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Dosimetric Impact of Ac-227 in Accelerator-Produced Ac-225

Actinium-225 (225Ac) has a 10-day half-life and a decay scheme that yields four alpha-particle emissions. This radionuclide is produced by a generator system from the decay of thorium-229. Accelerator-produced 225Ac via thorium-232 irradiation (denoted 225/7Ac) contains a low percentage (0.1-0.3%) 227Ac; (21.77 year half-life) at end of bombardment. The biological consequences of this contamination have been recently examined [1]. We examine the contribution of 227Ac and its daughters to tissue absorbed doses when the level of contamination is 0.7% (by radioactivity) at time of injection. The dosimetric analysis was performed for antibody-conjugated 225/7Ac administered intravenously to treat patients with hematological cancers.

Published pharmacokinetic models are used to obtain the distribution of 225/7Ac -labeled antibody and also the distribution of either free or antibody-conjugated 227Th. Since 227Th is obtained from the beta decay branch (99% yield) of 227Ac rather than a more energetically disruptive alpha-emitter decay, it is possible that a significant fraction of the 227Th generated remains antibody-conjugated. A pharmacokinetic model representing the distribution of radiolabeled antibody in patients with hematologically distributed cancer is adapted from reference [2] to obtain the pharmacokinetics for 225/7Ac and 227Th-labeled-antibody. A model representing the pharmacokinetics of free 227Th is used to model the distribution of unconjugated 227Th [3]. Under both circumstances, 223Ra generated by 227Th decay is simulated using a pharmacokinetic model that is relevant to free 223Ra [4]. The 1% of 227Ac that decays to francium-223 (223Fr, T ½ = 22 min) is considered to have a negligible impact on tissue absorbed dose relative to that from 227Th which is already expected to be very low because of the low initial amount of 227Ac in 225/7Ac. The tissue absorbed dose from 227Ac is negligible in the context of therapy; less than1.4 mGy/MBq for the top 5 highest absorbed tissues and < 0.007 mGy/MBq for all other tissues. Compared to that from 225Ac, the absorbed dose from 227Ac makes up a very small component (<0.4%) of the total absorbed dose delivered to the 5 highest dose tissues: red (active) marrow, spleen, endosteal cells, liver and kidneys when accelerator produced 225/7Ac-conjugated anti-CD33 antibody would be used to treat leukemia patients. For all tissues, the dominant contributor to the absorbed dose arising from the 227Ac is 227Th, the first daughter of 227Ac which has the potential to deliver absorbed dose both while it is antibody-bound and while it is free. The results suggest that the dose arising from 227Ac to normal organs is negligible for 225/7Ac-labeled antibody that targets hematological cancer.

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