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 those 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 ^{225}Ac and its precursor ^{225}Ra are discussed. ^{225}Ac [4] and its decay product ^{213}Bi 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 ^{213}Bi from the ^{225}Ra/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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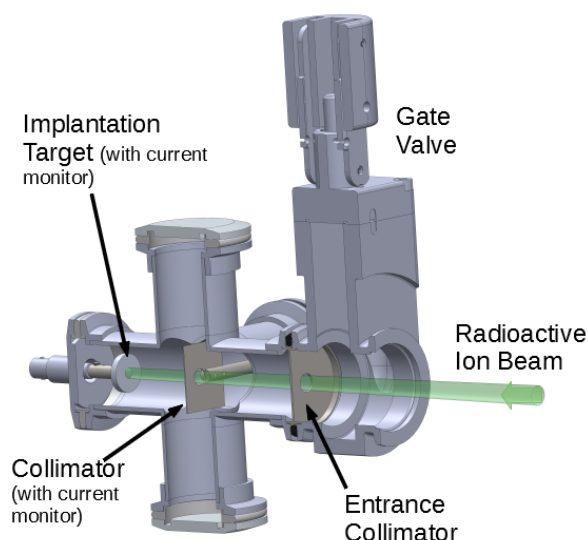
Fig. **1.** Section view of the ISAC Implantation chamber. The RIB is focused though a set of collimators on the implantation target in the back of the chamber.

tors that determine the maximum feasible beam power on target. The extraction of a beam from the ion source is only efficient under high-vacuum conditions ($< 10^{-5}$ mbar) [6]. The vapor pressure depends strongly on the target temperature which depends on power deposition and the efficiency of power dissipation, governed by the thermal conductivity of the target material and the emissivity of the target container. The resulting target temperature limitations can be detrimental to the efficient and fast release of isotopes through diffusion and effusion which benefits from high operating temperatures. The best balance between these two opposing requirements can be achieved by using refractory materials with high thermal stability, low vapor pressure and good thermal conductivity. Another aspect considering target material properties are diffusion times. Slow diffusion reduces the release efficiency of short-lived isotopes. This effect can be mitigated by using high-porosity materials. For example, the average bulk density of the uranium carbide used for ISAC targets is typically around 3.3 g/cm^3 [7], about 1/3 of the theoretical density of UC$_2$. In comparison to bulk UC$_2$, the thermal conductivity of this porous material is reduced by a factor of 6. In order to still achieve sufficient power dissipation, composite ceramic target materials [8], consisting of disks made of a 100-250 μm thick carbide layer on a 130 μm graphite backing foil have been developed. 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, UO$_2$) 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).

For the ionization process a variety of ion source options can be utilized [9]. 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.

For the production of heavy isotopes for targeted alpha therapy research, composite ceramic uranium carbide targets [7] are currently used. They have typical thicknesses between 0.05 and 0.1 mol U/cm^2 and are irradiated with a proton beam of max. 10 μA for up to 5000 μAh (current operation license limits) at an operating temperature of approximately 1950 °C. Neutron-deficient isotopes for medical applications in the lanthanide region are efficiently produced from tantalum metal foil targets, which are filled with several hundred 25 μm thick Ta foil disks up to a total thickness of 0.14 mol/cm^2. They are operated at up to 70 μA proton beam current and a target core temperature of 2300°C [6].

2.1 ISAC Implantation Station (IIS)

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 it's 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.

The design of the ion collection chamber used for the examples presented in this paper is shown in figure 1. It is made of a standard KF40 6-way cross. Attached are vent and sampling valves to test for airborne contamination, a vacuum gauge, a collimator with current readout for beam centering and the implantation target mounted on an electrical feedthrough to allow current monitoring during the implantation process. In principle the target can have any form and composition. The only condition is that it must be electrically conductive to avoid charging and enable a current readback. For the experiments in this paper we used a standard aluminium SEM sample holder ($\varnothing$25 mm) with a machined-in 2 mm deep cut-out ($\varnothing$16 mm), see figure 2. The cut-out is required for the etching process described in 2.2. A manual KF40 gate valve serves as an interface to section 1. Once an implantation is finished the gate valves in both sections are closed and the volume between them is vented. Now, the ion collection chamber can be detached and - still under vacuum - be transferred to the radiochemistry laboratory. This way, the collected activity can be considered a closed source, which is important particularly for alpha emitters where the spread of contamination through recoil emission can be a problem.
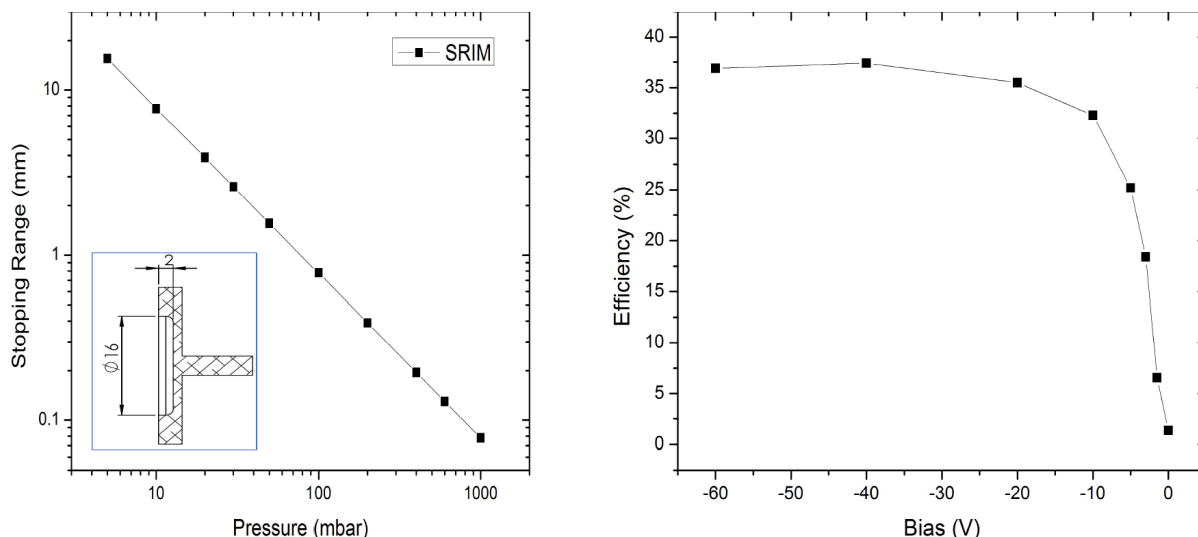
Fig. 2. ^{225}Ac recoil collection depends on the stopping range of approx. 100 keV alpha decay recoils (left) and the bias between the implantation target (insert, dimensions in mm) and an identical ion catcher target. The measured ^{213}Bi collection efficiency (right) at normal air pressure for a configuration in which the catcher target was pressed against the implantation target, separated by a thin insulator. A negative bias was applied to the catcher.

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 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 ^{213}Bi from a ^{225}Ac source involves 3 alpha decays in the chain. The decays of ^{221}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 $1.3 \cdot 10^8$ ions/s from a uranium carbide target / laser

Table 1. Selected isotopes for potential medical applications from ISAC targets. The table lists primary collection beam, target material, ion source and established yields [3] and the activity that can be accumulated within a typical 24h beam collection period.

Isotope	Half-life	Application	Primary beam	Target material	Ion source	Measured yield [ions/s]	Accumulated 24h Activity [Bq]
225Ac	9.92 d	TAT^a	225Ac	UC	LIS^{ff}	1.30E+08	8.60E+06
225Ac	9.92 d	TAT^a	225Ra	UC	SIS^{gg}	1.70E+08	3.40E+06
224Ra	3.66 d	TAT^a	224Ra	UC	SIS^g	1.60E+09	2.70E+08
223Ra	11.43 d	TAT^a	223Ra	ThO	SIS^g	6.90E+08	4.00E+07
213Bi	45.6 m	TAT^a	225Ac	UC	SIS^g	6.70E+07	2.25E+06
212Pb	10.64 h	TAT^a	224Ra	UC	SIS^g	1.60E+09	1.00E+08
212Bi	60.6 m	TAT^a	224Ra	UC	SIS^g	1.60E+09	7.80E+07
211At	7.22 h	TAT^a	211Rn	UO	FEBIAD^h	1.00E+08	2.40E+07
211At	7.22 h	TAT^a	211At	UO	FEBIAD^h	8.40E+07	7.40E+07
211At	7.22 h	TAT^a	211Fr	UC	SIS^g	1.90E+09	4.30E+07
209At	5.4 h	SPECT^b	213Fr	UC	SIS^g	1.80E+09	8.50E+08
209At	5.4 h	SPECT^b	209At	ThO	LIS^f	1.90E+08	1.70E+08
177Lu	6.65 d	BT^c	177Lu	Ta	LIS^f	6.50E+08	6.40E+07
169Yb	32.02 d	SPECT^b	169Yb	Ta	LIS^f	5.10E+10	1.00E+09
166Yb	2.36 d	AT^d	166Yb	Ta	LIS^f	1.50E+11	3.70E+10
165Er	10.3 h	AT^d	165Yb/165Tm	Ta	LIS^f	9.32E+10	3.90E+10
161Ho	2.5 h	AT^d	161Ho	Ta	LIS^f	9.96E+09	9.30E+09
161Ho	2.5 h	AT^d	161Er	Ta	LIS^f	1.03E+10	3.90E+09
149Tb	4.12 h	TAT^a/SPECT^b	149Tb	Ta	SIS^g	5.78E+08	5.75E+08
140Nd	3.37 d	PET^e/AT^c	140Sm	Ta	LIS^f	9.70E+08	1.70E+08
124I	4.18 d	PET^e	124I	UO	FEBIAD^h	2.20E+08	3.20E+07
123I	13.22 h	PET^e	123I	UO	FEBIAD^h	3.80E+07	2.60E+07
82Sr	1.35 d	PET^e	82Sr	Nb	SIS^g	1.00E+10	2.10E+08
77Br	57.0 h	Labeling	77Rb	Nb	SIS^g	1.60E+09	3.70E+08
67Ga	78.28 h	Imaging	67Ga	ZrC	LIS^f	8.10E+09	1.50E+09
67Cu	2.58 d	BT^c	67Cu	Ta	LIS^f	1.40E+08	3.10E+07
64Cu	12.70 h	PET^e/therapy	64Cu	Nb	LIS^f	3.20E+09	2.20E+09
61Cu	3.33 h	PET^e	61Cu	Nb	LIS^f	7.80E+08	7.50E+08

^{a} targeted alpha therapy, ^{b} single-photon emission computed tomography, ^{c} beta therapy, ^{d} Auger therapy, ^{e} positron emission tomography, ^{f} laser ion source, , ^{g} surface ion source , ^{h} forced electron beam induced arc discharge ion source

ion source combination accumulates an activity of up to $8.6 \cdot 10^6$ Bq. The accompanying ^{225}Ra ($T_{1/2} = 14.8$ d) beam is collected simultaneously. At a rate of $1.7 \cdot 10^8$ ions/s from a uranium carbide target / surface ion source combination a total of $1.4 \cdot 10^{13}$ atoms ($7.5 \cdot 10^6$ Bq) can be collected in 24 hours. ^{225}Ra decays via β-decay into ^{225}Ac, reaching a maximum activity of $3.4 \cdot 10^6$ 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]. The collection of ^{213}Bi via recoil transfer was employed during chelation studies. In this case the collected activities were significantly lower, in the kBq range, but still sufficient for this kind of experiment. The recoil transfer from the low energy beta decay of ^{225}Ra is insignificant compared to the implantation energy and, therefore, stays in the implantation target, while it's decay product ^{225}Ac can escape, thus, extending the lifetime of the ^{213}Bi source significantly.

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 209/211At via the implantation of $^{211/213}$Fr beams for At-based α-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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