

## Production and Quality Control of $^{223}\text{RaCl}_2$ and $^{224}\text{RaCl}_2$

Among all radium isotopes, at least two are used in nuclear medicine. Bayer-manufactured  $^{223}\text{RaCl}_2$  (trade name Xofigo) is applied for palliative care of bone metastasis. Microsources containing  $^{224}\text{Ra}$  are under clinical trials to treat malignant tumors of skin and mucous membrane using diffusing  $\alpha$ -emitter radiation therapy (DaRT) that involves controlled migration of  $^{220}\text{Rn}$ .

These two radium isotopes have one common feature – they can be produced from radionuclide generators containing long-lived parent radionuclides  $^{227}\text{Ac}$  and  $^{228}\text{Th}$ . The essential quality control parameter is the content of the long-lived parent radionuclide in the final product. However, the direct measurement using alpha, beta or gamma spectrometry does not ensure the required detection limit. In alpha spectra the lines corresponding to  $^{227}\text{Ac}$  and  $^{228}\text{Th}$  are on the low-energy tail of alpha peaks for  $^{223}\text{Ra}$ ,  $^{224}\text{Ra}$  and their daughter products. As for  $^{227}\text{Ac}$ , the situation gets more complicated due to low alpha-particle emission probabilities (1.38%) causing the detection limit of  $\sim 1\%$  with the acquired statistics being 1 million counts in the alpha spectrum. The detection limit for  $^{228}\text{Th}$  in  $^{224}\text{Ra}$  under similar conditions is  $\sim 0.1\%$ . Conversion electrons and beta radiation of  $^{223}\text{Ra}$  decay products ( $^{211}\text{Pb}$  and  $^{211}\text{Bi}$ ) are hurdles in measuring the activity of  $^{227}\text{Ac}$  by beta radiation. Compton scattering of gamma radiation from  $^{212}\text{Pb}$  and  $^{208}\text{Tl}$  becomes an obstacle in measuring the activity of  $^{228}\text{Th}$  with the use of gamma spectrometry. Decay  $^{227}\text{Ac}$  is not accompanied by emission of characteristic gamma radiation.

There are two basic approaches to determine long-lived parent radionuclides in  $^{223}\text{Ra}$  and  $^{224}\text{Ra}$ . One approach is that the left-off preparation sample is stored for a long time for  $^{223}\text{Ra}/^{224}\text{Ra}$  to decay, and alpha/gamma spectra are measured. Another approach is based on the chemical extraction of  $^{227}\text{Ac}$  and  $^{228}\text{Th}$  traces from a preparation aliquot and further measurement of their activity.

JSC “SSC RIAR” performs experiments to generate trial samples of  $^{223}\text{RaCl}_2$  and  $^{224}\text{RaCl}_2$ . For the purpose of long-lived impurities quantification, an aliquot with the activity ranging from 10 to 100 MBq is taken from every batch. The impurities are extracted chemically by sorption of radium isotopes on BioRAD AG-50x8 strong acid cation-exchange resin with EDTA in ammonium acetate buffer solution with a pH from 4.5 to 6.0. In these conditions actinium and thorium form stable complexes, and they are not sorbed on the cation-exchange resin. It has been found that the presence of EDTA, acetic acid and ammonium acetate in the solution does not affect the quality of obtained alpha spectra and impurity detection limits. Therefore, the analysis can be done without pre-desalting or diluting the obtained solutions. The achieved detection limits for long-lived impurities are  $\sim 10^{-5}\%$  of the activity of radium isotopes, which is enough for their application in nuclear medicine.

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Poster

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