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Estimation of cyclotron–based ^{161}Tb production yields via ^{160}Gd(d, n)^{161}Tb nuclear reaction

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Abstract. Theoretical yield of cyclotron-based production route for ^{161}Tb isotope using enriched oxide target, relying on the nuclear reaction ^{160}Gd (d, n)^{161}Tb, is calculated. The yield of ^{161}Tb and radioactive impurities (^{160}Tb and ^{161}Gd) is calculated for range of initial deuteron energies up to 30 MeV, as well as suitable target thickness for each of the energies. Initial particle energy of 20 MeV can be considered preferable in such production line, since further increase of energy (over 10-12 MeV) leads to cross section decrease for the targeted isotope and the yield curve slightly flattens, and is yet achievable for existing cyclotrons. It is concluded that evaluated production route cannot produce carrier-free ^{161}Tb under considered conditions. To obtain results on stopping power and particle range SRIM software was used.

1. Introduction

Nowadays most of the nuclear medicine diagnostic procedures are carried out using ^{99m}Tc, production of which seems to be endangered, due to aging reactor production facilities [1]. Different isotopes are proposed to be substitutes for ^{99m}Tc, one of them being ^{152}Tb. Due to the same chemical properties as ^{152}Tb other isotopes of terbium also came into the focus, and are planned to be combined with it as suitable theranostic pairs.

First in vivo introduction of the so called “terbium quadruplet” is done by Muller et al. in ref. [2] and stressed the clinic study importance of ^{149}Tb, ^{152}Tb, ^{155}Tb and ^{161}Tb.

Following the idea of pairing one diagnostic and one therapeutic isotope, which is a common practice for theranostic medication labelling, Qaim et al. in ref. [3] suggested terbium pairs ^{152}Tb/^{161}Tb and ^{152}Tb/^{149}Tb, where ^{161}Tb acts as the therapeutic component.

For a long time, the golden standard for therapy has been considered to be ^{177}Lu, thus the two can be compared. The main similarity between the two is the same decay mode. In pre-clinical studies Muller et al. in ref. [4] showed that tracers with ^{161}Tb show minimal or nil effect on kidney function, while ^{177}Lu labelled ones can damage it.

The scope of this research is to evaluate possibility to produce ^{161}Tb in clinical setting. Work conducted with the same goal was published by Tarkanyi et al. in ref. [5]. They used gadolinium powder targets with natural isotopic composition and irradiated them with highly accelerated deuterons. They noted that impurities are inevitable, and recommended usage of enriched targets.

To increase the production rate, in this research highly enriched ^{160}Gd oxide targets irradiated by deuterons with initial energy up to 30 MeV are used.

2. Target material selection

For ^{161}Tb cyclotron production, ideal target needs to fulfill several requirements, connected with both projectile and target properties.

Using cyclotron, not a wide range of particles can be used as projectiles – mostly protons, deuterons or alpha particles, occasionally light nuclei. Accordingly, only the transformation of elements with similar nuclear structure can be used for the production. That being said, both dysprosium and gadolinium isotopes are suitable candidates, since they have structures of nuclei which are easily transformed to terbium by light particles (or light nuclei). To meet practical side of the work no nuclei will be used as projectile particles, since there are very few of such facilities nowadays.

Both of the mentioned target materials (Dy and Gd) are fully suitable for further consideration, but are used in combination with different projectiles. Dysprosium target can produce ^{161}Tb if irradiated by protons, while gadolinium needs to be irradiated by deuteron beam [5]. The last reaction is presumed to have higher cross section, thus the higher production rate.

In the present work highly enriched gadolinium oxide will be used as a target material. It is expected that such a target will have higher production rate of ^{161}Tb compared to a natural isotope mixture. Since gadolinium is rare-earth metal and high-enrichment procedures are demanding and expensive, economical aspect of the process will not be described. Moreover, deuteron sources can be more expensive than the proton ones, that also raises the summary cost of the production route.

From chemical aspect, the most abundant and stable form of gadolinium is its oxide, a powder-like substance.

Consequentially, ignoring the economical aspect in which natural dysprosium irradiated by protons is absolutely preferable, further work will be done on highly enriched ^{160}Gd in oxide form via ^{160}Gd(d,n)^{161}Tb reaction.

Thickness of $^{160}Gd_2O_3$ powdery target is calculated in such way, that all of the particles are completely stopped inside the target. The calculation is done by adding the 10% to maximum range of the particle in the target material [6]. In that way, all possible particle ripples are excluded. Optimal thickness of the target as function of deuteron energy is presented on Figure 1.

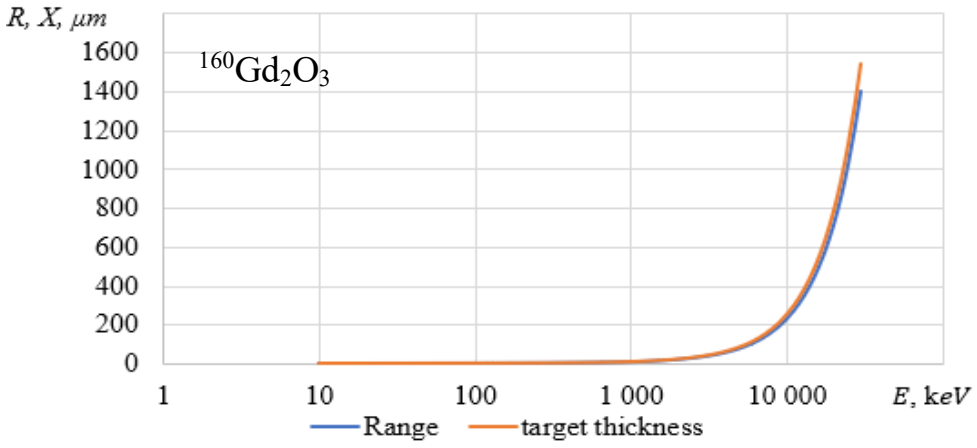

Figure 1. Range of deuterons in Gd_2O_3 target and target thickness (X)

3. Research methods

Range, stopping power (v. Figure 2) and effective cross sections are obtained from the SRIM [7] (publicly available at www.srim.org) simulation results and TENDL-2019 database [8], respectively.

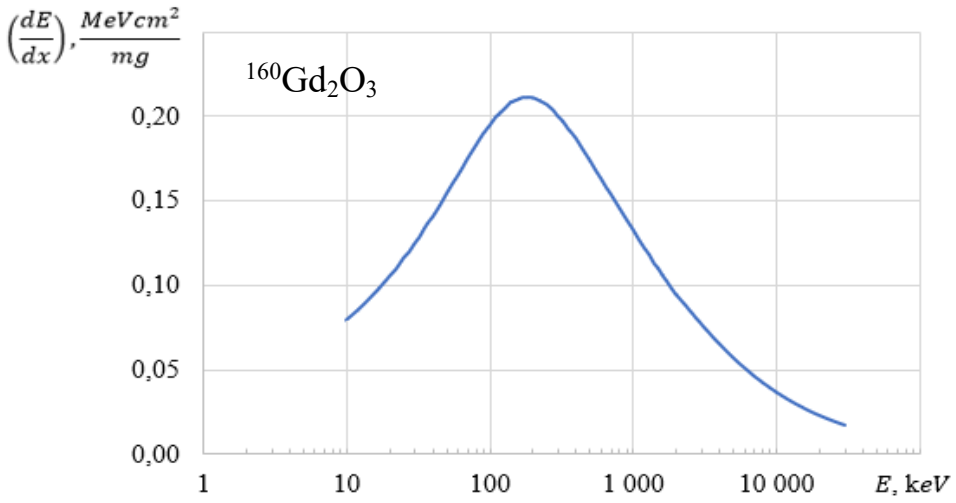

Figure 2. Stopping power for deuterons in proposed target

Initial parameters used for the calculation of range, stopping power and target thickness are the following:

- projectile particle: hydrogen nucleus with one excess neutron (deuteron setting is not available in the standard database of available particles). Addition is done by manually changing the mass of the nucleus to 2.014102 amu;
- target structure: uniformly dispersed mix of gadolinium and oxygen in ratio 2:3.
- target mass ratio – 86.76% of gadolinium and 13.24% of oxygen;
- density of the target is 7.41 g/cm^3 and atomic concentration of $6.15 \cdot 10^{22}$ 1/cm^3;
- calculation is done without any Bragg's correction coefficient.

To make the results applicable for as wide range of operating regimes as possible, all the obtained values will be normalized over one hour of production. The end-of-bombardment (EOB) yield is calculated as follows [9]:

$$A = KF\left(1 - e^{-\frac{0.7t}{T}}\right)\int_0^{E_p} \sigma \left(\frac{dE}{dx}\right)^{-1} dE \quad (1)$$

where A is EOB yield, K is a numerical constant, F is particle flux, T is the half-life constant of the desired isotope, t is the time of irradiation, E_p is the initial energy of incoming particles, σ is the effective cross section and dE/dx is the stopping power of particle in the target.

Constant K is calculated as follows:

$$K = \frac{fNa}{w} \quad (2)$$

where Na is Avogadro's number, w is the atomic weight of the target, f is the abundance of the isotope.

Particle flux is calculated from the beam current, by the definition of electric current:

$$F = \frac{6.25 \cdot 10^{12} I}{z} \quad (3)$$

where z is charge number of the projectile particle and I is beam current (in μA) [9].

Firstly, the general data for the isotope needs to be clarified, in order to take into account its decay during the production process. Important parameters for the calculation of constant values are (all nomenclature is in accordance to formulas (1), (2) and (3)):

- Half-life of ^{161}Tb: T = $0.59 \cdot 10^{6}$ s;
- molar mass of the target: M = 367.852 g/mol;
- charge of the projectile: z = $1.66 \cdot 10^{-19}$ C;
- abundance of the ^{160}Gd in target: f = 100%·2/5;
- atomic weight of the oxide: w= 367,8 g/mol.

For calculation of the radioactive impurities, several significant reaction channels are considered. Reaction channel is considered significant if its effective cross section is comparable or higher than the cross section of ^{160}Gd(d,n)^{161}Tb reaction. Estimation is done on pure ^{160}Gd target and reaction cross sections are presented on Figure 3, based on data from ref. [8]. Difference in cross sections for oxide and pure ^{160}Gd is taken into account in the calculations using parameter f.

Special attention is given to reactions (d, n) and (d, p), cross sections of which do not agree with experimental data, thus are obtained from ref. [5].

It is important to note, that several works do agree with Tarkanyi et at. to reasonable extent, including Szelecsenyi et al. in ref. [10]. However, for final comparison the work of Nigron et al. [11] will be used, since their data were obtained using more reliable spectral line.

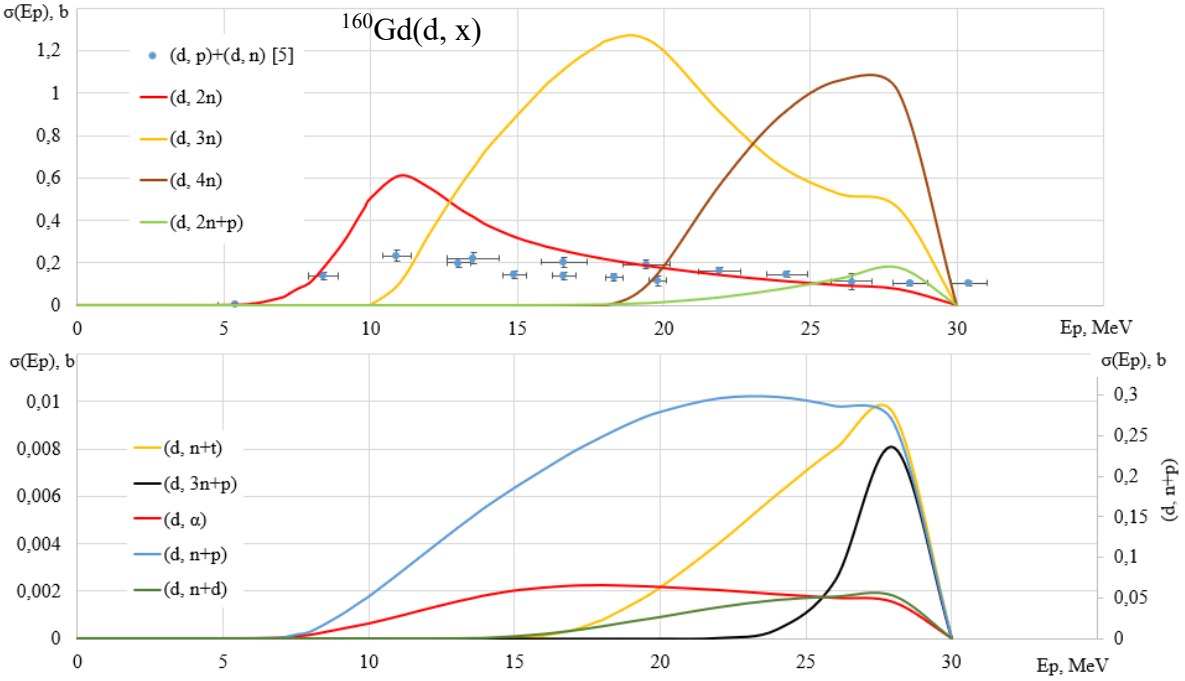

Figure 3. Cross section comparison for relevant reaction channels on pure ^{160}Gd target

4. Results

Having stopping power and effective cross sections for all of the reactions with significant yield, production rates can be calculated for desired and byproduct isotopes.

As already concluded in ref. [5], getting the isotopically clean product by the proposed route is not possible, since several possible reaction channels are strongly influencing the outcome. Both radioactive and stabile isotopes would be present in the mixture (Table 1). Some of those with significantly higher effective cross section then the desired one (v. Figure 3).

Table 1. Decay characteristic and contributing reactions for production of ^{161,160,159,158}Tb, ^{161,160,159}Gd and ^{158}Eu [12]

Nuclide	Decay mode	Half-life (abundance)	Contributing reaction[a]
^{161}Tb	β^-: 100%	6.89 d	^{160}Gd (d, n)^{161}Tb ^{160}Gd(d, p)^{161}Gd→^{161}Tb
^{160}Tb	β^-: 100%	72.30 d	^{160}Gd (d, 2n)^{160}Tb
^{158}Gd	stabile	24.84%	^{160}Gd (d, n+t)^{158}Gd ^{160}Gd (d, 2n+d)^{158}Gd ^{160}Gd (d, 3n+p)^{158}Gd ^{160}Gd (d, 4n)^{158}Tb→^{158}Gd
^{159}Tb	stabile	100%	^{160}Gd (d, 3n)^{159}Tb ^{160}Gd (d, n+d)^{159}Gd→^{159}Tb
^{160}Gd	stabile	21.86%	^{160}Gd (d, n+p)^{160}Gd
^{159}Gd	β^-: 100%	18.48 h	^{160}Gd (d, n+d)^{159}Gd ^{160}Gd (d, 2n+p)^{159}Gd
^{158}Tb	$\varepsilon+\beta^+$: 83.4% β^-: 16.6%	180 y	^{160}Gd (d, 4n)^{158}Tb
^{161}Gd	β^-: 100%	3.66 min	^{160}Gd (d, p)^{161}Gd
^{158}Eu	β^-: 100%	45.90 min	^{160}Gd (d, α)^{158}Eu

[a] Decay reaction are not included in EOB calculations.

Several radioactive products are expected to be widely present in the final product, independent of the irradiation time. Presuming burn-up of products is way less probable than one-time deuteron capture, radioactive isotopes such as ^{161}Tb, ^{160}Tb, ^{161}Gd are expected and their production rate is estimated – Figure 4.

The impurities are of different importance, since, for instance, ^{158}Tb is not produced in considerable quantity. The most valuable of all impurities for further consideration is ^{161}Gd, which undergoes beta decay in a rapid pace, resulting in additional ^{161}Tb source. That rapid decay should be considered in procedures following the irradiation, since the peak activity of ^{161}Tb will be shifted in time.

However, there is no cross section data dedicated only for such (n,p) reaction, so the production of ^{161}Tb and ^{161}Gd is carried out together. The same data were obtained in ref. [5] and [11], so the comparison between the three can be made – Figure 5.

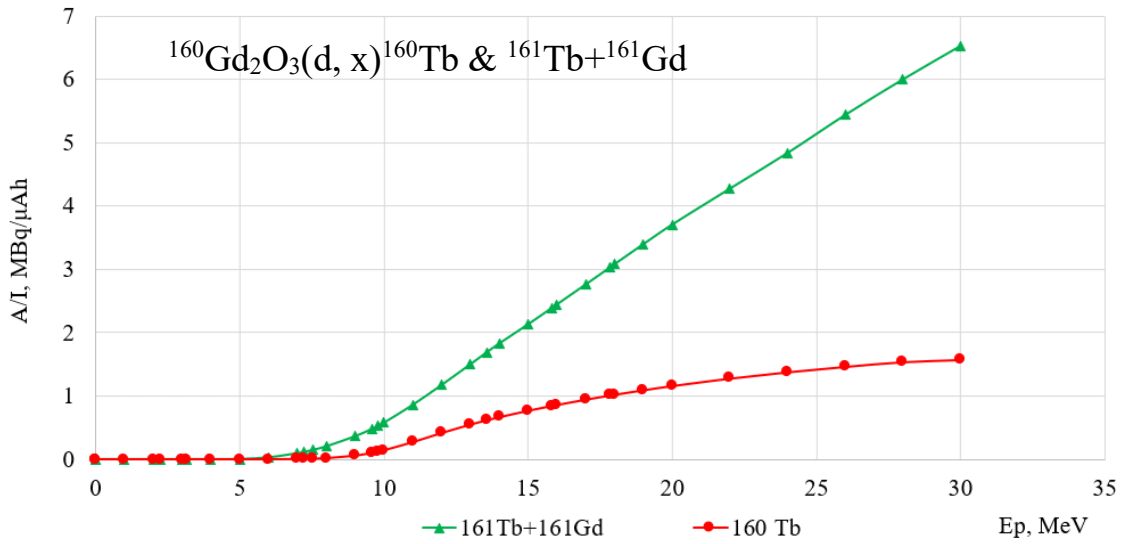

Figure 4. Production rate of ^{161}Tb+^{161}Gd and ^{160}Tb from oxide target

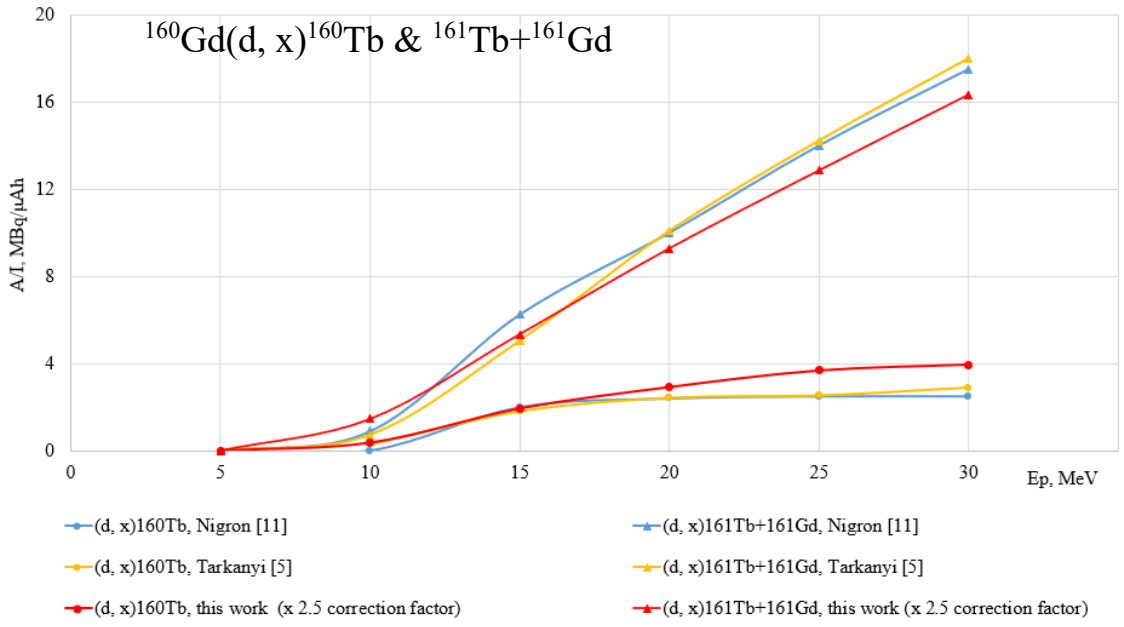

Figure 5. Comparison of integral yields for ^{160}Gd(d, x)^{160}Tb & ^{161}Tb+^{161}Gd between this work and ref. [5] and [11]

To evaluate obtained yields, comparison with experimental data is necessary. As shown on Figure 5, calculated yield match satisfactory with the data from ref. [11] and [5] for energies lower than 15 MeV. In the reaction cross section peak region (v. Figure 3), results mostly agree, and the discrepancy of Tarkanyi's data can be due to manual extraction from the graphs in ref. [5].

For higher energies discrepancy is increasing for both reactions, reaching up to 11.5% for ^{161}Tb+^{161}Gd at 25MeV. Results for ^{160}Tb are overestimated on whole range of comparation. The discrepancy occurs due inconsistency of data used for the cross section calculations, since data from ref. [8] and [5, 10] do not necessarily agree. That effect is mostly present in the higher

energies, which can be due to fitting curve smoothing effect, since data from ref. [5] were obtained in discrete form.

5. Conclusions

In the proposed production route, impure ^{161}Tb is produced from the highly enriched ^{160}Gd target. Evaluation of several possible target materials suggested that gadolinium oxide targets irradiated by deuteron beam can be preferable for the reaction yield, but are economically unviable.

Evaluated reaction gives two possible channels for the desired isotope production – directly from the bombardment and via decay of byproduct ^{161}Gd (v. Table 1).

As can be seen on Figure 4, direct production yield shows the biggest dependence of initial energy in range 6–20 MeV. In other two energy intervals (0-6 MeV and 20-30 MeV) change in energy has nil or insignificant effect on the reaction yield, considering the amount of energy consumed.

From the mathematical model used in the estimation, it is clear that yield is inevitable rising with the rise of the initial energy. Therefore, the energy of 20 MeV is considered optimal and suitable target thickness is considered to be 7.7 mm. However, even at 20 MeV produced activity of combined ^{161}Tb and ^{161}Gd is considerably high only after long irradiation period. Due to combined production and rapid decay of ^{161}Gd, spike of targeted isotope concentration can be expected right after the irradiation. However, after the ^{161}Gd decay (~30 min), all the residual of ^{161}Tb activity can be tracked and estimated by the decay law of ^{161}Tb alone.

Besides the production rate of the desired isotope, production rates of radioactive impurities via proposed reaction are estimated. It was concluded, that ^{158}Tb, ^{160}Tb, ^{161}Gd can be expected, though the presence of ^{158}Tb is negligible. However, the separation process will also be necessary and, possibly, complex, since all the impurities have rather similar properties as ^{161}Tb.

Knowing that some clinical procedures take up to 1.2–2.6 GBq of activity, i.e., pain palliation in skeletal metastases [13], it is clear that in reasonable period of irradiation, such activities are hard to achieve by this production route. That being said, conclusions on cyclotron production insufficiency for ^{161}Tb stated by Tarkanyi et al. [5] and Nigron et al. [11] are once more confirmed.

6. Acknowledgments

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References

[1] Ruth T J 2020 *Annu. Rev. Nucl. Sci.* **70(1)** 77–94
[2] Müller C *et al* 2012 *J. Nucl. Med.* **53 (12)** 1951-59
[3] Qaim S M, Scholten B, Neumaier B 2018 *J. Radioanal. Nucl. Chem.* **318 (3)** 1493–1509
[4] Müller C *et al* 2019 *Eur. J. Nucl. Med. Mol. Imaging* **46(9)** 1919–30
[5] Tárkányi F, Hermanne A, Takács S, Ditrói F, Csikai J and Ignatyuk A V 2013 *J. Radioanal. Nucl. Chem.* **298(2)** 1385–92
[6] Wibowo F A and Kambali I 2021 *J. Phys.: Conf. Ser.* **1816** 012099
[7] Ziegler J F, Ziegler M D and Biersack J P 2010 *Nucl. Instr. Meth.* **B 268** 1818
[8] Koning A J, Rochman D, Sublet, J Ch, Dzysiuk N, Fleming M, Van der Marck S 2019 *Nucl. Data Sheets* **155** 1-55
[9] Chaudhri A J, Qaiser J and Qammar N 1995 *14th International Conf. on Cyclotrons and their Applications*
[10] Szelecsényi F, Kovács Z, Nagatsu K. Zhang M R and Suzuki K 2016 *J. Radioanal. Nucl. Chem.* **307** 1877–81

[11] Nigron E, Guertin A, Haddad F, Granger L, Rayer M and Rintaud A 2023, *Appl. Radiat. Isot.* **200** 110927
[12] National Nuclear Data Center 2000 National Nuclear Data Center. Brookhaven National Laboratory (http://www. nndc. bnl. gov/exfor/exfor00. htm)
[13] Dash A, Pillai M R A and Knapp F F 2015 *Nucl. Med. Mol. Imaging* **49** 85–107