

^{47}Sc production with proton beams on isotopically enriched ^{48}Ti and ^{49}Ti targets

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Abstract. The theranostic emerging radionuclide ^{47}Sc is under the spotlight of the scientific community due to its medically favorable decay characteristics ($t_{1/2}=3.3492$ d, $E_{\gamma}=159.381$ keV, $E_{\beta^{-},mean}=162.0$ keV) for both the diagnostic and treatment procedures. In the framework of the LARAMED (LABoratory of RADionuclides for MEDicine) program at INFN-LNL (National Institute of Nuclear Physics-Legnaro National Laboratories), the investigation of the possible ^{47}Sc production routes using a 70 MeV proton beam is one of the goals of the REMIX (Research on Emerging Medical radIonuclides from the X-sections) project, funded by INFN for the years 2021-2023. Since the LARAMED bunkers are currently under completion, experiments are performed in collaboration with the GIP ARRONAX facility (Nantes, France), where a 70 MeV multi-particle cyclotron is operational. In this work, the cross-section measurements using enriched $^{48,49}\text{Ti}$ targets are reported and the results presented in comparison to the previous literature data, when available. The ^{47}Sc excitation functions are analyzed in relation to the contaminants' ones since the co-produced radionuclides can affect the dose delivered to a patient. ^{46}Sc cross-section curves are mainly taken into account since ^{46}Sc cannot be chemically separated from ^{47}Sc and its half-life ($t_{1/2}=83.79$ d) is longer than the ^{47}Sc one ($t_{1/2}=3.3492$ d).

1. Introduction

Theranostics, the new standpoint of nuclear medicine, benefits from the physical properties of some radionuclides to perform both the diagnosis and treatment of human diseases. The radionuclides employed in such procedures should have similar chemical characteristics to label the same biologically active molecule. For this reason, it is advantageous if the theranostic pair encompasses two radioisotopes of the same element or even only one radioisotope if the decay characteristics are suitable for both the diagnosis and the therapy. The latter is the case of ^{47}Sc , which emits a γ -ray at 159.381 keV (see table 1) suitable for SPECT (Single Photon Emission Computed Tomography) imaging, accompanying a low-energy β -particle ($E_{\beta^{-},mean}=162.0$ keV, $I_{\beta^{-}}=100\%$ [1]) that can be employed for RadioNuclide Therapy (RNT).



The scientific community interest in the ^{47}Sc , highlighted in the IAEA (International Atomic Energy Agency) CRP (Coordinated Research Project) "Therapeutic Radiopharmaceuticals Labelled with New Emerging Radionuclides (^{67}Cu , ^{186}Re , ^{47}Sc)" [2], requires the investigation of the possible production routes of this radionuclide. In the context of LARAMED [3, 4], at INFN-LNL, two projects focused on the study of production cross-sections of ^{47}Sc and its contaminants. The first one, the PASTA (Production with Accelerator of Sc-47 for Theranostic Applications) project [5, 6, 7, 8], funded by INFN for the years 2017-2018, considers the use of protons on ^{nat}V and enriched ^{48}Ti . The second one, the REMIX (Research on Emerging Medical radionuclides from the X-sections) project, funded by INFN for the years 2021-2023, is considering the proton-induced reactions on enriched ^{49}Ti and ^{50}Ti .

In this work, the $^{48}\text{Ti}(p,x)^{47}\text{Sc}$ cross-section is reported in comparison to the ^{46}Sc excitation function to search for a possible energy interval where the ^{47}Sc production is maximized while the ^{46}Sc one minimized. Among all the co-produced contaminants that can potentially contribute to the dose delivered to a patient, particular attention is given to ^{46}Sc which has two high branching ratio γ -rays highly impacting on the total dose ($E_{\gamma 1}=889.381$ keV, $I_{\gamma 1}=99.984$ %, $E_{\gamma 2}=1120.545$ keV, $I_{\gamma 2}=99.987$ %). Moreover, ^{46}Sc cannot be chemically separated from ^{47}Sc or waited for its decay since its half-life ($t_{1/2}=83.79$ d) is longer than the ^{47}Sc one ($t_{1/2}=3.3492$ d). Also preliminary values of the $^{49}\text{Ti}(p,x)^{47,46}\text{Sc}$ cross-sections are presented.

2. Materials and methods

Thin (about $1\text{ }\mu\text{m}$) enriched $^{48,49}\text{Ti}$ targets, manufactured at INFN-LNL, were used for cross-section measurements. The ^{48}Ti enriched metallic powder, purchased from TRACE Sciences International (Richmond Hill, Ontario, Canada) with an isotopical enrichment purity of 99.32%, was deposited on a $25\text{ }\mu\text{m}$ thick Al foil using the HIVIPP (High energy Vibration Powder Plating) technique [9, 10]. The ^{49}Ti powder instead, supplied by Oak Ridge (Oak Ridge, Tennessee, USA) with an isotopical enrichment of 96.25%, was delivered in a sponge-like shape and required a cryogenic milling process before the deposition on Al supports. The targets were characterized by Elastic Backscattering Spectroscopy (EBS) analysis to quantify the exact amount of enriched powder deposited and the level of impurities.

Since the LARAMED bunkers are still under completion, targets were irradiated with the tunable 35-70 MeV proton beams delivered by the IBA cyclotron at the GIP ARRONAX facility (Saint Herblain, Nantes, France) [11]. The samples were arranged in stacked-foil targets including Ni monitor and Al thick degrader layers to bombard several enriched Ti targets in each irradiation run. In total, 7 targets of ^{48}Ti and 12 targets of ^{49}Ti have been bombarded. Beam current of at least 100 nA was used and the irradiation runs lasted about $1\div 1.5$ h. After a proper cooling time from the End Of Bombardment (EOB), each enriched Ti target was measured with a HPGe detector calibrated in efficiency and energy to obtain the activity of all produced radionuclides. For several days after the irradiation, additional γ -spectra of each foil were collected (at least 5 acquisitions) to follow the decay of all the produced radionuclides and to check eventual γ -interferences. The γ peaks identified in the spectra to quantify the activity of ^{47}Sc and ^{46}Sc are reported in Table 1.

3. Experimental results and discussion

3.1. ^{48}Ti results

The cross-section values for the production of ^{47}Sc and ^{46}Sc obtained using protons on ^{48}Ti are graphed together with the few previous literature data available [12, 13] and a theoretical curve produced by TALYS 1.95 code [14] run with default parameters. In figure 1(a), the trend reported by our new data is in agreement with the literature and TALYS estimations. However, our obtained values have a difference up to 20% with the Gadioli *et al* [12] and the corrected Levkovski* [13, 15] results. It has to be noted that the theoretical estimation

Table 1. Half-life, decay mode, energy and intensity of the γ -ray used in the analysis for the radionuclides considered [1].

Radionuclide	$t_{1/2}$ (d)	Decay mode	E_γ (keV)	I_γ (%)
^{47}Sc	3.3492 (6)	β^- (100%)	159.381 (15)	68.3 (4)
^{46}Sc	83.79 (4)	β^- (100%)	889.277 (3)	99.984 (1)

largely overestimates all experimental values. The ^{46}Sc cross-section values, in figure 1(b), are in agreement with the Gadioli *et al* [12] data and with TALYS, in the energy range investigated.

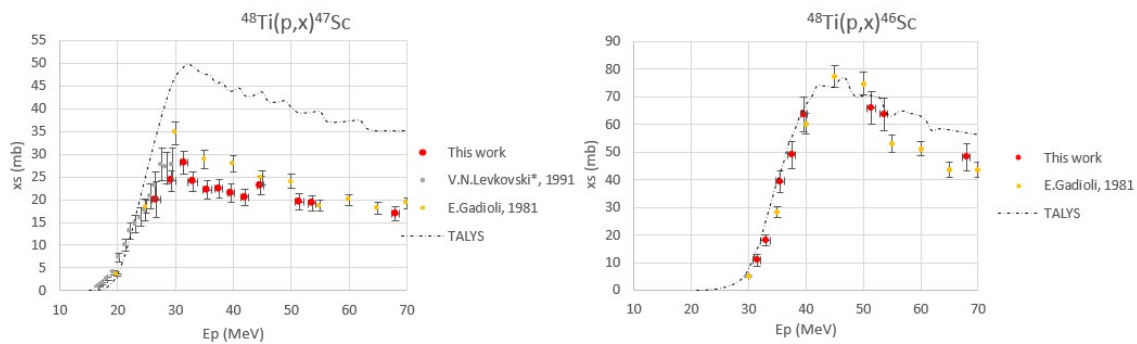


Figure 1. Cross-sections of $^{48}\text{Ti}(p,p)^{47}\text{Sc}$ reaction (a), and of $^{48}\text{Ti}(p,x)^{46}\text{Sc}$ reaction (b).

3.2. ^{49}Ti results

The preliminary cross-sections of ^{46}Sc and ^{47}Sc induced by protons on ^{49}Ti targets are graphically represented in figure 2. The results are still preliminary because the EBS analysis are not yet completed. Our measurement, in figure 2(a), is the first for the $^{49}\text{Ti}(p,x)^{47}\text{Sc}$ reaction so only the results about ^{46}Sc , in figure 2(b), are shown with a previous set of data by Levkovski* [13].

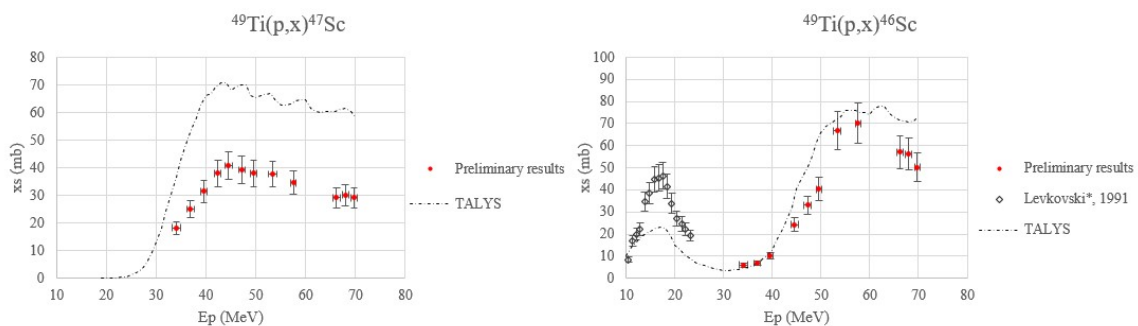


Figure 2. Cross-sections of $^{49}\text{Ti}(p,x)^{47}\text{Sc}$ reaction (a), and of $^{49}\text{Ti}(p,x)^{46}\text{Sc}$ reaction (b).

Similarly to the previously presented $^{48}\text{Ti}(p,x)^{47}\text{Sc}$ data, our ^{47}Sc cross-section points are well below the theoretical values while the ^{46}Sc values are in good agreement with the TALYS estimations.

4. Conclusions

The aim of the PASTA and REMIX projects is to determine the optimal irradiation conditions to maximize the production of ^{47}Sc while minimizing the co-production of radioisotopic contaminants. To achieve a precise knowledge about the cross-sections, different target materials (^{nat}V and Ti isotopes) have been irradiated and some measurements are still ongoing. In this work, proton-induced nuclear reactions on enriched metallic $^{48,49}\text{Ti}$ targets are presented. Particular attention is given to ^{46}Sc since it cannot be decreased by extending the post-irradiation decay time. From a preliminary evaluation of the results it seems that these nuclear reactions cannot be used for the ^{47}Sc production due to the presence of other isotopic contaminants. Anyways, further investigations concerning thick targets yields and dosimetric calculations have to be done to evaluate the feasibility of these ^{47}Sc production routes.

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References

- [1] National Nuclear Data Center (NNDC) NuDat 3.0 webpage: <https://www.nndc.bnl.gov/nudat3/>
- [2] Jalilian A R *et al* 2021 *Curr Radiopharm.* **14** 306-14
- [3] Pupillo G *et al* 2020 The Laramed project at LNL: ^{67}Cu and ^{47}Sc production for theranostic applications *AIP Conf. Proc. (On-line)* vol 2295 p 020001
- [4] Esposito J *et al* 2019 LARAMED: a laboratory for radioisotopes of medical interest *Molecules* **24** 20
- [5] Pupillo G *et al* 2019 Production of ^{47}Sc with natural vanadium targets: results of the PASTA project *J. Radioanal. Nucl. Chem.* **322** 1711-18
- [6] Pupillo G *et al* 2021 Correction to: Production of ^{47}Sc with natural vanadium targets: results of the PASTA project *J. Radioanal. Nucl. Chem.* **328** 1407
- [7] Barbaro F, Canton L, Carante M P, Colombi A, De Dominicis L, Fontana A, Haddad F, Mou L and Pupillo G 2021 New results on proton-induced reactions on vanadium for ^{47}Sc production and the impact of level densities on theoretical cross sections *Phys. Rev. C* **104** 0044619
- [8] De Nardo L, Pupillo G, Mou L, Furlanetto D, Rosato A, Esposito J and Meléndez-Alafort L 2021 Preliminary dosimetric analysis of DOTA-folate radiopharmaceutical radiolabelled with ^{47}Sc produced through $^{nat}\text{V}(p,x)^{47}\text{Sc}$ cyclotron irradiation *Phys. Med. Biol.* **66** 025003
- [9] Cisternino S, Skliarova H, Antonini P, Esposito J, Mou L, Pranovi L, Pupillo G and Sciacca G 2022 Upgrade of the HIVIPP deposition apparatus for nuclear physics thin targets manufacturing *Instruments* **6** 23
- [10] Skliarova H, Cisternino S, Pranovi L, Mou L, Pupillo G, Rigato V and Rossi-Alvarez C 2020 HIVIPP deposition and characterization of isotopically enriched ^{48}Ti targets for nuclear cross-section measurements *Nucl. Instrum. Methods Phys. Res. Sect. A Accel. Spectrometers Detect. Assoc. Equip.* **981** 164371
- [11] Haddad F, Ferrer L, Guertin A, Carlier T, Michel N, Barbet J and Chatal J F 2008 ARRONAX, a high-energy and high-intensity cyclotron for nuclear medicine *Eur. J. Nucl. Med. Mol. Imaging* **35** 1377-87
- [12] Gadioli E, Gadioli-Erba E, Hogan J J and Burns K I 1981 Emission of alpha particles in the interaction of 10-85 MeV protons with $^{48,50}\text{Ti}$ *Z. Physik A* **301** 289-300
- [13] Levkovski V N 1991 Cross-section of medium mass nuclide activation ($A=40-100$) by medium energy protons and alpha particles ($E=10-50$ MeV) *Inter-Vesi*
- [14] Koning A J, Hilaire S and Duijvestijn M C 2008 Proc. Int. Conf. on Nuclear Data for Science and Technology Nice (EDP Sciences) pp 211-14
- [15] Takács S, Tárkányi F, Sonck M and Hermanne A 2002 Investigation of the $^{nat}\text{Mo}(p,x)^{96m,g}\text{Tc}$ nuclear reaction to monitor proton beams: New measurements and consequences on the earlier reported data *Nucl. Instr. Meth. B* **198** 183-196