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Various chromatographic schemes for separation of 213Bi from 225Ac

Among alpha emitters suitable for targeted alpha-therapy, 225Ac (T1/2 = 9.9 days) and the product of its decay 213Bi (46 min.) are the most promising. Clinical trials are confirming higher efficacy and less toxicity of the radiopharmaceuticals labeled with these radionuclides in comparison with similar beta-emitting ones. A prospective method of producing 225Ac (more than 1 Ci for a 10-day run) by irradiation of natural thorium with medium-energy protons followed by chemical isolation has been developed at the Institute for Nuclear Research of the Russian Academy of Sciences (INR RAS). A long-lived 227Ac (21.7 years) is also formed (~0.1% of 225Ac at the end of irradiation), and direct medical application of the product seems questionable. However, 225Ac with small impurity of 227Ac is appropriate as a mother radionuclide for 225Ac/213Bi generator.

225Ac/213Bi generators based on ion exchange (AG MP-50, AG 1, BioRad) and extraction chromatography resins (Actinide Resin, UTEVA Resin, Triskem Int.) are well described.

All the proposed generator systems can be classified as follows:
1. The «direct» generator, where Ac-225 is firmly retained by the sorbent, and Bi-213 is eluted with various complexing agents. Such generator based on the cation-exchange resin of the type AG MP-50 is commonly applied for clinical trials;

1. The «direct» generator, where Ac-225 is firmly retained by the sorbent, and Bi-213 is accumulated and concentrated due to the separation and decay of the short-lived Fr-221 on the second sorbent. This type of generators is under development at INR RAS;
2. A «reverse» generator, where periodically accumulating Bi-213 is selectively adsorbed from solution of Ac-225, and then desorbed for use. Systems of so-called multicolumn selective inversion generators (MSIG) was developed at PNNL, USA. Generators of this type based on inorganic sorbents is also under development at INR RAS.

The «direct» generator is most convenient for clinical application, however, in the presence of Ac-227 in Ac-225, the content of Ac-227 and its decay products in Bi-213 eluate may be important. Generators developed at INR RAS can provide higher degree of purification from these radionuclides.

The initial activity of generator (not more than 50-100 mCi) is limited not only by 225Ac production capabilities but also by the radiation resistance of the sorbents used in the generator. Since the developed method of 225Ac production allows increasing the activity of 213Bi injected into a patient (at least to 4 GBq (100-150 mCi)), both radiation and radiolytic destruction of the sorbent also grow up. In this case, generators assigned to the 2nd and 3rd categories will have an advantage.

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