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A dual generator concept to yield 226Th: an isotope of interest for targeted alpha therapy

Introduction-Thorium-226 (t1/2=30.6m) is an isotope of interest for targeted alpha therapy (TAT). It decays via a four alpha decay chain to long-lived (t1/2=22.3 y) Pb-210 with a 111 keV gamma-line (3.29%) that can be used for SPECT imaging; thus providing theranostic capabilities. A generator concept is necessary to provide a consistent supply of Th-226 from its parent U-230 (20.23 d) [1]. Furthermore, Th-226 needs to be supplied in a form that is amenable to direct labeling with the chelate; minimizing the amount of time required for its preparation for use. Uranium-230 is best obtained by the proton irradiation of thorium targets via formation of Pa-230 (17.4 d), which partially decays to U-230. To yield a consistent supply of Th-226, a dual generator concept was developed: first to yield U-230 from the decay of Pa-230, and second, to separate Th-226 from the parent U-230.

Methods-Protactinium-230 used in this work was obtained from Oak Ridge National Laboratory as a side product from the production of Ac-225 [2]. An extraction chromatography resin approach was used for both the design of a Pa-230/U-230 generator, and a U-230/Th-226 generator. Uranium-230 and its decay product Th-226 were first sorbed on a solid phase in acid media. Uranium-230 was then eluted in acid as Th-226 remained on the stationary phase. In a third step, Th-226 was eluted from the resin in acidic media.

Results-The Pa-230/U-230 generator provided U-230 in high radiochemical yield and purity (>99.9%). The U-230/Th-226 generator yielded approximately 90% of the Th-226 with a >99.5% recovery of parent U-230 for each elution cycle. Thorium-226 was obtained with high radiochemical purity (>99.9%). Multiple elutions have been performed successfully with consistent radiochemical yields and purities.

Conclusions-A dual generator system was successfully designed and tested to provide a relibale supply of Th-226. Uranium-230 can be conveniently supplied from a Pa-230/U-230 generator. The U-230/Th-226 generator, in turn, provides Th-226 in high radiochemical yield and purity and in a form that is amenable to direct labeling with chelates for use in targeted alpha therapy.

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