^{155}Tb production via proton beams on enriched ^{155}Gd targets: simulations from cross sections to dosimetry

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INTRODUCTION

Terbium radioisotopes are of particular interest in nuclear medicine thanks to their decay features, such as half-lives, the type and energy of the emission products [1]. Among Tb-isotopes, the γ emitter ^{155}Tb is suitable for SPECT imaging. Moreover, the diagnostic ^{155}Tb could be paired with one of the Tb therapeutic counterparts (α or β^-emitter) for personalized precision-medicine therapy known as theranostics. In view of possible applications of ^{155}Tb in medical imaging, it is important to identify an adequate production route that guarantees a high level of purity and an acceptable risk introduced by the co-produced contaminants in terms of dose released to the patient's organs. An example of a possible production route for ^{155}Tb is the proton-induced reaction on Gd targets [2]. Since ^{nat}Gd is made of seven isotopes, it is not the optimal option as target material to obtain a high purity production. On the other hand, enriched Gd targets could enhance the level of purity by limiting the Gadolinium components that are responsible for the production of contaminants, especially of ^{156g}Tb, since its half-life is comparable to ^{155}Tb, and its γ emissions have severe impact to the dose released. Very recently Dellepiane et al. [3] measured the cross section of ^{155}Tb and co-produced contaminants by using gadolinium oxide targets with a ^{155}Gd enrichment of 91.9%. In this theoretical study a comparison with the measured cross-section reactions is presented, with focus on the effects of the other Gd isotopes present in small quantities in the target. The study includes a discussion on the radionuclidic purity (RNP) and dose increase (DI) to healthy organs caused by administration of co-produced contaminants to the patient.

RESULTS

The nuclear reaction code Talys has been used to model the theoretical cross sections of both ^{155}Tb and the contaminants ^{153}Tb, ^{154g,m1,m2}Tb, and ^{156g,m1,m2}Tb. Simulations have been performed assuming the same isotopic composition of the target employed in the experimental setup of Dellepiane and Favaretto [4], and listed in Table 1. The analysis has been performed considering the Talys default calculation [5], since for the main radionuclide the cross section is equally reproduced by all Talys models up to 10 MeV, while some limited model variability appears at higher energies. Fig. 1 shows the cross section of the main contaminant ^{156}Tb. The black line, referring to the ^{156t}Tb cumulative cross sections of ^{156g,m1,m2}Tb, is in good agreement with the data. The disentanglement of the cross-section contributions caused by the different isotopic components of the target are also illustrated (colored lines). The larger contribution to the ^{156}Tb contamination comes from the ^{156}Gd component (5.87%), followed by the ^{157}Gd component (0.81%), while the production of ^{156}Tb from ^{155}Gd remains quite small in the entire range of energies.

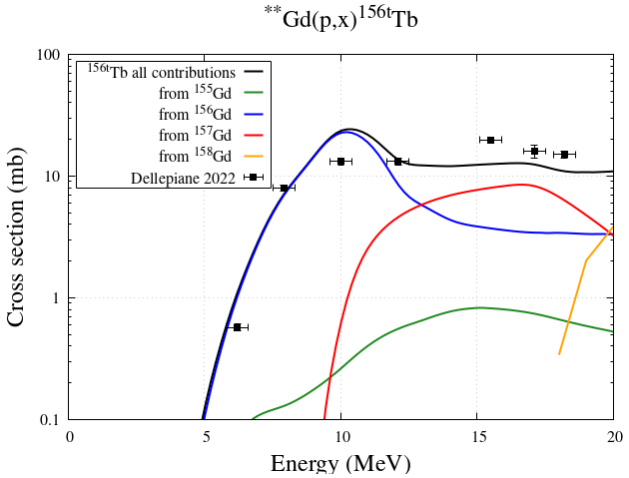

Fig. 1. Theoretical and experimental ^{155}Gd(p,n)^{156t}Tb cross section. The colored lines represents the contribution to the ^{156t}Tb production from the Gadolinuim isotopes reported in Table 1.

Table 1. Gadolinium isotopic percentages of enriched ^{155}Gd oxide employed in [3, 4].

	^{152}Gd	^{154}Gd	^{155}Gd	^{156}Gd	^{157}Gd	^{158}Gd	^{160}Gd
^{155}Gd-enr. [%]	<0.02	0.5	91.90	5.87	0.81	0.65	0.27

From the simulated cross sections of ^{155}Tb and co-produced contaminants the analysis of rates, yields, and

purities has been carried out. The radionuclidic purity (RNP), Fig. 2, that is the fraction of the total activity for ^{155}Tb, reaches a maximum value of about 0.938.

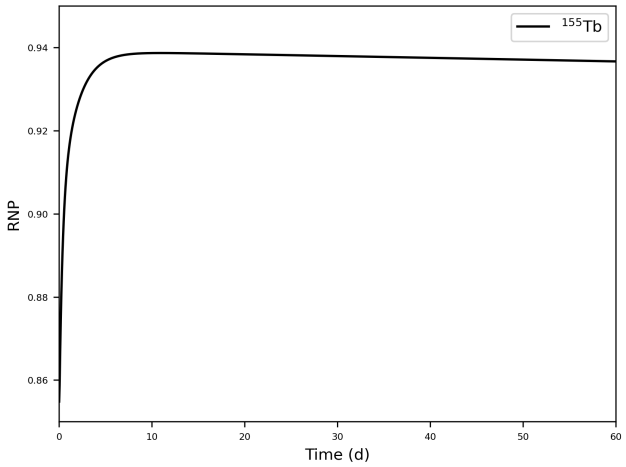

Fig. 2. Radionuclidic purity for the reaction ^{155}Gd(p,n)^{155}Tb, considering a 91.90% enrichment of the target.

However, RNP below 99% is not necessarily related to a high dose. For this reason, it is important to assess the dose increase, which describes the dosimetric impact of the contaminants. For an extensive discussion about DI see [6].

Absorbed doses to human organs due to different Tb-radioisotopes were calculated with the OLINDA software 2.2.3 using the activity concentrations of the DOTA-folate radiopharmaceutical (RF), ^{161}Tb-cm09, in the different source organs of tumor-bearing mice [7] and the relative mass scaling method as reported before [8, 9]. Then effective dose (ED) for each Tb-radioisotopes was evaluated by summing the product of organ equivalent dose and the corresponding tissue-weighting factor recommended by ICRP 103 [10].

Table 2. Main organ absorbed doses (mGy/MBq) and ED values (mSv/MBq) per unit-administered activity calculated for ^{XXX}Tb-cm09 with the OLINDA 2.2.3 software for male ICRP 89 phantoms.

Target Organ	^{153}Tb	^{154}Tb	^{155}Tb	^{156g}Tb	^{156m1}Tb	^{156m2}Tb
Adrenals	6.7E-02	1.7E-01	6.6E-02	4.7E-01	6.8E-03	1.4E-03
Gallbladder Wall	3.0E-02	7.8E-02	2.7E-02	2.0E-01	3.1E-03	1.3E-03
Kidneys	2.9E-01	3.9E-01	3.5E-01	1.3E+00	4.3E-02	4.0E-02
Liver	4.7E-02	1.0E-01	5.1E-02	2.8E-01	6.1E-03	4.7E-03
Salivary Glands	4.2E-02	6.4E-02	4.7E-02	1.7E-01	6.6E-03	8.3E-03
Osteogenic Cells	7.5E-02	6.0E-02	8.6E-02	1.8E-01	1.8E-02	1.1E-02
Spleen	3.3E-02	7.7E-02	3.3E-02	2.1E-01	3.5E-03	1.7E-03
Effective Dose	**2.0E-02**	**4.4E-02**	**1.9E-02**	**1.1E-01**	**2.5E-03**	**2.1E-03**

Table 2 shows that the ED values of ^{156}Tb and ^{154}Tb are the largest, 5.9 and 2.4 times higher than those of ^{155}Tb-cm09 respectively. The total effective dose (ED_t) of Tb-cm09 was calculated considering that the radiopharmaceutical was injected immediately after labelling with the mixtures of Tb-radioisotopes present at the different times after the end of bombardment (EOB), using the following equation: $ED_t(t) = \Sigma\, f_i(t) ED_i$ where $f_i(t)$ is the fraction of total activity corresponding to each radioisotope i at the time t after EOB. The dose increase (DI) has been evaluated as the ratio between ED_t and the $ED_{^{155}Tb}$. Fig. 3, shows an increase of the dose above the standard limit of 10%.

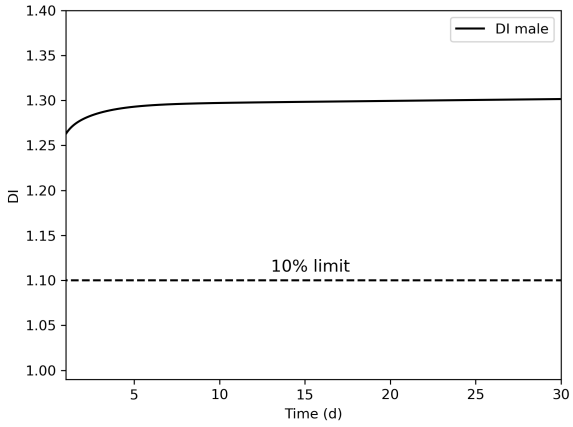

Fig. 3. Dose increase for the production route ^{155}Gd(p,n)^{155}Tb, due to the isotopic composition of the target listed in Table 1.

CONCLUSIONS

This study focuses on the analysis of the production route ^{155}Gd(p,n)^{155}Tb, simulating an enriched Gadolinium target similar to the one used in Dellepiane work. The analysis of the radionuclidic purity exposes the level of contamination of the production route. In addition, the high dose increase, above the recommended limit, discourage the feasibility of this channel for medical applications. However, it is fundamental to emphasize that the low purity and high dose achieved depend on the presence of the main contaminant ^{156g}Tb, and so they are target dependent. Higher enrichment of the ^{155}Gd target could lead to a different and more favourable outcome, since it is clear that the contamination originates mostly from the ^{156}Gd component.

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