**Exploring novel direct reactions for the production of terbium-149 using Hyperion**

L.A. McCann,[1,2] A.B. McIntosh,[1] L.A. McIntosh,[1] P. Adsley,[1,3] J.G. Duarte,[4] M. Gott,[5] J.T. Harke,[4] Y. Mishnayot,[4] J.T. Morrell,[6] A.S. Tamashiro,[4] C.E. Vermeulen,[6] and S.J. Yennello[1,2]

[1] *Cyclotron Institute, Texas A&M University, College Station, TX 77843, USA*
[2] *Department of Chemistry, Texas A&M University, College Station, TX 77843, USA*
[3] *Department of Physics, Texas A&M University, College Station, TX 77843, USA*
[4] *Lawrence Livermore National Laboratory, Livermore, CA, 94550, USA*
[5] *Physics Division, Argonne National Laboratory, Lemont, IL 60439, USA*
[6] *Los Alamos National Laboratory, Los Alamos, NM 87545, USA*

Targeted alpha therapy (TAT) is an emerging field in cancer research that links an alpha-emitting radionuclide to a targeting agent that can travel to the tumor location, allowing most of the damage due to the radioactive decay to occur within the tumor, reducing damage to healthy cells. There are several factors that need to be considered when selecting a TAT isotope such as its half-life and toxicity of nuclide and its decay products. While there are a number of isotopes that meet biologically relevant criteria, there is only one that has been identified to decay via both alpha and positron emission, allowing it to be used in TAT, but also to be imaged via positron emission tomography (PET) without the use of another imaging isotope [1-3]. This unique isotope is terbium-149. Its dual functionality of both therapy and diagnostic properties is termed "theranostic" and is very valuable as it eliminates the need for a chemically similar homolog to be used for imaging purposes [4]. Despite the potential value of $^{149}$Tb as a TAT isotope, there are a number of challenges facing its production including its biologically-relevant half-life of 4.1 hours, its low neutron-to-mass ratio, and the favorable production of the metastable state which does not decay via alpha emission.

Although $^{149}$Tb has been made via a variety of pathways over the years, none of these currently produce the yields that are necessary for isotope production with worldwide availability [5,6]. Many experiments, particularly heavy-ion direct reactions, have attributed these low production rates to the competing production of the 4 minute half-life metastable isomer, but none have been designed to quantify this contribution [7-9]. In an effort to explore new pathways for the production of $^{149}$Tb, it is valuable to know this ratio of population of the ground state to the excited state based on projectile energy and mass. With this in mind, the Hyperion high-purity germanium (HPGe) detector array was chosen [10], to allow measurement of the decay of all of the isotopes produced in the reaction immediately after beam, including the short-lived $^{149m}$Tb. The reaction chosen for this experiment was a $^{6}$Li beam impinging on a variety of enriched samarium targets (Z = 147-149), due to its high predicted cross-sections found using PACE4 [11,12]. While PACE4 is known to overpredict cross-sections, it is also unable to distinguish between production of the ground state or other excited states of a given nucleus, likely a large source of error particularly in the case where the excited state population is high

and does not decay to produce the ground state. It is, however, accurate for choosing beam energies, allowing us to choose our maximum yield energies for this experiment.

A series of reactions were then measured at TAMU using Hyperion. The reactions that were measured include $^{147}$Sm($^{6}$Li,4n)$^{149}$Tb at 45 MeV, $^{148}$Sm($^{6}$Li,5n)$^{149}$Tb at 55 MeV, and $^{149}$Sm($^{6}$Li,6n)$^{149}$Tb at 55, 60, and 65 MeV. These systems were chosen to experimentally measure for the first time the cross-sections of these reactions, and determine the contribution to the total predicted cross section of $^{149}$Tb by the metastable isomer. From the resulting measurements, the effect of the differing target mass could be measured, and to determine how close to the actual peak cross section our single-energy measurements were based on PACE4 predictions. A week of beam was necessary for these experiments with overnight irradiations, while the decay measurements, beam tuning, and target changing occurred during the day. Given the 4.1 h half-life of the isotope of interest, this amount of time allowed for maximum production of $^{149g}$Tb, and the subsequent immediate decay measurement of the products, followed by delayed target extraction and movement to an offline HPGe detector for further measurement of isotopes with longer half-lives.

In order to prepare for these experiments, a series of samarium targets needed to be prepared. An aluminum backing was chosen for the foils so that it would result in a limited number of known activation lines interfering with the measured production gamma rays. Additionally, the short-lived $^{28}$Al peak ($t_{1/2}$ = 2.25 m) should allow for better characterization of the beam current during the overnight irradiations. Since enriched samarium comes only in the oxide form, it was necessary to reduce it in order to create the desired metallic targets. Samarium is also considered to be a low melting point lanthanide, meaning that these targets were able to be produced via physical vapor deposition (PVD) at Argonne National Laboratory. The enriched

**Fig. 1**. Tantalum pinhole boat containing a pressed pellet of Sm2O3 and Zr.

samarium oxide was measured and pressed into a pellet with an excess of zirconium metal, and placed into a tantalum pinhole boat (Fig. 1). From there, a current is passed through the boat,

heating up the pellet, allowing the zirconium to reduce the samarium oxide powder to samarium metal, and then selectively evaporate it onto the overhead aluminum frames. Targets of thickness 1 mg/cm2 were prepared using this method, shown in Fig. 2.

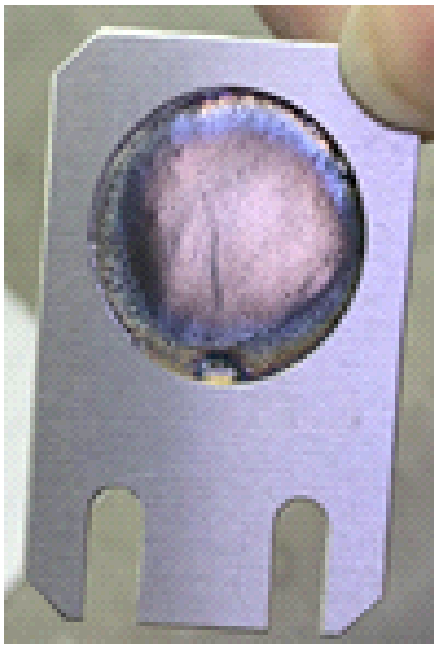

**Fig. 2**. PVD Sm target with Al backing mounted on a Hyperion frame.

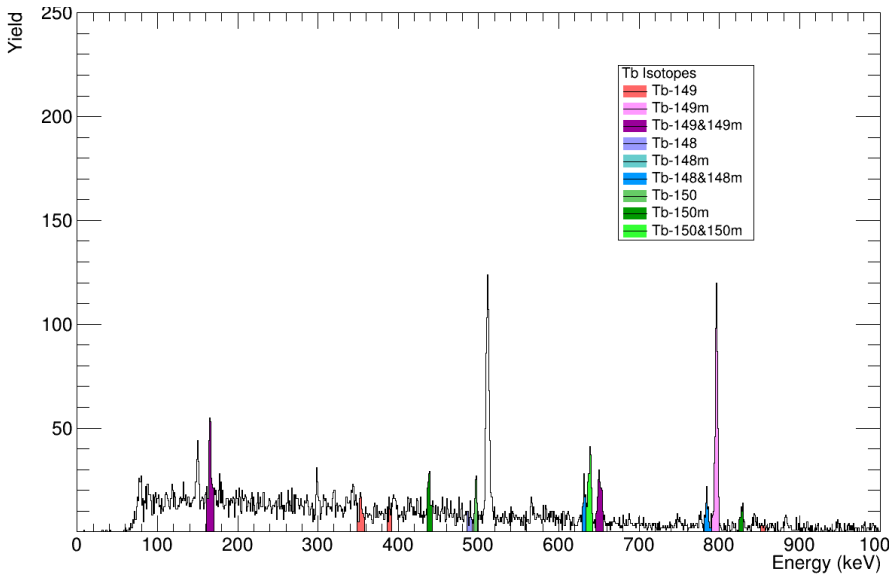


**Fig. 3**. HPGe clover spectrum taken 8 min after the end of beam for the $^{6}$Li on $^{147}$Sm system. The highlighted peaks indicate the gamma emissions associated with the $^{149}$Tb isomers (pinks), $^{148}$Tb isomers (blues), and $^{150}$Tb isomers (greens).

From analyzing the resulting HPGe spectra in Fig. 3, it can be seen that both $^{149g}$Tb and $^{149m}$Tb were produced in the reactions. Terbium-148 and $^{150}$Tb were also able to be confirmed through peak

analysis. Cross sections for every isotope measured in the experiment are currently being calculated, to get a comprehensive picture of the isotopes produced in the reaction to better inform nuclear codes in this region, and determine if these reactions pose a viable pathway for the large-scale production of $^{149}$Tb for medical applications.


## Acknowledgements

This work is indebted to the operations staff at the Texas A&M Cyclotron Institute and Radiological Safety program for their contributions to this work. This work was supported by the U.S. DOE Isotope Program, Award No. DE-SC0020958, DE-SC0022539 and DE-SC0022550 (HIPPO program); U.S. DOE under Award No. DE-NA0003841 and DE-FG02-93ER4077; the NSF GRFP; TAMU through the Bright Chair in Nuclear Science, the Nuclear Solutions Institute and a T3 grant: TAMU NLO and LANL through the joint collaborative research program. Work at ANL was supported by the U.S. DOE, Office of Science, Office of Nuclear Physics, under Award No. DE-SC-0017208. Argonne's ATLAS facility, which is a DOE Office of Science User Facility. Hyperion Array made possible by DE-AC52-07NA27344.



[1] M.R. McDevitt *et al.*, Eur. J. Nucl. Med. Mol. Imaging **25**, 1341 (1998); DOI: 10.1007/s002590050306

[2] D.S. Wilbur, Curr. Radiopharm **4**, 214 (2011); DOI: 10.2174/1874471011104030214

[3] M.R. Zalutsky and M. Pruszynski; Curr. Radiopharm. **4**, 177 (2011); DOI:10.2174/1874471011104030177

[4] C. Kratochwil *et al.*, J. Nucl. Med. **57**, 1941 (2016); DOI: 10.2967/jnumed.116.178673

[5] C. Ducheminet *et al.*, Front. Med. **8**, 625561 (2021); DOI: 10.3389/fmed.2021.625561

[6] H. Verhoeven, MSc Thesis, KU Leuven (Belgium), 2018; CERN-THESIS-2018-157.

[7] R.D. Macfarlane, Phys. Rev. **126**, 274 (1962); DOI: 10.1103/PhysRev.126.274

[8] M. Maiti *et al.*, Radiochim. Acta. **99**, 527 **(**2011); DOI: 10.1524/ract.2011.1839

[9] J.T. Wilkinson *et al.*, Appl. Rad. Isot. **178**, 109935 (2021); DOI: 10.1016/j.apradiso.2021.109935

[10] R.O. Hughes *et al*., Nucl. Instrum. Methods Phys. Res. **A856**, 47 (2017); DOI: 10.1016/j.nima.2017.03.012

[11] O.B. Tarasov and D. Bazin, Nucl. Instrum. Methods Phys. Res. **B266**, 4657 (2008).

[12] A.Gavron, Phys.Rev. C **21**, 230 (1980).