Development of Radioisotopes Production Method

by Accelerator-based Neutron

-activity at Kyushu- university 2020 -

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Radioisotopes (RIs) production using deuteron accelerator-based neutrons has been studying at Kyushu University. We primarily focus on neutrons generated via the C or Be(d, n) reactions in a target whose thickness is thicker than the deuteron range. These reactions are selected because (1) high intense neutrons having high kinetic energy can generate by the elastic and non-elastic breakup reaction of deuterons, and (2) neutron energy spectrum has a maximum of around a half incident deuteron energy, i.e., varying deuteron energy guides the spectrum shape adjustment. The two approaches have conducted the study: proposal of new production routes and new RIs with the accelerator-based neutron method and systematic measurements of double-differential thick-target neutron yields (DDTTNYs) up to 40 MeV. The present paper shows some examples of past works (^{92}Y production for biodistribution assessment and 132Cs production for alternative environment tracer as ^{137}Cs), and current status (systematic DDTTNY measurement results) of our project.

1. Introduction

Recently, the accelerator-based neutron has been widely applied in various fields. In this decade, medical radioisotopes (RIs) production using the neutron has been proposed by Nagai et al. First in the research, the production method of ^{99}Mo, which is the mother nuclide of the most used medical RI, ^{99m}Tc, was proposed [1,2]. In the study, deuterons are accelerated to around 100 keV and bombarded on a tritium target to obtain neutrons by DT fusion reactions. Generated neutrons have nearly monoenergetic around 14 MeV, where the ^{99}Mo production reaction ^{100}Mo(n,2n) has a large cross section. The study reveals that the production method can generate a sufficient amount of ^{99}Mo of the world demand. We have also proposed the ^{64}Cu and ^{67}Cu production methods for other applications by using accelerator-based neutron via the C(d,n) reaction [3]. These copper RIs are new promising candidates of theranostics, which means combining therapy and diagnosis. In the proposed route, 40-MeV deuterons are used to generate accelerator-based neutrons to obtain intense flux. The amount of the RIs is estimated to be sufficient for clinical use (a few hundreds of MBq for diagnosis, a few GBq for therapy). The accelerator-based neutron method by deuterons was summarized as a GRAND system in Ref.[4].

We started studying the RI production method by the accelerator-based neutron in 2012 when I moved from Prof. Nagai's group at JAEA to Prof. Watanabe's laboratory at Kyushu University. At that time, Kyushu University already gets started a nuclear data study on deuteron-induced reactions[5,6]. Thus, our research has not only been a part of the GRAND project but also combined with the nuclear data study[7–12].

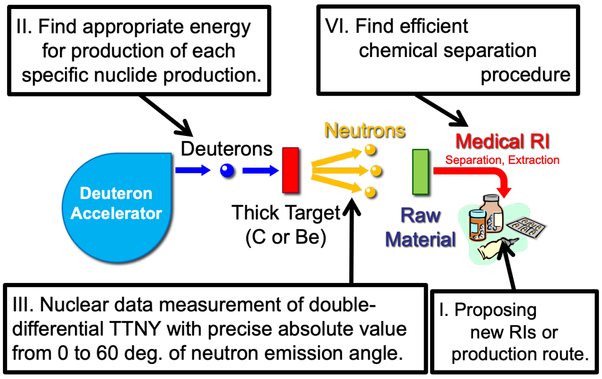

Fig. 1 Objectives of radioisotopes production by the accelerator-based neutron method.

In our study, the C or Be(d,n) reactions have been used to produce the accelerator-based neutron because the neutron energy distribution can be adjusted by incident deuteron energy. It means users can roughly control the radioactive and isotopic purity of produced RIs. Some of RIs have been investigated to find the appropriate deuteron energy to obtain sufficient quantity with high purity. Moreover, for clinical use, the chemical separation process has also been studied. In this paper, first, two RI (^{92}Y and ^{132}Cs) production routes proposed in our study are reviewed[7,12].

Second, I introduce the latest publication of systematic measurement of thick-target neutron-yield of C(d,n) [10]. Third, the preliminary result of uncertainty propagation in neutron spectra [13]. Finally, I summarize the paper and show prospects.

2. New Route to Produce ^{92}Y and ^{132}Cs

2.1. Yttrium-92 production for Assessment of Biodistribution of ^{90}Y-labeled ibritumomab tiuxetan

This section reviews a proposal of ^{92}Y to improve the precision of assessment for metabolic distribution of ^{90}Y ibritumomab tiuxetan (see Ref. [7] for detail).

Yttrium-90 ibritumomab tiuxetan is the first radio immune therapy agent approved by the US Food and Drug Administration (USFDA) and followed by more than 40 other countries, including Japan. Until November 2011, biodistribution is assessed using a single photo emission computed tomography (SPECT) scan by administering ^{111}In-ibritumomab tiuxetan before ^{90}Y-ibritumomab tiuxetan therapy was required in the United States, Japan, and Switzerland to predict radiation dose to normal tissues and organs. The FDA, however, removed this procedure based on a clinical study. The main reason was “analysis of data in 253 patients showed that the In-111 imaging was not a reliable predictor of altered Y-90 Zevalin (the trade name of ibritumomab tiuxetan) bio-distribution”. Suppose a yttrium isotope that emits gamma rays labels the ibritumomab tiuxetan that emits positron or suitable gamma rays. In that case, such a procedure will constitute a reliable monitor by the adoption of positron emission tomography (PET) or gamma-ray imaging. Two radioactive yttrium isotopes have been proposed by Rösche et al. [14] and Nagai et al. [15]. In the present study, we have proposed gamma-emitter, ^{92}Y, which can be produced only by accelerator-based neutrons, for precise assessment of biodistribution (see Fig. 2).

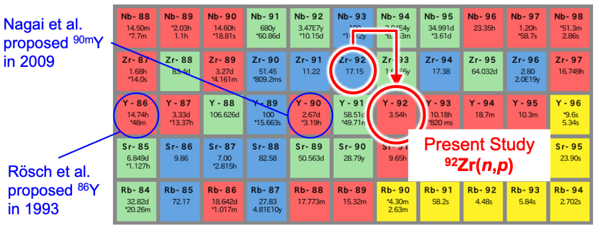

Fig. 2 Production routes of radioactive yttrium isotopes. The ^{92}Y proposed in the present study can only be produced via the fast neutron-induced method.

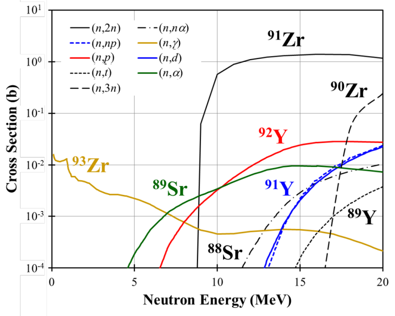

Fig. 3 Neutron excitation functions of ^{92}Zr stored in JENDL-4.0u.

The production route is ^{92}Zr(*n*,*p*) reactions, and its theoretical neutron excitation function is shown in Fig. 3 together with other ones of byproduct for ^{92}Zr (note that the functions are available in JENDL-4.0u [16]). We have conducted a thick-target neutron yield (TTNY) measurement of C(d,n) reactions for 20-MeV deuterons at Cyclotron and Radioisotope Center (CYRIC) at Tohoku University to estimate the production amount and isotopic purity of ^{92}Y product. We adopted the multiple foils activation methods to derive the TTND. As shown in Fig. 4, deuterons were accelerated up to 20 MeV by AVF930 cyclotron and guided to the thick carbon target installed in the 32 course to irradiate multiple foils made of Al, Fe, Co, Ni, Zn, Zr, Mo at the irradiation point for 19 hours. The average beam current on the carbon target was 2 μA.

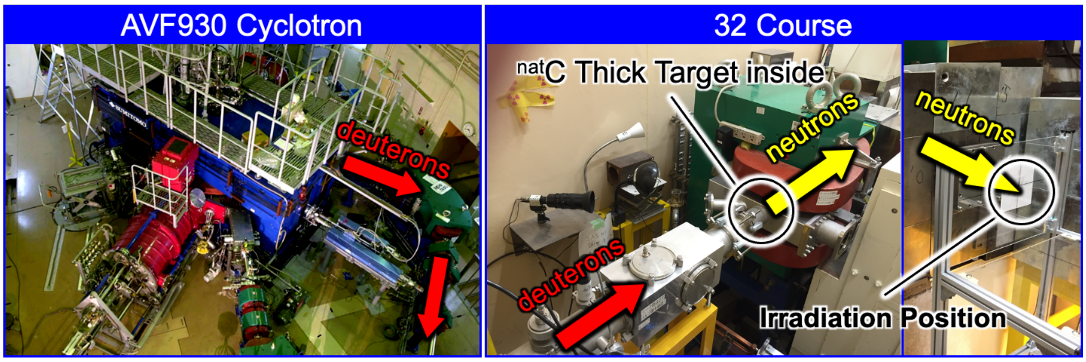

Fig. 4 AVF930 type accelerator used to measure the thick-target neutron yield of C(d,n) reactions using the multiple foils activation methods at the 32 course. Neutrons emitted around 0 degrees concerning the beam axis were collimated and bombarded on the multiple foils at the irradiation point.

The TTNY was derived from activities induced by the neutron irradiation by unfolding process using GRAVEL code [17]. For the next step, using the derived TTNY, a production simulation was conducted for 20 g of enriched ^{92}Zr target irradiation to estimate the production amount and purity. As a result, we found 1.32 GBq of high isotopic purity (94.9%) ^{92}Y can be produced by a 2-mA deuteron beam on the carbon target for 7.5-h irradiation. This amount can be used for around ten patients of biodistribution assessments.

2.2. Environment tracer Cs-132, the alternative of Cs-137

In the environment study of radioactive cesium, ^{137}Cs ($T_{1/2}$ = 30 y) has been well used to know environmental dynamics even if some studies are focused on the short period (around from a few days to a few weeks) dynamics. The half-life is too long for the task, and management of the tracer after an experiment has been a heavy load of research works. To improve this situation, we have proposed ^{132}Cs as an alternative tracer of ^{137}Cs for studies of the short period dynamics, e.g., a few days dynamics (dominant period for absorption into the soil) of radioactive cesium released by the Fukushima Daiichi Nuclear Power Plant Accident. The radioactive material management is straightforward because it has a drastically shorter half-life (6.5 d) than ^{137}Cs. In the present study, we conducted a production experiment of the ^{132}Cs using an accelerator-based neutron method to investigate production amount and radioactive purity. The accelerator-based neutron irradiated a 12-g Cs2CO3 sample via the C(*d*,*n*) reactions by 1.2 μA of 30-MeV deuterons as a similar irradiation system in Fig. 4. As a result, 102 kBq/g of ^{132}Cs was obtained with higher than 98.5% radioactive purity. Following that, a feasibility study of cesium distribution measurement in andosol soil, which is a typical species of soil in Japan, was performed. The NaI(Tl) detector was placed through a lead collimator having a 1-cm window, as shown in Fig. 5 (left). First, we flow cesium aqueous into the soil and measure the initial distribution (the blue line in Fig. 5 (right)). After 8-h adsorption time, distilled water was flowed to remove free cesium. Finally, adsorbed distribution was measured as shown in the red line in Fig. 5 (right). We found almost all of the cesium is adsorbed in andosol soil in a short period, 8 hours. The property is well known, but we concluded the produced ^{132}Cs tracer could be an alternative to environment tracer ^{137}Cs.

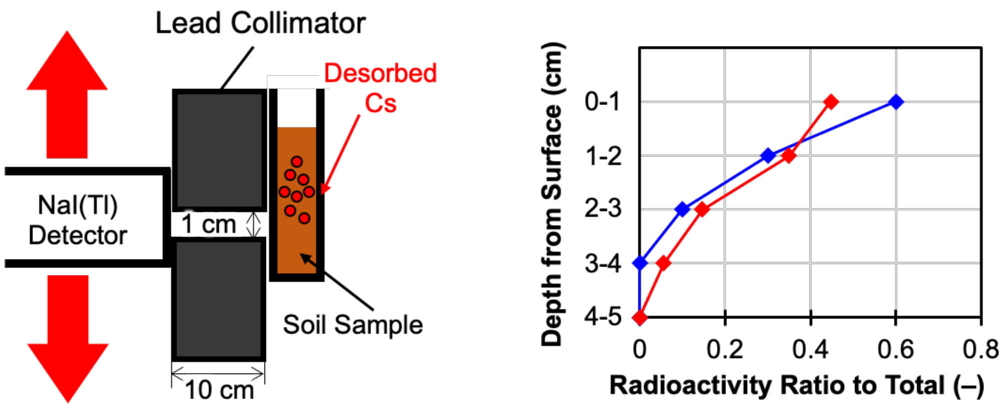

Fig. 5 Setup of measurement of radioactive cesium distribution (left) and its results. The blue line shows the initial allocation, and the red line shows the distribution after water flow with an 8-hour adsorption time.

3. Systematic Measurement of Double-differential Thick-target Neutron Yield of C(*d*,*n*) reaction

The neutron generation by the C(*d*,*n*) reaction on a thick target is promising for radioisotope production by accelerator-based neutron method. As mentioned above, an intense neutron field is possible coincidently with adjustment of neutron energy distribution by incident deuteron energy. For this application, the thick-target neutron yield of wide neutron emission angles (0-90degs) from 10 to 40-MeV incident deuterons is necessary to estimate production amount and isotopic purity. However, the nuclear data has not been systematically measured by a single facility with the same irradiation conditions. To improve this situation, we have conducted a series of double-differential thick-target neutron yield measurements for C(*d*,*n*) reaction at 12, 20, and 30 MeV deuterons for neutron emission angles 0, 10, 20, 30, and 45 degrees at Tandem accelerator facility of JAEA. The experimental results are compared with close deuteron energy and neutron emission angles. See Ref. [10] for the results and details.

4. Summary

We have proposed new radioisotopes (RIs) or new production routes possible by accelerator-based neutron methods. Experiments of RIs production to know production amounts and find appropriate chemical separation methods. Also, double-differential thick-target neutron yields (DDTTNYs) of the proposed route have been measured to estimate isotopic purity, including stable isotope byproducts.

Furthermore, the DDTTNYs have been systematically (in neutron emission angle and incident deuteron energy) measured for storing nuclear data of deuteron-induced reactions. The experiments have been conducted at Cyclotron and Radioisotope Center at Tohoku University and Tandem accelerator at Japan Atomic Energy Agency. At this moment, we conclude the DEURACS model [18] gives precise DDTTNYs for C(*d*,*n*) reactions in the measured incident energy range from 12 to 35 MeV, especially at around 0 degrees.

The effort to find the new route or RIs will be continued in the future. Moreover, we will analyze nuclear data uncertainty contributions in the unfolding process by random sampling method using covariance for worthful nuclear data measurement.

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