IL NUOVO CIMENTO **42 C** (2019) 139
DOI 10.1393/ncc/i2019-19139-1

Colloquia: EuNPC 2018

Preliminary results of the PASTA project

G. Pupillo(1)(*), A. Fontana(2), L. Canton(3), F. Haddad(4), H. Skliarova(1), S. Cisternino(1), P. Martini(1), M. Pasquali(1), A. Boschi(5), J. Esposito(1), A. Duatti(5) and L. Mou(1)

(1) *INFN, Laboratori Nazionali di Legnaro - Legnaro, Padova, Italy*
(2) *INFN, Sezione di Pavia - Pavia, Italy*
(3) *INFN, Sezione di Padova - Padova, Italy*
(4) *GIP ARRONAX and SUBATECH - Nantes, France*
(5) *Università di Ferrara - Ferrara, Italy*

received 5 February 2019

Summary. — ^{67}Cu, ^{186}Re and ^{47}Sc are theranostic radionuclides in the spot-light of the scientific community: the insufficient availability is limiting their use in clinical and pre-clinical studies. The aim of this work is the analysis of ^{47}Sc production by using high-energy and high-intensity cyclotrons, as the one installed at INFN-LNL in the framework of SPES project, by exploring promising nuclear reactions induced by proton-beams.

1. – Introduction

The worldwide increasing interest on theranostic radiopharmaceuticals, allowing the selection of patients with higher chance to respond to specific treatments and the application of individually customized dosimetry, is well represented by the recent Coordinated Research Project (CRP), promoted by the International Atomic Energy Agency (IAEA), focused on *^{67}Cu, ^{186}Re and ^{47}Sc as Emerging Theranostic Radionuclides* (No. F22053) [1]. The aim of this work is the analysis of ^{47}Sc production by using proton cyclotrons, as the one installed at INFN-LNL in 2015. The applied research in the field of nuclear medicine through the LARAMED project, acronym of LAboratory of RAdionuclides for MEDicine, is currenty conducted in partnership with different italian and international research institutions, since the infrastructure at LNL (beam-lines and laboratories) is currently under construction. Cross section measurements are carried out at the ARRONAX facility (Nantes, France), where a 70 MeV cyclotron is operative and produces radionuclides for medicine [2]. Among the isotopes of interest for LARAMED and ARRONAX, ^{47}Sc is of particular interest for its great potential in theranostic but

(*) Corresponding author. E-mail: `gaia.pupillo@lnl.infn.it`

Fig. 1. – Photograph of the foils of a stacked-target.

also in radioimmunotherapy: its relatively long half-life (3.3492 d) permits to follow the slow biodistribution of monoclonal antibodies; the β^- particles of low-medium energy (mean energy 162.0 keV; intensity 100%) are useful to deliver cytotoxic dose to small-medium sized tumours while the emitted $\gamma-$rays are suitable for SPECT or SPECT/CT cameras (energy 159.381 keV; intensity 68.3%). Moreover, β^+ counterparts such as ^{44}Sc or ^{43}Sc exist and may also allow the theranostic approach to be used with PET imaging.

The PASTA project, acronym of Production with Accelerator of Sc-47 for Theranostic Applications, is focused on the production of ^{47}Sc by using enriched metal targets of ^{48}Ti, ^{49}Ti, ^{50}Ti and ^{nat}V metal targets. In fact, no experimental data are available for the ^{49}Ti(p,x)^{47}Sc reaction, while only few measurements were performed with the ^{48}Ti and ^{50}Ti targets in oxide form [3]. In view of an optimized production, the co-production of contaminant radionuclides, especially the isotopic impurities that cannot be chemically separated from the desired product and affect the RadioNuclidic Purity (RNP), is a keypoint. For this reason, experiments are designed in order to measure not only the nuclear cross section of the radionuclide of interest (*i.e.* ^{47}Sc), but also the production of isotopic contaminants (*e.g.* ^{46}Sc) and other impurities (*e.g.* ^{51}Cr) that may affect the radiochemical procedure aimed at the radionuclide extraction and purification.

2. – Materials and Methods

Considering the high cost of the enriched metal powders ^{49}Ti and ^{50}Ti (natural abundance 5.41% and 5.18% respectively), first experiments at the ARRONAX facility were performed with ^{nat}V and ^{48}Ti (natural abundance 73.73%) metal targets, arranged in stacked-foils structures (fig.1). The ^{nat}V metal foils were purchased by Goodfellow, while enriched ^{48}Ti metal targets were realized by using the High energy VIbrational Powders Plating (HIVIPP) method [4], to homogeneously deposit the enriched titanium powder (>99%, purchased by TraceScience) on an aluminium support. Considering the use of enriched expensive materials, a dedicated target holder ($\oslash$ 11 mm), a graphite collimator ($\oslash$ 9 mm) and a plastic support have been designed and realized at the INFN-LNL workshop and used to precisely define the beam size on target during these irradiation runs. The duration of a typical run was 1.5 h with a constant current of about 100 nA, monitored during the bombardment by using an instrumented beam dump.

In the meantime, a fruitful collaboration with experts in nuclear codes such as EMPIRE, FLUKA and TALYS [5-7] started, in order to compare the different nuclear reactions and identify the most promising energy region for ^{47}Sc production. Among the radionuclidic impurities of ^{47}Sc coproduced during the irradiation, ^{46}Sc (83.79 d half-life) causes the major concern since it is the only radioisotope with a longer half-life than ^{47}Sc. For this reason, a cooling time after irradiation may only decrease the ^{47}Sc/ ^{46}Sc activity ratio: it is thus crucial to minimize as much as possible the ^{46}Sc production by carefully selecting the target material and the energy range. Aiming at this goal, the different nuclear codes are employed to estimate the cross sections to produce ^{47}Sc and ^{46}Sc by using the enriched and expensive material of interest (^{49}Ti and ^{50}Ti).

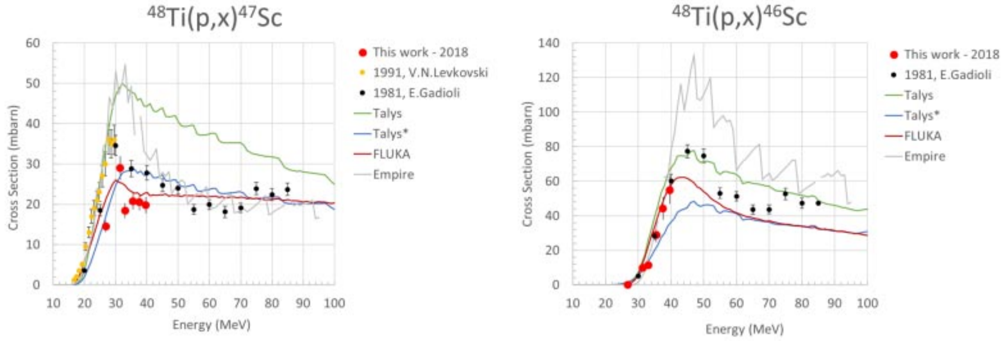

Fig. 2. – Preliminary results of the ^{48}Ti(p,x)^{47}Sc,^{46}Sc nuclear cross sections (red dots).

3. – Results and Discussion

Figure 2 shows the preliminary results of the measurement of ^{48}Ti(p,x)^{47}Sc,^{46}Sc nuclear cross sections (red dots). The reaction for ^{46}Sc production shows a regular trend in the entire energy range investigated; on the contrary, the trend of the ^{48}Ti(p,x)^{47}Sc cross section is irregular at around 30-35 MeV; however, data anlysis is still in progress.

Preliminary results of the ^{nat}V(p,x)^{47}Sc, ^{46}Sc cross sections are shown in fig.3 (red dots) and compared with previous measurements [3]. In both cases an overall good agreement can be found with previous measurements; however, in the energy range 50-60 MeV our values for ^{47}Sc production seems to be lower than previous data. For brevity, results regarding the production of ^{44m}Sc, ^{44}Sc, ^{48}Sc, ^{43}Sc, ^{43}K, ^{48}V, ^{48}Cr, ^{49}Cr and ^{51}Cr are not shown here; in case of ^{44m}Sc and ^{44}Sc decay contribution was taken into account in the data analysis; for ^{43}Sc, the interference with the $\gamma-$ray at 373 keV emitted by ^{43}K was corrected; in case of ^{48}Sc, the nuclear cross section is calculated by considering the $\gamma-$rays at 175 keV and 1037 keV, in order to avoid the interference with ^{48}V at the 938 keV and 1312 keV $\gamma-$lines.

Figure 4 reports the theoretical estimations of ^{47}Sc/^{46}Sc cross section ratio for ^{49}Ti (left) and ^{50}Ti (right) by using FLUKA (blue line), TALYS (red line) and EMPIRE

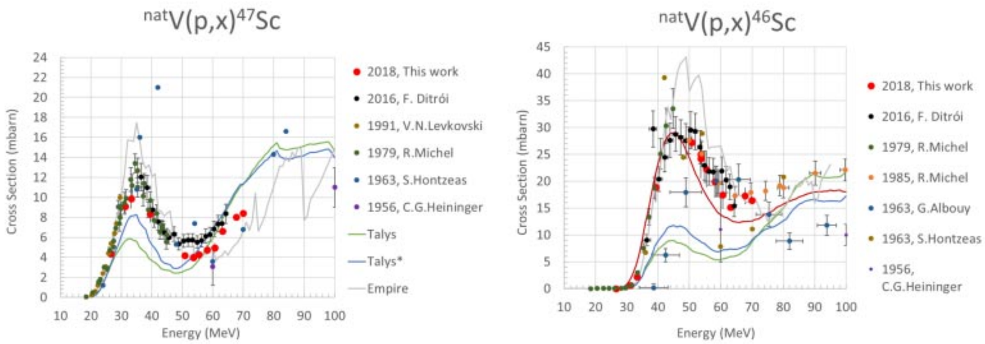

Fig. 3. – Preliminary results of the ^{nat}V(p,x)^{47}Sc,^{46}Sc nuclear cross sections (red dots).

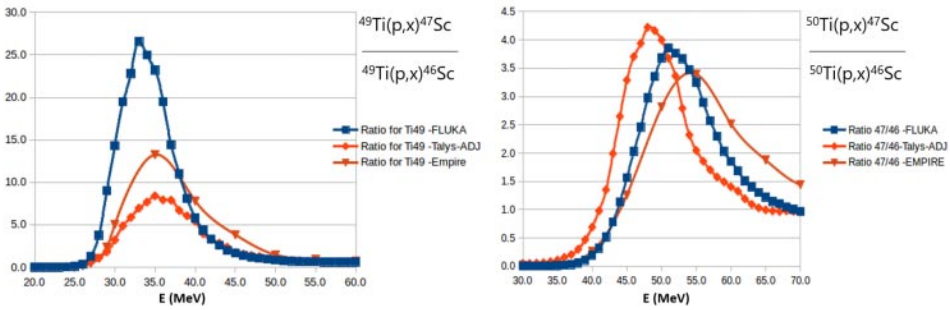

Fig. 4. – ^{47}Sc/^{46}Sc cross section ratio for ^{49}Ti (left) and ^{50}Ti (right) targets.

(brown line) nuclear codes. These estimations show that the nuclear reaction on ^{49}Ti may be preferable than the nuclear reaction on ^{50}Ti targets: in particular, the most promising energy range with ^{49}Ti enriched material is 25-45 MeV; on the contrary, in case of ^{50}Ti targets the best energy range is at higher energies, *i.e.* $E_P > 40$ MeV.

4. – Conclusion

This work reports preliminary results of the PASTA project, an interdisciplinary research activity that ranges from nuclear physics up to material science and radiochemistry.

* * *

This work was funded by INFN with the research project *PASTA-Production with Accelerator of Sc-47 for Theranostic Applications* (CSN5 Bando N. 18203, 2017-2018). It is developed in the framework of the CRP by IAEA (No. F22053) on *Therapeutic Radiopharmaceuticals Labelled with New Emerging Radionuclides (^{67}Cu, ^{186}Re, ^{47}Sc)*. It has been also, in part, supported by a grant from the French National Agency for Research called *Investissements d'Avenir*, Equipex Arronax-Plus (ANR-11-EQPX-0004) and Labex IRON (ANR-11-LABX-18-01).

REFERENCES

[1] IAEA, CRP, http://cra.iaea.org/cra/explore-crps/all-active-by-programme.html.
[2] Haddad F. *et al.*, *Eur. J. Nucl. Med. Mol. Imaging*, **35** (2008) 1377–1387.
[3] EXFOR, Database, https://www-nds.iaea.org/exfor/exfor.htm.
[4] Sugai I. *et al.*, *Nucl. Instr. and Meth. A*, **397** (1997) 81-90.
[5] Herman M. *et al.*, *Nucl. Data Sheets*, **108** (2007) 2655-2715.
[6] Boehlen T.T. *et al.*, *Nucl. Data Sheets*, **120** (2014) 211-214.
[7] Koning A.J. *et al.*, *EDP Sciences*, (2008) 211-214.