Investigation of deuteron-induced reactions on ^{nat}Gd up to 30 MeV: possibility of production of medically relevant ^{155}Tb and ^{161}Tb radioisotopes

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Abstract

Excitation function for the ^{nat}Gd(*d,xn*)^{155}Tb and ^{nat}Gd(*d,n*)^{161}Tb nuclear reactions were measured using the standard stacked-foil activation technique in the deuteron energy range of 30 MeV down to 4.2 MeV. The measured cross-section data were compared not only with the earlier reported experimental values but also with the results of a theoretical model as well. Integral yields for ^{155}Tb and ^{161}Tb and for their contaminating radioisotopes were also deduced to evaluate the production circumstances. The results revealed that the investigated radioisotopes can not be produced in no-carrier-added form via deuteron way even using 100% enriched targets (^{155}Gd and ^{160}Gd).

Keywords

Gadolinium target; Terbium radioisotopes; Deuteron irradiation; TENDL 2014 library

Introduction

Recently the element Terbium, member of the lanthanide row, attracted special attention since it offers a set of radionuclides which are potentially suitable both for therapy and diagnosis. These radioisotopes possess one or several advantages compared to radionuclides currently used in radiopharmacy with respect to decay energies and half-life [1-4]:

a) For imaging with PET, the ^{152g}Tb seems to be a proper candidate. The positron intensity of 17% (and the mean positron energy of 1.1 MeV) is acceptable. The only strong gamma line of 344 keV ($I\gamma$ = 65%) is far away from the annihilation line of 511 keV to avoid coincidence events.

c) For targeted particle radionuclide therapy both the ^{149}Tb ($T_{1/2}$ = 4.1 h, I_α = 17%) and ^{161}Tb ($T_{1/2}$ = 6.89 d, $I_{\beta-}$= 100%) seems to be promising. ^{161}Tb has a similar half-life and beta energy as the already useful ^{177}Lu.

c) For diagnostic imaging the ^{155}Tb seems to be an ideal nuclide. Its half-life (5.32 d) is long enough to observe even slower metabolic processes. The gamma energies of 87 and 105 keV are ideal for most SPECT cameras.

Despite of the opportunity, only a few in vivo applications of Tb-radionuclides are reported particularly using ^{152}Tb and ^{155}Tb [1-3]. The widespread application of Tb-labeled macromolecules is limited because of the lack of well established and reasonable production routes of the Terbium radioisotopes. In the case of ^{155}Tb Levin *et al*. [5] have already investigated its formation via the ^{156}Dy(γ,*n*)^{155}Dy→^{155}Tb route. Although relative high radionuclidic purity (>99.9%) was obtained, the available yields are not enough for practical purposes. For ^{161}Tb, large-scale production method was developed using highly enriched ^{160}Tb as target and intensive neutron beam from a research reactor [1, 6]. Heavy ions (^{12}C-beam) induced nuclear reactions can be also employed for ^{149}Tb formation however, the accessibility of this type of beam with high intensity, is very limited [7-9]. Proton-induced spallation of Tantalum target, followed by an online isotope separation process, seems to be useful for high scale productions of ^{149,152,155}Tb, however, the

number of laboratories equipped with these devices is very limited [1]. Nowadays several laboratories are involved in research to elaborate practical production methods of the above Terbium radioisotopes using light charged-particle accelerators [10-13].

This study reports on the work of a collaboration established to measure production cross sections for the formation of medically relevant Terbium radioisotopes using deuterons available from commercial medical cyclotrons (*e.g*. 30/15 and 18/9 MeV for protons/ deuterons) and enriched Gadolinium targets. Detailed cross-section measurements are presented here for the ^{nat}Gd(*d,xn*)^{155,156}Tb and ^{nat}Gd(*d,xn*)^{160,161}Tb nuclear processes up to 20 MeV. Based on the reliable excitation functions, we calculate also the available yields for ^{155}Tb and ^{161}Tb to estimate their possible production circumstances. Until now only Tárkányi *et al*. [10, 11] reported cross sections for ^{nat}Gd+*d* processes resulting different Tb, Gd and Eu radioisotopes including ^{155}Tb and ^{161}Tb. Using the cross-section results they have estimated the practical production possibility of ^{161}Tb. Since their excitation function results showed discrepancies for the ^{nat}Gd(*d,xn*)^{160,161}Tb reactions, especially at lower energies (below 10 MeV), we found it necessary to re-measure these processes to get reliable cross-section databases for yield estimations. The limited number of their cross-section data for the ^{nat}Gd(*d,xn*)^{155,156}Tb reactions also motivated us to re-measure these reactions as well. The measured cross sections were also compared with the predictions by means of the TALYS code [14], according to the TALYS-based evaluated nuclear data library TENDL 2014.

Experimental

Natural Gd metal foils (^{152}Gd: 0.2 %, ^{154}Gd: 2.18 %, ^{155}Gd: 14.8 %, ^{156}Gd: 20.47 %, ^{157}Gd: 15.65 %, ^{158}Gd: 24.84 %, ^{160}Gd: 21.86 %) with thicknesses of 8.61, 23.4 μm (obtained from Goodfellow Metals, UK) and 31.87 μm (supplied by New Metals, UK), were used for the targets stacks. The thin metal Ti foils (10, 20 and 25 μm) which were employed for energy degradation and beam intensity monitoring were also supplied by Goodfellow. The cross-section data were collected in three separate experimental runs. The samples were irradiated in the form of stacks. In Debrecen two activations were

performed with energetic deuteron particles (10 MeV; both cases) accelerated by the MGC20 cyclotron of ATOMKI. The irradiations lasted 2.6 h and 2.06 h with beam currents of 50 nA in both cases. The investigated energy regions were 9.58 to 4.2 MeV. The stacks in Debrecen contained 5 and 5 Gadolinium foils of 31.87 μm. In Japan one experiment was performed at the NIRS cyclotron with extracted deuteron energy of 30.24 MeV. The beam current was 50 nA. The target consisted of five 'thicker' (thickness: 23.4 μm) and four 'thinner' (thickness: 8.61 μm) Gadolinium foils. The 5 thick samples (and the degrader foils) slowed down the deuteron beam to 15.4 MeV while energy of the outgoing beam, leaving the last thin target, was 4.2 MeV. The beam current was measured via electric charge collection in a Faraday-cup at both laboratories. Good agreement between direct current measurements and results from deuteron monitor activations has consistently been obtained. For this purpose the reference cross-sections of the ^{nat}Ti(*d,xn*)^{48}V monitor process have been used [15]. The induced radioactivity of the samples and monitor foils were measured non-destructively using HPGe detector gamma-ray spectrometry, analyzing the dominant gamma-rays of the investigated radionuclides. The accurately calibrated detectors had relative efficiencies of 10% and 30%, (ATOMKI and NIRS respectively), with corresponding resolutions of 2.1 keV FWHM and 1.8 keV FWHM at 1.33 MeV. The photo-peak areas were determined using a quantitative analysis software package at NIRS (supplied by Laboratory Equipment Japan) and the FGM program at ATOMKI [16]. The decay data of ^{155}Tb, ^{156}Tb, ^{160}Tb and ^{161}Tb and their dominant contributing reactions are collected in Table 1. The cross sections were calculated by applying the well-known activation formula. The total uncertainties of the measurements were calculated according to Gaussian error propagation and are given together with the cross-section data in Table 2. The errors of non-linear parameters (time etc.) were not considered but their contribution is negligible compared to the linear parameters. The average total cross-section uncertainty was around 14%. The uncertainty of the energy was estimated from the uncertainties of the primary incident deuteron beams and the target thicknesses taking also into account the energy straggling.

Table 1. Decay characteristic and contributing reactions for production of ^{155}Tb, ^{156}Tb, ^{160}Tb and ^{161}Tb

Nuclide	Half-life (day)	Gamma energy used for identification (keV)	Contributing reaction	Q-value (MeV)
^{155}Tb	5.32	180.08	^{154}Gd(*d,n*),	2.61
		1340.67	^{155}Gd(*d,2n*)	-3.83
			^{156}Gd(*d,3n*)	-12.36
			^{157}Gd(*d,4n*)	-18.72
^{156}Tb	5.35	534.29	^{155}Gd(*d,n*)	3.09
		1222.44	^{156}Gd(*d,2n*)	-5.45
			^{157}Gd(*d,3n*)	-11.81
			^{158}Gd(*d,4n*)	-19.75
^{160}Tb	72.3	879.38	^{160}Gd(*d,2n*)	-3.11
^{161}Tb	6.89	74.57	^{160}Gd(*d,n*)	4.58
			^{160}Gd(*d,p*)^{161}Gd→^{161}Tb	-3.41

Results and Discussion

The measured cross sections for the formation of end products ^{155}Tb, ^{156}Tb, ^{161}Tb and ^{160}Tb are shown in Figs.1-4 and compared to the available literature results. Additionally, theoretical curves taken from TENDL-2014 library (calculated by TALYS code) are also added to the figures [14]. The presently measured cross-section values are also collected in Table 2. Since we investigate here only the production possibilities at low energies, all measured cross-section values above 22 MeV will be published separately.

Excitation functions of the ^{nat}Gd(d,xn)^{155,156}Tb nuclear processes

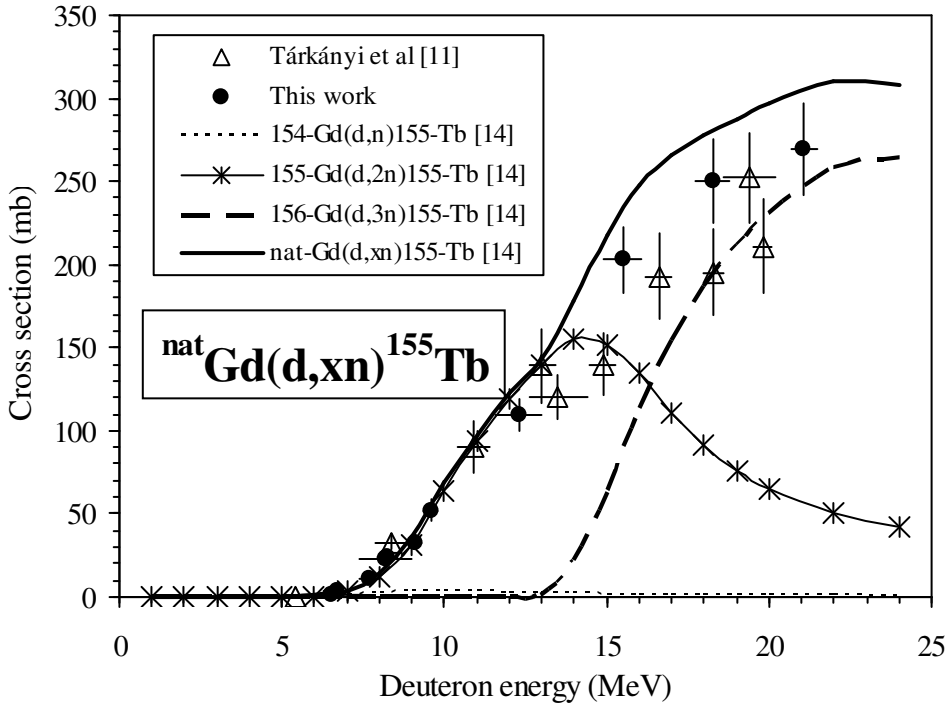
Below 20 MeV three reactions (^{154}Gd(*d,n*), ^{155}Gd(*d,2n*) and ^{156}Gd(*d,3n*)) contribute to the formation ^{155}Tb using natural Gd target. Due to this fact, it was possible to evaluate only the 'natural' cross-sections for its formation. (Natural cross-section is the sum of cross sections of the contributing nuclear reactions weighted by the natural isotopic abundance of the target nucleus.)

Table 2. Measured cross sections for the production of ^{155,156,160,161}Tb radionuclides in the irradiation of ^{nat}Gd with deuterons

Deuteron energy (MeV)	Cross section (mb) ^{155}Tb	^{156}Tb	^{160}Tb	^{161}Tb
4.2±0.4	-	-	0.3±0.1	2.1±0.6
4.9±0.5	-	-	0.3±0.1	4.0±0.5
6.5±1.0	1.1±0.1	0.7±0.1	4.3±0.7	10.4±11.3
6.7±0.4	4.1±0.6	3.1±0.4	6.3±0.8	9.7±1.2
7.7±0.3	10.6±1.1	10.6±1.2	15.9±1.8	17.0±1.9
8.2±0.9	23.2±2.5	42.2±5.2	25.1±2.8	29.3±3.2
8.2±0.3	23.5±3.2	23.6±2.6	32.7±3.9	26.0±2.9
9.1±0.2	32.9±3.8	42.7±4.7	56.3±6.3	33.3±3.6
9.6±0.2	52.0±6.5	67.6±7.4	81.5±9.2	39.3±4.3
12.3±0.8	110±12	174±21	100±12	36.4±3.9
15.5±0.6	203±21	234±25	74.3±9.4	24.9±2.7
18.3±0.5	250±26	240±26	48.9±5.5	24.2±2.6
21.1±0.4	269±28	236±25	-	19.3±2.1

Our data are in good agreement with the values of Tárkányi *et al.* [11] over the whole investigated energy region. The TENDL-2014 estimation for the ^{nat}Gd+*d* process, however, overpredict the experimental results especially above 13 MeV. The theoretical excitation functions of the contributing reactions are also added to Fig.1. (The original TENDL-2014 values were multiplied by us with the natural abundances of the target nucleus in ^{nat}Gd). Taking into account the natural abundances of the possible targets, the cross-section maximums and the available energy region, the ^{155}Gd(*d,2n*)^{155}Tb reaction would be useful for production purposes. Although the irradiation of ^{nat}Gd could produce useful amount of ^{155}Tb, the co-formation of other (long-lived) Tb radioisotopes [11] resulted in unacceptably high radioisotope contamination level of the final product. To decrease this level, however, there is no other choice than using highly enriched ^{155}Gd (>99.9) target. In this case the only major contamination would be ^{156}Tb ($T_{1/2}$ = 5.35 d) which is formed via the ^{155}Tb(*d,n*) reaction. Unfortunately it has a half-live comparable to ^{155}Tb, therefore it will be present in any final product. To estimate its formation circumstances, we measured also the excitation function curve of the ^{nat}Gd(*d,xn*)^{156}Tb process up to 21 MeV. The results can be seen in Fig.2. The cross sections of the

143 contributing processes, namely ^{155}Gd(*d,n*), ^{156}Gd(*d,2n*) and ^{157}Gd(*d,3n*), taken from the
144 TALYS-based evaluated nuclear data library TENDL 2014, are also added to Fig.2 [14].



145

146 **Fig.1**. Excitation functions for the production of ^{155}Tb in the bombardment of ^{nat}Gd with
147 deuterons

148 The present measurement is in relative good agreement with the data of Tárkányi *et al.*
149 [11]. However, the natural cross-section predictions of TENDL-2014 are closer to our
150 data especially in the energy range from 10 to 15 MeV.

151 It can be seen that the impact of ^{155}Gd(*d,n*) reaction to the production of ^{156}Tb is almost
152 negligible. However, since the starting energies of the ^{155}Gd(*d,2n*) and ^{155}Gd(*d,n*) are
153 close to each other, there is no energy window where the ^{155}Tb can be produced without
154 ^{156}Tb contamination even if 100% enriched target is used. The ^{156}Tb/^{155}Tb contamination
155 level, using the theoretical (TALYS) excitation functions, strongly depends on the energy
156 window used for production. For example, at 14 MeV this contamination level is around
157 5 %.

Excitation functions of the $^{nat}Gd(d,xn)^{161,160}Tb$ processes

The ^{161}Tb is formed on one Gadolinium nuclide (^{160}Gd) via a direct reaction ($^{160}Gd(d,n)^{161}Tb$) and through the decay of ^{161}Gd ($T_{1/2}$= 3.66 m) ($^{160}Gd(d,p)^{161}Gd \rightarrow ^{161}Tb$) in the case of deuteron activation.

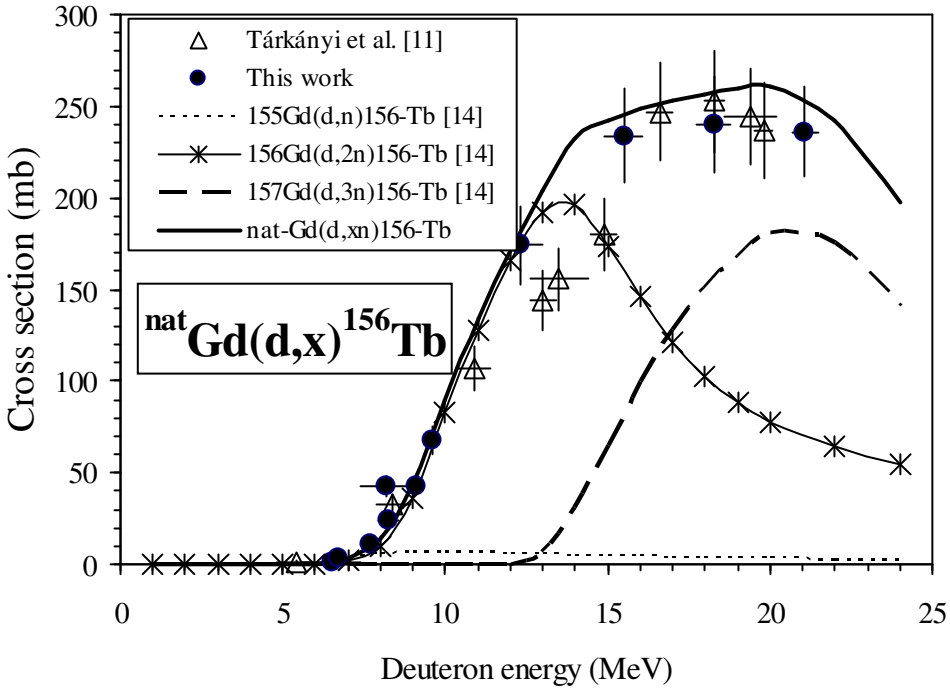


Fig.2. Excitation functions for the production of ^{156}Tb in the bombardment of ^{nat}Gd with deuterons

All cross-section values on Fig.3, including the present results are cumulative data calculated after the complete decay of the ^{161}Gd precursor and refers to the natural isotopic abundance of ^{160}Gd (21.86%). Our numerical cross-section data are collected in Table 2. The two data sets of Tárkányi *et al.* [10, 11] are also reproduced on this figure. Our excitation function seems to support the most recent result of Tárkányi *et al*. [11]. As usual in the case of (*d,n*) reactions in this mass region, the theoretical results published in TENDL-2014 library significantly underestimate the experimental values.

Based on the experimental results, this reaction seems to be useful for production purposes if highly enriched (>99.9%) ^{160}Gd is employed. Our calculation predicts somewhat lower yields (10-15%) than it was reported by Tárkányi *et al*. in their first article [10], but still acceptable for practical purposes.

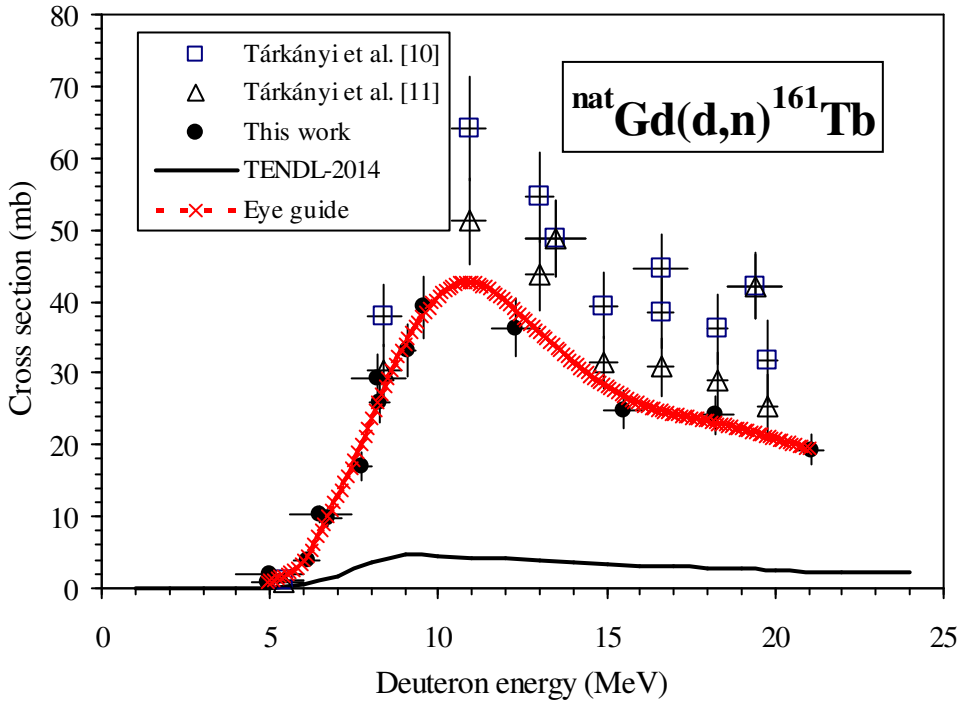


Fig. 3. Excitation functions for the production of ^{161}Tb in the bombardment of ^{nat}Gd with deuterons

In the investigated energy range one radio-contaminant will be co-formed even if 100% enriched ^{160}Gd is used as target. Unfortunately this radioisotope (^{160}Tb) has almost 10 times longer half-life than the ^{161}Tb (see Table 1) therefore its influence can not be neglected from the point of view of medical applications. We have also re-measured the excitation function of the ^{160}Gd(*d,2n*)^{160}Tb nuclear reaction, which only responsible for ^{160}Tb formation. Our results together with the literature results and the predicted curve of the TENDL-2014 calculation can be seen in Fig.4. (Note that all values refer to the natural abundance of ^{160}Gd). While the present data support the most recent values of Tárkányi *et al.* [11], the theoretical calculation seems to show better agreement with the earlier literature values [10]. The recent cross-section results for both of the above

investigated reactions confirm the conclusion reported in [10]: Due to the high level of the ^{160}Tb contamination in the final product there is no energy window where the ^{161}Tb can be produced for medical purposes.

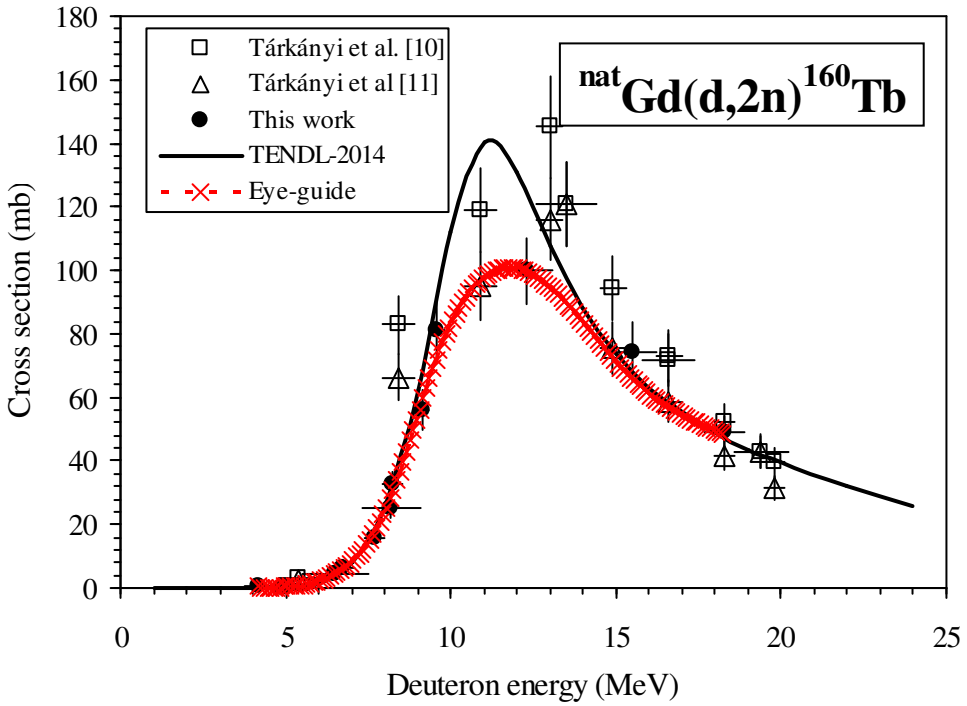


Fig. 4. Excitation functions for the production of ^{160}Tb in the bombardment of ^{nat}Gd with deuterons

Since the number of the co-produced ^{160}Tb is much higher (around twice) than the ^{161}Tb, this production route seems to be useful only for developmental studies. Note that the ^{160}Tb/^{161}Tb contamination level increases as function of irradiation time.

Conclusion

The detailed cross-section measurement of this work not only extended the databases of the ^{nat}Gd(*d,xn*)^{155,156,160,161}Tb nuclear processes up to 21 MeV, but also pointed to the disagreement between the experimentally measured data of the literature. Cross-section results revealed that both ^{155}Tb and ^{161}Tb can not be produced in no-carrier-added form

even using 100% enriched ^{155}Gd and ^{160}Gd targets, respectively. Their practical application therefore is limited to supply radioactive Terbium for developmental studies. At present the only practical method for production of medically relevant ^{161}Tb radioisotope is the spallation-type reaction followed by mass separation.

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