

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

Actinium-225 (^{225}Ac) 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 ^{225}Ac via thorium-232 irradiation (denoted $^{225}/^{232}\text{Ac}$) contains a low percentage (0.1-0.3%) ^{227}Ac ; (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 ^{227}Ac 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 $^{225}/^{232}\text{Ac}$ administered intravenously to treat patients with hematological cancers.

Published pharmacokinetic models are used to obtain the distribution of $^{225}/^{232}\text{Ac}$ -labeled antibody and also the distribution of either free or antibody-conjugated ^{227}Th . Since ^{227}Th is obtained from the beta decay branch (99% yield) of ^{227}Ac rather than a more energetically disruptive alpha-emitter decay, it is possible that a significant fraction of the ^{227}Th 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 $^{225}/^{232}\text{Ac}$ and ^{227}Th -labeled-antibody. A model representing the pharmacokinetics of free ^{227}Th is used to model the distribution of unconjugated ^{227}Th [3]. Under both circumstances, ^{223}Ra generated by ^{227}Th decay is simulated using a pharmacokinetic model that is relevant to free ^{223}Ra [4]. The 1% of ^{227}Ac that decays to francium-223 (^{223}Fr , $T_{1/2} = 22$ min) is considered to have a negligible impact on tissue absorbed dose relative to that from ^{227}Th which is already expected to be very low because of the low initial amount of ^{227}Ac in $^{225}/^{232}\text{Ac}$. The tissue absorbed dose from ^{227}Ac is negligible in the context of therapy; less than 1.4 mGy/MBq for the top 5 highest absorbed tissues and < 0.007 mGy/MBq for all other tissues. Compared to that from ^{225}Ac , the absorbed dose from ^{227}Ac 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 $^{225}/^{232}\text{Ac}$ -conjugated anti-CD33 antibody would be used to treat leukemia patients. For all tissues, the dominant contributor to the absorbed dose arising from the ^{227}Ac is ^{227}Th , the first daughter of ^{227}Ac 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 ^{227}Ac to normal organs is negligible for $^{225}/^{232}\text{Ac}$ -labeled antibody that targets hematological cancer.

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