Production of ${}^{44}\text{Ti}$ via the ${}^{45}\text{Sc}(p,2n){}^{44}\text{Ti}$ reaction for ${}^{44}\text{Ti}/{}^{44\text{g}}\text{Sc}$ generator development

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Table 1. Activities of $^{44}\mathrm{Ti},\,^{44\mathrm{m},\,46}\mathrm{Sc}$ at EOB.

 $^{44\mathrm{g}}\mathrm{Sc}$ is a promising radionuclide for PET imaging applications. Its direct production via the $^{44}\mathrm{Ca}(p,n)^{44\mathrm{m},\,\mathrm{g}}\mathrm{Sc}$ and $^{44}\mathrm{Ca}(d,2n)^{44\mathrm{m},\,\mathrm{g}}\mathrm{Sc}$ reactions were investigated by several groups.^{1–4}) Owing to the short half-life of $^{44\mathrm{g}}\mathrm{Sc}$ $(T_{1/2}=3.9~\mathrm{h})$, daily irradiations close to the site where it is used are required to maintain a constant supply of $^{44\mathrm{g}}\mathrm{Sc}$. An alternative approach to obtain $^{44\mathrm{g}}\mathrm{Sc}$ is the production by the $^{44}\mathrm{Ti}$ $(T_{1/2}=59.1~\mathrm{y})/^{44\mathrm{g}}\mathrm{Sc}$ generator.⁵⁾ In this work, we investigated the production of $^{44}\mathrm{Ti}$ via the $^{45}\mathrm{Sc}(p,2n)^{44}\mathrm{Ti}$ reaction to develop the $^{44}\mathrm{Ti}/^{44\mathrm{g}}\mathrm{Sc}$ generator.

A metallic ⁴⁵Sc (99.99%) disk target with a diameter and thickness of 10 mm and 0.90 g/cm², respectively, was placed in an irradiation chamber with helium gas and water cooling.⁶) The target was irradiated for 1.25 h with a 0.25- μ A proton beam from the RIKEN AVF cyclotron. The incoming and outgoing proton beam energies were 30 MeV and 15 MeV, respectively.

Large amounts of ${}^{44\mathrm{m}}\mathrm{Sc}$ $(T_{1/2} = 58.6 \text{ h})$ and ${}^{44\mathrm{g}}\mathrm{Sc}$ were also produced in the 45 Sc $(p, x)^{44m, g}$ Sc reactions. The short-lived ^{44g}Sc fully decays in several days. Thus, the activities of ^{44m}Sc and ⁴⁴Ti at the end of bombardment (EOB) were determined by fitting the decay curve of the 1157-keV gamma line of ^{44g}Sc after radioactive equilibrium. The yields of ⁴⁴Ti and ^{44m}Sc with the beam energy range of 30–15 MeV were calculated based on the cross-section data reported by L. Daraban.⁷⁾ The calculated results agree well with the experimental results. In addition, $^{46}\mathrm{Sc}~(T_{1/2}$ = 83.8 d) was co-produced via the secondary-neutron-induced reaction of ${}^{45}Sc(n,\gamma){}^{46}Sc$. The activity of ${}^{46}Sc$ was determined by the 889-keV and 1121-keV gamma lines after 76 days of cooling. The results from the two gamma lines agree well with each other and are listed in Table 1.

⁴⁴Ti was separated from the target with ZR resin. Firstly, the irradiated ${}^{45}Sc$ target (0.71 g) was dissolved in 20 mL of 6 M HCl and heated to dryness. Subsequently, the residue was dissolved in 5 mL of 6 M HCl and fed into a column filled with conditioned ZR resin (100–150 μ m, 5 mm *i.d.* × 5 mm). Scandium passed through the column while titanium was adsorbed on the resin. Finally, 44 Ti was eluted with 6 mL of 3 M HCl/0.325 M H₂O₂ solution.⁸⁾ The Ti/Sc separation factor was determined by the activity ratio of 44 Ti and 46 Sc before and after separation. The recovery yield of ⁴⁴Ti was 95%, and the Ti/Sc separation factor was $>10^3$ in this scheme. The gamma-ray spectrum of ⁴⁴Ti after the chemical separation is shown in Fig. 1. Small amounts of long-lived ⁵⁶Co ($T_{1/2} = 77.3$ d) and ⁵⁴Mn ($T_{1/2} =$ 312.3 d) found in the irradiated target were successfully

Calc. yield γ-ray Activity at EOB (Bq) Nuclide energy $(Bq/\mu Ah)$ Calc. Exp. (keV) ⁴⁴Ti 1114 ± 55 1157 3338 1043 $4.1 \times 10^{7} \pm$ ^{44m}Sc 1.3×108 1157 4.2×107 2.5×10⁵

889

1121

⁴⁶Sc



Fig. 1. Gamma-ray spectrum of ⁴⁴Ti after separation.

removed by the chemical separation. Only gamma lines from 44 Ti and its daughter, 44g Sc, were identified in the gamma-ray spectrum. The radionnuclidic purity of 44 Ti after chemical separation was evaluated to be >99%.

By assuming experimental conditions (incident beam energy: 30 MeV; beam intensity: 10 μ A; target thickness: 0.9 g/cm²; irradiation time: 10 d), 8 MBq of ⁴⁴Ti can be produced at the EOB.

In the future, we will develop a prototype of the ${}^{44}\text{Ti}/{}^{44\text{g}}\text{Sc}$ generator with long-term stability, high yield of ${}^{44\text{g}}\text{Sc}$, and no ${}^{44}\text{Ti}$ breakthrough.

References

- 1) C. Alliot et al., Nucl. Med. Biol. 42, 524 (2015).
- 2) G. W. Severin et al., Appl. Radiat. Isot. 70, 1526 (2012).
- 3) C. Müller *et al.*, J. Nucl. Med. **54**, 2168 (2013).
- 4) R. Hernandez et al., Mol. Pharm. 11, 2954 (2014).
- 5) D. Filosofov et al., Radiochim. Acta 98, 149 (2010).
- 6) S. Yano *et al.*, RIKEN Accel. Prog. Rep. **50**, 261 (2017).
- L. Daraban *et al.*, Nucl. Instrum. Methods Phys. Res. B 267, 755 (2009).
- 8) V. Radchenko et al., J. Chromatogr. A 1477, 39 (2016).

 454 ± 15

 459 ± 15

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