The REMIX Project: Research on the Emerging Medical radIonuclides from the X-sections

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INTRODUCTION

REMIX is a three-years project funded by INFN-CSN5 in 2021, with the goal of finding possible ^{47}Sc and medical Terbium isotopes (^{149}Tb, ^{152}Tb, ^{155}Tb and ^{161}Tb) production routes by using accelerators. All the radionuclides of interest in the REMIX project, except for the therapeutic ^{161}Tb, can be used to obtain theranostic radiopharmaceuticals, since they emit radiation suitable for both therapeutic and diagnostic purposes, as shown in Table 1 [1].

The study of the possible production routes is important since until now the limiting factor for clinical and preclinical studies with ^{47}Sc-labeled radiopharmaceuticals is the lack of ^{47}Sc availability. Studies to find the best proton-induced nuclear reaction that allows enough ^{47}Sc production must also consider the simultaneous minimization of the co-production of all possible contaminants. Particular attention must be paid to the other Sc-isotopes since they cannot be chemically separated from the produced ^{47}Sc. Among the Sc-isotopes, the most critical is the ^{46}Sc (83.79 d) as it has a longer half-life than the ^{47}Sc (3.3492 d). As already reported, ^{47}Sc was first studied in the PASTA project [2, 3, 4, 5] and the goal of REMIX is to measure the proton-induced nuclear reactions by using isotopically enriched ^{49}Ti [6,7] and ^{50}Ti targets. The enriched powders, purchased during 2018, were not suitable for target manufacturing with the HIVIPP technique, as previously described. For this reason, during 2019 and 2021 a cryomilling procedure was studied and optimized using the cheaper ^{nat}Ti metallic sponges to mimic the process and obtain metallic powders suitable for the HIVIPP deposition. During 2021, the first enriched ^{49}Ti targets were realized [8,9] and characterized with IBA (Ion Beam Analysis) methods, exploiting the AN2000 accelerator at the LNL (HIX project, PI: S. Cisternino).

On the other hand, the medical relevant Tb-isotopes have not been studied at the LNL during 2021 but are under investigation within the REMIX project [10].

Table 1. Nuclear data of ^{47}Sc, ^{149}Tb, ^{152}Tb, ^{155}Tb and ^{161}Tb [1].

	Half-life	Imaging radiation	Therapeutic radiation
^{47}Sc	3.3492 d	γ: 159.381 keV intensity 68.3%	Mean β^- energy 162.0 keV intensity 100%
^{149}Tb	4.1 h	Mean β^+ energy: 730 keV Intensity 7% γ energy: 164.98 keV Intensity 26.4%	Auger and IC electrons: E_{mean} = 32 keV Intensity 85% α particle: Energy 3967 keV Intensity 16.7%
^{152}Tb	17.5 h	Mean β^+ energy: 1140 keV Intensity 20.3% γ energy: 344.28 keV Intensity 63.5%	Auger and IC electrons: E_{mean} = 36 keV Intensity 69%
^{155}Tb	5.32 d	Main γ energy: 105 keV Intensity 25%	Auger and IC electrons: E_{mean} = 19 keV Intensity 204%
^{161}Tb	6.89 d	γ energy: 74.57 keV Intensity 10.2%	Mean β^- energy 154 keV intensity 100% Auger and IC electrons: E_{mean} = 19 keV Intensity 227%

REMIX ORGANIZATION

The project is organized in working packages (WP):

WP1. Target manufacturing and characterization (resp. S. Cisternino)**.** During 2021 and up to June 2022 the WP1 will realize with the HIVIPP method and characterize with IBA techniques the isotopically enriched ^{49}Ti and ^{50}Ti thin targets to be irradiated at the ARRONAX facility for nuclear cross section measurements [8,9]. From July 2022 to December 2023, the WP1 will study the manufacturing of Gd_2O_3 targets by Spark Plasma Sintering (SPS) to be irradiated at the Sacro Cuore Don Calabria Hospital (SCDCH, Negrar, VR, Italy), first by using ^{nat}Gd and then by using the isotopically enriched ^{155}Gd to produce ^{155}Tb.

WP2. Nuclear cross section (XS) measurements with ^{49}Ti and ^{50}Ti targets (resp. L. Mou). The thin targets realized by WP1 will be irradiated with the proton-beam available at ARRONAX (Nantes, France) that has a tunable energy 35-70 MeV (Figure 1). Due to the pandemic, during 2021 only two irradiation runs have been performed on ^{49}Ti targets [6,7]. WP2 experiments with ^{50}Ti targets are scheduled for 2022.

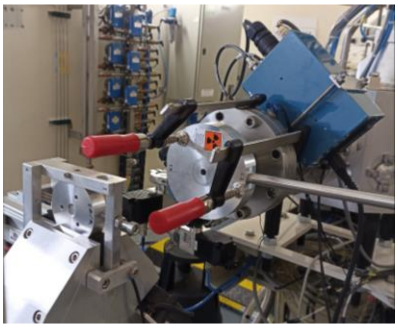

Fig. 2 The ARRONAX beam line during a REMIX run with ^{49}Ti.

WP3. Nuclear XS measurements with ^{nat}Dy, ^{159}Tb and ^{nat}Eu targets (resp. S. Manenti). These thin targets are available on the market and will be irradiated at the ARRONAX facility to find out the best production parameters for Tb-radionuclides, in collaboration with WP4. The γ-spectrometry measurements will be carried out at the LASA lab. Due to the pandemic, during 2021 only two irradiation runs have been performed on ^{nat}Dy targets [10].

WP4. Nuclear XS modeling (resp. L. Canton and A. Fontana). The nuclear codes TALYS, EMPIRE and FLUKA will be used to estimate the production of ^{47}Sc [3, 11], ^{155}Tb and ^{161}Tb. Experimental data from WP2 and WP3 will be compared with theoretical results, to find out the most promising production routes for these radionuclides. It is important to remind the need to estimate the co-production of contaminants, in collaboration with WP2 and WP3, to find out the best irradiation parameters for the medical radionuclides of interest.

WP5. Dosimetric calculations (resp. L. Meléndez-Alafort and L. De Nardo). As already done for ^{47}Sc production using ^{nat}V targets [4], the OLINDA code will be used to estimate the dose increase due to the presence of contaminants in the labelling of specific radiopharmaceuticals. These results, carried out with both ^{47}Sc and Tb-isotopes, will indicate whether radionuclides obtained with the production route under investigation could be used in clinical practice.

WP6. ^{155}Tb Thick Target Yield (TTY) measurements (resp. P. Martini). During 2023, the enriched $^{155}Gd_2O_3$ target realized by WP1 will be irradiated at the 19 MeV cyclotron of the SCDCH. Dissolution of the target will be performed to take an aliquot of the solution and measure ^{155}Tb RadioNuclidic Purity (RNP) by γ-spectrometry, in collaboration with WP2.

WP7. Apparatus design and realization for irradiation tests with the L3c beam-line (resp. G. Sciacca). The target-station and the beam-dump to be installed in the LARAMED beam-line devoted to XS measurements will be designed and realized at the LNL. Additional mechanical devices, useful for the REMIX project (e.g. collimator, capsule, etc.), will be designed and realized within WP7.

RESULTS AND DISCUSSION

REMIX project started in 2021, a year still affected by the pandemic. However, results have been achieved without delay, also thanks to the solid network of collaborations and the mutual support in the team. A more detailed description of REMIX major outcomes can be found in specific LNL Annual Reports.

REFERENCES AND FINAL NOTES

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