Leon et al. (Leon (1998)). After 36.4 h from the end of the irradiation, the Al catcher foil was moved in front of a high-purity germanium (HPGe) detector for off-line $\gamma$-ray analysis as described in the following sections.

3. Data analysis and results

3.1. Off-line $\gamma$-ray analysis

The radioactivity of the produced $^{67}$Cu and the other coproduced radioisotopes was determined by off-line analysis of the $\gamma$-ray spectra. The foil was placed at a distance of d = 17.2(10) mm from the end cap of the detector. Under this condition, the dead time of the counting system was around 2-3%, thus avoiding the pile-up effect. The energy resolution of the detector system was 2.5–4.0 keV FWHM.

The energy calibration was performed using known $\gamma$-rays obtained in the spectra. The absolute efficiencies were obtained using photopeak efficiency predictions generated from a Geant4 (Agostinelli (2003)) simulation, considering the source and the detector geometry. The spectrum of the room background was measured for 67.3 h.

The radioactivity levels of the isotopes were determined by the quantification of the photopeaks of the $\gamma$-rays taking into account the branching ratios and the absolute efficiencies of the detector. A detailed description of the $\gamma$-ray analysis of all the observed $\gamma$-ray peaks will be presented in Rodrigues (2019).

In figure 3, we present the background-subtracted $\gamma$-ray spectrum obtained during an accumulation period of 68.0 h, starting 36.4 h after the end of the irradiation. We note that the peaks at 92 keV and 185 keV are characteristic of $^{67}$Cu decay. The peak at 439 keV is due to the main radioimpurity of $^{69}$mZn ($T_{1/2}$ = 13.8 h) from the $^{70}$Zn+p reaction. We observe a small contribution, around 3% of the $^{65}$Cu production, from $\gamma$-ray at 300.2 keV characteristic of the presence and decay of $^{67}$Ga ($T_{1/2}$=78 h) with a branching ratio of 16.7%. We note that this radioimpurity, decaying to the same levels of $^{67}$Cu as $^{67}$Cu, is intensely co-produced in the main production route via $^{69}$Zn(p,2p)$^{67}$Cu with high energy protons (Smith (2013)). This $\gamma$-ray for $^{67}$Cu has a branching ratio of only 0.8%. Similarly, the peak at 1115.5 keV, characteristic of $^{65}$Zn ($T_{1/2}$ = 244 d), is significantly suppressed (0.2% of the $^{67}$Cu production). This radionuclide is notoriously produced in the high-energy $^{67}$Cu production methods and requires radiochemical separation.

In the spectrum of figure 3, we observe peaks from a series of radionuclides that are mainly due to nuclear reactions on the Havar windows and the Al catcher foil. More specifically, the radionuclides $^{86}$Y, $^{87}$Y, $^{89}$Zr, $^{90}$Nb and $^{93}$Mo are fusion-evaporation products of the reaction $^{70}$Zn+$^1$H (with the beam of $^{70}$Zn entering the Al catcher at 7.0 MeV/nucleon, see section 3.2). Furthermore, the heavier radionuclides $^{111}$In, $^{117}$Sn and $^{119}$Te are residues of the reaction of the $^{70}$Zn beam with the constituents of the Havar alloy (42% Co) of the gas-cell windows. We also identified the presence of $^7$Be ($T_{1/2}$=53 d, $E_x$=477.6 keV) possibly coming from the activation of the small Be or C
the gas and the exit window of the gas cell. The calculated energy losses of the beam in the entrance window, 7.5 mg 70 K
kBq/pnA (or equivalently, 0.8(3) MBq/h/pnA). This is a rather low activity that can be further reduced by an appropriate cooling period (of, e.g., 2 days).

3.2. Comparison of measured 67Cu activity with estimates

In this section, we estimate the activity of the radionuclide 67Cu produced in the inverse kinematics reaction 70Zn (15 MeV/nucleon) + p. The cross sections for the direct kinematics reaction 70Zn(p,α)67Cu have been reported in Kastleiner (1999). We take into account that the 10 cm long gas target cell was filled with H2 gas at a pressure of 2.7 atm and was at a temperature of 87 K via the thermal contact with the LN2 Dewar. Under these conditions, the H2 gas target thickness was 7.5 mg/cm2. Using the code SRIM (Ziegler (2013)), we calculated the energy losses of the beam in the entrance window, the gas and the exit window of the gas cell. The 70Zn beam hit the entrance window at 15 MeV/nucleon, exited it at 14.2 MeV/nucleon, traversed the gas and reached the exit window at 8.0 MeV/nucleon and, finally exited it at 7.0 MeV/nucleon (figure 2).

Using the data of Kastleiner et al. (Kastleiner (1999)), we estimated the integral of the excitation function in the region 14.2–8.0 MeV, resulting in an average value for the cross section of 7.5 mb for 67Cu. Using this cross section value and the H2 gas target thickness, we obtained the production rate of 67Cu. Subsequently, we obtained the produced activity, assuming 1h of irradiation with a beam intensity of 1 pnA. This activity is calculated to be 1.8 kBq/h/pnA (or equivalently, 1.8 MBq/h/pnA). We notice that the measured activity of 0.8(3) kBq/h/pnA is about 2.2 times lower than the expected activity, as obtained with the procedure described above.

In this section, we discuss several possible sources for the discrepancy between the experimental and the theoretical activity of 67Cu: a) the spread of the recoiling 67Cu nuclei that may result in an incomplete collection on the Al catcher foil. As previously mentioned, the Al foil was mounted on an Al frame with a 12.7 mm hole. The 67Cu activity of the target frame was measured to be 0.12 kBq which is 7.5% of the main activity collected on the Al catcher foil; b) the use of an unsuppressed Faraday cup to measure the beam current. As it is well known, the sputtering of electrons from the side of the Faraday cup hit by the heavy-ion beam results in an increase of the measured positive current leading to a lowering of the obtained production rate and, thus, the specific activity. The cup should be biased to a positive voltage (in the range 200–400V). Such electron suppression of the Faraday cup was not performed in the present experiment. This effect may account for about 20–30% of the discrepancy, but it should be quantified for the present heavy-ion setup (as performed in Carzaniga (2017), figure 4, for proton beams); c) the reduction of the pressure of the H2 gas due to local heating along the path of the primary beam. As
reported in a previous study (Brinkley (2003)), this effect has been observed in the behavior of this gas cell during its use for radioactive beam production with the MARS recoil separator. The rate of radioactive beams has been observed to drop when intense primary beams were used, but no quantitative estimates have been reported. A related quantitative account of this effect is reported by Amadio et al. (Amadio (2008)) for the production of a low-energy radioactive beam of $^7$Be in a cryogenic hydrogen gas cell. In that setup, circulation of the hydrogen gas cooled at LN$_2$ temperature indicated that the effect of the local pressure reduction may amount to 60–70% at high primary beam currents [figure 4 of (Amadio (2008))]. Similar measurements are necessary for the present gas cell. We note that a magnetic stirring system was operated in this cell, but its effect was rather inadequate.

Finally, we mention that, by using the cross section data of Kasteliner (1999), the production cross section of $^{67}$Cu drops to nearly zero at about 7 MeV. Thus, in the energy range 14.2–8.0 MeV/nucleon of the $^{70}$Zn beam in the hydrogen gas, almost the full thickness of the target was exploited to produce $^{67}$Cu.

3.3. Use of the neutrons from the primary reaction for secondary radioisotope production

The interaction of $^{70}$Zn at 15 MeV/nucleon with the proton target produces about 1.6 neutrons per reaction, as calculated with the code TALYS (Koning (2012); Duchemin (2015)). Along with the heavy reaction products, these neutrons are also kinematically focused in the forward direction and can be exploited for further radioisotope production by simply letting them interact with a secondary target, e.g., a $^{60}$Zn or $^{nat}$Zn target for additional production of $^{67}$Cu. In this work, we performed such a test by placing a block of twenty 25.4x25.4 mm$^2$ foils of $^{nat}$Zn with 1 mm thickness behind the Al catcher (figure 2).

Because this production is from the secondary neutrons, the yield is expected to be about 2 orders of magnitude lower than the main production channel. However, given the long mean free path of the neutrons (with a typical value of several cm), production of different isotopes is conceivable with these neutrons impinging on different targets. This production scheme shares some similarity with the one recently published in (Auditore (2017)) employing secondary neutrons from the target of a standard $^{18}$F radioisotope-producing setup. The advantage of our approach of inverse kinematics is the strong focusing of the secondary neutrons that can be directed to a target stack of much smaller size than the one used in (Auditore (2017)), which essentially encloses the target. The results of our neutron-production test are promising. The analysis work is currently in progress and will be presented in Rodrigues (2019).

4. Discussion and plans

The present preliminary study that we performed at the Cyclotron Institute of TAMU confirms that important medical radionuclides, such as $^{60}$Cu, can be effectively produced using inverse kinematics. The main advantages of the present novel approach along with necessary developments and relevant implementations are discussed below.

First, the produced radionuclides are strongly focused along the beam direction and, thus, can be easily collected. In this respect, with the appropriate choice of the reaction channel(s) and the subsequent cooling time of the products, it is possible to minimize the production of radioimpurities coming from the main reaction. Moreover, it is possible to minimize the radioimpurities resulting from the primary beam interacting with the Havar windows of the gas target and the catcher material. Of course, we cannot avoid reactions at the entrance window, where the beam enters with the full energy of 15 MeV/nucleon and induces reactions on the foil. However, the products coming from peripheral or semiperipheral (deep-inelastic) collisions on the isotopes of Havar (Co, Cr, Ni, W, etc.) have rather wide angular distributions [e.g., (Fountas (2014)) and (Papageorgiou (2018)) figure 4] and are expected to mostly miss the catcher (depending on its diameter). On the other hand, the products of complete or nearly complete fusion are forward focused, but are heavier and slower than the beam and, thus, may mostly stop in the gas.

Regarding the exit window, it is possible to adjust the gas cell parameters (pressure, temperature and length) so that the primary beam reaches this window at low energy, i.e. near or below the Coulomb barrier of the relevant reactions (e.g., 4.0 MeV/nucleon). Consequently, nuclear reactions can be suppressed or fully eliminated on that window. Of course, under these conditions, the low energy primary beam exiting the gas cell will not induce reactions in the catcher material. For example, referring to the $^{70}$Zn+$^{27}$Al reaction, the Coulomb barrier corresponds to a projectile energy of 3.5 MeV/nucleon. We realize that detailed simulations and further experimental tests are necessary to achieve optimum conditions for the experimental setup and production procedure. Under properly fine-tuned conditions, water or other materials (salt, sugar, etc.) can be used to collect the radioisotopes in a convenient chemical form, so that, post radiolabelling, they may be used for tests on animals.

As we briefly mentioned, secondary neutrons from the primary reaction can be used to irradiate other targets for further radioisotope production of the same or different type (e.g. Cu, Sc, etc.). However, in this case, radiochemical methods are needed to separate the medical radionuclides, as in the traditional production schemes (Smith (2012)).

From a financial point of view, material costs may be considerably reduced, since the heavy (and usually rare) element is used as the projectile (for instance, $^{70}$Zn has 0.6% natural abundance). Also, the radiochemical processing is substantially minimized or, desirably, completely eliminated because the radioisotope of interest is collected and essentially used directly after production (and appropriate cooling). However, the primary requirement of our approach is the use of a heavy-ion accelerator (e.g., cyclotron or LINAC) that can deliver high-intensity heavy-ion beams in the energy range 10–20 MeV/nucleon. Fortunately, such accelerators are available at a number of facilities worldwide and, with appropriate planning, a fraction of their beam time may be devoted to non-standard radionuclide production following our inverse-kinematics approach.
According to our estimates, with a primary beam of 1 particle μA, we can reach activities of 1.8 MBq/h and, thus, obtain milliCurie quantities of $^{67}$Cu within 24 h of irradiation. The μA heavy-ion beam intensities are achievable with the current ion-source and accelerator technology.

We note that the use of the cryogenic gas cell has the additional advantage that its cooled windows can withstand the necessary high beam currents. Appropriate circulation of the ion-source and accelerator technology.

...the length, and, furthermore, lowering the temperature below under intense beam irradiation, even with thinner windows, we may consider lowering the pressure to 1.0–1.5 atm, increasing the length, and, furthermore, lowering the temperature below LN$_2$ temperatures with the use of modern cryocoolers [e.g., a Gifford-McMahon refrigerator [Radebaugh (2009)].

Taking advantage of the development of thin liquids, it is conceivable to substitute the hydrogen gas cell by a liquid H$_2$ cell with thin windows. The development of a liquid H$_2$/D$_2$ target with typical thickness of a few mm is reported in [Jaechle (1994)]. More recently, a liquid H$_2$ target for fragmentation reactions has been reported in [Ryutin (2003)]. This target was operated at temperatures about 20 K, achieved with a Gifford-McMahon refrigerator. The cell had a length of 30 mm and a density of 200 mg/cm$^2$. We propose the implementation of a similar system for the production of medical isotopes, but for this purpose the length has to be only 1-2 mm to achieve the required thickness of about 8–10 mg/cm$^2$.

In the case of the Cyclotron Institute of TAMU, the facility houses two cyclotrons: a) the K150 cyclotron which, in principle, can produce high-intensity heavy-ion beams (up to around Kr) with energies up to around 12–15 MeV/nucleon, suitable for the production of relatively large activities of radioisotopes and, b) the K500 cyclotron, employed in the present experiment, which can produce lower currents of heavy-ion beams (upto $^{238}$U) and in a broader energy range (up to 20–40 MeV/nucleon depending on the isotope). We anticipate that both the K150 and the K500 cyclotrons may be successfully used for the development and production of a variety of non-standard radioisotopes at activities appropriate for medical studies on small animals. For this purpose, however, beams of 30–100 pNA have to be developed, which should be possible with a modest investment at the existing ion-source and accelerator infrastructures.

To summarize, the aforementioned considerations for the development of a viable route of medical radioisotope production in inverse kinematics are based, first, on the successful results of the present study and, second, on the current experience and developments on ion-source and accelerator technologies worldwide. We think that a fruitful application of our proposed method is achievable with timely planning and allocation of relatively modest resources. Along with the other production approaches, the proposed route may contribute to a broad and diversified program of production and use of non-standard medical radionuclides.

5. Conclusions

An innovative method for the production of important medical radioisotopes was presented in this article. The approach is based on realizing the nuclear reaction in inverse kinematics by sending a heavy-ion beam of appropriate energy on a light target (e.g., H, d, He) and collecting the isotope of interest on an appropriate catcher after the target. In this work, as a proof-of-principle, we studied the production of the radionuclide $^{67}$Cu ($T_{1/2}$=62 h) via the reaction of a beam of 15 MeV/nucleon $^{70}$Zn with a cryogenic hydrogen gas target. The $^{67}$Cu radionuclide (along with other coproduced isotopes) was collected after the gas target on an Al catcher foil and the radioactivity was measured by off-line γ-ray analysis. After the end of the irradiation, the main radioimpurity in the Al catcher coming from the $^{70}$Zn+p reaction was $^{68}$Zn ($T_{1/2}$=13.8 h), which can be suppressed by cooling for a period of 2–3 days. Other identified radioimpurities are understood to come from the interaction of the beam with the window material and the catcher and can be eliminated by careful tuning of the parameters of the setup. The present successful test and the ensuing considerations indicate the possibility of producing important non-standard radionuclides of high radionuclide purity with the approach of inverse kinematics. In parallel to the main production scheme, secondary neutrons from the primary reaction were used to irradiate a secondary target of Zn for further radioisotope production with promising results. The main requirement necessary to achieve production of activities appropriate for preclinical studies is the availability of high-intensity (particle μA) heavy-ion primary beams.

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