

The New BLIP Raster System and Associated Target Modifications

L.Mausner^{a,1}, R. Michnoff^a, C. Cullen^a, D. Raparia^a,

^aBrookhaven National Laboratory, Upton NY

Introduction

Among the most important isotopes produced at Brookhaven Linac Isotope Producer (BLIP) are Sr-82 and Ac-225, and demand currently exceeds our capacity. Efforts to improve supply with increased intensity have been difficult. The beam is pulsed and the instantaneous beam current can be as high as 50mA with plans to increase further. Combined with a sharply peaked Gaussian-shaped beam intensity profile this creates very high power density at the beam spot center ($>4 \text{ kW/cm}^2$) and has caused target reliability and lifetime issues due to overheating, as well as somewhat erratic isotope yields. A raster scanning system has been installed to provide a better distribution of the proton beam on the targets, allow higher beam intensities to be used, and ultimately increase production yield of the isotopes. The upgrade consists of horizontal and vertical dipole magnets sinusoidally driven with 90 deg phase separation to produce a circular raster pattern, and a suite of new instrumentation devices to measure beam characteristics and allow adequate machine protection. Modifications to the targets for Sr-82 and Ac-225 were implemented to adapt to the new beam profile.

Material and Methods

The raster system sweeps the H^+ beam in a circular pattern at 5 kHz, which corresponds to 2.25 revolutions per 450 microsecond beam pulse. Using only a single sweep radius generates a donut intensity pattern that is not optimum. Therefore a dual radius repeating pattern was developed as follows: 3 consecutive beam pulses at a radius of 12.5 mm, then 1 pulse at a 5.5 mm radius. Figure 1. shows the initially planned raster pattern. In order to optimize the thermal profile for different targets it is possible to vary the radius value, the number of beam pulses for each radius and even the shape (eg. elliptical). In this manner near uniform energy deposition and temperature on the target can be achieved. The layout of the new BLIP beamline section is shown in Fig. 2. A beryllium window converts the H^+ beam to just protons on target.

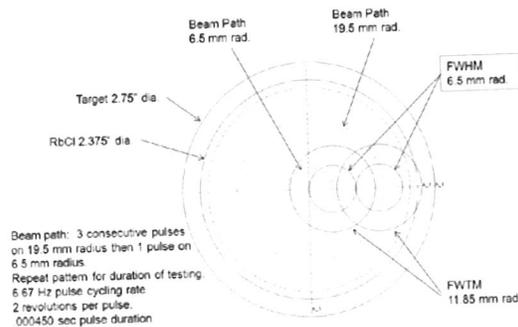


Figure 1. Diagram of circular raster pattern on target.

The new instrumentation systems include two plunging multi-wire profile monitors, a laser profile monitor, two beam current transformers, and a beam position monitor. An elaborate interlock system was designed as a combination of machine protection and target failure prevention upon raster malfunction. Sensors monitor raster magnet amplitude, frequency, phase, current, temperature, and more.

The raster magnet consists of one horizontal pair and one vertical pair of water-cooled coils surround on an 8" OD ceramic beam tube with transitions to stainless steel flanges at each end. The coil/tube assembly is housed in ferrite. A ceramic beam-tube was selected to limit eddy currents produced by the 5 kHz sinusoidal oscillations of each magnet coil. The interior of the ceramic beam tube has a thin conductive coating to dissipate static charge. Four small coils were installed in the magnet to monitor the induced magnetic field.

Power amplifiers in combination with a custom-resonant circuit were designed to deliver 225 A RMS (318 A peak), 470 V RMS (664 V peak), 105 KVA apparent power to the magnet. Low resistance Litz wire (4/0 gauge) with polyimide insulation for radiation resistance was used. The power supply controls are based on National Instrument's PXIe system and Labview. Frequency feedback loops were implemented to keep the frequency on resonance with software feedback loops for amplitude control. More detail on the raster components can be found in reference 2.

¹Corresponding author, E-mail: lmausner@bnl.gov

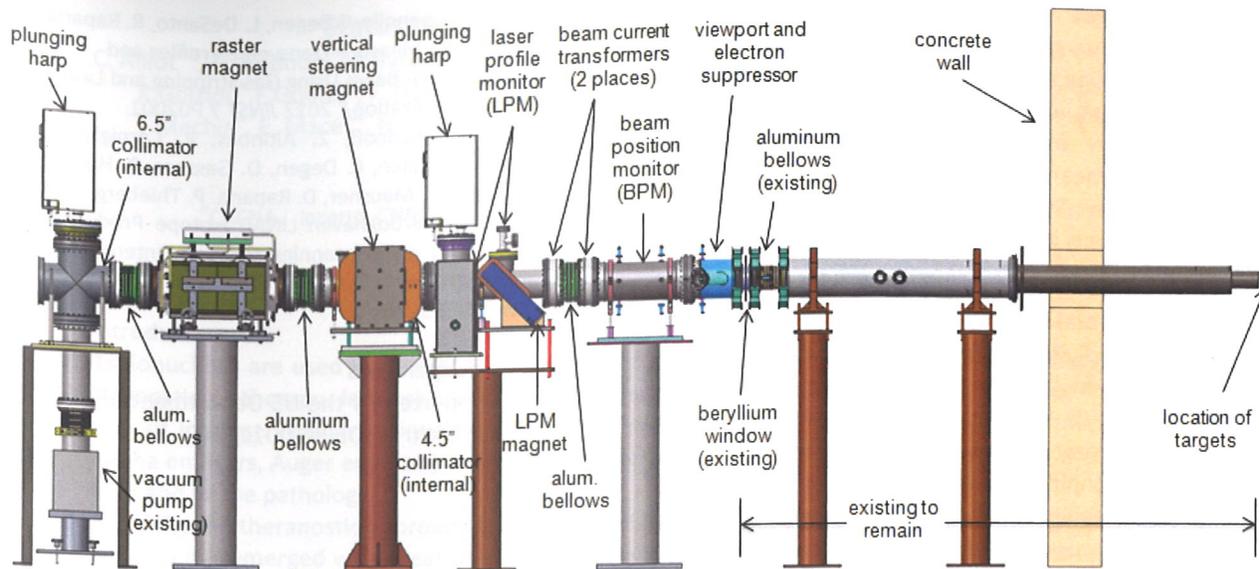


Figure 2: New BLIP beam-line layout. Length from vacuum pump center to beryllium window flange is 141.18".

Sr-82 is produced by irradiating two RbCl pressed pellet targets. RbCl has poor thermal conductivity, and with the previous fixed Gaussian beam spot (FWHM 22mm) the salt melts only in the beam strike area. Upon melting the RbCl expands 20% and moves outward, refreezing into void space on the target's periphery, and thus reducing the amount of RbCl remaining in the irradiation zone by an

estimated 10%. This effect also shifts the proton energy on downstream targets higher than optimum leading to reduced and variable Sr-82 yield. The raster parameters, 5 kHz sweep with dual radius, are driven by the thermal properties of RbCl. In addition the raster should minimize material creep as most of the target is consistently molten, but with lower overall temperatures than previously achieved.

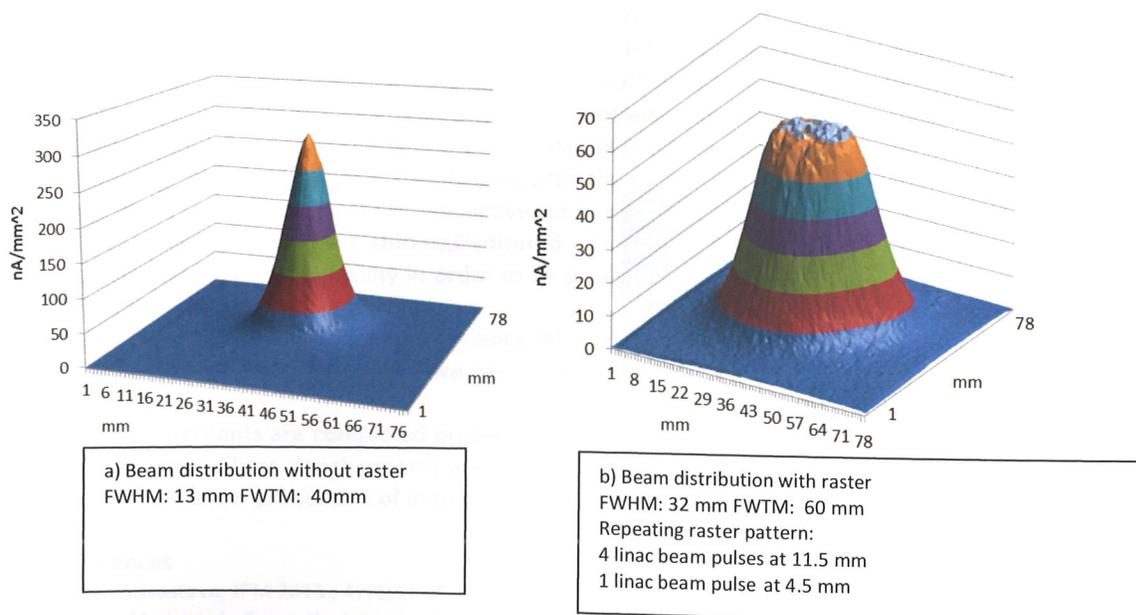


Figure 3: a) & b) Beam distribution on target.

¹Corresponding author, E-mail: lmausner@bnl.gov

Our most important research effort involves irradiation of thorium metal targets at 200 MeV to produce Ac-225. The target type used was an aluminum clad bolted design with an active diameter of 27.9mm. The use of the raster would mean considerable beam outside the Th diameter. Therefore a larger Inconel clad electron beam welded target was fabricated with a 60mm Th diameter, 0.38mm thick.

Results and Conclusion

Dual radius raster scanning has been demonstrated in late December 2015 and has been used routinely since early January 2016. Under the present and foreseeable future beam operating conditions, we do not expect to require a radius as high as the initially planned 19.5 mm. The adopted sequence was a repeating raster pattern was 4 linac cycles at 11.5 mm and 1 linac cycle at 4.5 mm. The measured beam distribution on target, with and without the raster is shown in Figure 3a,b. The average power density has decreased more than 4 fold.

A computational fluid dynamics code (ANSYS FLUENT) was used to model the thermal profile of the RbCl target irradiated for 20 seconds of beam with the above raster parameters as shown in Figure 4. Even this quickly over 70% of the target volume is predicted to melt. An increase of the raster sweep radii was then implemented to 12.5mm outer radius and 5.5mm inner radius. Visual observation of RbCl targets irradiated at 150 μ A with these raster parameters showed complete melting had occurred. Production efficiency (mCi/ μ Ah) has improved by 9% compared to past non raster irradiations. In addition the large diameter Th target was irradiated successfully with the raster.

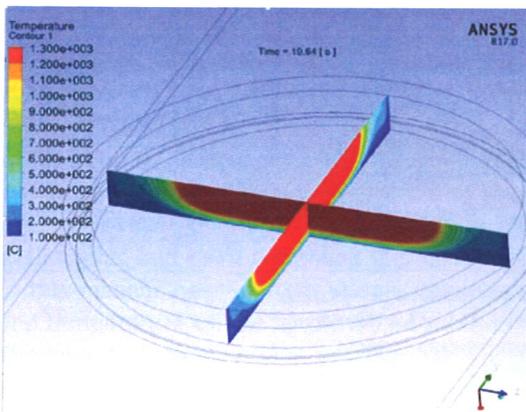


Figure 4. Transient thermal profile of RbCl target

References

1. R. Connolly, C. Degen, L. DeSanto, R. Raparia, A Detector to Measure Transverse Profiles and Energy of an H- Beam Using Gas Stripping and Laser Photo Neutralization," 2012 *JINST* 7 P02001.
2. R. Michnoff, Z. Altinbas, P. Cerniglia, R. Connolly, C. Cullen, C. Degen, D. Gassner, R. Hulsart, R. Lambiase, L. Mausner, D. Raparia, P. Thieberger, M. Wilinski, The Brookhaven LINAC Isotope Production Facility (BLIP) raster scanning upgrade, International Beam Instrumentation Conference, Monterey CA, September 2-5, 2014.

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¹Corresponding author, E-mail: lmausner@bnl.gov

Selective Extraction of Medically-Related Radionuclides from Proton-Irradiated Thorium Targets

Valery Radchenko^{*1}, Jonathan W. Engle¹, Roy Copping², Justin Griswold², Francois Meiring Nortier¹, Eva R. Birnbaum¹, Mark Brugh¹, Saed Mirzadeh², Kevin D. John¹, Michael E. Fassbender^{*1}

¹Los Alamos National Laboratory, Los Alamos, NM, USA

²Oak Ridge National Laboratory, Oak Ridge, Tennessee, USA

Introduction

Clinicians rely on nuclear medicine for the treatment of numerous diseases [1, 2] impacting millions of patients annually. Recently, Targeted Radiotherapy (TR) has been successfully advanced with the US FDA approval of several radionuclide based drugs [3]. Combinations of several types of radionuclide emissions for therapy (i.e., α -therapeutic agent combined with β^- therapeutic) could lead to even more effective treatment options [4]. One of the limiting factors in the development of TR as a widely adopted treatment option is the availability of radionuclides with optimum emission properties. A challenge in developing a suite of radionuclides for clinical use is the wide variety of target materials and/or nuclear reaction pathways for their formation.

Material and Methods

We recently published a successful strategy for the isolation of $^{225/227}\text{Ac}$ from proton-irradiated thorium targets [5], and have expanded this to include the recovery of Pa isotopes [6] from the same matrix. In this work, we describe the isolation of several other medically relevant radionuclides, namely ^{103}Ru , $^{223/225}\text{Ra}$, ^{111}Ag , from the same target material.

Results and Conclusion

Several methods based on ion exchange chromatography and solid phase extraction show promise for the co-extraction of ^{103}Ru , ^{111}Ag and Ra isotopes from thorium irradiated targets. Anion exchange in HCl media proves to be an efficient method for the isolation of ^{103}Ru . The Ru fraction can be further purified with Cl and DGA resins. Ra isotopes can be isolated via a combination of cation exchange resin / citrate and DGA resin/ HNO_3 sorption steps to separate the ^{225}Ac source ^{225}Ra . Additionally, ^{223}Ra and ^{224}Ra can be harvested after 20 days post separation from the decay of ^{227}Th and ^{228}Th respectively, via the same strategy. To remove Ba impurities from the Ra fraction, and additional step with cation exchange/ HNO_3 , citrate was tested. ^{111}Ag can potentially be isolated with Cl resin.

Production yields for the proposed radionuclides were evaluated by comparison of actual product yields with calculated (predicted) yields. Radiochemical strategies for co-extraction of ^{103}Ru , ^{111}Ag and $^{223/224/225}\text{Ra}$ isotopes based on ion exchange and solid phase extraction chromatography will be discussed.

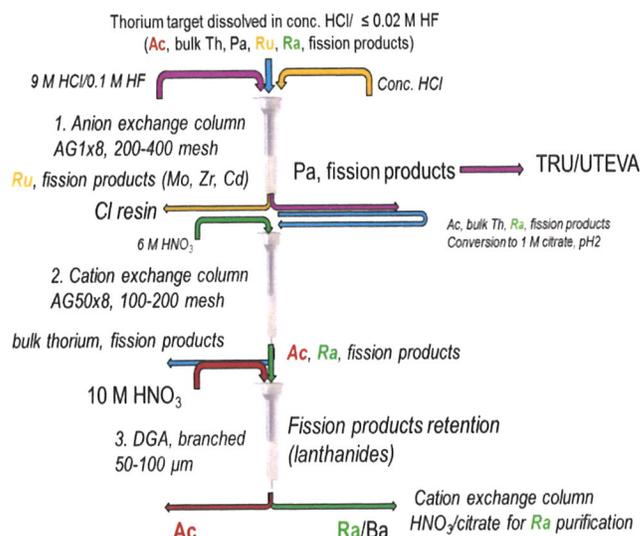


Figure 1. Proposed multi-nuclide separation strategy.

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References

1. T. Stigbrand, et al. *Targeted Radionuclide Tumor Therapy*, Springer 2008, ISBN 978-1-4020-8696-0.
2. F. Fahey, et al. *J. Nucl. Med.* 2014 55(2): 337.
3. www.fda.gov
4. A. Dash, et al., *Curr Radiopharm.* 2013 6(3): 152.
5. Radchenko et al., *Chromatography A*, 2014 1380: 55.
6. Radchenko et al. available online, *Radiochimica Acta* DOI: 10.1515/ract-2015-2486

*Corresponding authors. E-mail: varad@lanl.gov (V. Radchenko), E-mail: mifa@lanl.gov (M. E. Fassbender)

Radiochemical separation of ^{44}Ti from proton-irradiated scandium

C.A.L. Meyer^{a,1}, V. Radchenko^{a,1}, J.W. Engle^a, D.G. Medvedev^b, C.M. Naranjo^a, G.A. Unc^a, M. Brugh^a, E.R. Birnbaum^a, K.D. John^a, F.M. Nortier^a, M.E. Fassbender^{a,1}

^aLos Alamos National Laboratory, Los Alamos, NM, USA

^bBrookhaven National Laboratory, Upton, NY, USA

Introduction

Positron emission tomography (PET), a functional imaging technique that can reveal cancers, can be improved through the development of medical radionuclide generator systems that produce relatively long-lived positron-emitting daughters. The $^{68}\text{Ge}/^{68}\text{Ga}$ system is widely used for ^{68}Ga -labelled PET radiopharmaceuticals but the clinical value is limited by the physical half-life of ^{68}Ga (67.7 min [1]). Thus, it is of increasing interest to investigate other candidate systems- one of which is the $^{44}\text{Ti}/^{44}\text{Sc}$ generator. ^{44}Sc bears promise as a PET imaging radionuclide due to its high positron branching ratio of 94.3%, the appropriate mean energy range of 0.632 MeV, and its physical half-life of 3.97 hours which enables imaging of longer lasting biological processes and allows more time for preparation of the radiopharmaceutical [2]. Previous work on the subject reported on the design and irradiation of a Sc metal target ($^{45}\text{Sc}(p,2n)^{44}\text{Ti}$) and developed a bulk radiochemical separation scheme[3]. In this study, we examine alternative separation strategies for the isolation of ^{44}Ti using DGA and Zr hydroxamate extraction chromatographic resins, and propose a novel generator system.

Materials and Methods

The previously reported procedure involves a two-step purification for ^{44}Ti using anion exchange resin for the bulk removal of Sc, and cation exchange resin for fine purification[3]. In this study, we explore the effectiveness of branched DGA resin and a Zr hydroxamate resin for Ti/Sc separations. First, K_d studies were performed to determine the acid dependency of Ti/Sc retention on each resin in HCl media (0.1 – 10 M). Distribution coefficients were determined using γ ray spectrometry and ^{44}Ti and ^{46}Sc as radiotracers. The K_d study results informed preliminary separation experiments for which elution profiles were obtained. To better understand the behavior of Ti/Sc on the resins, capacity experiments were performed using increased $^{45}\text{Sc}:^{44}\text{Ti}$ mass ratios. Furthermore, the suitability and clinical viability of the Zr hydroxamate resin as the solid phase in a generator was evaluated by way of a labeling study with ^{44}Sc and DOTA.

Results and Conclusions

The optimal conditions for Ti/Sc separations on DGA and hydroxamate resins are reported in Table 1. Unlike the DGA resin, the Zr hydroxamate resin pre-

ferentially adsorbs Ti to a high degree ($K_d >1000$) across all tested concentrations (with only weak affinity for Sc). In preliminary separation experiments with DGA, a Ti/Sc separation factor $\geq 10^5$ was achieved (representing a ten times increase in separation factor compared with cation exchange resin). However, DGA resin failed to elute Ti without Sc breakthrough when the mass of ^{45}Sc was increased from 2.8 mg to 30 mg (in 5 mL resin). Thereby, DGA resin could be an alternative to the cation column in the current process for fine purification as long as the Sc capacity (<6 mg Sc/1 mL resin) is not exceeded.

In capacity experiments for Zr resin, the resin remained selective for Ti despite the bulk mass of Sc on the column (1 g ^{45}Sc on 1 mL resin). Further proof of principle is demonstrated in a scaled-up separation using 4 g ^{45}Sc on 5 mL resin. Separation factors $\geq 10^3$ were achieved. The Ti is removed from the column using 6 M HCl/0.65 M H_2O_2 as the eluent. Given that the Zr hydroxamate resin allows for straightforward elution of Sc with high retention of Ti, this brings about the possibility of this resin as the stationary phase in a $^{44}\text{Ti}/^{44}\text{Sc}$ generator. Labeling studies with ^{44}Sc and DOTA indicate maximum labeling yield occurs with 30 nM DOTA and 15 minutes heating. A prototype generator was constructed with reverse-type elution mode capabilities with performance that remains to be addressed.

Resin	[HCl] M	K_d	
		Ti	Sc
DGA	4	0	730
Zr	6	>1000	0.21

TABLE 1. Ti/Sc retention factors in HCl media.

Acknowledgments

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References

1. F. Roesch: *Curr. Radiopharm.* **5**, pp. 187-201, 2012.
2. D. V. Filosofov, N. S. Laktionova, F. Roesch: *Radiochim. Acta.* **98**, pp. 149-156, 2010.
3. V. Radchenko, J. W. Engle, D. G. Medvedev, ... M. E. Fassbender: *Proton induced production and radiochemical isolation of ^{44}Ti for $^{44}\text{Ti}/^{44}\text{Sc}$ generator development*, Manuscript in preparation, 2015.

¹Corresponding authors. E-mail: catherinem@lanl.gov (C.A.L. Meyer). E-mail: varad@lanl.gov (V. Radchenko). E-mail: mifa@lanl.gov (M.E. Fassbender)

Production of ^{186}Re and ^{189}Re via Proton Induced Reactions on Natural Tungsten Disulfide-Graphite, Natural Osmium Disulfide, and Natural Osmium-Graphite Targets

T. E. Phelps^{a,b}, M. D. Gott^{a,b}, D. E. Wycoff^a, A. R. Ketring^b, E. R. Balkin^c, D. S. Wilbur^c, M. E. Fassbender^d, C. S. Cutler^e, S. S. Jurisson^{a,1}

^aDepartment of Chemistry, University of Missouri, Columbia, MO 65211

^bUniversity of Missouri Research Reactor, Columbia, MO 65211

^cDepartment of Radiation Oncology, University of Washington, Seattle, WA 98105

^dIsotope Production Facility, Los Alamos National Laboratory, Los Alamos, NM 87545

^eCollider-Accelerator Department, Brookhaven National Laboratory, Upton, NY 11973

Introduction

Radionuclides are the workhorse of nuclear medicine and are powerful tools for diagnosis and therapy. Rhenium is the chemical analogue to the widely used Technetium-99m. Rhenium-186 has a 3.72 day half-life, which allows sufficient time for transportation and synthesis of radiopharmaceuticals. ^{186}Re emits a therapeutic 1.07 MeV β^-_{max} , which travels up to 3.6 mm in tissue. Furthermore, its low abundance 137 keV γ -ray (9.4%) allows for *in vivo* tracking via SPECT. Rhenium-189 is a novel radionuclide for nuclear therapy and diagnostic imaging due to its 1.1 MeV β^- endpoint energy, its low abundance 216 keV γ -ray (5.5%), and its 24.3 hour half-life. ^{186}Re is produced in a reactor via the $^{185}\text{Re}(n, \gamma)$ reaction; however, this results in a low specific activity of 0.11 GBq/ $\mu\text{g}^{[1]}$, which is marginally applicable for clinical use. Production via accelerators yields in a theoretical specific activity of 6.88 GBq/ $\mu\text{g}^{[2]}$ – a 62 fold increase over reactor production of ^{186}Re .

The studies reported herein focus on the evaluation of accelerator-based reaction pathways for production of high specific activity (HSA) ^{186}Re and ^{189}Re . The following proton and deuteron induced reactions on osmium and tungsten targets are being investigated: $^{186}\text{W}(p, n)^{186}\text{Re}$, $^{186}\text{W}(d, 2n)^{186}\text{Re}$, $^{189}\text{Os}(p, \alpha)^{186}\text{Re}$, $^{192}\text{Os}(p, \alpha)^{189}\text{Re}$.

Materials and Methods

Tungsten disulfide (WS_2) and osmium disulfide (OsS_2) targets were chosen over tungsten and osmium metals because they are robust and easy to recycle. However, the disulfide chemical forms exhibit poor thermal conductivity. Graphite was incorporated in

the target design to improve thermal conductivity and to enable the use of higher currents.

WS_2 -graphite, OsS_2 , and Os -graphite targets were prepared using a unilateral press with a 13 mm diameter die to form pressed pellets. The target holder (Figure 1) was designed to accommodate the graphite and to allow for a stable base during pressing.

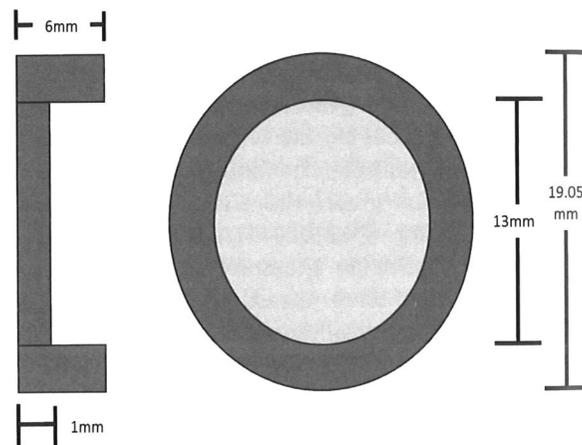


FIGURE 1. Aluminum holder for WS_2 -graphite, OsS_2 , and Os -graphite targets.

Irradiations were performed using a 16 MeV PETtrace cyclotron at the University of Missouri Research Reactor (MURR). $^{\text{nat}}\text{WS}_2$ -graphite targets were irradiated with proton beam currents of 10 μA and 30 μA for 1 hour. Preliminary $^{\text{nat}}\text{Os}$ -graphite targets plan to be irradiated at 15 μA for 1 hour. Thin $^{\text{nat}}\text{OsS}_2$ targets were previously irradiated at 10 μA for 1 hour.

Post irradiation, $^{\text{nat}}\text{WS}_2$ -graphite targets were digested in H_2O_2 , adjusted to pH 14 with NaOH , and graphite was removed with a glass wool filter.

¹Dr. Silvia Jurisson, Email: jurissons@missouri.edu

Perrhenate was extracted using methyl ethyl ketone (MEK), with tungstate remaining in the aqueous solution. The MEK was evaporated and the perrhenate resuspended in saline, which was passed through an acidic alumina column to remove any tungsten impurities. Activity determination was done by gamma spectroscopy with an HPGe detector (Table 1). The aqueous solution was passed through a strong anion exchange column to recover tungstate for recycling^[3]. Addition of concentrated HCl to the tungstate solution resulted in precipitation of tungstic acid, which was washed with water and acetone and then sintered in a tube furnace to recover tungsten trioxide, the precursor for WS₂ synthesis.

Isotope	t _{1/2}	Gamma Energy (Intensity)
¹⁸² Re	64.0 h	1121 (22%), 169 (11.3%)
^{182m} Re	12.7 h	1121 (32%)
¹⁸³ Re	70.0 d	162 (23.3%)
¹⁸⁴ Re	35.4 d	792 (37.7%)
¹⁸⁶ Re	89.2 h	137 (9.42%)

TABLE 1. Identified rhenium isotopes with their half-lives and utilized gamma emissions.

^{nat}OsS₂ targets were dissolved in NaOCl and pH adjusted with NaOH. Volatile OsO₄ was trapped in KOH to form perosmate. Addition of sodium hydrosulfide to the recovered perosmate resulted in precipitated OsS₂, which was washed with water and acetone and then sintered in a tube furnace to recover dried OsS₂ in high yield^[4]. MEK aliquots were added to the final aqueous solution to extract perrhenate, with iridium and osmium remaining in aqueous phase^[4]. MEK extracts were evaporated and resuspended in saline. The saline solution was passed through an acidic alumina column to purify rhenium from the iridium and osmium contaminants^[4]. Activity and radionuclidic purity determination was done by gamma spectroscopy with an HPGe detector (Table 2).

Isotope	t _{1/2}	Gamma Energy (Intensity)
¹⁸⁶ Ir	16.64 h	137 (41%), 297 (62%)
¹⁸⁷ Ir	10.5 h	913 (4.3%)
¹⁸⁸ Ir	1.72 d	155 (29.7%), 1210 (6.9%)
¹⁸⁹ Ir	13.2 d	245 (6%)
¹⁹⁰ Ir	11.8 d	187 (52.4%)
¹⁸⁶ Re	89.2 h	137 (9.42%)
¹⁸⁸ Re	17.0 h	155 (15%)
¹⁸⁹ Re	24.3 h	216 (5.5%)

¹Dr. Silvia Jurisson, Email: jurissons@missouri.edu

TABLE 2. Identified rhenium and iridium isotopes with their half-lives and utilized gamma emissions.

Results and Conclusion

Two ^{nat}WS₂-graphite targets were irradiated with 10-11 MeV protons at 10 μAh and 30 μAh, and ¹⁸⁶Re produced was analyzed by HPGe. These conditions produced rhenium isotopes in microcurie quantities, and although the presence of graphite impeded ¹⁸⁶Re production, no target failure was observed at higher currents (Table 3). Future irradiations at 9-10 MeV with larger proton beam currents and more graphite are planned to enable increased ¹⁸⁶Re production. After optimizing conditions, enriched ¹⁸⁶WS₂ targets will be irradiated to maximize ¹⁸⁶Re production and reduce production of unwanted rhenium isotopes.

Isotope	A ^{EOB} (10 μA)	A ^{EOB} (30 μA)
¹⁸² Re	1.91 μCi	7.54 μCi
^{182m} Re	121. μCi	426. μCi
¹⁸³ Re	0.67 μCi	1.80 μCi
¹⁸⁴ Re	2.31 μCi	7.01 μCi
¹⁸⁶ Re	24.0 μCi	58.1 μCi

TABLE 3. Total activities of rhenium isotopes produced at EOB using 225 mg WS₂ with 10-11 MeV at 10 μAh and 30 μAh.

^{nat}Os-graphite targets plan to be irradiated with 14 MeV protons at 15 μAh and the ¹⁸⁶Re and ¹⁸⁹Re produced will be analyzed by gamma spectroscopy with an HPGe detector. ^{nat}OsS₂ targets were irradiated with 16 MeV at 10 μAh and produced nanocurie quantities of ¹⁸⁶Re and ¹⁸⁹Re while iridium isotopes were produced in microcurie quantities (Table 4). Higher proton irradiations with ^{nat}OsS₂ and ^{nat}Os are expected to result in increased ¹⁸⁶Re and ¹⁸⁹Re production and decreased iridium production. After optimizing irradiation parameters, enriched ¹⁸⁹Os and enriched ¹⁹²Os irradiations will be conducted to minimize unwanted radionuclides and maximize production of ¹⁸⁶Re and ¹⁸⁹Re, respectively.

Isotope	A^{EOB} (Total)
^{186}Ir	3.00 μCi
^{187}Ir	143. μCi
^{188}Ir	10.0 μCi
^{189}Ir	9.00 μCi
^{190}Ir	1.34 μCi
^{186}Re	4.99 nCi
^{188}Re	4.19 nCi
^{189}Re	6.58 nCi

TABLE 4. Activities of iridium and rhenium isotopes produced at EOB using 46 mg OsS₂ with 16 MeV at 10 μAh .

In conclusion, production of HSA ^{186}Re and ^{189}Re via accelerator induced reactions are being evaluated using natural WS₂, natural Os, and natural OsS₂. Irradiation of thin ^{nat}OsS₂ targets demonstrated the feasibility of producing rhenium via the ^{nat}Os(p, α)Re reaction. Results suggest higher proton energies are required to reduce production of unwanted iridium isotopes and to increase rhenium production. After irradiation conditions are optimized, enriched ^{189}Os and enriched ^{192}Os targets will be used to maximize ^{186}Re and ^{189}Re production, respectively. Irradiation of ^{nat}WS₂-graphite targets established the feasibility of ^{186}Re production at higher proton beam currents via the $^{186}\text{W}(p, n)^{186}\text{Re}$ reaction.

References

1. G. J. Ehrhardt, M. E. Blumer, F. M. Su, J. L. Vanderheyden, A. R. Fritzberg: *Appl. Radiat. Isot.* **48**, pp. 1-4, 1997.
2. M. L. Bonardi, F. Groppi, S. Manenti, E. Persico, L. Gini: *Appl. Radiat. Isot.* **68**, pp. 1595-1601, 2010.
3. M. D. Gott, B. D. Ballard, L. N. Redman, J. R. Maassen, W. A. Taylor, J. W. Engle, F. M. Nortier, E. R. Birnbaum, K. D. John, D. S. Wilbur, C. S. Cutler, A. R. Ketring, S. S. Jurisson, M. E. Fassbender: *Radiochim. Acta* **102**, pp. 325-332, 2014.
4. M. D. Gott, C. R. Hayes, D. E. Wycoff, E. R. Balkin, B. E. Smith, P. J. Pauzaskie, M. E. Fassbender, C. S. Cutler, A. R. Ketring, D. S. Wilbur, S. S. Jurisson: *Appl. Radiat. Isot.* **114**, pp. 159-165, 2016.

Acknowledgments

¹Dr. Silvia Jurisson, Email: jurissons@missouri.edu

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Investigation of ^{72}Se Production via High Energy Proton Induced Reactions on Arsenic Metal Targets for Application of a Clinical $^{72}\text{Se}/^{72}\text{As}$ Generator

T. E. Phelps^{a,b}, D. E. Wycoff^a, M. D. Gott^{a,b}, A. J. DeGraffenreid^d, D. Medvedev^d, C. S. Cutler^d, A. R. Ketring^b, M. F. Embree^b, S. S. Jurisson^{a,1}

^aDepartment of Chemistry, University of Missouri, Columbia, MO 65211

^bUniversity of Missouri Research Reactor, Columbia, MO 65211

^dCollider-Accelerator Department, Brookhaven National Laboratory, Upton, NY 11973

Introduction

Radioisotopes advance the field of nuclear medicine and demonstrate a host of applications in imaging and therapy. Diagnostic imaging allows for early disease detection by non-invasive *in vivo* tracking of gamma emitting radiolabeled compounds. $^{99\text{m}}\text{Tc}$ is a well-established imaging agent that is eluted daily from a $^{99}\text{MoO}_4^{2-}/^{99\text{m}}\text{TcO}_4^-$ generator. However, the 6 hour half-life of $^{99\text{m}}\text{Tc}$ is too short for monoclonal antibodies and large proteins. Positron Emission Tomography (PET) is a non-invasive imaging method that allows for higher resolution and is more easily quantitated than Single Photon Emission Computed Tomography (SPECT). With the extensive use of short half-life PET agents, such as ^{18}F (110 minutes) and ^{68}Ga (68 minutes), longer half-life agents are desirable for use with large proteins. Arsenic-72, (^{72}As) emits β^+ particles in high abundance and has a 26.0 hour half-life, which would allow for longer biological half-life molecules to sufficiently localize and acquire more complete data of tissue uptake and clearance. ^{72}As is the daughter product of ^{72}Se , which decays by electron capture over 8.4 days and emits a 46 keV γ -ray (57%). Therefore, the production of ^{72}Se has potential use in a $^{72}\text{Se}/^{72}\text{As}$ generator based system to obtain no carrier added ^{72}As for radiolabeling studies.

The studies reported herein focus on investigating proton induced reaction pathways for production of high specific activity (HSA) ^{72}Se for applications as a clinical $^{72}\text{Se}/^{72}\text{As}$ generator. The pathway of interest is the $^{75}\text{As}(p, 4n)^{72}\text{Se}$ reaction. Preliminary cross sectional measurements for this reaction suggest sufficient ^{72}Se is produced (50 mCi) above 100 MeV for application as a generator. The following information explains the conditions utilized for the separation of bulk As from Se prior to application as a $^{72}\text{Se}/^{72}\text{As}$ generator.

Materials and Methods

Arsenic is a monoisotopic element, which makes targets relatively inexpensive and makes target recovery unnecessary.

Irradiations will be conducted using the Brookhaven Linac Isotope Producer (BLIP). 2.375 inch diameter and 0.02 inch thick As metal targets will be prepared by welding in an aluminum capsule under helium. Targets will be irradiated with 105 MeV protons with $\geq 11800 \mu\text{Ah}$. Targets will be processed post irradiation at the Target Processing Laboratory (TPL).

Separation of bulk As from ^{72}Se was performed by anion exchange chromatography. Initially, the target was dissolved to oxidize As and Se to their highest oxidation states, As(V) and Se(VI). Large loading volumes were used to minimize ionic strength and Se breakthrough. After loading, the column was eluted with several bed volumes of water to allow arsenate to equilibrate on the column. As was eluted as arsenic acid and Se was retained as selenate with 0.03 M HNO_3 ^[1]. After all bulk As(V) was eluted, ^{72}Se was stripped with 1 M HNO_3 , diluted, and reapplied to a new AG 1-X8 anion exchange column for use as a $^{72}\text{Se}/^{72}\text{As}$ generator.

Results and Conclusions

Initial anion exchange chromatography was performed at the University of Missouri Research Reactor (MURR) using HCl and HNO_3 eluents that were eluted through 8 mL bed volumes, 9.6 milliequivalents (meq) at 1.2 meq per mL, of DOWEX AG 1-X8 anion exchange columns^[1]. Bulk amounts of anhydrous monobasic potassium arsenate, KH_2AsO_4 , were dissolved in H_2O and spiked with $^{75}\text{Se(VI)}$ and $^{76}\text{As(V)}$ radiotracers. The final loading solution was pH 4-5. Elution profiles were monitored by using

¹Dr. Silvia Jurisson, Email: jurissons@missouri.edu

gamma spectroscopy with an HPGe detector (Table 1).

Isotope	t _{1/2}	Gamma Energy (Intensity)
⁷⁵ Se	120 d	136 (54%)
⁷⁶ As	26.2 h	559 (45%)
⁷² As	26.0 h	834 (81%)

TABLE 1. Identified arsenic and selenium isotopes with their half-lives and utilized gamma emissions.

Elutions with HCl resulted in no Se breakthrough when column capacity meq exceeded arsenate meq. However, HCl eluted As slowly and half of the As coeluted with Se in 0.6 M HCl. More dilute loading solutions that exceeded the column capacity resulted in significant Se recovery, but similar loading solutions with higher ionic strength resulted in poor Se recovery (Table 2).

Arsenate (meq)/ Load Volume (mL)	Fractions (% Se)	Fractions (% As)
5.2 / 15	Load (0%)	Load (12%)
5.2 / 15	H ₂ O (0%)	H ₂ O (11%)
5.2 / 15	0.03 M HCl (0%)	0.03 M HCl (25%)
5.2 / 15	0.6 M HCl (100%)	0.6 M HCl (52%)
7.8 / 15	Load (0%)	Load (12%)
7.8 / 15	H ₂ O (0%)	H ₂ O (21%)
7.8 / 15	0.03 M HCl (0%)	0.03 M HCl (13%)
7.8 / 15	0.6 M HCl (100%)	0.6 M HCl (49%)
16.0 / 15	Load (30%)	Load (42%)
16.0 / 15	H ₂ O (17%)	H ₂ O (16%)
16.0 / 15	0.03 M HCl (0%)	0.03 M HCl (5%)
16.0 / 15	0.6 M HCl (53%)	0.6 M HCl (37%)
16.0 / 30	Load (2%)	Load (34%)
16.0 / 30	H ₂ O (2%)	H ₂ O (11%)
16.0 / 30	0.03 M HCl (0%)	0.03 M HCl (6%)
16.0 / 30	0.6 M HCl (96%)	0.6 M HCl (49%)

TABLE 2. Percent selenate and arsenate in combined elutions using HCl with various KH₂AsO₄ loading masses and 9.6 meq column capacity.

HNO₃ elutions were performed when column capacity meq and arsenate meq were equal. Nitrate ions have increased AG 1-X8 resin selectivity over chloride ions. Therefore, column elutions with HNO₃ resulted in more efficient arsenate removal but also coeluted selenate (Table 3). Based on the percent Se eluted using 1 M HNO₃ with 0.51 M and 0.69 M loading ionic strengths, this suggests loading solutions must have low ionic strengths to recover Se in high yield.

Arsenate (meq) /[Arsenate] (M)	Fractions (% Se)	Fractions (% As)
9.6 / 0.69	Load (17%)	Load (35%)
9.6 / 0.69	H ₂ O (23%)	H ₂ O (32%)
9.6 / 0.69	.03 M HNO ₃ (2%)	.03 M HNO ₃ (33%)
9.6 / 0.69	1 M HNO ₃ (57%)	1 M HNO ₃ (0%)
9.6 / 0.51	Load (13%)	Load (42%)
9.6 / 0.51	H ₂ O (12%)	H ₂ O (22%)
9.6 / 0.51	.03 M HNO ₃ (1%)	.03 M HNO ₃ (36%)
9.6 / 0.51	1 M HNO ₃ (74%)	1 M HNO ₃ (52%)

TABLE 3. Percent selenate and arsenate in combined elutions using HNO₃ with various KH₂AsO₄ concentrations and 9.6 meq column capacity.

In conclusion, bulk As(V) solutions with ⁷²Se require pH > 3 and low ionic strength during column loading in order to prevent Se breakthrough. AG 1-X8 chromatographic resin has higher selectivity towards nitrate, which caused greater Se breakthrough and more As elution with HNO₃. Future investigations of anion exchange chromatography will include more chromatographic resin and will utilize lower ionic strength loading solutions to separate irradiated As targets and maximize recovery of ⁷²Se. After ⁷²Se is purified in high yield, it will be applied to a second AG 1-X8 anion exchange column for use as a ⁷²Se/⁷²As generator. Future plans include an As metal irradiation at the BLIP to evaluate the separations.

References

1. D. E. Wycoff, M. D. Gott, A. J. DeGraffenreid, R. P. Morrow, N. Sisay, M. F. Embree, B. Ballard, M. E. Fassbender, C. S. Cutler, A. R. Ketring, S. S. Juisson: *J. Chromatogr. A* **1340**, pp. 109-114, 2014.

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¹Dr. Silvia Jurisson, Email: jurissons@missouri.edu

Production of $^{72}\text{Se}/^{72}\text{As}$ in Clinically Relevant Quantities at the BLIP

A. J. DeGraffenreid^a, D. G. Medvedev^a, S. V. Smith^a, M. D. Gott^c, T. E. Phelps^b, S. S. Jurisson^b, C. S. Cutler^{a1}

^aBrookhaven National Laboratory—Upton, NY 11973, ^bUniversity of Missouri—Columbia, MO 65211, ^cInstitute of Radiopharmaceutical Cancer Research, Helmholtz-Zentrum Dresden-Rossendorf—Dresden, Germany—Mainz, 01328

Introduction

Arsenic-72 (^{72}As ; 2.49 MeV β^+ , 26 h) has been identified as a possible radioisotope for PET imaging with novel targeting vectors such as peptides and monoclonal antibodies.¹ Arsenic-72 can be produced directly and via decay from selenium-72 (^{72}Se ; EC, 8.4 d), from which a portable generator system can be implemented. To this end, $^{72}\text{Se}/^{72}\text{As}$ generator systems have been previously reported.²⁻⁴ However production of a clinically relevant amount of ^{72}Se has long been problematic.^{5,6}

The Brookhaven Linear Isotope Producer (BLIP) is one of the few facilities in the world capable of producing high energy protons (up to 200 MeV) at high currents (up to 150 $\mu\text{A}/\text{h}$). Production of suitable quantities of medical isotopes at the BLIP has centered on production of $^{82}\text{Sr}/^{82}\text{Rb}$ and therefore requires the production of other radioisotopes at alternative energies (outside of 30-96 MeV). Two positions within the array are available, from 96-105 MeV (front of box; Fig. 1) and up to 30 MeV (back of box; Fig. 1). The latter is typically slated for the production of ^{68}Ge using a metal gallium target. The former slot has been relatively unused since its energy is often too high for the optimal production of large quantities of radioisotopes. It is hypothesized that significant quantities of ^{72}Se could be produced using the 96-106 MeV slot at the BLIP, however little is known on the cross section for the production of $^{72,75}\text{Se}$ at energies greater than 50 MeV on natural arsenic containing targets.^{7,8}

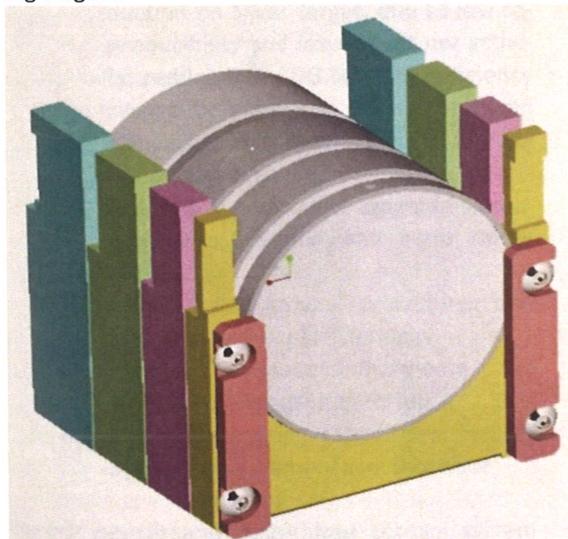


Figure 1. Model of the target box array used at the BLIP.

Material and Methods

Cross section data from 50-105 MeV were measured using commercially available gallium arsenide disks, 2.0" dia. x .005" thick (University Wafer; Boston, MA) and high purity (99.999%) 0.001" thick aluminum as monitoring foils (Alfa Aesar; Ward Hill, MA). Gallium arsenide disks and aluminum foil were cut to a 1.1" diameter at BNL and packaged into custom target holders for irradiation (Fig. 2). Targets were irradiated for 2 h at various incident energies with a current of 37-41 $\mu\text{A}/\text{h}$ in a Gaussian beam (FWHM 10 mm). Irradiated GaAs samples were dissolved in concentrated nitric acid and 30% H_2O_2 (1:1), quantitatively transferred to a 100 mL volumetric flask with 0.1 M HNO_3 , and diluted to volume. Aluminum foils were dissolved in concentrated HCl, with a few drops of concentrated HNO_3 , and quantitatively transferred to a 50 mL volumetric flask with milliQ H_2O and diluted to volume. All samples were counted on a calibrated high purity germanium detector (Ortec; Oak Ridge, TN) in a similar geometry with dead time less than 18% for all.

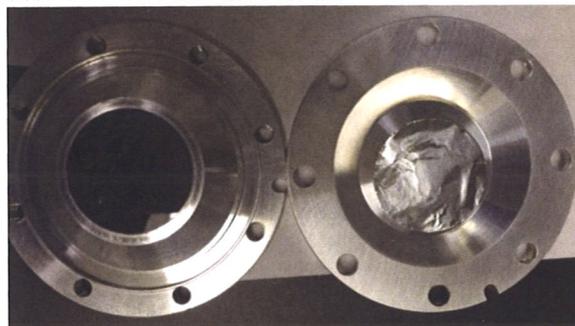


Figure 2. Custom bolted aluminum target holders containing GaAs disk (left) and aluminum foil (right) for cross section measurements.

Following cross section measurements, a production sized target (3" dia. x 0.02" thick) obtained from University Wafer was cut (2.375" dia. x 0.02" thick) on site. The target was laser welded in an aluminum can under an inert atmosphere of helium by EB Industries (Farmindale, NY) and irradiated for 72 hours at 150 $\mu\text{A}/\text{h}$ and 105 MeV in a rastered beam (FWHM 34 mm). The target was removed, dissolved as previously mentioned, and taken to dryness. After dissolving the target into 2 M NaOH and adjusting the solution to contain 0.1-0.3 M HNO_3 bulk gallium was removed using cation exchange chromatography, AG50W-X8 (Bio-Rad Laboratories; Berkeley, CA). The eluted material was taken to dryness, and dissolved into dilute

¹Anthony J. DeGraffenreid, E-mail: adegraffenreid@bnl.gov

NH₄OH, then added to an Anion exchange, AG1-X8, (Bio-Rad Laboratories; Berkeley, CA) column whereby arsenic and selenium would be retained. Bulk arsenic was selectively eluted in 0.03 M HNO₃ prior to eluting the product ^{72/75}Se in ≥0.6 M HNO₃.³

Results and Conclusion

While the cross sections for ⁷²Se production are highest at 60-80 MeV, the cross section measured at 97.5 MeV, 28.1 mb, suggest irradiation yield of >50 mCi of ⁷²Se in 72 hours at full current. Cross section data from 50-105 MeV, EOB production and chemical recovery of ⁷²Se using the production sized GaAs target as well as plans to transition to an arsenic metal target will be presented.

References

- (1) Jennewein, M.; Lewis, M. A.; Zhao, D.; Tsyganov, E.; Slavine, N.; He, J.; Watkins, L.; Kodibagkar, V. D.; O'Kelly, S.; Kulkarni, P.; Antich, P. P.; Hermanne, A.; Rosch, F.; Mason, R. P.; Thorpe, P. E. Vascular imaging of solid tumors in rats with a radioactive arsenic-labeled antibody that binds exposed phosphatidylserine. *Clinical cancer research : an official journal of the American Association for Cancer Research* **2008**, *14*, 1377-1385.
- (2) Ballard, B.; M. Nortier, F.; R. Birnbaum, E.; D. John, K.; R. Phillips, D.; E. Fassbender, M. Radioarsenic from a Portable ⁷²Se/⁷²As Generator: A Current Perspective. *Current Radiopharmaceuticals* **2012**, *5*, 264-270.
- (3) Wycoff, D. E.; Gott, M. D.; DeGraffenreid, A. J.; Morrow, R. P.; Sisay, N.; Embree, M. F.; Ballard, B.; Fassbender, M. E.; Cutler, C. S.; Ketrings, A. R.; Jurisson, S. S. Chromatographic separation of selenium and arsenic: A potential ⁷²Se/⁷²As generator. *Journal of Chromatography A* **2014**, *1340*, 109-114.
- (4) Chajduk, E.; Doner, K.; Polkowska-Motrenko, H.; Bilewicz, A. Novel radiochemical separation of arsenic from selenium for ⁷²Se/⁷²As generator. *Applied radiation and isotopes : including data, instrumentation and methods for use in agriculture, industry and medicine* **2012**, *70*, 819-822.
- (5) Ellison, P. A.; Barnhart, T. E.; Chen, F.; Hong, H.; Zhang, Y.; Theuer, C. P.; Cai, W.; Nickles, R. J.; DeJesus, O. T. High Yield Production and Radiochemical Isolation of Isotopically Pure Arsenic-72 and Novel Radioarsenic Labeling Strategies for the Development of Theranostic Radiopharmaceuticals. *Bioconjugate Chemistry* **2016**, *27*, 179-188.
- (6) Ballard, B.; Wycoff, D.; Birnbaum, E. R.; John, K. D.; Lenz, J. W.; Jurisson, S. S.; Cutler, C. S.; Nortier, F. M.; Taylor, W. A.; Fassbender, M. E. Selenium-72 formation via natBr(p,x) induced by 100 MeV Protons: Steps towards a novel ⁷²Se/⁷²As generator system. *Applied Radiation and Isotopes* **2012**, *70*, 595-601.
- (7) Mushtaq, A.; Qaim, S. M.; Stöcklin, G. Comparative evaluation of ⁷³Se-production via several routes. *Journal of Labelled Compounds and Radiopharmaceuticals* **1989**, *26*, 148-149.
- (8) Mushtaq, A.; Qaim, S. M.; Stöcklin, G. Production of ⁷³Se via (p, 3n) and (d, 4n) reactions on arsenic. *International Journal of Radiation Applications and Instrumentation. Part A. Applied Radiation and Isotopes* **1988**, *39*, 1085-1091.

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¹Anthony J. DeGraffenreid, E-mail: adegraaffenreid@bnl.gov

Production of Ti-44 from natural Scandium target at low energy at BLIP

D. Medvedev^{a,1}, V. Radchenko^b, L. Muench^a, A. Degraffenreid^a, C. Cullen^a, L. Mausner^a, C. Cutler^a

^aMedical Isotope Production group, Collider Accelerator Department, Brookhaven National Laboratory, Upton, NY, USA

^bLos Alamos National Laboratory, Los Alamos, NM, USA

Introduction

Radionuclide Ti-44 ($T_{1/2}=60$ y) and its daughter nuclide Sc-44g ($T_{1/2}=3.97$ h) form a radionuclide generator suitable for medical applications. The radionuclide Sc-44g decays by emitting positrons (mean $E_{\beta^+}=632$ keV, $I=94.27\%$) and several gamma rays of which the most abundant is 1157 keV (99.97%). These nuclear properties make Sc-44g suitable for PET imaging particularly of the processes involving proteins and peptides where the standard PET emitters are too short-lived.

There has been elevated interest in Sc-44g nuclide and its application in the last few years. The number of records returned by the Web of Science search engine is steadily above 10 per year which is appreciable for a research isotope. Research applications expanded when Sc-44(m+g) was produced on a small cyclotron using the Ca-44(p,n) reaction^{1,2}. Since metastable Sc-44m ($T_{1/2}=2.44$ d) decays primarily by internal transition (98.8%, $E_{\gamma}=271.2$ keV, 86.7%) to Sc-44g it was used as an *in-vivo* generator of Sc-44g³.

Both direct and generator routes of Sc-44g production are challenging. While the direct route requires highly enriched target material (2.09% natural abundance), the Ti-44 production route requires long irradiation times and high beam current. The excitation function for the $^{45}\text{Sc}(p,2n)^{44}\text{Ti}$ reaction exhibits a broad peak between 35 and 15 MeV reaching 45 mbarns at about 28 MeV (Figure 1).

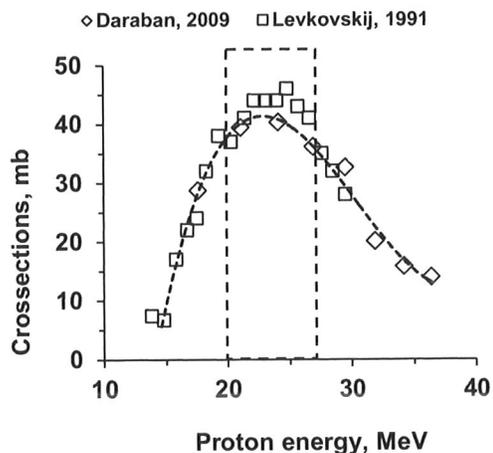


Figure 1. Excitation functions for the $^{45}\text{Sc}(p,2n)^{44}\text{Ti}$ reaction. The dotted rectangular indicates the energy range captured by the Sc target irradiation.

diated in this work.

Due to relatively low cross sections and the long half-life of Ti-44 dedicated irradiations aiming to produce only this isotope may not be practical. To date there have been only a couple of instances of dedicated Ti-44 production when ~ 1.5 g of Scandium was irradiated^{4,5} and only one of those was carried out to produce Ti-44 for generator use⁵.

Brookhaven (BNL) and Los Alamos National laboratories (LANL) operate high energy/high current linear accelerators whose mission in part is to support radioisotope production. Brookhaven Linac Isotope Producer (BLIP) at BNL and its sister program Isotope Production Facility (IPF) at LANL utilize proton energy from ~ 93 MeV down to 40 MeV to produce the PET radioisotope Sr-82. The energy slot below 40 MeV is suitable for (p,2n), (p,n) reactions if the excitation function peak of the target isotope is well separated from those of the undesirable impurities. Irradiation of Ga metal targets aiming to produce Ge-68 has been carried out in both facilities in this manner. With the increase of Ge-68 availability from private industry the low energy slot at BLIP has been mainly occupied by a Copper beam stop. Under these circumstances production of a long lived radionuclide like Ti-44 in this slot is advantageous.

The challenges associated with this approach are of a physical and chemical nature. To fully stop the beam of 30-35 MeV of protons the Sc target has to be substantial (tens of grams) and be able to withstand the energy deposition of 30-35 Watt per each μA of beam current.

This amounts to ~ 5.7 kW of power at 165 μA beam current achievable at BLIP. Since Sc thermal conductivity is low (15.8 W/m.K compared to Cu 401 W/m.K) long term survival of the target under these conditions remains uncertain.

Further, while Filosofov et al⁵ successfully separated Ti-44 by retaining 1.5 g of Sc on two cation exchange columns, a multigram target approach will require either multiple steps or substantial quantity of the resin.

In this paper we report the results of irradiation of a massive 17.5 g Sc target at the low energy slot at BLIP. The target was used to assess the yield and feasibility of production as well as to

¹Corresponding author, E-mail: dmedvede@bnl.gov

produce Ti-44 for chemical processing and generator development. Since Titanium adsorbability in the form of anionic complexes in >11M HCl solutions has been reported^{4,6} separation of Ti/Sc by adsorption of Ti has been tested in this work first. In the middle of the project we became aware of exceptional selectivity for Ti over Sc by the novel extraction chromatography resin (Zr resin) developed by Triskem International (Bruz, France). Preliminary data for the separation using this resin is reported here.

Material and Methods

Targetry and irradiation

Scandium (TREM>99.92%, Sc/TREM>99.99%) metal was purchased from Symcon® (Charlotte, NC, USA). The disk d×h=2.38×0.060 inch (60.45×1.52 mm), 17.5 g was electron beam welded in an Aluminum can with 0.020 inch (0.508 mm) windows. The target was irradiated with a focused proton beam having a Gaussian profile (FWHM 17 mm) in the low energy slot behind RbCl targets for 7 days at 116 μA.

Target cooling was facilitated by constant water flow along the can windows. The propagation of proton energy through the target stack was calculated using dE/dx tables generated by SRIM 2013. The calculated proton energy for the Sc disk was 27.3→20.1 MeV (Figure 1). Theoretical yield was estimated using an activation equation based on cross section data reported by Daraban⁷ and Levkovskij⁸

Target dissolution and processing

After irradiation the Aluminum can was cut open and the Sc disk was dissolved in 2N HCl exceeding stoichiometric amount. The resulting solution was filtered and the filtrate (92.3 mL) was assayed by gamma spectroscopy. Ti-44 activity was determined using both 78.3 keV (96.4%) peak emitted directly by Ti-44 and Sc-44g 1157 keV peak. The measurements were carried out >40 days after end of bombardment after directly produced Sc-43, Sc-44, Sc-44m decayed.

About half of the solution was evaporated to dryness and brought up in 12.3 N HCl (150 ml) to carry out Ti-44 separation in highly acidic HCl media. A total of 3 anion (AG1-X8 200-400 mesh) exchange columns (18, 30 and 40 ml) were used for process development. Elution of Ti-44 was carried out with 8 N HCl. When the amount of Sc was reduced to mg levels, Ti-44 was further purified using cation exchange column in 1N HCl, where Sc was adsorbed and Ti was not.

The remaining unprocessed half of Sc target solution was used to develop separation on Zr resin (TRISKEM). Adsorption of Ti-44 on 7 ml bed volume column was carried out with 2N HCl. A solution of 132 ml containing 6.5 g of Sc was loaded in 2N HCl. The radioisotope Ti-44 was eluted using 0.2 N oxalic acid, followed by 2N HCl-2.5% H₂O₂ solution.

Collected fractions in both separation processes were assayed by gamma spectroscopy. Distribution of stable Sc in the fractions was followed using Sc-46 (E_γ=889.3 keV, I=99.98%, T_{1/2}=83.79 d). Ti-44 was quantified using Sc-44. The later was allowed to grow in for the period exceeding 10 half-lives before the assay.

Results and Discussion

After irradiation the Sc target exhibited an insignificant heat mark in the center. This was anticipated as the beam was stopped in the water gap behind the target. In addition to Ti-44 a substantial quantity of Sc-46 was generated by secondary neutrons (Table 1).

Nuclide	Activity at EOB, mCi (MBq)	
	Ti-44	0.48 (14.8) via 78.32 keV
Sc-46	307.7 (11385)	

Table 1. Activities of isotopes in the Sc target.

The Sc-46 gamma emissions were the major contributors to the dose rate hence the target solution was handled inside a hotbox.

The measured irradiation yield of Ti-44 was about 50% of the expected theoretical prediction (1.06 mCi). This may be due to several factors, such as uncertainty in energy propagation calculation, proton straggling as well as beam adsorption upon propagation through the target stack with uncertainty in energy being the most significant contributor. The Sc target was designed to capture only the cross section peak of the ⁴⁵Sc(p,2n)⁴⁴Ti reaction, hence there was uncertainty in both the entrance and exit energy.

Irradiation of a target thick enough to stop the proton beam may result in a higher irradiation yield of Ti-44 as the uncertainty in the exit energy will be eliminated and a larger portion of the cross section curve will be captured.

The extent of benchtop experiments for Ti-44/Sc separation chemistry development was limited by the high cost of Scandium. Therefore, most of the process optimization was carried out with

¹Corresponding author, E-mail: dmedvede@bnl.gov

the irradiated target. The 18 and the 30 ml columns were loaded with increasing amounts of Ti/Sc solution in 12.3 N HCl until Ti-44 breakthrough was observed. The process was performed successfully on a 40 ml column (Table 2).

	Bed volume	Ti-44	Sc-46
Load	2.1	n/d	52.4%
Wash	2.1	n/d	45.0%
Elution	3.5	90.0%	0.08%

Table 2. Distribution of Sc-46 and Ti-44 on a 40 ml anion exchange column. Solution contained 3.4 g of Sc.

The remaining 0.08% of Sc was removed with a cation exchange column. Based on ICP-OES analysis the final Ti-44 solution contained: Cu 4.83 mg, Ca 2.32 mg. Both of these elements originated from the Sc target material which had 10 ppm of Ca, and 30 ppm of Cu based on certificate of analysis.

The 7 ml Zr resin column demonstrated excellent selectivity for Ti-44 over Sc (Figure 2).

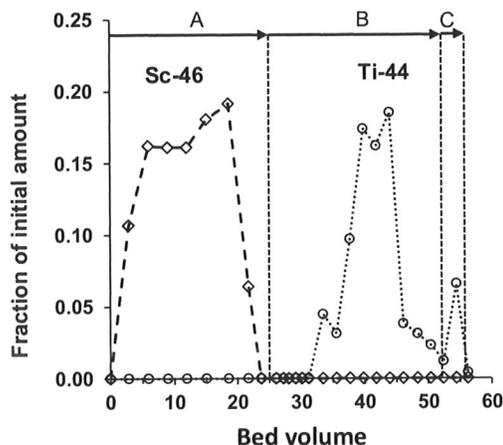


Figure 2. Loading and elution profile of Ti-44 and Sc-46 on Zr resin. The solution contained 6.5 g of Sc. Solvents: A-2N HCl, B-0.2 M oxalic acid, C-2N HCl-2.5% H_2O_2

No Ti-44 breakthrough was observed during the solution loading and washing steps. The total elution volume of 0.2 N oxalic acid was however substantial (30 bed volumes). This preliminary data indicates that a combination of hydrogen peroxide and HCl may elute Ti-44 more efficiently.

Conclusions

The low energy slot at BLIP offers opportunities for production of Ti-44 for a Ti-44/Sc-44g generator. Disks of Sc-45 of various sizes and purities can be purchased and used for irradiation. With development and implementation of the raster system at BLIP the Sc target will tolerate higher beam currents.

Chemical separation of Ti in highly acidic media was successful but generated a lot of highly acidic waste. Separation using Zr resin looks very promising. The purification from Sc was close to 100%. Additional work is required to decrease the elution volume of Ti-44 from the column.

References

1. G. W. Severin, J. W. Engle, H. F. Valdovinos, T. E. Barnhart and R. J. Nickles, *Appl. Radiat. Isot.* **70** (8), 1526-1530 (2012).
2. S. Krajewski, I. Cydzik, K. Abbas, A. Bulgheroni, F. Simonelli, U. Holzwarth and A. Bilewicz, *Radiochimica Acta* **101** (5), 333-338 (2013).
3. C. Alliot, R. Kerdjoudj, N. Michel, F. Haddad and S. Huclier-Markai, *Nuclear Medicine and Biology* **42** (6), 524-529 (2015).
4. R. Lange, J. D'Auria, U. Giesen, J. Vincent and T. Ruth, *Nuclear Instruments & Methods in Physics Research Section a-Accelerators Spectrometers Detectors and Associated Equipment* **423** (2-3), 247-255 (1999).
5. D. V. Filosofov, N. S. Loktionova and F. Rosch, *Radiochimica Acta* **98** (3), 149-156 (2010).
6. K. A. Kraus, F. Nelson and G. W. Smith, *The Journal of Physical Chemistry* **58** (1), 11-17 (1954).
7. L. Daraban, R. Adam Rebeles, A. Hermanne, F. Tarkanyi and S. Takacs, *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms* **267** (5), 755-759 (2009).
8. V. N. Levkovskij, in *Activation cross sections by protons and alphas*, edited by V. N. Levkovskij (Inter-Vesny, Moscow, 1991).

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¹Corresponding author, E-mail: dmedvede@bnl.gov