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INVITED LECTURE - A renaissance of radionuclide generators for versatile application

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Introduction: Radionuclide generator systems continue to play a key role in providing both diagnostic and therapeutic radionuclides for various applications in nuclear medicine, oncology and interventional cardiology. In parallel to the well established ⁹⁹Mo/^{99m}Tc generator used for SPECT imaging, new generators for PET/CT imaging attract attention. In particular the ⁶⁸Ge/⁶⁸Ga system (⁶⁸Ge: t½ = 270.95 d; ⁶⁸Ga: t½ = 67.7 min, β⁺ branching = 89.1%) has found impressive and established clinical application, the ⁴⁴Ti/⁴⁴Sc generator (⁴⁴Ti: t½ = 60 a; ⁴⁴Sc: t½ = 3.97 h, β⁺ branching = 94.3) represents a promising system providing a longer-lived daughter, and a ¹⁴⁰Nd/¹⁴⁰Pr system (¹⁴⁰Nd: t½ = 3.37 d d; ¹⁴⁰Pr: t½ = 3.39 min, β⁺ branching = 51.0%) may be used in terms of an in vivo generator.
Challenges: (1) Different to the established ⁹⁹Mo/^{99m}Tc generator used for SPECT imaging, new generators for PET/CT such as the ⁶⁸Ge/⁶⁸Ga system [1] and the ⁴⁴Ti/⁴⁴Sc generator ask for special generator designs because of the long half-life of the parent nuclide. Both represent secular equilibrium systems (different to the transient ⁹⁹Mo/^{99m}Tc generator) as well as long shelf-life. Both generators may be used over periods of many month and many years, respectively. Still the elution yield of the daughter should be high and the breakthrough of the parent low.
(2) While the generators mentioned all separate parent and daughter nuclides due to different chemical properties of the chemical elements involved, i.e. Mo vs. Tc, Ge vs. Ga, Ti vs. Sc), the ¹⁴⁰Nd/¹⁴⁰Pr system involves two neighbored lanthanides of very similar chemical behavior.
Experiments and Conclusion: (1) It appears to be a rather general feature of radionuclide generators based on longer-lived parent nuclides, that effective elution modes [2] as well as post-elution processing [3] are mandatory. With those aspects managed in an effective way, the radionuclide generator systems may be tuned to medical systems. This was demonstrated in detail for the ⁴⁴Ti/⁴⁴Sc radionuclide generator. Very low breakthrough of ⁴⁴Ti and high yield of ⁴⁴Sc is guaranteed by sophisticated generator designs (anion exchange resin as column material, HCl / oxalic acid mixtures for elution), but in addition by a scheme of reverse elution directions. Particular attention was paid to the application of a reverse elution mode, which helps to retain the parent nuclide along the chromatographic column even after many hundred elutions. A 5 mCi generator provides about 170 MBq of ⁴⁴Sc after direct elution and about 150 MBq following online post-processing similar to the ⁶⁸Ge/⁶⁸Ga generator. The final content of ⁴⁴Ti is as low as < 10 Bq, representing a separation factor of > 10⁷..
(2) With no-carrier-added ¹⁴⁰Nd produced by irradiations of CeO₂ and Pr₂O₃ targets [4], an efficient ¹⁴⁰Nd/¹⁴⁰Pr radionuclide generator system was developed and evaluated. The principle of the radiochemical separation is based on physico-chemical transitions (hot-atom effects) of the daughter ¹⁴⁰Pr following the electron decay process of ¹⁴⁰Nd. The parent radionuclide ¹⁴⁰Nd(III) is quantitatively adsorbed on a solid phase matrix in the form of ¹⁴⁰Nd-DOTA-conjugated complexes. ¹⁴⁰Nd generated is released from the ¹⁴⁰Pr-DOTA core as an ionic species. It is easily separated using low volumes of various aqueous eluents. The elution yield is at least 93%, if an optimized eluent, such as DTPA solution is applied. The system remains stable at least over three half-lives of ¹⁴⁰Nd, with high radiolytic stability and low ¹⁴⁰Nd breakthrough of ca. 0.025% [5].

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