Medical isotope collection from ISAC targets

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Abstract. The ISAC facility (Isotope Separation and Acceleration) at TRIUMF has recently started to provide isotopes for pre-clinical nuclear medicine studies. By irradiating ISOL (Isotope Separation OnLine) targets with a 480 MeV proton beam from the TRIUMF H-cyclotron, the facility can deliver a large variety of radioactive isotope beams (RIB) for research in the fields of nuclear astrophysics, nuclear structure and material science with half-lives down to a few milliseconds via an electrostatic beamline network. For the collection of medical isotopes, typically with half-lives in the range of hours or days, we have developed a compact apparatus for the implantation of mass-separated RIB on a target disc at energies between 20-55 keV. In this paper, we also discuss two different retrieval methods of the implanted activity from the implantation target: by chemical etching of the target surface and by recoil collection of implanted alpha emitters.

1 Introduction

The ISAC facility features two target stations for the irradiation of ISOL-type thick targets with up to 100 μA of a 480 MeV proton beam from the TRIUMF H-cyclotron. Using a variety of refractory target materials (metal foils, composite ceramic carbides, oxides) a large number of radioactive isotope beams (RIB) can be produced by spallation, fragmentation or fission from elements such as C, Si, Ti, Ni, Nb, Ta, Th and U. Only sufficiently volatile isotopes in atomic or molecular form for which the average release time doesn’t exceed their half-life too much can be released, ionized, mass-separated and distributed through the ISAC electrostatic beamline network. Therefore, to accommodate a fast and efficient release, ISAC targets are generally operated at temperatures as high as permissible by the properties of the target material – mainly vapor pressure, thermal conductivity, sintering behavior and chemical stability. Operating temperatures range from 1100 °C for nickel oxide targets to 2300 °C for tantalum metal foil targets [1]. The facility is mainly used for research in the fields of nuclear astrophysics, nuclear structure and material science [2]. In addition to these applications, the facility is now also producing radioisotopes for pre-clinical nuclear medicine research. Some of these isotopes are of interest for imaging or therapeutic applications or both (theranostic isotopes). They generally have half-lives in the range of hours or days and can be produced in sufficient quantities for pre-clinical research from a variety of target materials. The current status of verified RIB yields is available for ISAC users in the ISAC Yield Database [3].

This paper is providing an overview of of isotopes that have already been collected as well as potential candidates for future applications related to nuclear medicine research. In particular, the collection of the heavy, alpha emitting isotope 225Ac and its precursor 225Ra are discussed. 225Ac [4] and its decay product 213Bi are promising candidates for targeted alpha therapy (TAT). Furthermore, methods to transfer the collected activity from the implantation target have been investigated. Sample preparation methods such as chemical etching of implantation targets and the recoil collection of 213Bi from the 225Ra/Ac decay chain are discussed.

2 Experimental

The two target stations at the ISAC facility are operated alternately. The 480 MeV proton beam can be directed at either one of them where it impinges on a production target with a beam current of up to 100 μA with a maximum achievable beam power of 48 kW. In order to accommodate the full capacity of the cyclotron, high-power tantalum target containers [5] have been developed. The addition of cooling fins increases the emissivity to 92% and allows to dissipate up to 25 kW of beam power. This is sufficient since power deposition in the target material is usually less than 50% of the maximum beam power. Thickness, density, thermal conductivity, vapor pressure are fac-

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The RIB is focused though a set of collimators on the target. The spread of contamination through recoil emission can be a problem.

For the ionization process a variety of ion source options can be utilized. Which ionization method is most suitable, depends strongly on the ionization potential of the atoms or molecules released from the target. The ion beams discussed in this paper were ionized with a surface ion source or by resonant laser ionization.

The IIS is located a few meters behind the ISAC high-resolution mass separator on a short branch of the electrostatic beamline. It is divided in two sections. Section 1 contains ion beam optics for beam positioning, focusing or rastering. It ends at a gate valve with a pumping port on its downstream side which provides vacuum for the ion collection chamber (section 2). This chamber can be custom-build for specific applications and is attached to the gate valve by the user.

For the experiments in this paper we used a standard aluminium SEM sample holder (Ø 25 mm) and a machined-in 2 mm thick graphite backing foil. This configuration increases the overall thermal conductivity significantly due to the relatively high conductivity of the graphite backing foils. For low-thermal conductivity oxide materials (NiO, UO₂) 25 μm thick niobium metal backing foils serve as thermal conductivity booster.

The production rate for a specific isotope is the product of production cross section, proton beam intensity and target thickness. The actual isotope beam intensity that arrives at the experiment also depends on the release efficiency form the target, the ionization efficiency and the transport efficiency of the ion beam through the ISAC electrostatic beamline network. Beam transport includes the extraction and acceleration of ions from the ion source to energies between 10-55 keV, subsequent mass separation through a low resolution pre-separator, a high-resolution mass separator (m/Δm=2000).

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Once in the lab, the chamber can be vented and the implantation target can be retrieved for further processing.

2.2 Retrieval of activity from IIS targets

We have explored 2 methods to retrieve radioactive isotopes from the implantation target: chemical etching of the target surface (2.2.1) and recoil collection from implanted alpha emitters (2.2.2).

2.2.1 Chemical etching

The implantation depth of a heavy $^{225}$Ac/Ra ion beam at a typical ISAC extraction energy of 30 keV in aluminium is about 20 nm [10]. Therefore, the transfer of the implanted isotopes into an aqueous solution requires the removal of at least 20 nm of the implantation target surface.

To achieve this, 0.1 ml of 0.1N HCl is filled into the implantation target cut-out and then gently evaporated on a hot plate. Then the target is cooled down and a thin layer of AlCl$_3$, that has formed during the evaporation, is dissolved with 0.1 ml of 0.1N HCl. This solution is picked up with a micropipette and transferred to a vial. This etch-rinse procedure is repeated several times. 3 iterations already remove >95% of the implanted activity, leaving it in a small volume of acidic solution which can be used for further radiochemical experiments.

2.2.2 Recoil collection

Isotopes like $^{223-225}$Ra and $^{225}$Ac decay through relatively long chains, including multiple alpha decays. The recoil energy transferred during an alpha decay to the residual nucleus is around 100 keV, about 3 times larger than the typical ion beam implantation energy at ISAC. Therefore, the alpha decay recoils have sufficient kinetic energy to escape as long as the recoil vector points out of the target. For a thick implantation target, as was used in these experiments, this leads to a theoretical release efficiency of less than 50% for a single alpha decay. However, the collection of $^{211}$Bi from a $^{225}$Ac source involves 3 alpha decays in the chain. The decays of $^{211}$Fr and $^{217}$At contribute to the overall release efficiency, increasing it to 60% at an implantation energy of 30 keV. This result was confirmed with a GEANT4 [11] recoil track simulation.

Using a $^{225}$Ac/Ra target as shown in figure 2, $^{213}$Bi recoils were accumulated by placing an identical collection target, separated by a thin insulator, directly on top. The collection was ended when the activity of $^{213}$Bi (T$_{1/2}$ = 45.59 min) had reached saturation. Figure 2 (right) shows that a negative bias of >20 V lead to a collection efficiency for $^{213}$Bi of ~35%.

The stopping range of recoils in air under normal pressure is less than 0.1 mm, see figure 2 (left). Aligning the stopping range more accurately with the distance between source and collector by reducing the pressure to 50 mbar and using argon as a buffer gas increased the collection efficiency to 47%. However, for applications such as chelation studies a 35% efficiency was sufficient and sample collection under normal air pressure much more convenient.

3 Conclusion

All measured yield rates from ISAC targets are compiled in Ref. [3]. From these values, activities can be extrapolated either until saturation is reached or to a maximum 24 hour implantation period. This is a realistic time frame, considering that radioactive ion beam time is usually allocated for several experiments with one ISAC target. Within this period, a $^{225}$Ac beam (T$_{1/2}$ = 9.92 d) at a rate of $1.3 \cdot 10^6$ ions/s from a uranium carbide target / laser
ion source combination accumulates an activity of up to $8.6\times10^6$ Bq. The accompanying $^{225}$Ra ($T_{1/2} = 14.8$ d) beam is collected simultaneously. At a rate of $1.7\times10^8$ ions/s from a uranium carbide target / surface ion source combination a total of $1.4\times10^{12}$ atoms ($7.5\times10^6$ Bq) can be collected in 24 hours. $^{225}$Ra decays via $\beta$-decay into $^{225}$Ac, reaching a maximum activity of $3.4\times10^6$ Bq $^{225}$Ac approximately 18 days after the implantation.

The etching method (section 2.2.1) was used to extract Ac and Ra isotopes. Then the radium was separated from the actinium by well established extraction chromatography methods [12]. The remaining $^{225}$Ra can be recycled and used as an $^{225}$Ac generator. This has been demonstrated as part of the development of Multi-isotope SPECT imaging of the $^{225}$Ac decay chain by Robertson et al. [13].

| Isotope   | Half-life | Application | Primary beam | Target material | Ion source | Measured yield [Bq] | Accumulated 24h Activity [Bq] |
|-----------|-----------|-------------|--------------|-----------------|------------|---------------------|-----------------------------|
| $^{225}$Ac | 9.92 d    | TAT         | $^{225}$Ac   | UC              | LIS        | 1.30E+08            | 8.60E+06                    |
| $^{225}$Ac | 9.92 d    | TAT         | $^{225}$Ra   | UC              | SIS        | 1.70E+08            | 3.40E+06                    |
| $^{224}$Ra | 3.66 d    | TAT         | $^{224}$Ra   | UC              | SIS        | 1.60E+09            | 2.70E+08                    |
| $^{223}$Ra | 11.43 d   | TAT         | $^{223}$Ra   | ThO             | SIS        | 6.90E+08            | 4.00E+07                    |
| $^{213}$Bi | 45.6 m    | TAT         | $^{225}$Ac   | UC              | SIS        | 6.70E+07            | 2.25E+06                    |
| $^{213}$Pb | 10.64 h   | TAT         | $^{224}$Ra   | UC              | SIS        | 1.60E+09            | 1.00E+08                    |
| $^{212}$Bi | 60.6 m    | TAT         | $^{224}$Ra   | UC              | SIS        | 1.60E+09            | 7.80E+07                    |
| $^{211}$At | 7.22 h    | TAT         | $^{211}$Rn   | UC              | FEBIAD     | 1.00E+08            | 2.40E+07                    |
| $^{211}$At | 7.22 h    | TAT         | $^{211}$At   | UC              | FEBIAD     | 8.40E+07            | 7.40E+07                    |
| $^{211}$At | 7.22 h    | TAT         | $^{211}$Fr   | UC              | SIS        | 1.90E+09            | 4.30E+07                    |
| $^{209}$At | 5.4 h     | SPECT       | $^{213}$Fr   | UC              | SIS        | 1.80E+09            | 8.50E+08                    |
| $^{209}$At | 5.4 h     | SPECT       | $^{209}$At   | ThO             | LIS        | 1.90E+09            | 1.70E+08                    |
| $^{177}$Lu | 6.65 d    | BT          | $^{177}$Lu   | UC              | LIS        | 6.50E+08            | 6.40E+07                    |
| $^{169}$Yb | 32.02 d   | SPECT       | $^{169}$Yb   | UC              | LIS        | 5.10E+10            | 1.00E+09                    |
| $^{166}$Yb | 2.36 d    | AT          | $^{166}$Yb   | UC              | LIS        | 1.50E+11            | 3.70E+10                    |
| $^{165}$Er | 10.3 h    | AT          | $^{165}$Yb   | UC              | LIS        | 9.32E+10            | 3.90E+10                    |
| $^{161}$Ho | 2.5 h     | AT          | $^{161}$Ho   | UC              | LIS        | 9.96E+09            | 9.30E+09                    |
| $^{161}$Ho | 2.5 h     | AT          | $^{161}$Er   | UC              | LIS        | 3.60E+10            | 3.90E+09                    |
| $^{149}$Tb | 4.12 h    | SPECT       | $^{149}$Tb   | UC              | LIS        | 5.78E+08            | 5.75E+08                    |
| $^{140}$Nd | 3.37 d    | PET/AT     | $^{140}$Sm   | UC              | LIS        | 9.70E+08            | 1.70E+08                    |
| $^{124}$I | 4.18 d    | PET         | $^{124}$I    | UC              | FEBIAD     | 2.20E+08            | 3.20E+07                    |
| $^{123}$I | 13.22 h   | PET         | $^{123}$I    | UC              | FEBIAD     | 3.80E+07            | 2.60E+07                    |
| $^{82}$Sr | 1.35 d    | PET         | $^{82}$Sr    | Nb              | SIS        | 1.00E+10            | 2.10E+08                    |
| $^{77}$Br | 57.0 h    | Labeling    | $^{77}$Br    | Nb              | SIS        | 1.60E+09            | 3.70E+08                    |
| $^{67}$Ga | 78.28 h   | Imaging     | $^{67}$Ga    | Zn/C            | SIS        | 8.10E+09            | 1.50E+09                    |
| $^{67}$Cu | 2.58 d    | BT          | $^{67}$Cu    | UC              | LIS        | 1.40E+08            | 3.10E+07                    |
| $^{64}$Cu | 12.70 h   | PET/therapy | $^{64}$Cu    | Nb              | LIS        | 3.20E+09            | 2.20E+09                    |
| $^{61}$Cu | 3.33 h    | PET         | $^{61}$Cu    | Nb              | LIS        | 7.80E+08            | 7.50E+08                    |

* targeted alpha therapy, * single-photon emission computed tomography, * beta therapy, * Auger therapy, * positron emission tomography, * laser ion source, * surface ion source, * forced electron beam induced arc discharge ion source

With the example of $^{225}$Ac/Ra beams, it has been demonstrated that the ISAC facility at TRIUMF has the capability of providing pure isotope samples for pre-clinical nuclear medicine research [14]. Infrastructure for the ISAC Implantation Station and methods for production and retrieval of medical isotopes have been established. Similar implantation procedures have also been applied to the production of $^{209}$/$^{211}$At via the implantation of $^{211}$/$^{213}$Fr beams for At-based $\alpha$-therapy research [15][16]. In principle, the methods described above are applicable for any isotope beam from ISAC targets.

Table 1 lists the established yield rates (Ref. [3]) of isotopes of potential interest for nuclear medicine research from various targets and ion sources. Based on the established yields, the activity accumulated over a 24h implantation period was extrapolated. The data shows that in particular for some lanthanides very high activities can be collected. However, for relatively long-lived isotopes, such as $^{225}$Ra and $^{225}$Ac larger activities could be obtained by simply increasing the implantation period.

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