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The isotopes Tb-149 and Tb-152 in preclinical investigations: Report on the successes and challenges of the 2015 Medical Isotope Campaign for IS528.

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During the 2015 Ta target run, PSI concentrated on the collection and purification of ^{149}Tb and ^{152}Tb. Both isotopes could be harvested in sufficient quantities to allow transport to PSI, purification and significant imaging and therapy investigations. We report some of the successes and preliminary results of this campaign.

As in our previous ISOLDE campaigns the cumulative Tb yields were significantly boosted by use of resonant laser ionization of the respective Dy precursors. The new Dy laser ionization scheme using Ti-sapphire lasers instead of dye lasers provided excellent Dy yields and a very stable laser ionization. The ion beam composition was measured on-line with the ISOLTRAP MR-TOF mass spectrometer to validate the laser tuning and to quantify the contribution of Dy, Tb, Gd, Eu and the dominant oxide sidebands PrO, CeO, LaO. This enabled optimized collections in particular for ^{149}Tb. With 1.5 hours of collection and 2 hours decay before shipping, up to 200 MBq could be shipped to PSI.

Complementing our previous therapy studies with ^{149}Tb-cm09 and ^{161}Tb-cm09 that demonstrated therapeutic efficacy of these radiopharmaceuticals [1,2], we were now focusing on possible side effects of such a treatment. For this purpose healthy mice without tumors are injected at increasing activity levels for the purpose of investigating kidney damage after alpha therapy with ^{149}Tb-folate and compare it with the damage caused by ^{161}Tb-folate based beta therapy. These mice are currently being monitored regarding body weight and potential changes of blood plasma parameters. Raising levels of blood urea nitrogen and creatinine would be an indication for loss of kidney function. The plan is to follow the development over a period of about 8 months.
In 2014 we could inject 3 mice with 2 MBq/mouse and study their evolution, in 2015 we continued this ^{149}Tb-cm09 dose escalation study with 6 mice injected with 5 MBq/mouse.

For the ^{149}Tb pilot study with peptides we managed to label DOTANOC and DOTA-RGD at high specific activity of up to 10 MBq/nmol. This will allow the performance of a relevant therapy study in the next production run.

We also managed to label both peptides with the imaging isotope ^{152}Tb. They have been injected into AR42J and U87MG tumor-bearing mice which were imaged using a benchtop small animal PET/CT scanner (Genisys8, Sofie Biosciences). Tumor visualization was readily achieved with both targeting agents and, due to the high sensitivity of this scanner, it was possible to image tumors also at late time points after injection of the mice.

In order to facilitate an experiment at CHUV, we separated ^{152}Tb and sent 150 MBq to Lausanne where it was possible to label a neurotensin derivative (NT-20.3-Ile) and inject 4 tumor-bearing mice which were with 8 MBq each for scanning 1.5-2 h after injection using a small-animal PET scanner.

We would like to thank the RILIS team for excellent Dy ionization and the ISOLTRAP-MR-TOF-MS team for the on-line measurement of the beam composition as essential information to optimize the collection conditions. We are particularly grateful to CERN's and PSI's radioactive shipping services which did their best to cope with the constraints of the EDH system to minimize delays in shipping. In the longer run we aim at installing a setup for chemical separation of Tb from its unwanted pseudo-isobars (CeO sidebands) at MEDICIS. Thus the activity and dose rate of the shipped parcels could be reduced considerably.

[1] C. Müller et al., 2012

[2] C. Müller et al., 2014

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