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Testing the feasibility of 44mSc/44Sc as a potential in vivo generator for PET imaging and an alternative to the existing 44Ti/44Sc ?

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The use of radionuclides as potential therapeutic radiopharmaceuticals is increasingly investigated. Scandium isotopes (44Sc, 47Sc) become more easily available and their properties are convenient for either PET imaging or radiotherapy. Notably, the half-life of 3.97 h of 44Sc and its high positron branching (94%) lead us to consider this isotope for application in TEP radiopharmaceuticals. The high energy and high intensity ARRONAX cyclotron produces 44Sc together with its isomeric state 44mSc (T1/2=2.44 d) that may stimulate its use as a potential in vivo generator. For in vivo generators, it is not only the log K of complexation between the metal ion and the chelator that is important, but also whether the daughter radionuclide stays inside the chelator after decay of the parent radionuclide. From our previous work [1], we showed that the DOTA chelator exhibit the higher complexation constant value with Sc compared to other often used ligands such as DTPA, NOTA, ⋯In the perspective of medical applications, the Sc(III)-DOTA complex is stable over several days in the presence of a bone mimic and in rat serum. DOTA is also a good chelator of Ho and Nd but against all expectations, it was evidenced that 166Ho, from 166Dy/166Ho in vivo generator was released from DOTA [2]. It was evidenced that was not due to the low recoil energy (Q=0.486 MeV) but due to a "post-effect"as shown previously for the 140Nd/140Pr generator with an even lower recoil energy (Q=0.222 MeV) [3]. The post-effect is attributed to the physico-chemical process occurring after the primary radioactive decay (EC, IT, Auger electron ⋯).

This work presents the production route (targetry, extraction and purification) of 44mSc/44Sc at the ARRONAX facility and examines the effect of the recoil energy and the "post-effect"on 44mSc-DOTA complex in the aim of establishing an in vivo 44mSc/44Sc generator.

44mSc/44Sc production, Extraction and Purification

For this study, we have produced limited amount of scandium. A typical irradiation corresponds to 30 min at 0.1 µA during 33 MBq of 44Sc are produced. The 44Sc/44mSc activity ratio is found to be 50 at EOB. The extraction/purification process developed lead to a radionucledic purity of 100% and 43Sc, 46Sc, 48Sc<LOD.

Synthesis of (radio)metalled complex

From 90% to 99 % of radiolabelling yields were obtained for metal-to-ligand ratio ranging from 1/1 to 10/1 respectively; in agreement with published data [1, 4]. Detailed description of data will be given.

Study of the Post-effect

IT-TOF spectra showed that after a dosis of 1Gy delivered with a 9 MeV electrons beam at the maximum depth dose (external linear accelerator SATURN, ICO-Nantes), the pendant arms of Sc-DOTA complexes opened and the chelate released the metal. A detailed study on the comprehension of mechanisms is will be presented. The experiments with the in-vivo generator are on going.

References

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