Contribution ID: **4** Type: **talk**

Cyclotron production of theranostic pair 43/44Sc - 47Sc on calcium targets

Saturday, 9 October 2021 15:00 (20 minutes)

The 43Sc (T1/2 = 3.89 h) and 44Sc (T1/2 = 3.92 h) are an ideal β+ emitter in PET diagnosis. Both radionuclides can be used as an alternative to 68Ga, because 43/44Sc has a longer half-life and forms theranostic pair with β- emitter 47Sc, which is important in planning radionuclide therapy. However in comparison with 44Sc, 43Sc has half-life and beta plus radiation similar to 44Sc, moreover, gamma-ray energy emission and intensity is much lower (372 keV, 23%) than in the case of 44Sc (1157 keV, 99%) what is not negligible for the patient and medical personnel. On the other hand 47Sc as low energy β- emitter is an attractive candidate for radioimmunotherapy. In our work, we propose a new way for cyclotron production of 43Sc in 42Ca(d,n)43Sc nuclear reaction and 47Sc by proton irradiation of 48Ca target in 48Ca(p,2n)47Sc and 48Ca(p,d)47Ca→47Sc reaction.

In the present work, we used enriched 42CaCO3, 44CaCO3 and 48CaCO3 targets (Isoflex, Russia). To manufacture the targets enriched 42CaCO3, 44CaCO3 and 48CaCO3 powder was pressed with graphite powder (10-25%), mounted to a water-cooled target holder and irradiated with a beam of proton or deuteron at different energies. The activity of the samples was measured with high-resolution γ-ray spectrometry. CaCO3 targets were dissolved in 1 M HCl and a microfiltration process after alkalization of target material solution was used to separate 43/44Sc from calcium target materials and for production of 47Sc generator. The obtained by deuteron irradiation of 42Ca radionuclide of 43Sc and 44Ca radionuclide of 44Sc were radionuclidaly pure. In the case of proton irradiation of 48Ca obtained product contained a mixture of radionuclides 47Sc, 48Sc, and 47Ca which is a 47Sc mother radionuclide. After irradiation with 60 MeV proton beam followed by chemical separation of the Ca isotopes and waiting for the maximum growth of 47Sc by 5,6 days, 44 MBq/μAh of 47Sc can be eluted from the generator with no other contaminating scandium activity. After separation solution of 43/44/47Sc was loaded on cation exchange Dowex 50 resin for purification and change of environment.

The proposed methods allow obtaining high activity of 43Sc, 44Sc and 47Sc. Scandium isotopes were separated from the targets with the efficiency of more than 90% and eluted in the volume of 0.5 ml. The level of Ca2+ in 43/44Sc and 47Sc fractions is less than 3 μg/ml. The recovery of the calcium target is nearly quantitative making the proposed production process economically feasible.

Scandium radionuclides, separated by our method, have sufficient quality for labeling of the biologically active molecules, which has been confirmed by labeling bioconjugates of Trastuzumab, anti-HER2 nanobody and DOTA-TATE. For DTPA-Trastuzumab, DTPA-nanobody and DOTA-TATE efficiency of labeling was 99% and for DOTA-nanobody 60% (t=50°C).

This work was carried out as a part of the projects nr. IAEA-RC-23299-RO

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Session Classification: Saturday Afternoon Session