

## Production cross-section measurements of the medically relevant radionuclide thulium-167 using an 18-MeV medical cyclotron

E. Renaldin<sup>1,4</sup>, G. Dellepiane<sup>2</sup>, S. Braccini<sup>2</sup>, N. P. van der Meulen<sup>1,3</sup>, R. Eichler<sup>3,4</sup>, Z. Talip<sup>1\*</sup>

<sup>1</sup>Center for Radiopharmaceutical Sciences ETH-PSI-USZ, Paul Scherrer Institute, Villigen-PSI, Switzerland, <sup>2</sup>Albert Einstein Center for Fundamental Physics (AEC), Laboratory of High Energy Physics (LHEP), University of Bern, Bern, Switzerland, <sup>3</sup>Laboratory of Radiochemistry (LRC), Paul Scherrer Institute, Villigen-PSI, Switzerland, <sup>4</sup>Department of Chemistry, Biochemistry and Pharmaceutical Sciences, University of Bern, Bern, Switzerland

Auger electrons have gained significant attention for their potential capability of targeting individual tumor cells due to the deposition of a highly localized, cytotoxic radiation dose. By employing these particles in Targeted Radionuclide Therapy (TRT), healthy tissues could be spared from excessive radiation-induced damage, thereby, reducing potential severe, long-term side effects. Thulium-167 (100 % EC decay,  $t_{1/2} = 9.25$  d,  $E_{\gamma} = 207.8$  keV (42 %) [1]) is a promising candidate for TRT with Auger electrons due to its substantial emission of low-energy electrons [2]. In addition, the emission of an intense low-energy gamma ray, allows imaging by means of Single Photon Emission Computed Tomography (SPECT). This capability was previously demonstrated when thulium-167 was employed as a bone-scanning agent [3]. However, the understanding of the radiobiological effectiveness of Auger electron emitters is in its infancy, thereby, justifying the urgency for production to ensure systematic investigations. To achieve this objective, the knowledge of production cross sections of relevant thulium radioisotopes is essential to obtain high activities and assess radionuclidic purity of the radionuclide produced. Consequently, this study is aimed at measuring the cross sections of the proton-induced reactions producing thulium radioisotopes using enriched erbium-167 and erbium-168 in the chemically-stable oxide form.

The cross-section measurements were performed using the 18-MeV medical cyclotron in operation at the Bern University Cyclotron Laboratory, equipped with a Beam Transport Line (BTL). In this study, thin targets of erbium oxide were irradiated using nano-ampere (nA) proton currents with varying energy. The production cross sections of thulium-165, thulium-166, thulium-167, and thulium-168 were assessed over an energy spectrum ranging from 6.8 MeV to 18.2 MeV and compared with theoretical predictions obtained from the TENDL 2019 library. To validate the experimental cross-section data, a series of production tests bombarding thick targets were conducted employing the BTL. The production yields of each relevant thulium radioisotope were evaluated using the measured cross sections. This evaluation aimed to identify the optimal proton beam energy yielding maximum thulium-167 production. The theoretical predictions were compared to the corresponding experimental results.

Good agreement is found between the experimental cross-section measurements and the predictions by TENDL 2019. In addition, the production tests successfully validated the measured experimental cross-section data. According to experimental evidence, thulium-167 production yields were determined to be 2.4 MBq/ $\mu$ Ah and 8.4 MBq/ $\mu$ Ah when using 12.7 MeV and 18.2 MeV proton energies and  $^{167\text{enr}}\text{Er}_2\text{O}_3$  and  $^{168\text{enr}}\text{Er}_2\text{O}_3$  as target materials, respectively.

[1] M. Baglin, *Nucl. Data Sheets*, **2000**, 90 (3), 431–644

[2] Filosofov, E. Kurakina, and V. Radchenko, *Nucl. Med. Biol.*, **2021**, 94–95, 1–19

[3] Chandra, J. Hernberg, P. Braunstein, and W. Rosenfeld, *Radiology*, **1971**, 100 (3), 687–689