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Isolation of generator-produced 223Ra in NaCl isotonic solutions containing EDTA for radiotherapeutic studies

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The short range of α-particles (<100 μm) and high linear energy transfer (LET) in tissue make α-particle emitting radionuclides an ideal tool for targeted radiotherapy of cancer. A number of preclinical and clinical studies have shown the advantages of 223Ra for treatment of bone tumor and skeletal metastases due to its chemical similarity to calcium [1]. Therefore, Ra injected intravenously in isotonic solution is retained in skeletal metastases realizing in vivo generator for short-lived α-emitters of the decay chain:
223Ra(11.4d) α ⟶ 219Rn(3.9s) α ⟶ 215Po(1.78ms) α ⟶ 211Pb(36.1m) β ⟶ 211Bi(2.14m) β ⟶ 211Po(0.52s) and α ⟶ 207Tl(4.77m) β ⟶ 207Pb stab.

The first two ultra short-lived α-emitters are formed within four seconds of 223Ra decay and probably rest in the site of mother radionuclide. The more long-lived radionuclides, primary 211Pb and its α-emitting daughters 211Bi/211Po can be escaped from mother vicinity and transferred to another site. Obviously that strong chelating agents, which are able to form stable complexes with all radionuclides of the decay chain, could retain the daughters together with mother radionuclide. Furthermore, the Ra chelates attached to antibody or proteins could be used for targeted radiotherapy or preparation of novel radiopharmaceuticals.
The goal of the present work was to determine the conditions for formation of stable Ra/Pb-EDTA complexes in NaCl isotonic solutions using cation-exchange method. 223Ra was produced from 227Ac/223Ra generator developed earlier [2]. We studied in details the cation-exchange behavior of 211Pb and 223Ra in NaCl solutions in dependence on composition of solution, concentration of EDTA, pH and other factors.
Optimal conditions for elution of the 223Ra/211Pb EDTA complexes in 0.9% NaCl solutions were found. More than 90% of 223Ra can be eluted in a volume 1 mL of NaCl isotonic solution containing 0.05M Na2EDTA at pH=7-7.5.
A simple and efficient method for isolation of 223Ra in the form suitable for biomedical studies has been developed. The method is adaptable to automation for the routine clinical process, eliminates the need of evaporation of the solutions of high radioactivity that reduce the dangerous radiation to technical staff.

1. Carrasquillo J.A. et al. Eur J Med Mol Imaging. 2013. 40(9): 1384-1393.
2. Guseva L.I. J Radioanal Nucl Chem. 2009. 281(3): 577-583.

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