Research on Emerging Medical radIonuclides from the X-sections (REMIX): The Accelerator-based Production of ^{47}Sc, ^{149}Tb, ^{152}Tb, ^{155}Tb and ^{161}Tb

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Abstract. The REMIX project is focused on the cyclotron-based production of ^{47}Sc, ^{149}Tb, ^{152}Tb, ^{155}Tb and ^{161}Tb radionuclides, whose decay characteristics make them suitable for medical applications. This work will outline the main results achieved withing the REMIX collaboration, that is organized in the following Work Packages (WP): WP1. Target manufacturing (^{49}Ti, ^{50}Ti and $^{155}Gd_2O_3$) and characterization; WP2. Nuclear cross section (XS) measurements with ^{49}Ti and ^{50}Ti targets for ^{47}Sc production; WP3. Nuclear XS measurements with ^{nat}Dy, ^{159}Tb and ^{nat}Eu targets for ^{xx}Tb production; WP4. Nuclear XS modeling for ^{47}Sc and ^{155}Tb production; WP5. Dosimetric calculations for ^{47}Sc- and ^{xx}Tb-labelled radiopharmaceuticals; WP6. ^{155}Tb Thick Target Yield (TTY) measurements; WP7. Apparatus design and realization for irradiation tests with the LARAMED beamline. Since the LARAMED bunkers and ancillary laboratories are currently under completion at the INFN-LNL, the nuclear XS experiments are carried out in collaboration with the GIP ARRONAX facility (Saint-Herblain, France) and the Thick Target Yield (TTY) measurements are performed at the Sacro Cuore Don Calabria hospital (SCDCh, Negrar, Verona, Italy).

1. Introduction

REMIX is a project funded by INFN-CSN5 in 2021-2023, with the goal of studying ^{47}Sc and medical Terbium isotopes (^{149}Tb, ^{152}Tb, ^{155}Tb and ^{161}Tb) production routes by using accelerators. The framework of REMIX is the LARAMED (LAboratory of RADionuclides for MEDicine) program [1, 2], that will exploit the 70 MeV proton cyclotron installed at the INFN-LNL for the SPES project [3]. Since the LARAMED bunkers and ancillary laboratories are currently under completion (WP7), nuclear cross section (XS) experiments of the REMIX project are carried out in collaboration with the GIP (Groupement d'Intérêt Public) ARRONAX (Accélérateur pour la Recherche en Radiochimie et Oncologie à Nantes Atlantique) facility (Nantes, France) [4] while the Thick Target Yield (TTY) measurements are performed in collaboration with the Sacro Cuore Don Calabria hospital (SCDCh, Negrar, Verona, Italy). 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 [5].

Table 1. Main nuclear data of the radionuclides of interest in REMIX.

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

The study of the possible production routes of ^{47}Sc are under the spotlight of the scientific community since 2016, as underlined by the IAEA project focused on "Therapeutic Radiopharmaceuticals Labelled with New Emerging Radionuclides (^{67}Cu, ^{186}Re, ^{47}Sc)" (CRP no. F22053) [6, 7]. Studies to find the best ^{47}Sc production route have to consider not only the resulting ^{47}Sc yield but also the simultaneous minimization of the co-production of all possible contaminants: particular attention must be paid to the Sc-isotopes since they cannot be chemically separated from the produced ^{47}Sc and to their impact on the patient dose (WP5). As already reported, the proton-based production of ^{47}Sc was first studied in the PASTA project [8-11] and the goal of REMIX is to measure the proton-induced nuclear reactions by using isotopically enriched ^{49}Ti and ^{50}Ti targets (WP1, WP2). On the other hand, the medically relevant Tb-isotopes are obtaining increasing attention in the last years [12], but there are many challenges in their production. For this reason, within the REMIX project nuclear XS for Tb-production are investigated both experimentally (WP3) and theoretically (WP4), with a focus on the low energy ^{155}Gd(p,n)^{155}Tb route, investigated at the SCDCh (WP6).

2. Results from the Work Packages (WPs)

2.1. *WP1. Target manufacturing (^{49}Ti, ^{50}Ti and $^{155}Gd_2O_3$) and characterization* (resp. S. Cisternino). During 2021 and up to June 2022 the WP1 realized with the HIgh energy VIbrational Powder Plating (HIVIPP) method and characterized with Ion Beam Analysis (IBA) techniques the isotopically enriched ^{49}Ti and ^{50}Ti thin targets (ca. 550 µg/cm^2) [13], to be irradiated at GIP ARRONAX cyclotron for nuclear XS measurements (WP2). 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 SCDCh first by using ^{nat}Gd and then by using the isotopically enriched ^{155}Gd to produce ^{155}Tb (WP6). A dedicated capsule designed by WP7 will be used for this purpose.

2.2. *WP2. Nuclear cross section (XS) measurements with ^{49}Ti and ^{50}Ti targets for ^{47}Sc production.* (resp. L. Mou). The thin targets realized by WP1 are irradiated with the proton-beam available at GIP ARRONAX having a tunable energy 35-70 MeV. Considering the pandemic and up to mid-2022, no.6 irradiation runs have been performed: in total no.12 of ^{49}Ti and no.6 ^{50}Ti targets were irradiated. Figure 1 shows the preliminary results of the ^{49}Ti(p,x)^{47}Sc XS. Further WP2 experiments are scheduled for autumn 2022 and 2023.

WP3. Nuclear XS measurements with ^{nat}Dy, ^{159}Tb and ^{nat}Eu targets for ^{xx}Tb production (resp. S. Manenti). These thin targets are available on the market and are irradiated at the GIP ARRONAX facility to find out the best production parameters for Tb-radionuclides, in collaboration with WP4. The γ-spectrometry measurements are carried out at the LASA lab. Up to mid-2022, no.4 irradiation runs have been performed on no.16 ^{nat}Dy targets. Figure 2 shows the preliminary results of the ^{nat}Dy(d,x)^{155}Tb XS.

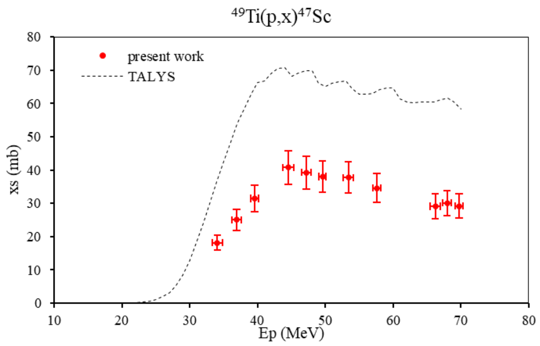

Figure 1. ^{49}Ti(p,x)^{47}Sc cross sections

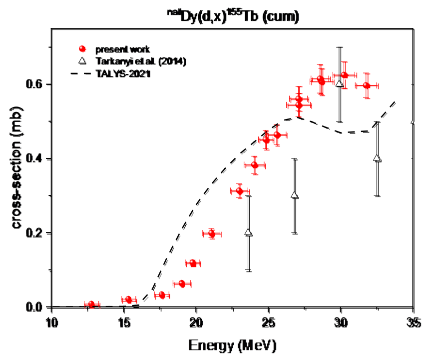

Figure 2. ^{nat}Dy(d,x)^{155}Tb cross sections

2.3. WP4. Nuclear XS modeling for ^{47}Sc and ^{155}Tb production (resp. L. Canton and A. Fontana). The nuclear codes TALYS [14], EMPIRE [15] and FLUKA [16] are used to estimate the production of ^{47}Sc [9], ^{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 properly estimate the co-production of contaminants, including the ones that are difficult to be measured, such as the fast-decaying ones and stable isotopes.

2.4. WP5. Dosimetric calculations for ^{47}Sc- and ^{xx}Tb-labelled radiopharmaceuticals (resp. L. Meléndez-Alafort and L. De Nardo). As already done for ^{47}Sc production using ^{nat}V targets [10], the OLINDA code is 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.

2.5. 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, determine thick target yield and measure ^{155}Tb RadioNuclidic Purity (RNP) by γ-spectrometry, in collaboration with WP2.

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

3. Conclusions: a mid-report of the REMIX project

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 works.

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