EPJ Web of Conferences **66**, 10007 (2014)
DOI: 10.1051/epjconf/20146610007

^{99}Mo Production via ^{100}Mo(n,2n)^{99}Mo using accelerator neutrons

Yasuki Nagai

Nuclear Engineering Research Collaboration Center, Japan Atomic Energy Agency,
Tokai-mura, Ibaraki-ken 319-1195, Japan

Abstract. A new production method of ^{99}Mo using accelerator neutrons via the ^{100}Mo(n,2n)^{99}Mo reaction was proposed. Intense neutrons with a most probable energy of 14 MeV can be produced by bombarding Be or C with 40 MeV deuteron beams. Research and development works of ^{99}Mo produced by neutrons from the ^{3}H(d,n)^{4}He reaction were carried out. High quality ^{99m}Tc was obtained by employing a sublimation method. Accelerator neutrons are shown to have a great potential to produce a wide variety of radioisotopes.

1 Introduction

Among various radioisotopes for medical use, ^{99m}Tc, the daughter nuclide of ^{99}Mo with a half-life ($T_{1/2}$) of 66 h is the most common radioisotope used in diagnosis, and more than 25 million diagnostic procedures in the world are carried out every year with ^{99m}Tc labeled tissue-specific radiopharmaceuticals [1]. Reliable and constant supply of ^{99}Mo is a key issue to ensure the routine application of ^{99m}Tc. About 95% of ^{99}Mo has been produced by the fission reaction of highly enriched ^{235}U (HEU) in five research reactors in the world. However, a number of unexpected accidents of the reactors highlighted shortcomings and unreliability in the supply of ^{99m}Tc [2]. Note that the use of HEU is an issue of public concern due to the proliferation of nuclear weapons. The shortage of ^{99}Mo due to these incidents has triggered widespread discussions on the medium- and long-term supplies of ^{99}Mo. A conversion from HEU to low-enriched ^{235}U was made, and succeeded in small-scale ^{99}Mo production. The ^{99}Mo production method by the neutron capture of enriched ^{98}Mo or natural Mo targets in reactors was demonstrated to be an attractive alternative. A variety of production methods of ^{99}Mo or ^{99m}Tc in accelerators without HEU or LEU have been also studied. A direct ^{99m}Tc production via ^{100}Mo(p,2n)^{99m}Tc has been investigated by a number of researchers [3,4]. ^{99}Mo productions by the ^{100}Mo(γ,n)^{99}Mo or ^{238}U(γ,fission)^{99}Mo reactions using bremsstrahlung photons from electron accelerators and by the ^{98}Mo(n,γ)^{99}Mo reactions using spallation neutrons have also been studied [5-7]. We propose a new route to produce ^{99}Mo by the ^{100}Mo(n,2n)^{99}Mo reaction [8].

2 ^{99}Mo production via ^{100}Mo(n,2n)^{99}Mo

There are several requirements in the domestic production of ^{99}Mo (^{99m}Tc). First, any method of ^{99}Mo production should have a potential to meet all, or a significant part, of the domestic demand of ^{99}Mo. The safety and efficacy of the ^{99m}Tc radiopharmaceutical preparation should be ensured, since ^{99m}Tc is used to form a ^{99m}Tc radiopharmaceutical for the parenteral administration. In fact, the

Corresponding author: nagai@rcnp.osaka-u.ac.jp

United States Pharmacopeia (USP) contains requirements concerning the radionuclide purity of ^{99m}Tc; the ^{99}Mo in the ^{99m}Tc product must be less than 0.015% and the total concentration of all other β- and γ-emitters must be less than 0.01%. The labeling efficiency of the ^{99m}Tc radiopharmaceutical complex, which reflects the chemical purity of ^{99m}Tc, should be above 90%.

Characteristic points of ^{99}Mo production by ^{100}Mo(n,2n)^{99}Mo are as follows. First, the cross section of the ^{100}Mo(n,2n)^{99}Mo reaction in the neutron energy (E_n) range between 11 and 18 MeV is as large as about 1.5 barn. Second, the cross sections of the (n,α), (n,$n'p$), and (n,p) reactions on ^{100}Mo producing impurity radionuclides other than ^{99}Mo are less than a few mb at E_n ~ 14 MeV. Third, a large amount of ^{100}Mo sample (> 100 g) can be used in the ^{100}Mo(n,2n)^{99}Mo reaction. Fourth, intense neutrons with the energy of 11 –18 MeV are available. In fact, at SPIRAL2 in GANIL in France, neutrons with a most probable energy of 14 MeV with a high flux of 10^{15} n/s are planned to be produced by ^{nat}C(d,n) using 40 MeV 5 mA deuterons [9].

The yield of ^{99}Mo is evaluated using the latest data of neutrons from ^{nat}C(d,n) at E_d = 40 MeV, assuming a beam intensity of 5 mA, and the evaluated cross section of ^{100}Mo(n,2n)^{99}Mo given in the Japanese Evaluated Nuclear Data Library (JENDL). In the calculation, an enriched ^{100}Mo sample (100% enriched in ^{100}Mo) is placed 2 cm downward from the carbon target, and the deuteron beam size is assumed to be 1 cm in diameter. Typically, 7.1 TBq of ^{99}Mo was obtained for a ^{100}Mo sample with a thickness of 2 cm and a radius of 2 cm (251g ^{100}Mo) at the end of irradiation [10]. The present result is compared with current ^{99}Mo demand in Japan, which is about 84 TBq per week before shipment from the producer's facility in Japan. On the basis of the present result, about 25 TBq/week of ^{99}Mo can be obtained at the end of irradiation (EOI) by repeating irradiation 3.5 times for two days. About 20-25% of the demand of ^{99}Mo in Japan could be obtained constantly with a single facility mentioned above, if one could obtain 40 MeV 5 mA deuteron beams.

Safety and efficacy of ^{99m}Tc radiopharmaceutical preparation is discussed in using ^{99m}Tc from ^{99}Mo of low-specific activity produced by accelerator neutrons. ^{99}Mo produced by fission reaction of ^{235}U has a high-specific-activity, about 10^3~10^4-times higher than that of any alternative production method. Therefore, the high-activity of ^{99m}Tc to meet customer expectation of the ^{99m}Tc activity concentration can be recovered from the fission-product ^{99}Mo using an alumina column (alumina cow) [1]. However, an alumina cow cannot be used for ^{99}Mo of low-specific activity. We use the thermochromatographic method to separate ^{99m}Tc from ^{99}Mo, which is based on a different volatility of technetium heptoxide (Tc_2O_7) and molybdenum trioxide (MoO_3); ^{99m}Tc produced in MoO_3 volatilizes at a temperature lower than that of the sublimation of MoO_3, which is 790°C [11].

3 Experimental study of ^{99}Mo produced via ^{100}Mo(n,2n)^{99}Mo

^{99}Mo was produced by irradiating a $^{100}MoO_3$ sample with ~14 MeV neutrons at Japan Atomic Energy Agency (JAEA). The thermochromatographic separation of ^{99m}Tc from the $^{100}MoO_3$ sample was performed by using an electric furnace. The irradiated $^{100}MoO_3$ sample was placed in a platinum boat placed in the furnace, and heated at around 820 °C so as to form gaseous materials containing vaporized technetium (^{99m}Tc) oxide in a stream of oxygen carrier gas. ^{99m}Tc-oxide, which was separated from the $^{100}MoO_3$ sample, was condensed at the exit of the furnace, and was eluted with a saline solution in a small beaker. The separation process of ^{99m}Tc was performed within one hour. γ-ray spectra of ^{99m}Tc were measured before and after the thermochromatographic separation by a HPGe detector. The upper limits of γ-rays from any impurity isotopes, such as ^{99}Mo, ^{97}Zr and ^{97}Nb, were found to be less than 0.01% of that of the 141 keV γ-ray (^{99m}Tc). Labeling efficiency was higher than 95% by formulating a radiopharmaceutical by using commercially available methylene diphosphonate (MDP) (FUJIFILM RI Pharma) kits, which is used for bone scans more than 50% of all routine ^{99m}Tc scans currently used in diagnostic nuclear medicine. The radionuclide purity of ^{99m}Tc and labeling efficiency were above the USP requirement [12]. Note that a thermochromatographic separation allows us to recycle any irradiated enriched ^{100}Mo.

4 Production of accelerator neutrons and prototype facility

The intensity of neutrons having energies of between ~10 and 18 MeV is the key issue for sufficiently producing ^{99}Mo by the ^{100}Mo(n,2n)^{99}Mo reaction. Recently significant progress has been achieved in accelerator technology to enable us in obtaining intense neutrons. In fact, at SPIRAL2 located at GANIL, neutrons with an intensity of 10^{15} n/s are expected to be produced by the ^{nat}C(d,n) reaction using 40 MeV 5 mA deuterons, as discussed above. A great advance has also been achieved with the development of a neutron converter, which can withstand the high power of the 40 MeV 5 mA deuteron beams, using a rotating carbon converter [13].

On the basis of the recent developments mentioned above, we propose to construct an AVF cyclotron with a deuteron beam intensity of 2 mA as a prototype facility to produce medical radioisotopes including ^{99}Mo [14]. Note that a fixed radiofrequency cyclotron is robust in operation, compact in size, and relatively cheap compared to a linear accelerator. Here, negative deuteron D^- ions are accelerated up to 40 MeV, and intense deuteron ions can be extracted with low loss by the stripping of D^- ions into positive deuteron (D^+) ions on a thin carbon foil. The D^+ ions can be extracted to two beam lines through the residual magnetic field in the AVF with a possibility to irradiate two targets simultaneously.

5 A wide variety of radioisotopes produced by accelerator neutrons

A charge exchange reaction, such as (n,p) and (n,α), of a sample nucleus with a medium-weight mass has a sizeable cross section at ~ $10 < E_n < 18$ MeV. Therefore, a wide variety of carrier-free radioisotopes can be produced using accelerator neutrons. In fact, we proposed new routes to produce carrier-free medical radioisotopes of ^{90}Y[15], ^{64}Cu, and ^{67}Cu [16] using accelerator neutrons. Note that a radiopharmaceutical agent containing a radionuclide ^{90}Y ($T_{1/2}$ = 64 h), a pure β^--ray emitter with a maximum energy of 2.28 MeV, has been used for cancer therapy. Currently, a carrier-free grade of ^{90}Y is obtained from the ^{90}Sr/^{90}Y generator, and is imported into Japan. Note that ^{90}Sr with $T_{1/2}$ = 28.8 y is obtained by the fission reaction of ^{235}U at reactors. Because of the short half-life of ^{90}Y, the domestic production of ^{90}Y is highly required. ^{64}Cu ($T_{1/2}$ = 12.7 h) is a promising radionuclide suitable for labeling many radiopharmaceuticals for PET imaging. As for the production of ^{64}Cu, the generally adopted route of ^{64}Cu production is ^{64}Ni(p,n)^{64}Cu. Since the natural abundance of ^{64}Ni is as low as 0.93%, the high price of ^{64}Ni is, however, a major drawback of the ^{64}Cu production route. ^{67}Cu ($T_{1/2}$ = 61.8 h) is believed to be a promising radionuclide to treat small distant metastases in Radio Immuno Therapy. Since ^{67}Cu emits low-energy γ-rays, which can be readily detected by a gamma-camera, it can be used simultaneously for diagnostic imaging and internal therapy. The ^{68}Zn(p,2p)^{67}Cu reaction is currently used to produce ^{67}Cu. Note that the proton energy used in the ^{68}Zn(p,2p)^{67}Cu reaction is high, a large amount of impurity radionuclide of ^{64}Cu is produced by ^{68}Zn(p,αn)^{64}Cu. We emphasized that both ^{67}Cu and ^{64}Cu can be produced by using accelerator neutrons.

6 Summary

We have shown that sufficient amount of ^{99}Mo can be produced via ^{100}Mo(n,2n)^{99}Mo using neutrons from ^{nat}C(d,n) with 40 MeV 5 mA deuterons. The result encourages us to employ the new ^{99}Mo production method to ensure a constant and assured supply of ^{99}Mo for domestic use, being free of significant amounts of radioactive waste production, and the inherent risk of worldwide radioactive shipment. On the basis of the results, we proposed a new prototype system for the generation of radioisotopes with accelerator neutrons by deuterons (GRAND). The system consists of a AVF cyclotron with a carbon converter to produce intense accelerator neutrons with a most probable energy of 14 MeV, and a sublimation system to recover ^{99m}Tc from an irradiated ^{100}Mo sample. The system has unique features in the production of a wide variety of radioisotopes, including ^{99}Mo, useful for nuclear medicine diagnosis procedures.

The present work was supported in part by Grant-in-Aid for Specially Promoted Research of the Japan Ministry of Education, Culture, Sports, Science and Technology, 23000005, and in part by an Adaptable and Seamless Technology Transfer Program through the Target-driven R&D (A-STEP) of Japan Science and Technology Agency (JST).

References

1. F. F. Knapp, Jr., S. Mirzadeh, Eur. J. Nucl. Med. **21**, 1151 (1994)
2. J. R. Ballinger, J. Labelled Compd. Radiopharm. **53**, 167 (2010)
3. M. C. Lagunas-Solar, Accelerator Production of 99mTc with Proton Beams and Enriched 100Mo Targets, in IAEA-TECDOC-1065, International Atomic Energy Agency, Vienna, 87 (1999)
4. B. Guérin, S. Tremblay, S. Rodrigue, J. A. Rousseau, V. Dumulon-Perreault, R. Lecomte, J. E. van Lier, J. Nucl. Med. **51**, 13N (2010)
5. S. Buono, N. Burgio, L. Maciocco, Technical evaluation of an accelerator-driven production of Mo-99 for Tc-99m generators at CERN (MolyPAN project) (2010)
6. R. Bennett, J. Christian, D. Petti,W. Terry, S. Grover, Nuclear Technology, **126**, 102 (1999)
7. C. Ross, R. Galea, P. Saull, W. Davidson, P. Brown, D. Brown, J. Harvey, G. Messina, R. Wassenaar, M. de Jong, Physics in Canada, **66**, 19 (2010)
8. Y. Nagai, Y. Hatsukawa, J. Phys. Soc. Jpn. **78**, 033201 (2009)
9. M. Fadil, B. Rannou, the SPIRAL2 project team, Nucl. Instrum. Method, B **266, 4318** (2008)
10. F. Minato, Y. Nagai, J. Phys. Soc. Jpn. **79**, 093201 (2010)
11. C. Perrier, E. Segre, J. Chem. Phys. **5**, 712 (1937)
12. Y. Nagai et al, J. Phys. Soc. Jpn. **80**, 083201 (2011)
13. M. Avilov, L. B. Tecchio, Nucl. Instr. Methods **B 266**, 4308 (2008)
14. Y.Nagai et al., J.Phys.Soc.Jpn.**82** 064201 (2013)
15. Y.Nagai, O. Iwamoto, N. Iwamoto, T. Kin, M. Segawa, Y. Hatsukawa, H. Harada, J. Phys. Soc. Jpn. **78**, 113201 (2009)
16. T. Kin, Y. Nagai, N. Iwamoto, F. Minato, O. Iwamoto, Y. Hatsukawa, M. Segawa, H. Harada, C. Konno, K. Ochiai, K. Takakura: J. Phys. Soc. Jpn. **82**, 034201 (2013)