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Alternative Options to Produce 225Ac for Nuclear Medicine

The 225Ac radiopharmaceuticals are at the final phases of clinical trials to treat various cancers. Hence, there is a relevant issue of establishing its scaled-up production. The easiest way to produce 225Ac is generating from 229Th extracted from 233U. However, the quantity of produced 225Ac is limited by the availability of stored 233U. For example, from 1 kg 233U aged for 35 years up to 32 mCi 229Th can be produced, which makes possible to accumulate up to 20 mCi 225Ac every two weeks.

An alternative way to produce 229Th is irradiation of 226Ra in the high neutron flux. JSC "SSC RIAR" has performed a series of experiments to irradiate trial radium targets, and experimental yields of radium activation products have been determined. Calculation based on these data demonstrated that the maximum yield of 229Th is ~21 mCi/g 226Ra after 6 months irradiation in the neutron trap of the SM high-flux reactor. The produced 229Th contains 228Th with the activity being 4500 times higher than that of 229Th. While there are no actinium isotopes in the 228Th decay chain, high activity of 228Th and its daughter decay products would cause a number of serious problems. Firstly, high alpha activity determines high heat and gas rates during irradiation, shipment and storage of radium targets, thus limiting the maximum mass of 226Ra per target. Secondly, continuous cooling is required when storing the purified isotope mixture between the 225Ac generation cycles. Finally, it is hard to use traditional methods of 225Ac extraction due to intense radiolysis of the reagents.

The content of 228Th in 229Th can be reduced if using a two-stage irradiation process. The first stage involves irradiation of radium up to the maximum yield of 227Ac (33 mg/g 226Ra). At the same time, a mixture of thorium isotopes is generated with the 228Th:229Th activity ratio of ~25000:1 that can be used to produce 224Ra and 212Pb. At the second stage, when irradiating 227Ac extracted from several radium targets, the maximum yield of 229Th is achieved on the 60th day of irradiation (72 mCi/g 227Ac). The ratio of 228Th and 229Th activities at this point is almost the same as that resulted from single irradiation. However, due to complete burnout of 227Ac, further irradiation would lead to a fast decrease in the 228Th:229Th activity ratio. In the course of irradiation during 5-6 months, the 228Th:229Th activity ratio would make up 1500:1, but the yield of 229Th would decrease to 35 mCi/g 227Ac.

Another way to produce 225Ac is irradiation of natural thorium in particle accelerators. The produced 225Ac contains an impurity of 227Ac and is not suitable for radiopharmaceutical synthesis. However, it can be used in 213Bi generators. To implement this option, it is necessary to cooperate with a partner company that has a proton accelerator with the beam energy of at least 100 MeV. Currently JSC "SSC RIAR" considers all three production options for 225Ac.

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