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INVESTIGATION OF THE PRODUCTION OF THE AUGER ELECTRON EMITTER ^{135}La USING MEDICAL CYCLOTRONS*

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Possible reactions leading to the production of ^{135}La are discussed in this study and corresponding theoretical yields calculated using Monte-Carlo (MCNPX) code are presented. The pilot ^{135}La production was performed employing the 16 MeV protons provided by a PETtrace cyclotron and a $^{\mathrm{nat}}$BaCO$_3$ target.

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1. Introduction

The Auger electron therapy is one of the most promising and important cancer therapies due to delivery of radiation dose only to individual cells [1]. Its effectiveness has been recently summarized in Refs. [2–4]. The Auger electron emitters cause much less off-target effects than β emitters [4]. ^{135}La with the half-life of 19.5 h and almost 100% decay to the stable ^{135}Ba [1] by electron capture is one of the important candidates for this kind of therapy. It also emits only low-intensity gamma rays (predominantly 480.5 keV, 1.5%) which contribute to the patient dose at a negligible level.

^{135}La can be produced using proton or deuteron bombardment of barium via ^{135}Ba$(p,n)^{135}$La, ^{136}Ba$(p,2n)^{135}$La, ^{134}Ba$(d,n)^{135}$La, ^{135}Ba$(d,2n)^{135}$La reactions and alpha bombardment of cesium ^{133}Cs$(\alpha,2n)^{135}$La.

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In 2015 and 2018, respectively, Mansel [5] and Fonslet [1] reported production of ^{135}La using protons bombarding a barium target. Nevertheless, to date, only few research works have been performed to study ^{135}La production routes. The cross sections are reported only for: $^{\rm nat}$Ba(d,x), $^{\rm nat}$Ba(p,x), $^{\rm nat}$La(p,x) and ^{133}Cs$(\alpha,2n)$ [2–10]. In this work, some possible routes of ^{135}La radionuclide production have been analysed in terms of production yield regarding the small medical cyclotron facilities and cost of targets needed for the discussed reaction. The production yield was calculated using the Monte Carlo N-Particle eXtended (MCNPX) code [11, 12].

2. Materials and methods

2.1. Theoretical calculations of TTY

The assessment of the applicability of a ^{135}La production route was mainly based on evaluation of Thick Target Yield (TTY) describing number of the produced radionuclides (activity) per unit of time and current of the applied beam. Theoretical TTY for production of the radionuclide of interest can be calculated using the following equation [13, 14]:

$$\mathrm{TTY} = \frac{H N_{\mathrm{A}} \lambda}{M Z\, e} \int\limits_{E_1}^{E_2} \frac{\sigma(E)}{\mathrm{d}E/\mathrm{d}(x\rho)} \mathrm{d}E\,, \tag{1}$$

where TTY is thick target production yield [Bq/Ah], N_{A} is the Avogadro number [1/mol], H is the isotope abundance of the target nuclide [%], M is the molar mass of the target element [g/mol], $\sigma(E)$ is the cross section at energy E [cm^2], $\mathrm{d}E/\mathrm{d}(x\rho)$ is the stopping power [MeV/(mg/cm^2)], λ is the decay constant of the product [1/h], $E_1 - E_2$ is the energy deposited in the target material [MeV], Z is the atomic number of the projectile, and e is the elementary charge [As].

In our calculations, we used the cross sections from the TENDL-2017 nuclear data library based on the TALYS code [15]. The stopping powers used in the calculation were derived from the SRIM 2013 code (Stopping and Range of Ions in Matter) [16].

The activity produced at the given irradiation time or the irradiation time needed to produce the required activity can be calculated from the following relation (considering decays of the produced radionuclide):

$$A_{\mathrm{EOB}} = \mathrm{TTY}\, I\, \frac{1}{\lambda}\left(1 - \mathrm{e}^{-\lambda\, t_{\mathrm{irr}}}\right)\,, \tag{2}$$

where A_{EOB} — activity at the End Of Bombardment, I — beam current, λ — decay constant, t_{irr} — irradiation time.

2.2. TTY predictions for ^{135}La production

^{135}Ba$(p,n)^{135}$La and ^{136}Ba$(p,2n)^{135}$La reactions

The optimal proton energy range for the ^{135}Ba$(p,n)^{135}$La reaction is of 16 to 5 MeV [15]. Since the natural abundance of ^{135}Ba is relatively low (6.5%) (Table I), a highly enriched barium target would be necessary for efficient production of ^{135}La in this reaction. The best energy range for the ^{136}Ba$(p,2n)^{135}$La reaction is between 35 to 12 MeV, however, it is worth mentioning that for the energy corresponding to the best range of the first reaction, the ^{135}La production yield is of comparable level. In other words, using natural barium both ^{135}La production channels have to be considered. The theoretical calculation shows the production yield at 16 to 5 MeV of proton energy range for the 100% enriched isotopes, ^{135}Ba and ^{136}Ba equals to 165.48 MBq/μAh and 151 MBq/μAh, respectively and 16 MBq/μAh for a natural Ba target (Table II).

TABLE I

Natural abundance of barium isotopes.

Isotope	^{132}Ba	^{134}Ba	^{135}Ba	^{136}Ba	^{137}Ba	^{138}Ba
Abundance [%]	0.1	2.4	6.5	7.8	11.2	71.7

TABLE II

^{135}La theoretical production yield in various reactions.

Reaction	Target yield [MBq/μAh]		Energy range [MeV]
	100% enrichment	Natural target	
^{135}Ba$(p,n)^{135}$La	165.48	16*	$16 \to 5$
^{136}Ba$(p,2n)^{135}$La	151.20		$16 \to 12$
^{135}Ba$(d,2n)^{135}$La	570.45		$35 \to 8$
^{134}Ba$(d,n)^{135}$La	33.27		$14 \to 8$
^{133}Cs$(\alpha,2n)^{135}$La	38.28		$40 \to 16$

*This TTY value was calculated for $16 \to 5$ MeV proton energy range, taking into account the contribution of the ^{135}Ba$(p,n)^{135}$La and ^{136}Ba$(p,2n)^{135}$La reactions.

Taking into account composition of the natural barium, it makes the ^{135}La production efficiency relatively high and considering the energy of protons delivered by cyclotrons such as PETtrace, C18/9 or Eclipse$^{\mathrm{TM}}$RD, this production route seems to be the most effective for the ^{135}La production in PET centres.

^{135}Ba$(d, 2n)^{135}$La reaction

The efficient energy range for the ^{135}La production in ^{135}Ba$(d, 2n)^{135}$La reaction is between 35 to 8 MeV. The theoretical calculation shows that the production yield in this energy range is 570.45 MBq/μAh (Table II). However, it requires high-energy deuterons that are not provided by the medical cyclotrons most commonly installed in the PET centres.

^{134}Ba$(d, n)^{135}$La reaction

The production energy range for the ^{134}Ba$(d, n)^{135}$La reaction is of 14 to 8 MeV [15]. The theoretical calculation shows that the production yield in the mentioned energy range equals 33.27 MBq/μAh (Table II). Due to the limited production efficiency and the very low abundance of ^{134}Ba in natural barium (2.4%), which would require the use of expensive enriched target material, the reaction cannot be considered as a good candidate for the efficient production of ^{135}La.

^{133}Cs$(\alpha, 2n)^{135}$La reaction

Regarding the best energy range of ^{133}Cs$(\alpha, 2n)^{135}$La production route (40–16 MeV), the calculation shows that the production yield equals 38.28 MBq/μAh (Table II). Taking into account that the yield is very low compared to other possible production routes, this reaction cannot be considered as a reasonable candidate.

2.3. Pilot production of ^{135}La using PETtrace cyclotron

2.3.1. Proton beam energy and beam current measurements

The verification of the experimental results requires measurements of the proton energy and the current of extracted beam. This is needed as well to optimize a target thickness and to reduce the radiation dose originating from the isotopes produced inside reactions [17].

Using the method proposed by Gagnon *et al.* [17], we verified the proton energy to be 15.98 ± 0.03 MeV. The beam current was measured by irradiating the copper and titanium foils of the same thickness (11 μm) and evaluating the activity of each radionuclide (^{62}Zn, ^{65}Zn and ^{48}V) produced respectively in Cu and Ti [18]. The obtained average beam current was 9.41 ± 1.85 μA which we found consistent with Faraday Cup measurements (10.2 ± 0.1 μA).

2.3.2. Target and irradiation condition

Considering the above TTY calculations and energy of protons delivered by PETtrace installed at HIL UW, the production of the ^{135}La via the $^{\rm nat}$Ba$(p, x)^{135}$La reaction was tested. Natural barium carbonate target ($BaCO_3$) with thickness of 427 mg/cm^2 prepared as a pellet [19] was bombarded for 10 minutes at the PETtrace cyclotron solid state target station [20] with a proton beam of 15.7 MeV energy and 9.4 μA intensity. The foils of Cu (11 μm) and Ti (11 μm) were placed in front of the barium carbonate pellet for off-line beam current verification. Target activity after irradiation was measured with a HPGe detector. Moreover, due to the fact that natural barium is composed of 6 stable isotopes (Table I), the co-produced impurities were also investigated.

3. Results and discussion

The activity of ^{135}La produced in our pilot irradiation was equal to 9.57 MBq at EOB what corresponds to about 6 MBq/μAh of TTY (Fig. 1, left panel). The activities of coproduced impurities (Fig. 1, right panel) namely ^{132}La and ^{132}Cs were measured as 0.43 MBq and 0.83 MBq, respectively (Table III).

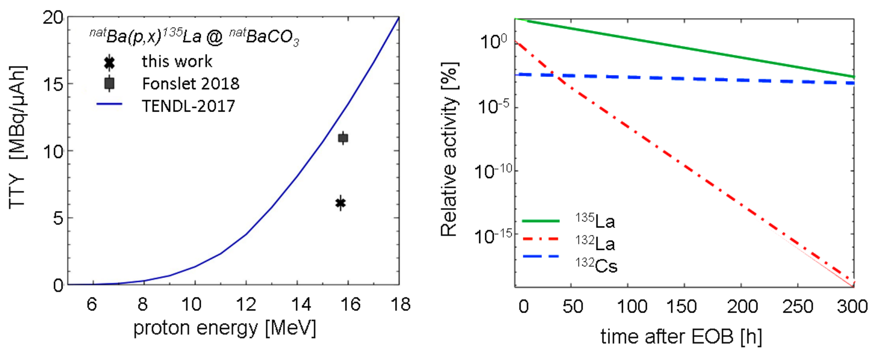

Fig. 1. Thick target yield for $^{\mathrm{nat}}$Ba$(p,x)^{135}$La reaction and measured evolution of ^{135}La activity relative to the activity of coproduced impurities.

TABLE III

Activity of ^{135}La and impurities produced in natural Ba target.

Isotope	Half-life	Activity at EOB
^{135}La	19.5 h	9.57 ± 0.20 MBq
^{132}La	4.72 h	0.43 ± 0.18 MBq
^{132}Cs	6.48 d	0.83 ± 0.31 MBq

4. Conclusion

The most important ^{135}La production routes were considered based on the production yield and natural isotope abundance. The theoretical production yield for each reaction was obtained using the MCNPX code and the results showed that ${}^{\mathrm{nat}}\mathrm{Ba}(p,x)^{135}\mathrm{La}$ reaction represents a reasonable production route considering common facilities of the PET centres. The activity of ^{135}La produced by bombarding a natural barium target with protons of 15.7 MeV (attenuated by Cu and Ti foils) for 10 minutes with the beam current of 9.4 μA was equal to 9.57 MBq with impurities on the level below 1% at EOB.

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