Photo-production of Alpha-emitting Isotopes with Thorium Target

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1. Introduction

With recent advancements of Theranostics, targeted radionuclide therapy (TRT) is getting attention as an effective cancer treatment [1]. Alpha-emitting isotopes have an advantage in targeted therapy when they are conjugated to an appropriate carrier, which is known as targeted alpha (*α)* therapy (TAT) [2]. An *α*-particle with high linear energy transfer (LET) and short range in human body can deliver radiant energy only to tumor cells and minimize damages in normal tissues. Despite of its high cell-killing ability in therapeutic applications, only a few *α*-emitting isotopes such as ^{225}Ac and ^{227}Th are appropriate as TAT due to a modest half-life and sequential emissions of *α*-particles by their daughter nuclei. Therefore, annual yield of these rare *α*-emitting isotopes are not enough to keep up with the global demand.

Most of the ^{225}Ac is supplied by the legacy ^{233}U stockpiles from thorium-based nuclear reactor in 1960s. It means that the rare ^{225}Ac is exclusively produced in US and Russia. Even the most probable way to produce ^{227}Th has issues about its procurement and treatment of radium target. Alternative methods of yielding ^{225}Ac and ^{227}Th should be developed to boost TAT applications and clinical tests. In order to answering the demand for *α*-emitting isotopes, we propose an innovative method to produce both ^{225}Ac and ^{227}Th from affordable thorium target bombarded by 500 kW electron beam.

2. Photo-transmutations in thorium target

We benchmarked the future converter with 500 kW electron beam and its cooling system in TRIUMF [3]. We evaluate the isotopic yield of ^{225}Ac and ^{227}Th based on TALYS-generated Evaluated Nuclear Data Libraries (TENDL) cross-sections for not measured photo-nuclear reactions [4]. Monte Carlo N-Particle transport (MCNP) version 6.2 code is used to estimate photon spectral density and transmutation rate in the thorium target [5], which will be described with Figs 1 and 2.

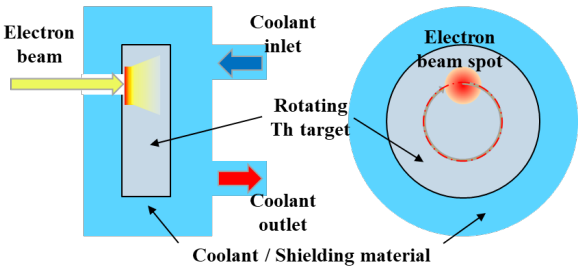

Fig. 1. Schematic diagram of *α*-emitters production system.

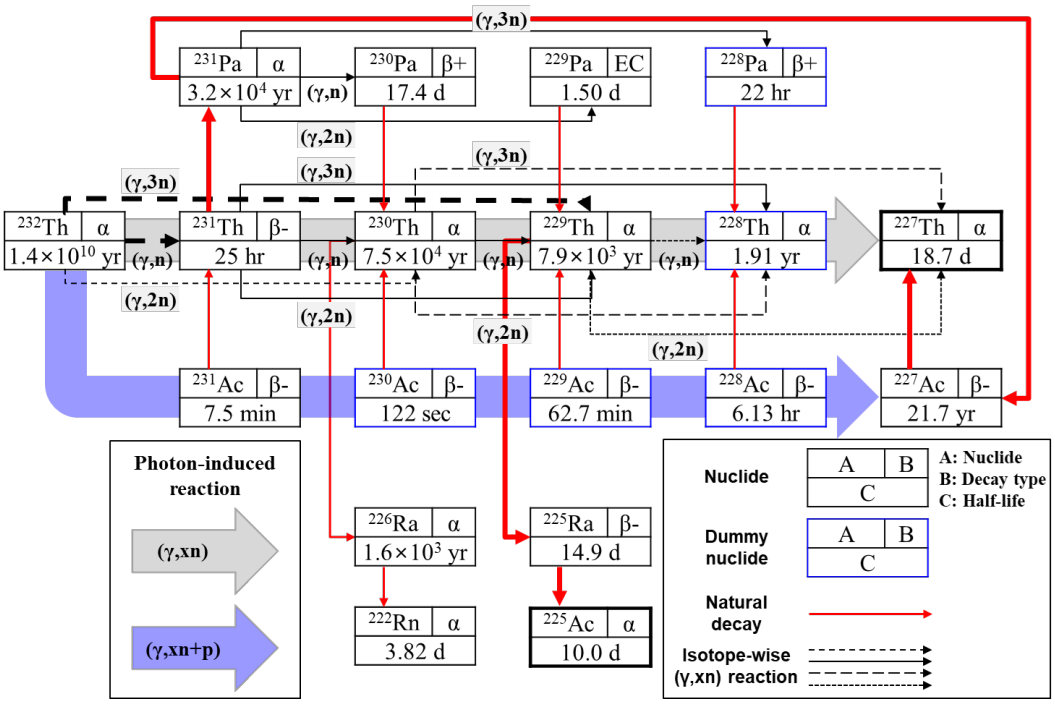

Fig. 2. Photonuclear reactions and natural decays in the Thorium target during electron beam bombardment.

2.1 Schematic diagram of α-emitters production system

Figure 1 shows schematic diagram of the α-emitters production system. A thorium target is bombarded by 500 kW electron beam as converter for Bremsstrahlung x-ray source and rotating at the same time to dissipate deposited heat in the target. The system should be equipped with a cooling and radiation protection system as in the TRIUMP Isotope Separator and Accelerator (ISAC) facility.

Figure 2 shows transmutation chains in the target induced by photon-induced reactions and natural decays. Although there happen several photon-induced reactions generating other actinium isotopes, we neglect them due to their extremely small cross-section and resulting reaction products except for ^{227}Ac. Moreover, prompt neutrons emitted from photonuclear reactions are simply leaking out from the target and cannot affect the production of ^{225}Ac and ^{227}Th.

2.2 Reliability of isotopic yields based on TENDL data

Most of the photonuclear reactions of thorium and protactinium isotopes have not been reported except for some of the reactions with ^{232}Th [6]. Figure 3 compares experimental cross-section of ^{232}Th with corresponding TENDL data. For the case of ^{232}Th, TENDL seems to give reliable data in that much of experimental data in Fig. 3 is within one standard deviation of TENDL data. Therefore, we alternatively adopt TENDL cross-section and estimate transmutation rate for isotopes in Fig. 2.

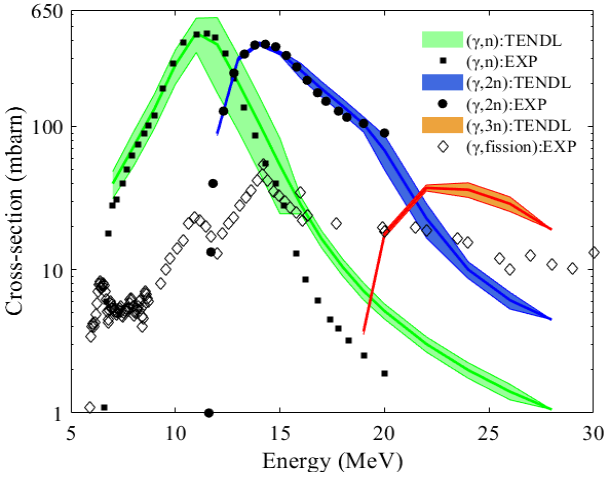

Fig. 3. Comparison between TENDL and experimental data for photon-induced reactions of ^{232}Th.

Bremsstrahlung photon energy of more than 6 MeV is needed to induce photo-neutron reactions. The number density of a certain nuclide in the target is calculated by following equations.

$$\frac{dN^A}{dt} = -\lambda_{Nat}^A N^A - \lambda_\gamma^A N^A + \lambda_{Nat}^{Other} N^{Other} + \lambda_{(\gamma,xn)}^{Other} N^{Other}, \quad \text{Eq. 1}$$

$$\lambda_{(\gamma,xn)}^A = \left(\int \sigma_{(\gamma,xn)}^A \frac{dN_\gamma}{dE} dE \right), \ \lambda_\gamma^A = \sum_{x=1}^{3} \lambda_{(\gamma,xn)}^A, \quad \text{Eq. 2}$$

where λ_{Nat} is natural decay constant, $\lambda_{(\gamma,xn)}$ is an effective decay constant for a (γ,xn) reaction, λ_γ is summation of the effective decay constants for all (γ,xn) reactions, and dN_γ/dE is the photon spectral density from MCNP 6.2. The last two terms in Eq. 1 denote production of 'A' nuclide due to decay or transmutation of other nuclides.

2.3 Strategy for extracting pure α-emitters

The essential idea for extracting pure α-emitters is to separate their mother nuclei. There exist various nuclei such as protactinium, actinium and radium except for thorium isotopes. Therefore, chemical procedures with a simple strategy are needed as shown in Fig. 4.

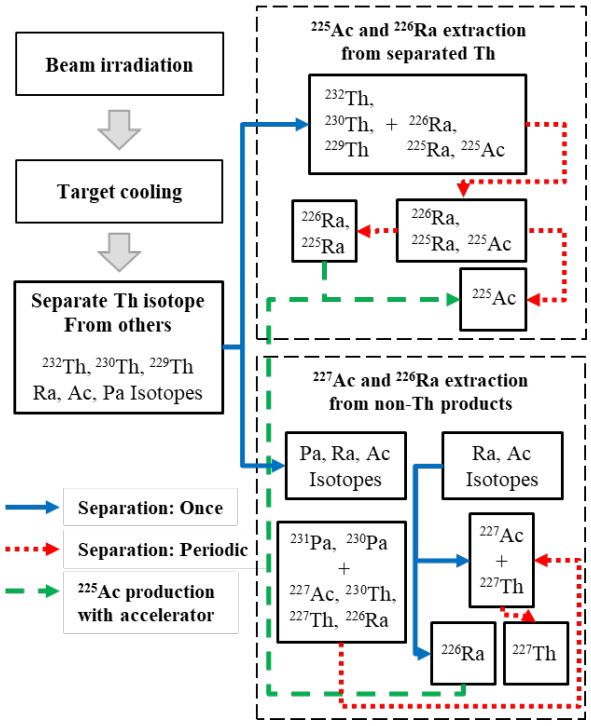

Fig. 4. Procedure for milking of ^{225}Ac and ^{227}Th.

Target cooling right after beam irradiation makes all ^{231}Th (mother nuclei of ^{227}Ac) decay out. There are no actinium isotopes in separated thorium stream where pure ^{225}Ac is accumulated by sequential decays of ^{229}Th. Now, it is possible to extract ^{225}Ac semi-permanently with a certain period. At the same time, pure ^{227}Th can be extracted from isolated non-Th products with Ra, Ac, and Pa isotopes. Due to a significant ^{232}Th(γ,n)^{231}Th reaction rate and a short half-life of ^{231}Th (25 hours), ^{231}Pa is the most abundant element in the thorium target except for ^{232}Th. ^{231}Pa slowly decays to ^{227}Ac decaying again to ^{227}Th with a half-life of 22 years. If ^{227}Th is directly extracted from the non-Th products without any

additional chemical separations, ^{230}Th can be blended with ^{227}Th, which may cause an accumulation of ^{226}Ra and its daughter nuclei. For high-purity ^{227}Th extraction, we partition the non-Th products into three parts: Ra, Ac, and Pa isotopes. ^{227}Ac can be extracted from the separated Pa and moves to the actinium part where pure ^{227}Th can be semi-permanently extracted. All chemical procedures in Fig. 4 are validated in ^{225}Ac productions with natural thorium bombarded by proton beam [7]. It is also noted that ^{226}Ra can be used as a target for other accelerator-based ^{225}Ac production methods.

3. Results

When a thorium target is bombarded by 500 kW electron beam with 15 mm diameter, isotopic yields can be affected by electron beam energy. This is because dominant photonuclear reactions are different for each mother nuclide of ^{225}Ac and ^{227}Th (^{229}Th and ^{231}Pa). Figure 5 describes their isotopic yields with different electron energy with the fixed beam power after a one-year beam irradiation. There exist asymptotic upper bounds for both isotopes as photo-neutron reactions are maximized below 30 MeV as shown in Fig. 3. Optimal energy for the ^{231}Pa is about 70 MeV while the yield of ^{229}Th is marginally increased in higher energy range. With considered simultaneous production of both isotopes, 70 MeV is considered as optimum electron energy.

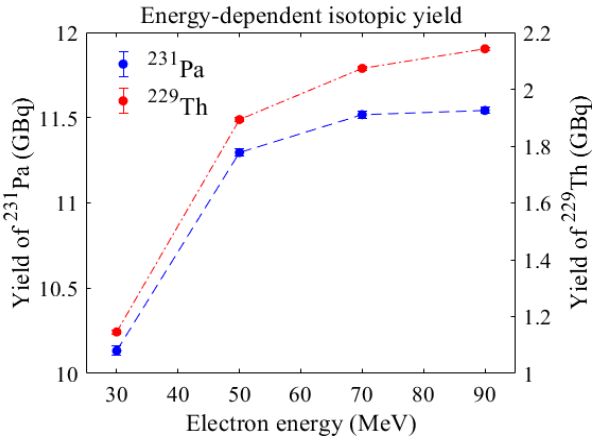

Fig. 5. Isotopic yields with different electron energies.

Figure 6 describes spatial distribution of ^{229}Th and ^{231}Pa yields after a one-year electron beam irradiation. Total yields of ^{229}Th and ^{231}Pa are ~2.07 GBq and ~11.5 GBq respectively. Most of them are spread out within 2cm outer region of electron beam. It is clear that the yield of these isotopes can be increased if the amount of ^{229}Th and ^{231}Pa in the target is increased with prolonged beam irradiation and higher electron current.

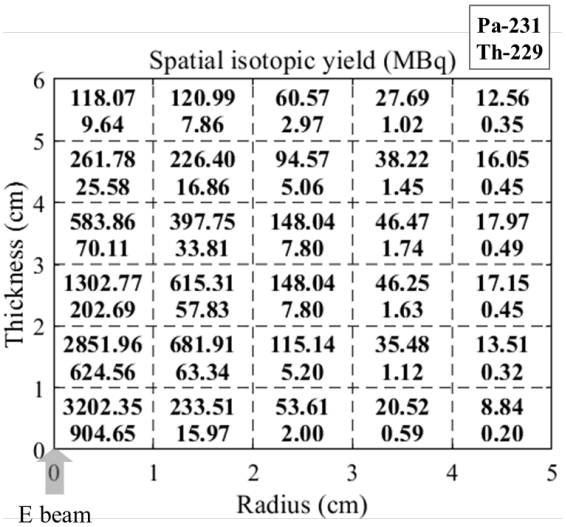

Fig. 6. Spatial distribution of the isotopic yields

Table 1 compares the proposed method with proton-based ^{225}Ac production using ^{226}Ra target, which is regarded as most probable method [8]. Beam and target parameters in other methods are optimized based on each experimental result to enhance isotopic yield [9].

The new method has an advantage that it requires only one 'long' irradiation and after that both isotopes are semi-permanently extracted. However, repetitive irradiations on Radium target are necessary for ^{225}Ac production. In order to compare a yearly yield with a same required time, based on engineering judgements, we assume that there is at least 12-hour preparation time between proton beam irradiations.

Table 1. Comparison with promising ^{225}Ac production method

Facility		Proton accelerator	Electron accelerator
Governing reaction		(p,2n) reaction	Photo-neutron reactions
Beam current		500 μA	7.14 mA
Irradiation time (day)		0.042	365
Particle energy		28 MeV	70 MeV
Target mass		210 mg	22 kg
Yield per irradiation (MBq)	^{225}Ac	743.7	-
	^{227}Th	-	-
Yearly yield (GBq)	^{225}Ac	501.1	11.7 (28.4)[2]
	^{227}Th[1]	-	47.0 (92.7)[2]

[1] 50-year averaged yield
[2] 2-year beam irradiation

Although the yearly ^{225}Ac yield of the proposed method is lower than that of proton-based method, the following advantages should be recalled: 1) pure ^{225}Ac can be produced in the new photo-production, while there should be some level of ^{227}Ac contamination in proton-beam based method, 2) a semi-permanent source is produced after a single irradiation with an affordable electron beam generator, 3) both ^{225}Ac and ^{227}Th are simultaneously produced.

4. Conclusions

A novel photo-production for rare α-emitting isotopes is proposed and seems to be viable. It can produce pure ^{225}Ac and ^{227}Th semi-permanently by irradiating a cheap thorium target with electron beam. We believe that this work helps activate clinical test with the rare isotopes and boost global supply of them. Still, the yield of ^{225}Ac is based on theoretical cross-section of ^{232}Th(γ,3n)^{229}Th reaction and it should be experimentally validated.

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