



# ***Horizon-broadening Isotope Production Pipeline Opportunities (HIPPO)***

*Poster Session*

*Bradbury Science Museum*

*Thursday July 28th, 2022*



## **Radiometal influences on tumor targeting and biodistribution properties of NM-600 in-vivo**

Abel Sebastian, **Reinier Hernandez(PI)**

PET imaging proxies have been the standard practice in the field of nuclear oncology for the prediction of biodistribution and dosimetry of targeted radionuclide therapy agents, especially since Lutetium-177, Actinium-225, and Bismuth-213 don't have a PET imaging surrogate even though they are promising at targeted radionuclide therapy (TRT) for neuroendocrine and prostate cancers. NM-600 is an alkylphosphocholine analog containing a DO3A chelating moiety that can be radiolabeled with the aforementioned radioisotopes, and it has been used in prior studies for the PET imaging of mice models for breast cancer. The aim of this study is to elucidate the causes of differing *in vivo* pharmacokinetics due to radioisotope selection. We will radiolabel NM600 (DOTA) with  $^{64}\text{Cu}$  and  $^{86}\text{Y}$ , NM620 (DFO) with  $^{89}\text{Zr}$ , and NM630 (NOTA) with  $^{64}\text{Cu}$ . Log P/D and HPLC will be carried out with each radiolabeled compound to assess the differences in polarity and radio stability respectively. The potential to be gathered from this study is the behavior of therapeutic analogs radiolabeled with various PET radioisotopes.



## **Measuring astatine-211 yield using a CdTe detector**

Alexandra Tabacaru, Lauren McIntosh and Sherry J. Yennello

It is important to know the amount of astatine-211 (At-211) produced by nuclear bombardment before the target is removed from the beamline, in order to protect personnel. The scope of this project is to remotely monitor the activity of At-211 produced during the time of irradiation. A Cadmium-Telluride (CdTe) detector was used for detecting the x-rays coming from the At-211 produced during the irradiation. For the experiment, CdTe spectra of a barium-133 source with a known activity were taken and then compared to previously collected At-211 spectra. MCA and Interspec software were used to analyze known At-211 peaks in these spectra. Based on previous correlations between counts in the At-211 peaks and real activity obtained after hours of irradiation, we correlate to the activity produced at different moments in time and we also understand the efficiency of the detector.



## Heavy-Ion Reaction Approach to Radionuclide Production

Anthony M. Miller, Gunnar M. Brown, Jerome Gan, Dr. Graham F. Peaslee (PI)

Positron-emitting radionuclides have been used for imaging various types of cancers. Proton, deuteron, and alpha particle accelerators have been used exclusively to produce these medical radioisotopes. However, novel radioisotopes such as  $^{76,77}\text{Br}$ ,  $^{70,71}\text{As}$ ,  $^{43,44}\text{g,44mSc}$  may benefit from production methods using heavy ions. Beams such as  $^{12}\text{C}$ ,  $^{16}\text{O}$ ,  $^{19}\text{F}$ ,  $^{28}\text{Si}$ ,  $^{32}\text{S}$ ,  $^{35,37}\text{Cl}$  incident on naturally monoisotopic targets can produce medically useful radioisotopes of interest. In some cases, these production methods demonstrate improved purity or more convenient target chemistry when compared to light ion production methods. Lists of potentially useful nuclear reactions were generated and filtered down using production rate predictions based on PACE4 and SRIM. Several reactions were selected for production rate measurements to investigate cross sections when compared to light ion methods. Preliminary thick target production rates at several incident energy between 40 and 60 MeV were measured for  $^{59}\text{Co}(^{16}\text{O}, \text{pxn})^{70,71}\text{As}$  and  $^{27}\text{Al}(^{19}\text{F}, \text{pxn})^{43,44}\text{g,44mSc}$  at the University of Notre Dame FN tandem facility, and will be reported here.



## Using Neural Networks To Predict The Density Profiles Of Isotopes

Austin Sides, Dr. Alessandro Lovato

There are over 3000 discovered radioisotopes, but only a couple hundred have known cross sections, which are the probabilities for a given reaction to occur. Terbium 155 ( $^{155}\text{Tb}$ ) is one such radioisotope and is known to emit both gamma rays and low-energy electrons called Auger electrons. Because of these properties, it shows immense promise for both therapeutic and diagnostic applications.  $^{155}\text{Tb}$ 's Auger electrons only penetrate 0.7-33  $\mu\text{m}$  into human tissue-comparable to the diameter of a human cell. With this property,  $^{155}\text{Tb}$  can be used for extremely precise cancer therapy because it targets the tumor itself while the surrounding healthy cells remain largely unaffected.

Neural Networks take a defined set of inputs, and through layers of digital neurons and their connections, produce a spread of data. Through training the network against a set of known data, neural networks can learn to recognize patterns and produce an output with considerable accuracy. In this work, we trained a digital neural network to reproduce the density profiles of known nuclei and predict those of  $^{155}\text{Tb}$  and  $^{156}\text{Gd}$ , the latter nucleus being useful to make  $^{155}\text{Tb}$  in fusion-evaporation reactions.

As a follow-up of this project, we plan on using neural networks to directly make predictions for compound nucleus reactions useful for  $^{155}\text{Tb}$  production. With this increased production of  $^{155}\text{Tb}$ , the radioisotope can be distributed for further research for the advancement of cancer treatments.



## Auger-Emitting Lanthanides for Radiobiological Studies.

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<sup>177</sup>Lu-PSMA-617 (Pluvicto™) and <sup>177</sup>Lu-DOTATATE (Lutathera®) are radiopharmaceuticals recently approved by the FDA for the treatment of prostate cancer and neuroendocrine tumors. <sup>177</sup>Lu (t<sub>1/2</sub>= 6.65d) is a β<sup>-</sup>-emitting radiolanthanide that's similar in chemical structure to other radiolanthanides, one of the most notable being <sup>161</sup>Tb (t<sub>1/2</sub>= 6.89d). The primary difference between <sup>177</sup>Lu and <sup>161</sup>Tb is the latter's co-emission of 12-13 conversion and Auger electrons (CAEs) per decay<sup>1</sup>. Radionuclides that emit high intensity, low energy CAEs have shown promise for cancer therapy due to their high linear energy transfer and short range<sup>2</sup>. This is advantageous due to the deposition of a high amount of radiation along a small path while minimizing the crossfire effect. To assess the advantages of these Auger emissions, radiobiological studies are necessary using radionuclides with primarily CAE emissions, such as <sup>165</sup>Er (t<sub>1/2</sub>=10.36h, 7–8 CAEs/decay), which can be produced by low energy cyclotron irradiation of holmium<sup>3</sup>. However, for radiobiological studies, the relatively short half-life of <sup>165</sup>Er can often be a limiting factor. Longer-lived Auger electron emitting lanthanides such as <sup>167</sup>Tm (t<sub>1/2</sub>= 9.25d, 13-14 CAEs/decay) and <sup>169</sup>Yb (t<sub>1/2</sub>= 32.03d, 29-30 CAEs/decay) may therefore prove useful in the investigation of Auger therapy.

An Excel-based tool for calculating nuclear reaction activity yield was created using experimental and TALYS-evaluated cross section values from TENDL<sup>4</sup>, proton stopping range values from SRIM<sup>5</sup>, target thickness, beam energy, beam intensity, radionuclide half-life, and length of irradiation. This was used to calculate <sup>165</sup>Er activity from the Ho(p,n)<sup>165</sup>Er nuclear reaction and these values were compared to those obtained using the IAEA Yield Calculator<sup>6</sup>. This program was then adapted to calculate <sup>167</sup>Tm activity from the Yb(p,2n)<sup>167</sup>Lu(β<sup>-</sup>)<sup>167</sup>Yb(β<sup>-</sup>)<sup>167</sup>Tm nuclear reaction and decay chain. This allowed insight into a low-energy cyclotron's ability to produce these longer-lived CAE-emitters. Using ICRP Nuclear Decay Data<sup>1</sup>, the electron and photons emitted through these radionuclide's decay were tabulated by their intensities, energies, tissue ranges, and linear energy transfer to understand the biological implications of their decay properties. In preparation for radiochemical separation experiments, a laboratory method of



quantification of ppm-level lanthanides in nitric acid solutions was developed. This method utilized Arsenazo III dye to complex the lanthanide and allow for absorbance measurement by UV-Vis spectrophotometer at 652 nm.

When using identical excitation functions for  $\text{Ho}(p,n)^{165}\text{Er}$ , the Excel-based program and IAEA Yield calculator agreed on  $^{165}\text{Er}$  activity production yield with an error of 1-3%. However, when applied to a more complex nuclear reaction and decay scheme such as  $\text{Yb}(p,2n)^{167}\text{Lu}(\beta^-)^{167}\text{Yb}(\beta^-)^{167}\text{Tm}$ , which involves the cyclotron production of a grandparent nuclide that decays to the radionuclide of interest, there is a ~700% disagreement between the IAEA calculator and the in-house developed Excel-based program.

The results demonstrate that it is possible to produce longer-lived Auger-emitting lanthanides for radiobiological testing using a low energy cyclotron. Although possible, production of other long-lived radionuclides needs to be considered and weighed against the activity produced of the desired radioisotope.

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## TRIGA Reactor Production and Synergistic Separation of $^{161}\text{Tb}$ from Enriched $^{160}\text{Gd}$ Targets

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**Abstract.** Terbium-161 ( $t_{1/2} = 6.95$  days) can be produced using nuclear reactors via the indirect  $^{160}\text{Gd}(n, \gamma)^{161}\text{Gd} \rightarrow (3.7 \text{ min}, \beta^-)^{161}\text{Tb}$  using both natural and enriched  $^{160}\text{Gd}$  targets. Significant yield depression using natural gadolinium targets ( $0.23 \mu\text{Ci}/\text{mg}$ ) was observed because of self-shielding due to the high neutron absorption cross-section of  $^{157}\text{Gd}$  compared to enriched  $^{160}\text{Gd}$  ( $5.69 \mu\text{Ci}/\text{mg}$ ) targets. Synergistic dual extractant liquid systems have been investigated to facilitate the Gd/Tb lanthanide separation using combinations of  $\beta$ -diketones and neutral extractants in 1,2-dichloroethane from  $\text{pH}$  0 – 3. Extraction was measured using radiotracer methods, UV-VIS spectroscopy, and inductively coupled plasma mass spectrometry (ICP-MS). In every  $\beta$ -diketone and neutral extractant combination, extraction efficiency increased over a range of acid concentrations depending on  $\text{p}K_{\text{a}}$  values of the  $\beta$ -diketone.

**1. Introduction.** One radionuclide of interest to nuclear medicine is terbium-161 ( $^{161}\text{Tb}$ ), which decays by beta emission and has similar beta decay properties as  $^{177}\text{Lu}$  (FDA approved as LUTATHERA<sup>®</sup>). In addition to beta emission,  $^{161}\text{Tb}$  emits a substantial number of conversion and Auger electrons.[1, 2] Auger electrons are of high interest in nuclear medicine because of the advantages over traditional beta therapy for the potential treatment of metastatic and disseminated disease. [3] The  $\beta^-$  particle ( $\beta_{\text{max}} = 518 \text{ keV}$ ) emitted from  $^{161}\text{Tb}$  has a low linear energy transfer (LET) depositing their energy over a long range (0.2 – 5 mm) in tissue. The Auger electrons emitted from  $^{161}\text{Tb}$  have high LET (1 – 10 keV/ $\mu\text{m}$ ), short ranges (0.1 – 50  $\mu\text{m}$ ) in tissue, and have been shown to provide a 2 – 3 fold increase in dose over  $^{177}\text{Lu}$  for distances between 10 – 100  $\mu\text{m}$  from the location of decay.[4] The production of  $^{161}\text{Tb}$  is achieved using nuclear reactors via the indirect method,  $^{160}\text{Gd}(n, \gamma)^{161}\text{Gd} \rightarrow (3.7 \text{ min}, \beta^-)^{161}\text{Tb}$ . One of the challenges with implementing  $^{161}\text{Tb}$  in nuclear medicine is separating target and product material to obtain high specific activity. Hundreds of liquid and solid phase systems have been investigated for adjacent lanthanide separations, but most systems fail to achieve selectivity in their separation. One technique for achieving enhanced separation is employing dual extractant systems that display synergism in separation and extraction efficiency.



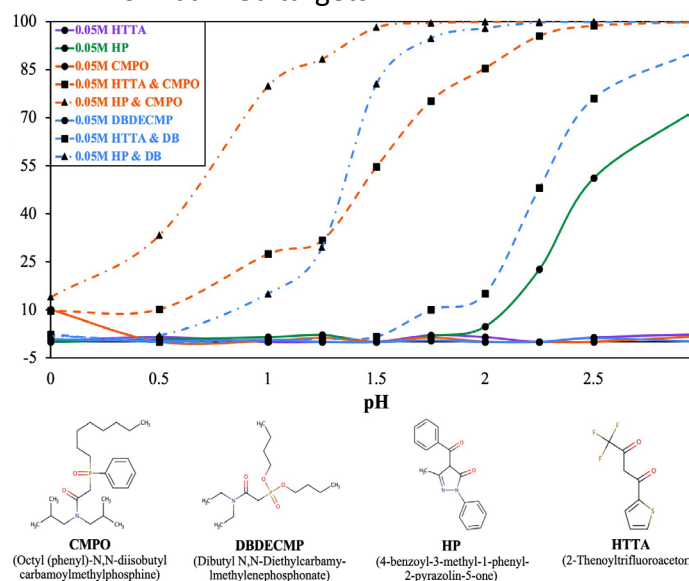


**2. Method & Materials.** Enriched  $^{160}\text{Gd}$  (10.0 mg) and Natural Gd (50.0 mg) targets were irradiated in the central irradiator at the University of Utah's TRIGA reactor at 90 kW for 3 hours. Theoretical yields were calculated employing a 16-group energy flux using a 3D Transport model. Experimental yields were measured via HPGe spectroscopy utilizing characteristic gamma rays for  $^{161}\text{Tb}$ . Extraction behavior of  $\text{Tb}^{3+}$  and  $\text{Gd}^{3+}$  in liquid-liquid systems was evaluated using extractants ( $\beta$ -diketones and neutral) alone and in combination at 0.05M in 1,2-dichloroethane. The extraction for terbium was evaluated using radiotracer  $^{160}\text{Tb}$ , while gadolinium extraction was evaluated using UV-VIS methods and Arsenazo III dye. Extraction was studied as a function of pH and extractant concentrations.

**3. Results & Discussion.** The experimental yield of  $^{161}\text{Tb}$  from natural targets was 11.62  $\mu\text{Ci}$  compared to the theoretical yield of 65.00  $\mu\text{Ci}$ . The experimental yield of  $^{161}\text{Tb}$  from enriched  $^{160}\text{Gd}$  targets was 56.89  $\mu\text{Ci}$  compared to the theoretical yield of 59.00  $\mu\text{Ci}$ . The low experimental yield in natural targets is caused by significant target self-shielding caused by the high neutron capture cross sections of  $^{155}\text{Gd}$  and  $^{157}\text{Gd}$ . Extraction with combined neutral and  $\beta$ -diketones synergistically increased extraction across all studied pH values. The  $\beta$ -diketone HP showed greater increase in extraction efficiency with > 95% from pH 1.5 – 3.0, whereas HTTA only achieved > 95% at pH 2.25 – 3.0. Preliminary separation factors give 1.35 for the CMPO/HP system and 1.52 for the DBDECMP system both at pH 1.50. Experiments are underway to determine the optimal ligand concentration

**4. Conclusion.** The dual ligand systems studied demonstrate synergistic extraction of Tb and Gd from nitric acid solutions ranging in pH from 1-3. Experiments are currently underway to determine optimum conditions (pH, ligand concentration) for the enhanced separation of Tb from Gd. Furthermore, conversion to a solid phase extraction chromatographic system is being explored as

and pH for maximum separation of  $^{161}\text{Tb}$  from bulk Gd targets.



Neutral Extractant +  $\beta$ -Diketone Extractant = Synergism

**Figure 1:** This figure shows the extraction percentage of  $\text{Tb}^{3+}$  (stable and  $^{160}\text{Tb}$  as a radiotracer) as a function of pH from a nitric acid medium with various extractants dissolved in 1,2-Dichloroethane.



these systems further enhance separation factor and significantly minimize mixed solvent waste.[5]

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## Solid-phase isotope harvesting of $^{88}\text{Zr}$

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During routine operation of the Facility for Rare Isotope Beams (FRIB), high-purity radioactive ion beams will be produced for nuclear science research experiments. During the beam purification process, byproduct radionuclides will accumulate along the beamline. There is interest in collecting, purifying, and using these radionuclides in a process called isotope harvesting. Preliminary isotope harvesting efforts have been ongoing at the National Superconducting Cyclotron Laboratory (NSCL), such as the aqueous collection of  $^{24}\text{Na}$ ,  $^{47}\text{Ca}/^{47}\text{Sc}$ ,  $^{48}\text{V}$ ,  $^{62}\text{Zn}$ ,  $^{67}\text{Cu}$ , and  $^{88}\text{Zr}$ . In this work, the viability of isotope harvesting using solid collection of  $^{88}\text{Zr}$ , an isotope relevant to stockpile stewardship, was examined by performing a proof-of-concept experiment at the NSCL where  $^{88}\text{Zr}$  beam was stopped in a series of collectors comprised of Al, Cu, W, and Au.  $^{88}\text{Zr}$  was radiochemically recovered from each of these collectors with yields exceeding 80% and decontamination factors on the order of  $10^5$  using a combination of solvent extraction and ion-exchange chromatography. Results of the harvesting experiment and the radiochemical recovery of  $^{88}\text{Zr}$  and its decay product  $^{88}\text{Y}$  from Cu and Al collectors will be discussed. For elements of interest that readily hydrolyze in near-neutral pH aqueous conditions, such as Zr, harvesting through solid-phase collection has been shown to result in higher recovery yields compared to aqueous harvesting.



## Mild and stable chelation strategies for small, rare earth radiometals

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Targeted nuclear medicine is an emerging clinical paradigm that harnesses radioactive isotopes for imaging and therapy by capitalizing on differential target expression of diseased and healthy cells. Development of clinically applicable radiopharmaceuticals requires carefully matching the physical half-life of the radioisotope with the biological half-life of the targeting vector to ensure optimal target accumulation within a relevant timeframe. Radioisotopes of scandium exhibit decay properties ideally suited for targeted imaging and therapy with small biologics, such as minibodies and fabs. Namely, <sup>43</sup>Sc ( $E\beta^+_{avg} = 476$  keV,  $t_{1/2} = 3.9$  h) and <sup>44</sup>Sc ( $E\beta^+_{avg} = 632$  keV,  $t_{1/2} = 4$  h) enable prolonged positron emission tomography (PET) imaging up to 24 hours post injection, while the emission properties of <sup>47</sup>Sc ( $E\beta^-_{avg} = 162$  keV,  $t_{1/2} = 80.4$  h) are well-suited for subsequent therapeutic intervention. However, strategies to chelate scandium isotopes under conditions compatible with thermally sensitive biologics to afford inert complexes is critically lacking.

Currently, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) is considered the gold standard Sc<sup>3+</sup> chelator, but the slow complexation kinetics require radiolabeling at 80 °C for at least 30 minutes. To overcome this, we rationally designed a triaza-macrocyclic derived chelator, L2, that is well-matched to the ionic radii and coordination preferences of Sc<sup>3+</sup>, as supported by computational studies and pH-dependent UV speciation. Radiolabeling studies with <sup>44</sup>Sc at room temperature indicate that L2 affords a 250-fold increase in apparent molar activity relative to our first-generation chelator, L1, and a 3-fold increase relative to DOTA at 80 °C. Room temperature scandium chelation enables us to explore radiolabeling of temperature sensitive targeting vectors, expanding the scope of potentially imageable and treatable disease targets.



## Photonuclear Production of the Theragnostic Agent $^{47}\text{Sc}$ from Natural Ti Targets

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Theragnostic medical radioisotopes have been of growing interest in the past decade, as they boast the ability to both allow diagnostic imaging as well as localized treatment of tumors.

Scandium-47 is an example of a theragnostic, with promising gamma-ray (159 KeV, 100%) and beta-particle emissions ( $E_{\text{avg}}$ ,  $\beta^-$  =162 keV) suitable for diagnostic and therapeutic applications in cancer treatment. The photonuclear production of  $^{47}\text{Sc}$  is being developed at Argonne National Laboratory. Natural Ti targets are irradiated (40 MeV, 3 kW, 10-12 hrs) and radioisotopes of Sc ( $^{46,47,48}\text{Sc}$ ) are isolated using DGA resin. Subsequent analyses of the  $^{47}\text{Sc}$  product with high purity germanium detectors (HPGe) and inductively coupled plasma mass spectrometer (ICP- MS) revealed high chemical purity product. The product was further analyzed by DOTA (2,2',2'',2'''-(1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetrayl) tetraacetic acid) titrations and provides high apparent molar activity (AMA). Advantages and drawbacks of the production method will be discussed.

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## Lanthanide Target Foils for the Exploration of Targeted Alpha Therapy Isotope Production Mechanisms

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Targeted alpha therapy (TAT) is rapidly coming to the frontiers of radiotherapeutic cancer research due to its high cell mortality rate when localized to the cancer site via a targeting agent. While radium-223, actinium-225, and astatine-211 are at the forefront of this research, all of these isotopes require separate isotopes for imaging (theragnostic pairs), since their alpha decays cannot be imaged outside of the body. A lesser known prospect for TAT is terbium-149, which decays via both positron and alpha emission, allowing it to be its own theragnostic pair, and eliminating the need for an imaging analog. However, it does not yet have a well-established production pathway via direct reaction. In order to probe potential reaction mechanisms for its production, a series of experiments will be executed which require the production of isotopically enriched samarium and gadolinium targets. Since there are few locations with the expertise and equipment to produce such targets, a collaboration was established between Texas A&M University (TAMU) and Argonne National Laboratory (ANL) to develop these targets using vapor deposition techniques. Lanthanide targets can be particularly challenging to produce, given the availability of the starting material as the metal oxide, and the high melting points of these compounds. Samarium is considered a low-melting point lanthanide, and therefore targets were produced via in-situ reduction with zirconium via vapor deposition. Targets were made on an aluminum backing, and self-supporting targets were also explored and able to be produced. Gadolinium is a high-melting point lanthanide making vapor deposition techniques difficult, so other methods such as electrodeposition are being explored for the production of these targets.



## Development and assessment of new resin materials for the efficient separation of Ti and Sc isotopes

Mariae Robis, Eszter Boros

The  $^{44}\text{Ti}/^{44}\text{Sc}$  generator has potential for clinical use in the production of  $^{44}\text{Sc}$ , a positron emitting radioisotope with a half-life of 4 hours. However, the state-of-the-art  $^{44}\text{Ti}/^{44}\text{Sc}$  generator technology is not suitable for clinical use due a) breakthrough of the long-lived parent isotope  $^{44}\text{Ti}$  b) the requirement of large elution volumes, and/or elution conditions that require post-processing to provide the  $^{44}\text{Sc}$  in a ready to use form. Therefore, there is a need to develop improved generator designs that efficiently address these shortcomings.

Towards the development to new  $^{44}\text{Ti}/^{44}\text{Sc}$  generators, we have designed 4 novel chelator-based resins which exploit the different solution behavior of Sc(III) and Ti(IV) ions. These novel resins have been evaluated for (i) their binding affinity for Sc and Ti in various acid media, (ii) their kinetic stability to retain Ti on resin, and (iii) the effect of trace metal contamination on ion separation. Inductively coupled plasma optical emission spectroscopy (ICP-OES) was used to quantify the degree of binding, as well as kinetic stability and stripping conditions for the various resins with citric acid, oxalic acid, and hydrochloric acid containing mobile phases.



## Comparing Efficiencies of $^{48}\text{Ca}$ Calcium Metal Removal and Recovery Methods

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The neutron abundant  $^{48}\text{Ca}$  isotope has a very low natural occurrence (0.187%). Highly enriched starting material for the production of nuclei in particle accelerators including the Argonne Tandem Linac Accelerator System (ATLAS) is exceptionally valued. We aim to recover enriched  $^{48}\text{Ca}$  metal from a mixed  $\text{CaCO}_3+\text{Zr}$  sample with unknown quantity of  $^{48}\text{Ca}$ . The goal is to carry out two chemical reactions within a standard ECR ion source resistively heated oven. A sample of natural  $\text{CaCO}_3+\text{Zr}$  with a ratio 1:2 of Ca:Zr by mass was prepared. An oven temperature calibration with power input set values was performed prior to baking the sample, expelling  $\text{CO}_2$  in a gaseous state and yielding  $\text{CaO}$  which is then reduced at a slightly higher temperature via reduction with Zr metal to form Ca metal and  $\text{ZrO}_2$ . The Ca metal is evaporated to a small area of a pre-weighed tantalum deposition plate while the  $\text{ZrO}_2$  remains in the oven crucible. The process was repeated using a resistively heated vapor deposition system to record and compare both Ca metal production efficiencies with a goal of finding a process for use with the enriched  $^{48}\text{Ca}$  material. In the vapor deposition system, a  $\text{CaCO}_3$  and Zr mixture with the same ratio is pressed and placed in a tantalum pinhole boat, which creates a directional vapor of Ca metal under high temperature. The Ca is deposited onto a pre-weighed glass substrate and reweighed after deposition to determine the Ca mass. Calcium metal recovery efficiencies will be reported.





## Liquid-liquid Extraction of Vanadyl as a Probe of Vanadium's Suitability as a Surrogate for Astatine

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The rapidly growing field of radiopharmaceuticals, specifically Targeted Alpha Therapy (TAT) agents, has necessitated the development of new radionuclides to treat various types of cancer. One promising isotope is At-211, currently of interest due to its simple decay scheme, stable granddaughter nuclei, and short half-life (roughly 7.2 h). Inquiry into At chemistry has been complicated by the lack of a stable, or long-lived isotope, where At-210 is the longest lived ( $t_{1/2} \sim 8.1$  h). This requires not only very efficient systems for separation and purification, but also that studies occur near facilities capable of synthesizing At-211. Along with its halogen-like properties, At also possesses metallic character, forming the unique oxocation  $\text{AtO}^+$  in acidic conditions. Knowing this, a non-radioactive chemical surrogate would allow for separation systems to be more extensively screened; the vanadyl cation,  $\text{VO}^{2+}$ , has a similar geometry to that of  $\text{AtO}^+$ , while only having metallic properties, as its frontier orbitals are d-orbitals compared to the p-orbitals of  $\text{AtO}^+$ . This project looks to probe the suitability of  $\text{VO}^{2+}$  as a surrogate for  $\text{AtO}^+$  by comparing the extraction behavior of both oxocations into either 1-octanol or 3-octanone from either nitric or hydrochloric acid.



## Development of Nanoparticles for Radionuclide Generator Systems of Alpha Emitting Radionuclide Pairs

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Radionuclide generator systems give access to short-lived radionuclides for basic research and clinical use. Traditional radionuclide generators use resin to bind the parent radionuclide and then elute the daughter after it grows in. When this is done with large activities of alpha emitting radionuclide pairs, like  $^{225}\text{Ac}/^{213}\text{Bi}$  and  $^{230}\text{U}/^{226}\text{Th}$ , the resin degrades due to the high linear energy transfer (LET) of the alpha particles causing the generator to fail. During alpha decay,  $\sim 100$  keV of kinetic energy is imparted to the daughter radionuclide causing it to travel significant distances from the point of decay. This process can be exploited to separate the parent from daughter radionuclides by trapping the parent radionuclide in a nanoparticle that is small enough to allow the daughter to escape. Super paramagnetic iron oxide nanoparticles (SPIONs) are of particular interest because they can be rapidly precipitated with a strong magnet allowing for the separation of the nanoparticles from the released daughter radionuclides in solution, and their metal framework may prove more radioresistant than organic based resins. To prevent the release of  $^{225}\text{Ac}$  from the SPIONs, we investigated adding a thin layer of gold coating. One potential issue is that daughter radionuclides ejected from one nanoparticle may implant into another, decreasing the amount that is recoverable. Monte Carlo simulations were performed with SRIM (Stopping and Range of Ions in Matter) to estimate the distance the ejected daughter radionuclides travel in water to determine the optimal number of nanoparticles per volume that minimizes reimplantation. Furthermore, the addition of PEG molecules to the surface of the Au-SPIONs was investigated to prevent nanoparticle aggregation in solution. Future research will investigate the recovery of  $^{213}\text{Bi}$  and  $^{226}\text{Th}$  while monitoring for any degradation of the nanoparticles.



## **Establishing Solvent Extraction Conditions with Tri-Butyl Phosphate for the Study of the Effects of Radiolysis on Pertechnetate Speciation**

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The build-up of tributyl phosphate (TBP) degradation compounds has been proven to reduce separation of U from fission products, but specific causes of this are poorly understood. To address this gap in fundamental knowledge, TBP degradation species and the radiolysis-induced redox chemistry of Tc must be studied with respect to their impact on separations under used nuclear fuel (UNF) reprocessing conditions. The work herein will detail the optimization of solvent extraction for Tc and other major fission products (Ce, Zr, U) in the HNO<sub>3</sub>/TBP/dodecane system, alongside the presence of TBP degradation compounds. Subsequent irradiation by <sup>60</sup>Co and characterization by IR, XAS, and multinuclear NMR will provide Tc extraction as a function of oxidation state for these systems. Deepening the understanding of Tc speciation in these conditions may influence the recovery valuable early actinides from used nuclear fuel

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## A Theranostic Application of Cobalt-55/58m

Wilson Lin, Jonathan W. Engle, Suzanne E. Lapi

### Background:

Neurotensin receptors (NTSR1,2,3) are known for stimulating tumor proliferation through neurotensin (NTS) activation and are expressed by a variety of cancers including breast, pancreatic, prostate, colon and non-small cell lung cancers. The high binding affinity, internalization efficiency and internalization rate of the NTS/NTSR1 complex make radiolabeled NTS derivatives interesting for cancer diagnosis and staging. Nuclear localization of NTS/NTSR1 also suggests therapeutic application with low energy electrons. We investigated [ $^{55,58\text{m}}\text{Co}$ ]Co-NOTA-NT20.3 (an NT analog) on NTSR1,3-positive HT29 human colorectal adenocarcinoma cells.

### Methods:

$^{55,58\text{m}}\text{Co}$  were produced via deuteron irradiation of iron and separated with ion exchange chromatography. NOTA-NT20.3 was labeled with  $^{55,58\text{m}}\text{Co}$  at pH 4.5 in 1 h at 95°C. Gentisic acid effectively mitigated radiolysis. Radiochemical purity was determined by radio-HPLC. Labelled compounds were purified and reconstituted in PBS. Neurotensin internalization rates were evaluated with [ $^{55}\text{Co}$ ]Co-NOTA-NT20.3 in HT29 cells (N=3) at a concentration of 4 nM, and surface bound activity was removed with stripping buffer (0.1 M citrate pH 2). Cytotoxicity studies incubated [ $^{58\text{m}}\text{Co}$ ]Co-NOTA-NT20.3 with HT29 cells and evaluated viability with ATP assays at 24h and 48h (N=3). IC50 was computed using GraphPad PRISM version 7.00. Female nude mice were xenografted with HT-29 cells. Nine days after tumor implantation approximately 7 MBq of [ $^{55}\text{Co}$ ]Co-NOTA-NT20.3 was administered by tail vein injection. PET imaging was performed at 1, 4, 9 and 24h post injection, then major organs were collected and quantified ex vivo to confirm image-derived uptake values.

### Results:

HPLC measured radiochemical purity of [ $^{55,58\text{m}}\text{Co}$ ]Co-NOTA-NT20.3 was >99% in all cases. [ $^{55}\text{Co}$ ]Co-NOTA-NT20.3 attained >80% of bound activity internalization in HT29 cells after 60 min. [ $^{58\text{m}}\text{Co}$ ]Co-NOTA-NT20.3 exhibited cytotoxicity for HT29 cells with IC50=7.0±4.3 MBq/mL. PET imaging with [ $^{55}\text{Co}$ ]Co-NOTA-NT20.3 showed uptake mainly in the kidneys and tumor.

### Conclusion:

We produced radiochemically pure [ $^{55,58\text{m}}\text{Co}$ ]Co-NOTA-NT20.3 suitable for in-vivo applications.



Our results demonstrate that [ $^{55,58m}\text{Co}$ ]Co-NOTA-NT20.3 exhibits specific binding and high internalization rates in NTSR1 positive HT29 cells. PET imaging quantified kidney and tumor accumulation of [ $^{55}\text{Co}$ ]Co-NOTA-NT20.3. Given the biodistribution profile and cytotoxicity data, [ $^{58m}\text{Co}$ ]Co-NOTA-NT20.3 shows potential for treatment of small cancers and warrants further research.



## **Synthesis of HOPO chelators for applications in separations of radionuclides, nuclear medicine imaging, and therapy**

Xena Soto, Prof. Lynn Francesconi (PI)

The synthesis of organic ligands plays an important role in all fields of radiochemistry including separations and nuclear medicine. For these applications, the chelator 3,4,3- L1(1,2 HOPO) is found to have strong selectivity and binding affinity to metals that are oxophilic with oxidation states of +4 and +3. In this work, the synthesis of 3,4,3- L1(1,2 HOPO), 3,3,3- L1(1,2 HOPO), and 3,2,3- L1(1,2 HOPO) was carried out. These chelators all bear four hydroxypyridinone (HOPO) groups but differ in the length of the carbon backbone chain and that difference may impact the binding and selectivity with +3 and +4 charged radiometal ions. We are synthesizing the three chelators and performing high-performance liquid chromatography, HPLC, to purify the chelators. Following that, we plan to test the binding affinity of the three chelators to metals such as Zr, Sc, and Lu and their radiometal analogs.



## Development of $^{52g}\text{Mn}$ for Diagnostic Applications in Positron Emission Tomography at UW-Madison

Yun-Hsuan Lee, Jonathan W. Engle, Kendall E. Barrett

The  $^{52g}\text{Mn}$  radionuclide has been of interest to the medical isotope production community due to promising imaging capabilities and its 6-day half-life that permits transportation. The production pathway chosen,  $^{nat}\text{Cr}(p,x)^{52g}\text{Mn}$ , not only has well-established targetry, but also facilitates  $^{52g}\text{Mn}$  production at low-energy medical cyclotrons. The  $^{52}\text{Cr}(p,n)^{52g}\text{Mn}$  cross section peaks at approximately 12 MeV and forms  $^{52g}\text{Mn}$  in high yield and purity, yet the separation and labeling processes for Mn isotopes still require further studies.

The production of  $^{52g}\text{Mn}$  ( $t_{1/2} = 5.591$  d,  $I_{\beta^+} = 29.4\%$ ,  $E_{\beta,avg} = 241.6$  keV) was observed at the University of Wisconsin - Madison GE PETtrace cyclotron [1]. Targets made of either hydraulically pressed or electroplated  $^{nat}\text{Cr}$  targets were irradiated with 12-16 MeV protons to produce the isotope of interest via the (p,n) reaction channel. Electroplating is favored for producing targets of high uniformity with powder Cr despite difficulties in recycling. After letting the undesirable  $^{52m}\text{Mn}$  ( $t_{1/2} = 21.1$  min,  $E_{\gamma} = 1434.06$  keV) decay overnight, separation of  $^{52g}\text{Mn}$  from the target material was performed through extraction chromatography [1]. The relatively higher affinity of the actinide resin for  $\text{Mn}^{2+}$  compared to  $\text{Cr}^{3+}$  in 0.01 M HCl was exploited to chemically remove impurities. Microwave plasma - atomic emission spectroscopy (MP-AES) was used to assess the purity of the final solution; three columns of AC resin effectively removes trace metals and Cr. Chelation of the isolated  $^{52}\text{Mn}$  was achieved with DOTA or other DOTA-based chelators, and the labeling was validated with thin-layer chromatography (TLC), followed by apparent molar activity (AMA) calculations. In order to reduce the chemically inseparable contamination of  $^{54}\text{Mn}$  ( $t_{1/2} = 312.20$  d,  $E_{\gamma} = 834.848$  keV) produced via the (p,n) reaction of the  $^{54}\text{Cr}$  in the  $^{nat}\text{Cr}$  targets (4.345%  $^{50}\text{Cr}$ , 83.789%  $^{52}\text{Cr}$ , 9.501%  $^{53}\text{Cr}$ , 2.365%  $^{54}\text{Cr}$ ), electroplated enriched  $^{52}\text{Cr}$  targets are currently being explored in hope of establishing a sustainable target production method [2].

[1] Yang Dong, Huo Junde, Nuclear Data Sheets **128**, 185 (2015)

[2] Yang Dong, Huo Junde, Nuclear Data Sheets **121**, 1 (2014)



## Production and Purification of $^{47}\text{Sc}$ from Natural Vanadium Targets

Putnam, E. E., Cingoranelli, S.J., Lapi, S.E.

**Objectives:** Proton irradiation on natural vanadium foils was conducted to produce high purity  $^{47}\text{Sc}$  for future radiochemical studies and development as a therapy isotope for the elementally matched “theranostic” pair of isotopes  $^{43}\text{Sc}$  and  $^{47}\text{Sc}$ .

**Methods:** Natural vanadium foils were bombarded at 24 MeV at 30  $\mu\text{A}$  for 1 h. The target was dissolved in 10 mL of 7 M  $\text{HNO}_3$ , dried down at 160  $^\circ\text{C}$  and reconstituted in 10 mL of 8 M  $\text{HCl}$ . The dissolved target was then added to an equilibrated AG MP-50 resin<sup>1</sup> followed by elutions of 20 mL of 8 M  $\text{HCl}$ , 15 mL of 4 M  $\text{HCl}$ , and 10 mL of MilliQ water to remove target material and impurities. The  $^{47}\text{Sc}$  was then collected in 4 separate elutions of 5 mL of 1 M ammonium acetate. The purity of the  $^{47}\text{Sc}$  was determined by High Purity Germanium Spectroscopy and Inductively Coupled Plasma Mass Spectroscopy. The  $^{47}\text{Sc}$  was then dried down and reconstituted in 100  $\mu\text{L}$  of 0.1 M  $\text{HCl}$ . The purified  $^{47}\text{Sc}$  and

2.5  $\mu\text{g}$  of DOTA were conjugated in 0.25 M ammonium acetate with 5  $\mu\text{Ci}$  of activity at 95  $^\circ\text{C}$ , 800 rpm, for 30 minutes. The percent complexation was analyzed using SG-iTLC page developed in 1 M citrate buffer pH 4.

**Results:** The average yield of the bombardment at 24 MeV, 30  $\mu\text{A}$  for an hour was approximately 125.2  $\pm$  4.7  $\mu\text{Ci}$ . The yield of 125.2  $\pm$  4.7  $\mu\text{Ci}$  is more than the predicted activity of 83.6  $\mu\text{Ci}$  provided by theoretical cross section calculations<sup>2</sup> for this reaction. The average recovery of  $^{47}\text{Sc}$  was approximately 89.5  $\pm$  17.6%. The vanadium target material is removed in the 20 mL of 8 M  $\text{HCl}$  and was not present within the purified  $^{47}\text{Sc}$  collection. Preliminary studies with DOTA radiolabeling showed that the utility of the  $^{47}\text{Sc}$  was promising as the iTLC depicted 100% labeling in each sample.

**Conclusions:** Pure  $^{47}\text{Sc}$  can be produced at a reasonable yield from natural vanadium foil targets with minimal impurities with a recovery of 89.5  $\pm$  17.6%. Preliminary study showed the utility of the produced  $^{47}\text{Sc}$  with DOTA radiolabeling.

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<sup>2</sup>A.J. Koning, D. Rochman, J. Sublet, N. Dzysiuk, M. Fleming and S. van der Marck, "TENDL: Complete Nuclear Data Library for Innovative Nuclear Science and Technology", Nuclear Data Sheets 155 (2019) 1



## Production of [ $^{43,47}\text{Sc}$ ] from [ $^{46,50}\text{Ti}$ ]TiO<sub>2</sub> targets.

Cingoranelli, S.J., Putnam, E. E, Loveless, C. S., Bartels, J.L., Elbahrawi R. T., Blanco J.R. , Lapi, S. E.

**Objectives:** Proton irradiation of enriched  $^{46, 50}\text{TiO}_2$  targets were investigated to produce high radionuclide purity  $^{43}\text{Sc}$  and  $^{47}\text{Sc}$  for radiochemistry development as a theranostic pair.

**Methods:** Enriched [ $^{46,50}\text{Ti}$ ]TiO<sub>2</sub> targets were bombarded with 18 MeV or 24 MeV protons at 20  $\mu\text{A}$ . Targets were dissolved using  $\text{NH}_4\text{HF}_2$  in a 3:1 ratio at 250°C for 2 h followed by 5 mL of concentrated HCl at 160°C for 1 h. The dissolved solution was diluted to 10 mL of 10.5 M HCl and purified on an equilibrated BDGA resin followed by washes of 9 M HCl, 7 M  $\text{HNO}_3$ , and 1 M  $\text{HNO}_3$ . The radioscandium was collected in 3 separate elutions of 3 mL 0.1 M HCl. The target material was recycled by diluting the flow-through and the first 9 M HCl to 500 mL MQ, precipitating out TiO<sub>2</sub> by pH adjustment to 8, filtered using 0.22  $\mu\text{m}$  mixed cellulose filter paper, and then heated at 350°C for at least 1 h. The purified  $^{47}\text{Sc}$  was evaporated to dryness and reconstituted in 200  $\mu\text{L}$  0.1 M HCl. Varying concentrations of DOTA were radiolabeled with  $^{43}\text{Sc}$  and  $^{47}\text{Sc}$  in 0.25 M ammonium acetate at 95°C, and 800 rpm for 30 minutes. PSMA-617 was radiolabeled with purified  $^{43}\text{Sc}$  at 95°C at varying concentrations using the same conditions.

**Results:** An average yield of  $1.5 \pm 1.3$  mCi of  $^{47}\text{Sc}$  was obtained for a 4 h irradiation and average  $^{43}\text{Sc}$  yield after 1.5 h bombardment was  $13.8 \pm 1.4$  mCi. The average recovery for  $^{43}\text{Sc}$  was  $88.4 \pm 5.2\%$  ( $98.7 \pm 0.2\%$  radiochemical purity) and the average recovery for  $^{47}\text{Sc}$  was  $90.2 \pm 10.2\%$  ( $90.2 \pm 2.9\%$  radiochemical purity after decay of short-lived isotopes ). The average recycled recovery for [ $^{46,50}\text{Ti}$ ]TiO<sub>2</sub> was  $96.5 \pm 3.5\%$  and  $96.6 \pm 4\%$ , respectively. The calculated molar activity for  $^{43}\text{Sc}$ -DOTA was 160.3 mCi/ $\mu\text{mol}$  and  $^{47}\text{Sc}$ -DOTA was 91.73 mCi/ $\mu\text{mol}$ .

**Conclusions:** Reasonable yields of high purity  $^{43,47}\text{Sc}$  were shown to be reproducible via proton bombardment of enriched [ $^{46,50}\text{Ti}$ ]TiO<sub>2</sub> with an average recovery yield of  $\geq 88\%$  for both  $^{43,47}\text{Sc}$ . The  $^{48}\text{V}$  is removed before radioscandium collection. Future experiments to improve production yields will be explored in addition to *in vivo* and *in vitro* applications of the theranostic pair  $^{43,47}\text{Sc}$ -PSMA-617.

**Acknowledgements:** This project was supported by the DOE isotope program through grant DESC0020197(P.I. Lapi). The authors acknowledge the support of all team members of Dr. Lapi's group, UAB cyclotron facility and the UAB machine shop.

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## Preparation and Evaluation of a SnO<sub>2</sub>-Based <sup>44</sup>Ti/<sup>44</sup>Sc Generator for Medical Applications

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<sup>44</sup>Sc has been gaining interest within the field of nuclear medicine as a potential radionuclide for positron emission tomography due to its relatively short half-life ( $t_{1/2} = 3.97$  h) and high positron branching ratio (94.3%). One convenient way to independently produce <sup>44</sup>Sc without the need for an on-site cyclotron is by the decay of the long-lived <sup>44</sup>Ti parent ( $t_{1/2} = 59.1$  y) via a <sup>44</sup>Ti/<sup>44</sup>Sc generator. However, current separation methods exhibit <sup>44</sup>Ti breakthrough during elution, potentially due to inadequate binding to the resin. This work focuses on the synthesis and use of tin dioxide (SnO<sub>2</sub>), a robust inorganic-based resin, as the column matrix for a <sup>44</sup>Ti/<sup>44</sup>Sc generator. The sorption behavior of <sup>44</sup>Ti/<sup>44</sup>Sc was tested on SnO<sub>2</sub> with varying acids, concentrations, and times. Preliminary batch study results showed relatively high <sup>44</sup>Ti retention to the resin at the lower acid concentrations (0.05 M HCl and 0.05 M HNO<sub>3</sub>) with equilibrium being established between 5-6.5 hours. From dynamic column studies, high <sup>44</sup>Sc elution yields were obtained with acid concentrations between 4-5 M. Additionally, using concentrations higher than 9 M to elute columns displayed greater than 1% <sup>44</sup>Ti breakthrough.



## Self-Supporting Samarium Targets for the Production of Terbium-149

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In the treatment of cancer by radiopharmaceuticals, it is necessary to identify the cancerous cells by imaging, which uses isotopes that go through gamma or positron decay. Then, the cells are killed by other isotopes that go through alpha, beta, or Auger electron decay.

Terbium-149 is a theragnostic isotope, going through positron and alpha decay, which makes it an excellent candidate for treating cancer. The reaction pathways to be evaluated as part of this research involve bombarding isotopically enriched samarium targets with a lithium-6 beam. To improve the post-irradiation analysis, the aim of this project was to create self-supporting targets of isotopic samarium that will be used for terbium-149 cross section evaluations. Initial studies were performed using natural samarium due to the high costs of the isotopically enriched materials. Based on existing literature, the methods of vapor deposition onto a substrate and subsequent floating were the best fit for the task. Testing was performed to determine the best parting agent; natural samarium was evaporated on surface of glass microscope slides treated with various parting agents: NaCl, Green Thunder, Green Soap, Cream Cote, and Teepol. These parting agents were later tested as to which coating was most efficient to release the evaporated samarium off the slide. The evaporation process involved reacting samarium oxide with zirconium in a tantalum pinhole boat at high temperature to produce a vapor of samarium metal, which was then deposited onto the substrate. Once a suitable parting agent was determined, the technique was transitioned to isotopic materials to produce targets for cross section measurements at Texas A&M University. The resulting targets will be presented.



## Investigating the Translation of Rn Gas Through Capillary Tubing of Different Materials

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Isotope production has been on the rise in hopes to provide new ways to offer medical treatment. Astatine-211 has the potential of being used for targeted alpha therapy, but it would be hard to distribute due to having a short 7.21-hour half-life. Instead, Radon-211, which has a 14.6-hour half-life, would allow enough time to produce the isotope and deliver to a wider community. In a well-constructed system Rn-211 could be produced via the bombardment of Li-6 beams on a Bi-209 target ( $^{209}\text{Bi}(^6\text{Li},4n)^{211}\text{Rn}$ ), the Rn-211 captured, and shipped to end users. During the shipping period the Rn-211 would decay to the desired At-211 and thus be ready for formulation upon receipt. However, Rn gas is a noble gas and requires investigation to determine an appropriate system for release, transfer, and trapping of the Rn followed by release of the At-211 daughter. Therefore, the transfer of Rn through capillary tubing of various materials and subsequent trapping of Rn gas is being investigated using surrogate Rn-222, a decay product of Ra-226, in order to develop a  $^{211}\text{Rn}/^{211}\text{At}$  generator system.

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## **Non Destructive Beam Monitor Prototype (ND-BMP)**

David Thomas, Dr. Gabriel Tabacaru, Dr. Lauren McIntosh, Dr. Sherry Yennello

Measuring beam current without interfering with and modifying the current is difficult. A nondestructive prototype simulates a method by which the current of a beam can be measured without destroying or obstructing the current.

In place of beam a copper rod is centered in a desktop prototype of a beam pipe and used to mimic beam. A section of the beam pipe contains the copper coil, in which an induced current is formed. This induced current, which is initially alternating is rectified and amplified using a circuit designed for this purpose. The current is then read using a picoammeter and compared to the current that is passed through the central copper rod and the output reading for the user is adjusted to match the current in the copper rod and displayed on a graphical user interface.

Using this method the current in the copper coil can be read without directly measuring the current. This prototype can then be expanded to a beam pipe where the current of a beam can be measured using the induced current around it. This is especially useful when trying to obtain the current of the beam without interfering or modifying it in facilities that irradiate targets.

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## Toward Automating the Separation of Adjacent Lanthanides: $^{165}\text{Er}$ from $^{\text{nat}}\text{Ho}$

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**1. Introduction.** With the FDA approvals of Lutathera ( $^{177}\text{Lu}$  dotatate) and Pluvicto ( $^{177}\text{Lu}$  PSMA-617), interest in the production of other radio-lanthanides for medical purposes has grown. The separation of the pure Auger-electron emitter  $^{165}\text{Er}$  from proton-irradiated  $^{\text{nat}}\text{Ho}$  is feasible in three steps: 1) cation exchange (CX) chromatography, 2) LN2 extraction chromatography (EXC), and 3) bDGA EXC [1]. This work reports the partial automation of this process and the plans to expand the LN2 separation to the adjacent lanthanides of reactor-generated  $^{161}\text{Tb}$  from target  $^{160}\text{Gd}$ .

**2. Method & Materials.** The main objective was to assess LN2 column performance (Ho/Er separation factor and  $^{165}\text{Er}$  yield) when directly loading the CX column eluant onto the LN2 column (Triskem LN2, 20-50  $\mu\text{m}$ , 5.5 mm  $\varnothing$  x 50 mm) without acidification. To test these direct loading conditions, tracer-level ( $\sim 155$   $\mu\text{Ci}$ )  $^{165}\text{Er}$  and 0.5 mg Ho were added to 70 mM alpha hydroxy isobutyrate ( $\alpha\text{HIB}$ , pH 4.7,  $\sim 225\text{mL}$ ) to simulate CX column eluent. Under previously published indirect loading conditions, this eluent was collected, assayed, and acidified prior to loading following the procedure in [1]. Activities of  $^{165}\text{Er}$  were quantified by dose calibrator measurement (Capintec CRC-15R, setting #260) and holmium concentrations by Microwave Plasma Atomic Emission Spectrometry (Agilent MP4200). Similar testing with 1 mg  $^{160}\text{Gd}$  and  $\sim 6$   $\mu\text{Ci}$   $^{161}\text{Tb}$  added to 70 mM  $\alpha\text{HIB}$  and loaded onto a LN2 column using a 24V peristaltic pump will be performed with the intent on finding the ideal nitric acid rinse concentration for separation. Activity will be quantified by a gamma counter and Gd concentrations via Arsenazo III spectrophotometry.

**3. Results & Discussion.** The LN2 column performance from the direct CX-to-LN2 loading test chemistries are compared with the published indirect loading procedure in Table 1. The separation factors and RCYs for the two methods are within each other's uncertainties. Separation products were reacted with PSMA-617 (at 80°C for 30 min, pH 4.0-4.2) with an end-of-bombardment [ $^{165}\text{Er}$ ]PSMA-617 molar activity of  $0.57 \pm 0.52$  Ci/ $\mu\text{mol}$  ( $n = 7$ ) for the direct loading, compared with  $1.6 \pm 1.0$  Ci/ $\mu\text{mol}$  ( $n = 6$ ) for [ $^{165}\text{Er}$ ]PSMA-617 synthesized following the indirect loading





procedure.

**Table 1.** Summary of key results from LN2 EXC direct loading.

	<b>Ho/Er Separation Factor</b>	<b><sup>165</sup>Er Percent Yield</b>	<b>n</b>
Direct Loading: Testing	419 ± 47	82 ± 9	3
Indirect Loading: Full-scale Separation	594 ± 450	80 ± 7	9

**4. Conclusion.** Partial automation of the <sup>165</sup>Er-Ho separation reduces operator exposure and scientist workload. However, more work is necessary to improve consistency and Ho/Er separation factor. Future work aims to apply this procedure to other adjacent lanthanides.

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**References.**

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