Optimized production of ^{155}Tb via ^{155}Dy decay for theranostics

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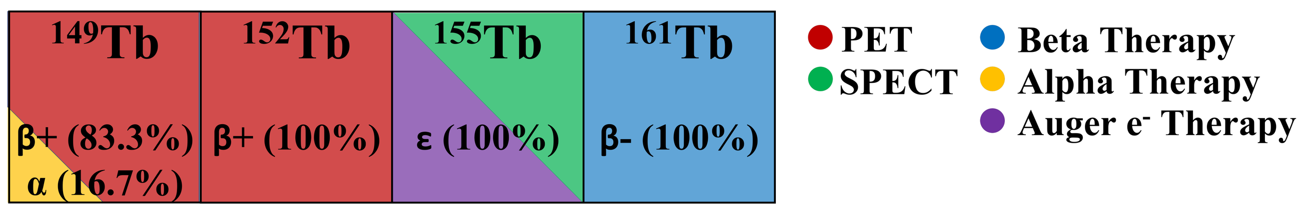
Reference paper

1. Introduction

Terbium: known as the *swiss-army knife* of Nuclear Medicine for its **four isotopes useful both for imaging and therapy**.

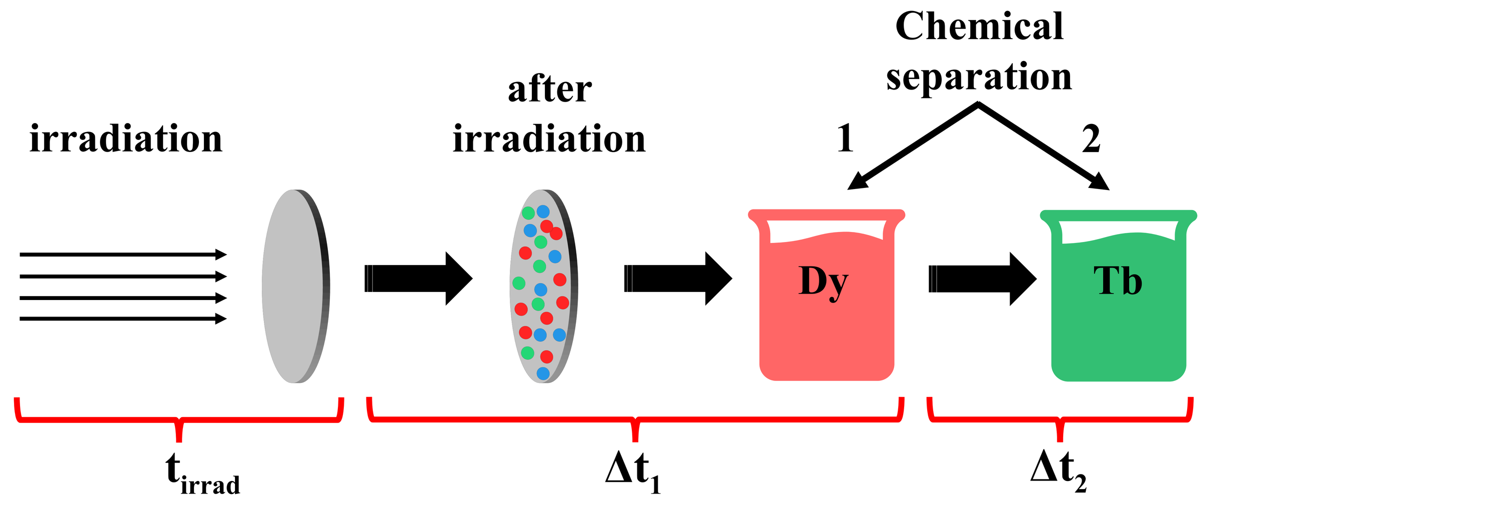


We focus here on **^{155}Tb** ($T_{1/2}$ = 5.32 d), **theranostic** radionuclide for Auger-electron therapy and SPECT imaging, with three cyclotron-based production routes:

$$^{159}\mathrm{Tb}(p,5n)^{155}\mathrm{Dy}, \qquad ^{159}\mathrm{Tb}(d,6n)^{155}\mathrm{Dy}, \qquad ^{nat}\mathrm{Gd}(\alpha,x)^{155}\mathrm{Dy}.$$

These **reactions** are **based on** the intermediate **formation and decay of the progenitor ^{155}Dy→^{155}Tb** and are ^{156}Tb-contaminant free, in contrast to **standard routes** that rely on direct **^{155}Tb** production with the **undesired generation of ^{156}Tb**.

During the irradiation (t_{irrad}), multiple isotopes are produced (isotope of interest + contaminants). **^{155}Tb generation involves two separation steps** (Dy extraction and subsequent Tb extraction) characterized by processing times Δt_1 and Δt_2.



Goals: 1) to identify the reaction with the **highest yield and purity**; 2) to define the **optimal energies and processing times** for production.

2. Methods

The study focused on two optimizations regarding: A) Dy-isotope production cross sections, B) irradiation and separation parameters to maximize ^{155}Tb yield and purity.

Theoretical calculations were performed with TALYS, including **rotational effects** for **deformed** nuclei, **linear binning** for continuum transitions, variations of **pre-equilibrium parameters**, **microscopic level-density models** with minimal parameter tuning for ^{153}Dy ($T_{1/2}$ = 6.4 h). **These settings are** referred to as ***TALYS modified***. We calculated the activity A(t) of each nuclide and the isotopic (IP(t)) and radionuclidic purity (RNP(t)) of ^{155}Tb:

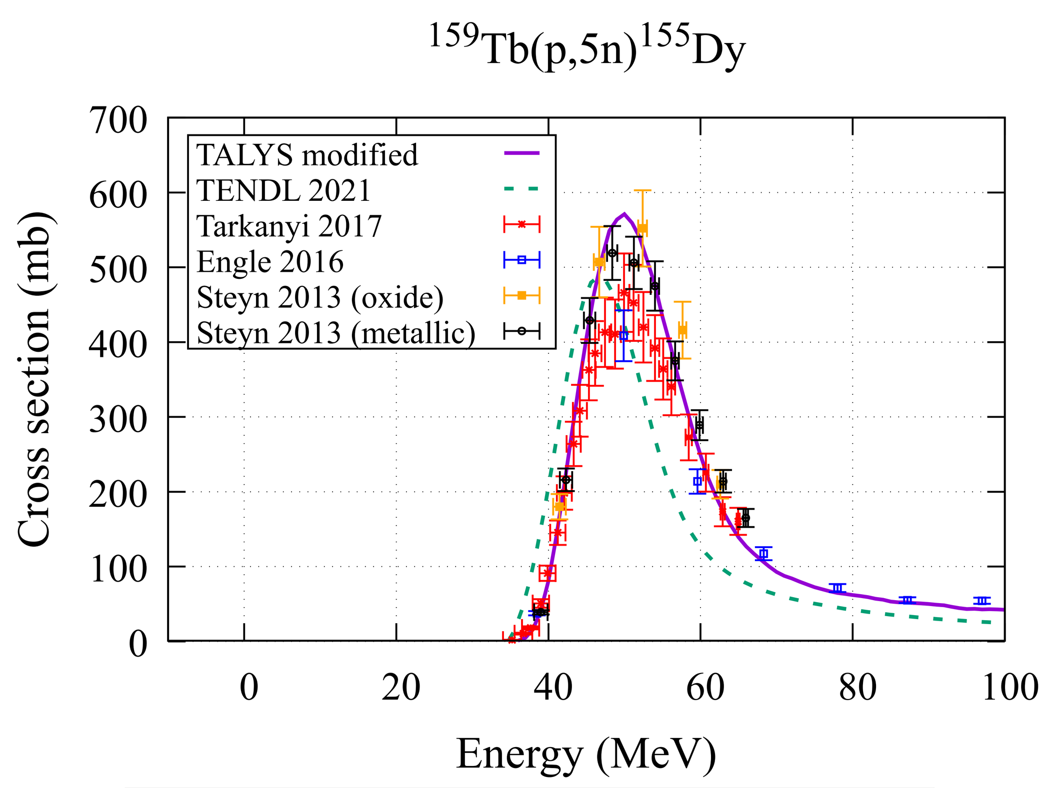
$$A_i(t) = \lambda_i N_i(t) \qquad IP_{155Tb}(t) = \frac{N_{155Tb}}{\Sigma_i N_i(t)} \qquad RNP_{155Tb}(t) = \frac{A_{155Tb}}{\Sigma_i A_i(t)}$$

To identify the most promising reaction, we evaluated the **integral saturation yield**:

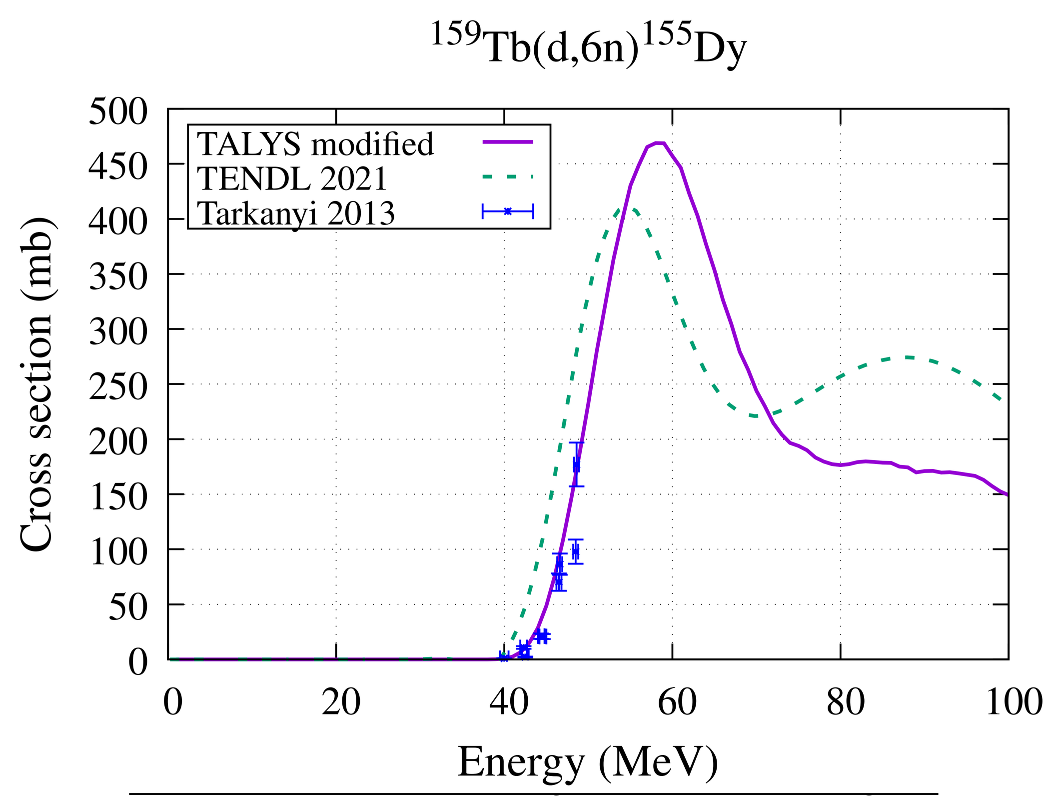
$$a_{sat}^{int} = \lim_{\substack{t_{irrad}\to+\infty \\ \Delta t_1 \to 0}} \frac{A_{155Tb}(t)}{I_0}$$

To address the second goal, we performed a **multi-objective optimization**, computing the **Pareto frontier** between ^{155}Tb integral production (IP) and activity (A), with the constraint RNP≥0.99, as recommended by the European Pharmacopoeia.

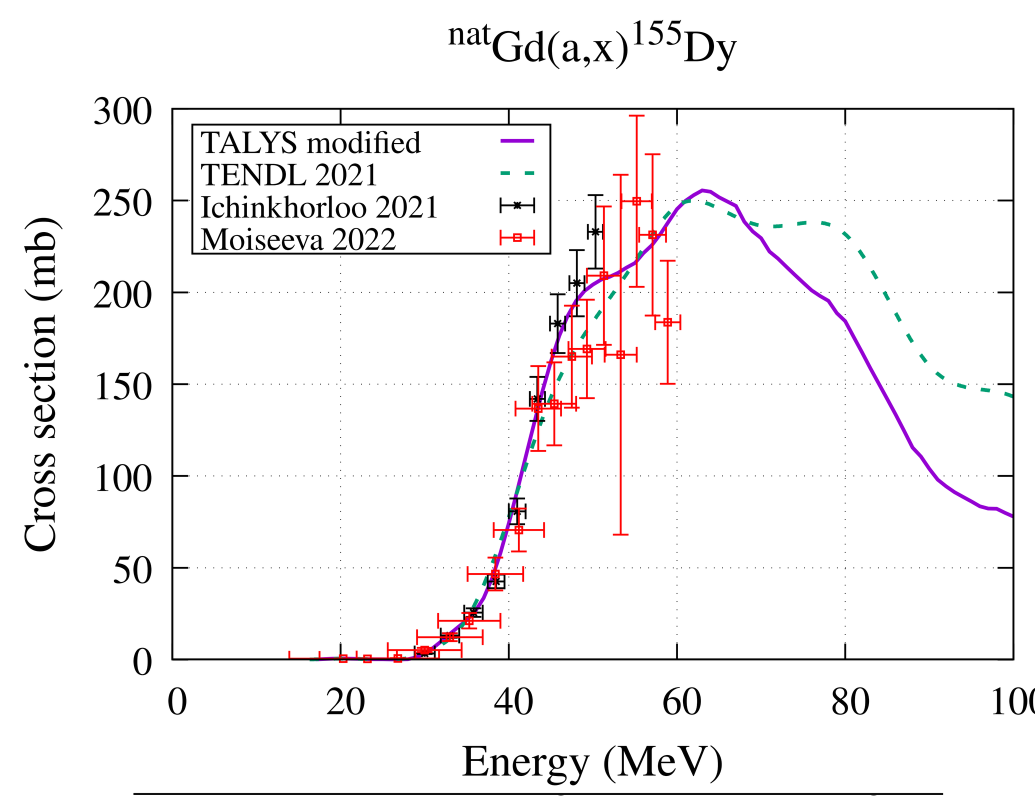
3. Selected results



TALYS modified χ^2_{tot}	TENDL χ^2_{tot}
1.7	3.6

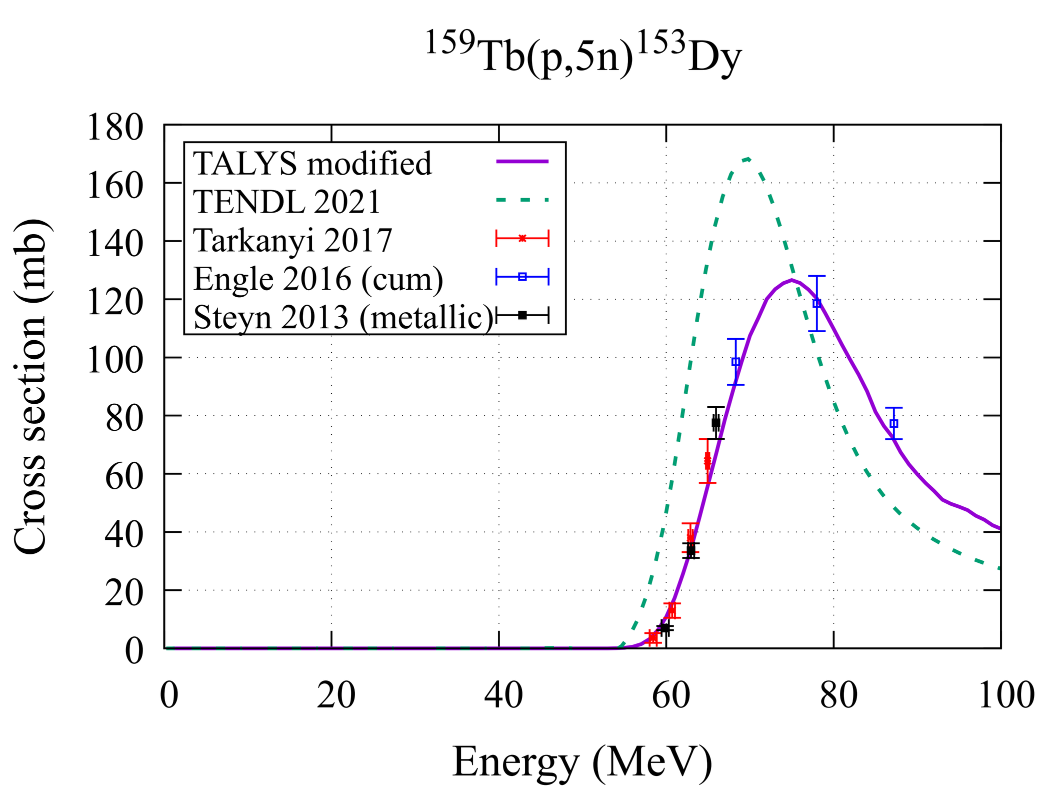


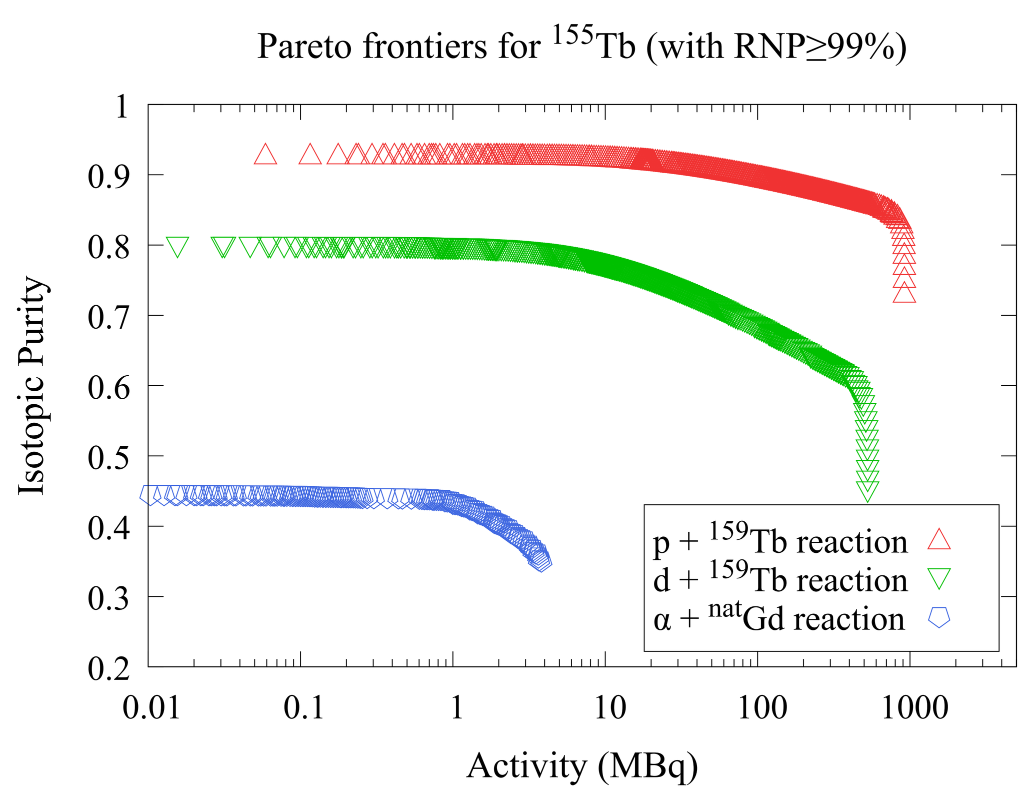
TALYS modified χ^2_{tot}	TENDL χ^2_{tot}
1.3	2.1



TALYS modified χ^2_{tot}	TENDL χ^2_{tot}
0.9	0.7

Top: **better description** is achieved with the calculations presented in Methods for all the three reactions with respect to the standard TENDL library. **Optimization** achieved especially for **contaminants**, as **^{153}Dy** shown below (**bottom left**), and validated with **total chi-square calculation** (considering all the Dy channels): **improvements** of **53%** for protons, **38%** for deuterons and **22%** for α reactions.





reaction	p	d	α
E_{in}–E_{th} (MeV)	60–35	67–38	53–12
Δx (mm)	4.6	3.5	0.55
a_{sat}^{int} (MBq/μA)	**1891**	**1139**	**19**
IP	0.7	0.41	0.07
RNP	0.997	0.992	0.98

Comparison of the three reactions by means of the saturation integral yield defined in the Methods section. The **proton-induced reaction is the most promising** route, providing the highest activity and purity levels.

Middle figure: Pareto frontier for the three reactions. Set of equally valid solutions that simultaneously maximize activity and isotopic purity, while also satisfying the required radionuclidic-purity constraint. The figure highlights **higher production of contaminants** in reactions with **deuterons** and **α-particles**. Additionally, **lower activities** are the result of lower cross section values.

4. Conclusions

Theoretically consistent and strong representation of the cross sections of ^{155}Tb and contaminants for all the reactions. Additionally we **optimized** the **activities and purities**, identifying the reaction with protons as the most promising. We developed a **robust framework** with **dedicated codes** available for further studies on the field. **Tools already applied with success** to other IAEA recommended isotopes, such as ^{67}Cu, ^{47}Sc and ^{52g}Mn.

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