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## An update on the chemical separation of $^{149}\text{Tb}$ and its subsequent application for preclinical therapy studies

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Terbium is a unique element, as it provides a quadruplet of radionuclides suited for diagnostics and therapy in nuclear medicine [1]. Much success has been gained from the PSI-ISOLDE collaboration, with the collection and purification of  $^{149}\text{Tb}$  ( $\alpha$ -emitter,  $T_{1/2} = 4.1$  h –for potential therapy), used for preclinical therapy studies [2] and PET imaging [3], and  $^{152}\text{Tb}$  ( $\beta^+$ -emitter,  $T_{1/2} = 17.5$  h –for use in PET imaging), for preclinical [4] and clinical [5] PET imaging, respectively.

A single campaign to produce  $^{149}\text{Tb}$  took place in June 2018. Initially, collections were performed using 0.2 mm thick Zn foils and the chemical separations performed using an updated method. The results were erratic, with low yields being obtained due to the tardiness of the separation process and poor labeling capability of the product. Similar yields were obtained when switching to Zn-coated gold foils as before, however, the product could label to PSMA –albeit poorly. Usable product (and yields around 100 MBq) were produced when reverting to the previously-used chemical separation method (which consisted of a smaller column), allowing the labeling of  $^{149}\text{Tb}$  to PSMA-617 and its use for preclinical studies.

$^{149}\text{Tb}$ -PSMA-617 was obtained with more than 98% radiochemical purity at up to 6 MBq/nmol specific activity. Groups of 6 mice bearing tumor PC-3 PIP xenografts were intravenously injected with  $\sim 6$  MBq  $^{149}\text{Tb}$ -PSMA-617 or 2 x 3 MBq  $^{149}\text{Tb}$ -PSMA-617 at Day 1 and 2 or at Day 1 and 4, respectively. The mice were monitored over several weeks with regard to the tumor growth and body weight. The tumor growth delay was more pronounced in the groups that received 2 x 3 MBq than in mice that received the whole activity in just one injection. The median survival time was 26 days in the group that received 1 x 6 MBq, significantly longer than in untreated control mice (median survival time 20 days). Mice which received 2 x 3 MBq at Day 1 and 2 or Day 1 and 4, respectively, had a median survival of 36 days and 32 days, respectively.

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[5] R. Baum et al., Dalton Transactions, 46, 14638 (2017).

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