PROTON-INDUCED NUCLEAR REACTIONS ON ^{NAT}V AND ^{49}TI FOR THE THERANOSTIC ^{47}SC PRODUCTION: PRELIMINARY CROSS-SECTION RESULTS

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^{47}SC DECAY PROPERTIES

^{47}Sc is a promising theranostic radionuclide for the realization of new radiopharmaceuticals due to its emissions.*

Half-life (d)	γ-emission			β-emission		
	Energy (keV)	Intensity (%)	Employment	Mean Energy (keV)	Intensity (%)	Employment
3.3492	159.381	68.3	SPECT imaging	142.6 203.9	68.4 31.6	Treatment of small-medium sized tumors

- Its half-life is long enough for labeling molecules with a slow biodistribution profile.
- Its lack of clinical employment is mainly due to its scarce availability → production only at reactors.

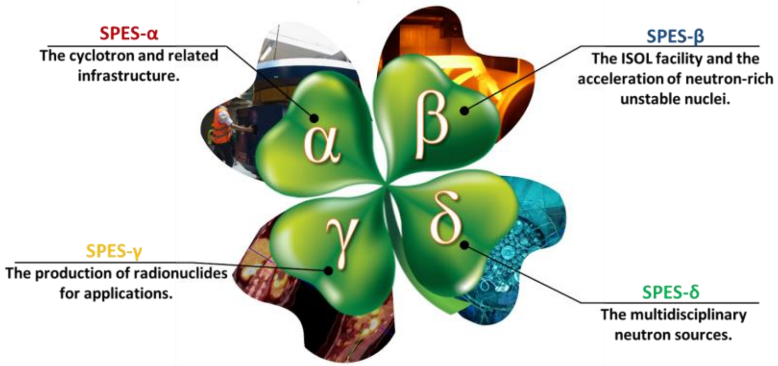
IAEA

*Therapeutic Radiopharmaceuticals Labelled with New Emerging Radionuclides (^{67}Cu, ^{47}Sc, ^{186}Re).

Coordinated Research Project (CRP) by the International Atomic Energy Agency IAEA (2016-2019).

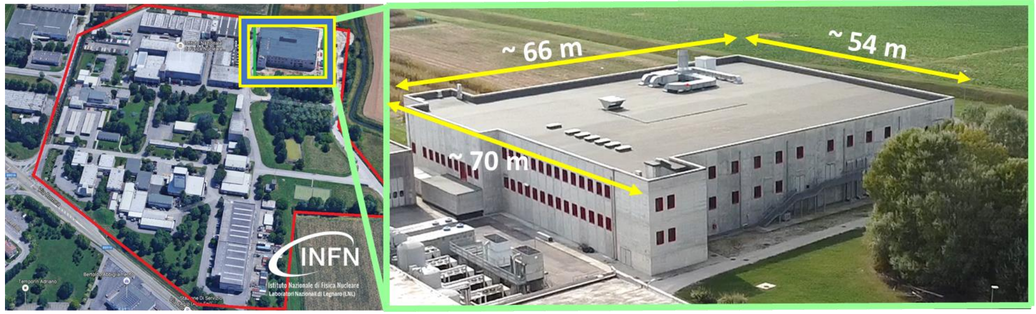
Is the ^{47}Sc production at cyclotrons possible?

SPES @ LNL: THE FACILITY



The SPES project

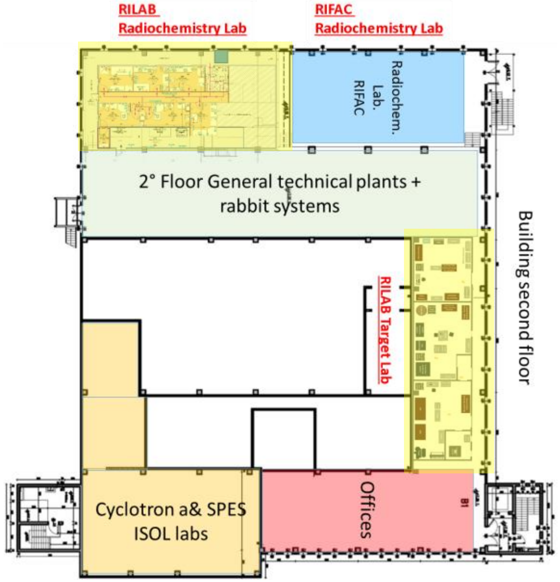
Selective Production of Exotic Species



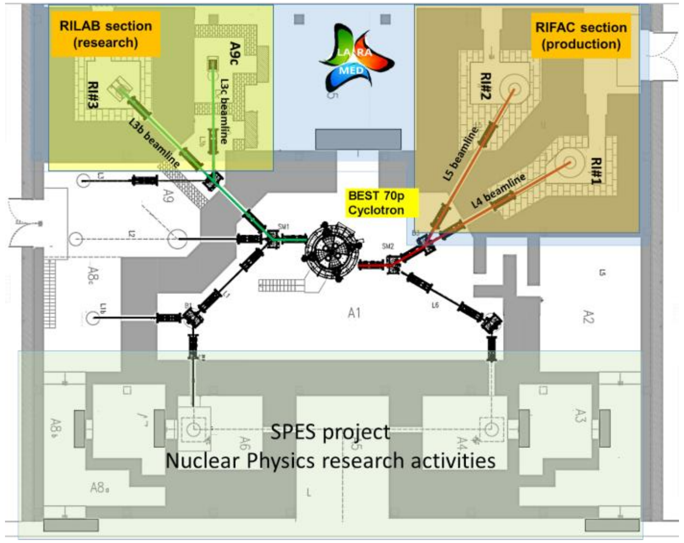
Tunable energy: 35-70 MeV

High output current: 500 μA

Dual extraction → fundamental and applied physics



Radioisotopes research area (LARAMED)



LARAMED PROJECT

LAboratory of RAdionuclides for MEDicine

LARAMED projects	
LARAMED (2012-2016)	LAboratory of RAdionuclides for MEDicine
APOTEMA (2012-2014) TECHNOSP (2015-2017)	Accelerator-Tc-99m alternative (direct) production route through hospital cyclotrons
IAEA CRP (2011-2015)	'Coordinated Research Project ' (CRP) on "Alternative, non HEU-based, Tc-99m /Mo99 supply"
COME (2016)	COpper MEasurement (Cu-67)
PASTA (2017-2018)	Production with Accelerator of Sc-47 for Theranostic Applications
IAEA CRP (2016-2019)	CRP on "Radiopharmaceuticals Labelled with New Emerging Radionuclides Cu-67, Re-186, Sc-47"
TERABIO (2016-2019)	High Power Target concepts R&D
E_PLATE (2018-2019)	High intensity vibrational powder plating
METRICS (2018-2020)	Multimodal pET/mRi Imaging with Cyclotron-produced Mn-52/51 and stable paramagnetic Mn iSotopes
REMIX (2021-2023)	Research on Emerging Medical radIonuclides from the X-sections
TOTEM (2021-2022)	TOTEM (magneTron sputtering cyclotrOn TargEt Manufacturing)

LARAMED network

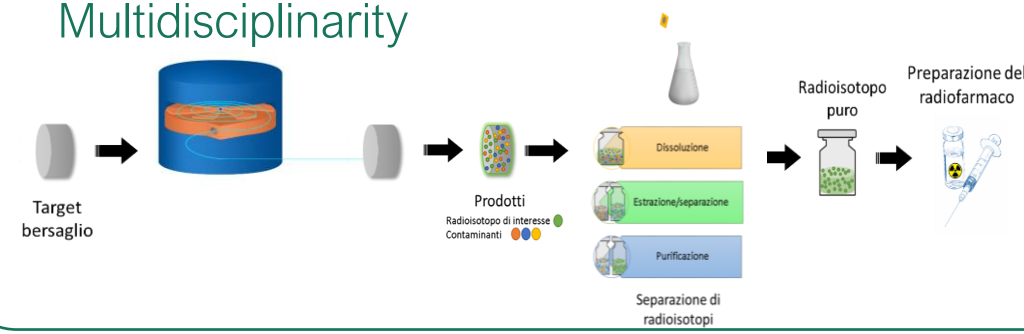
INFN PAVIA, INFN FERRARA, INFN PADOVA, INFN MILANO

Università di Pavia, Università degli Studi di Ferrara, Università degli Studi di Padova, Università degli Studi di Milano

L.E.N.A., Consiglio Nazionale delle Ricerche, Ospedale Sacro Cuore Don Calabria, Policlinico S. Orsola-Malpighi

UW-MADISON CYCLOTRON LAB, IAEA, Arronax Nantes

Multidisciplinarity



^{47}SC PRODUCTION: PASTA PROJECT

Production with Accelerator of Sc-47 for Theranostic Applications

Aim of the PASTA project

- Evaluation of the proton-induced nuclear reactions on ^{nat}V and ^{48}Ti.
- Optimization of the production parameters to minimize the co-production of contaminants: ^{44m}Sc (58.61 h, β^+); ^{44g}Sc (3.97 h, β^+); ^{46}Sc (83.79 d, β^-); ^{48}Sc (43.67 h, β^-).

^{nat}V targets composition

Element	Abundance (%)
^{51}V	**99.750**
^{50}V	0.250

✓ ^{nat}V foils purchased

^{48}Ti targets composition

Element	Abundance (%)
^{46}Ti	8.25
^{47}Ti	7.44
^{48}Ti	**73.72**
^{49}Ti	5.41
^{50}Ti	5.18

✓ Enriched ^{48}Ti metallic powder purchased (500 mg, about 6k€)

✓ Enriched ^{48}Ti targets realized with the HIVIPP technique @ LNL

^{47}SC PRODUCTION: REMIX PROJECT

Research on Emerging Medical radIonuclides from the X-sections

REMiX

LARAMED

Aim of the REMIX project

- Evaluation of the proton-induced nuclear reactions on ^{49}Ti and ^{50}Ti.
- Optimization of the production parameters to minimize the co-production of contaminants: ^{44m}Sc (58.61 h, β^+); ^{44g}Sc (3.97 h, β^+); ^{46}Sc (83.79 d, β^-); ^{48}Sc (43.67 h, β^-).

^{49}Ti and ^{50}Ti targets composition

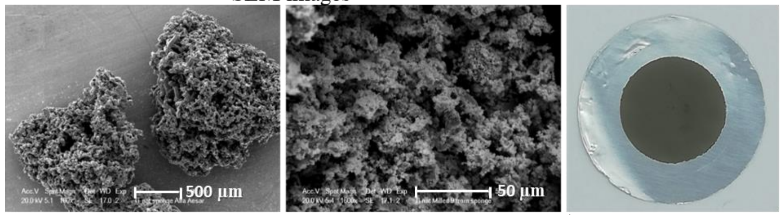
Element	Abundance (%)
^{46}Ti	8.25
^{47}Ti	7.44
^{48}Ti	73.72
^{49}Ti	5.41
^{50}Ti	5.18

✓ Enriched ^{49}Ti and ^{50}Ti metallic powder purchased (300 mg of ^{49}Ti and 150 mg of ^{50}Ti, about 27k€)

➔ **In metallic sponge form!**
(up to 2 mm size)

TARGET MANUFACTURING: E_PLATE PROJECT

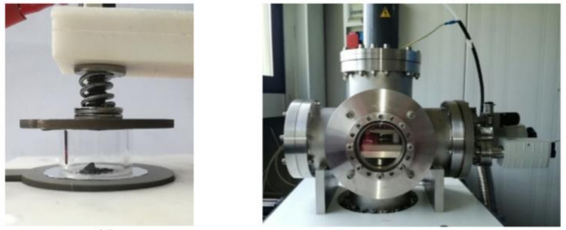
SEM images



^{nat}Ti material before cryomilling process | ^{nat}Ti material after cryomilling process | ^{nat}Ti target realized with cryomilled powder

Preliminary tests with ^{nat}Ti metallic powder.

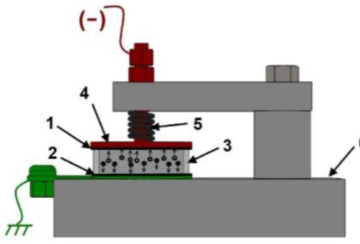
Cryomilling process.



(a) (b)

Fig. 3. Photograph of the HIVIPP setup assembly (a) placed inside the vacuum chamber (b).

Targets realization with the HIVIPP technique.



Setup scheme

1-backing (Upper electrode, cathode)
2-backing (Lower electrode, anode)
3-quartz cylinder
4-pressing plate
5-spring
6-Teflon holder

2 depositions each time with high efficiency (95-98%)!

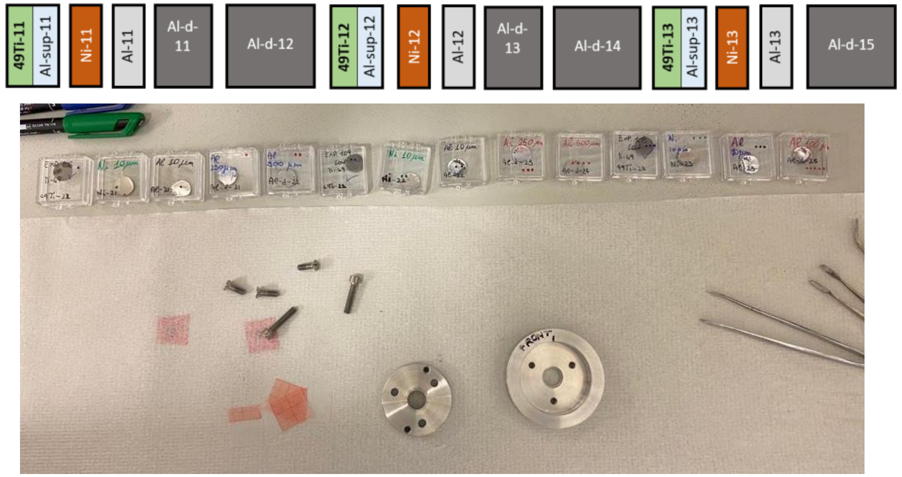
Homogeneity and Ti deposited amount analysis with the IBA (Ion Beam Analysis) method @ LNL.

→ **Analyses on ^{49}Ti are ongoing!**

"HIVIPP deposition and characterization of isotopically enriched ^{48}Ti targets for nuclear cross-section measurements"

H. Skliarova, et al., Nucl. Instrum. Methods Phys. Res A 981, 164371 (2020).

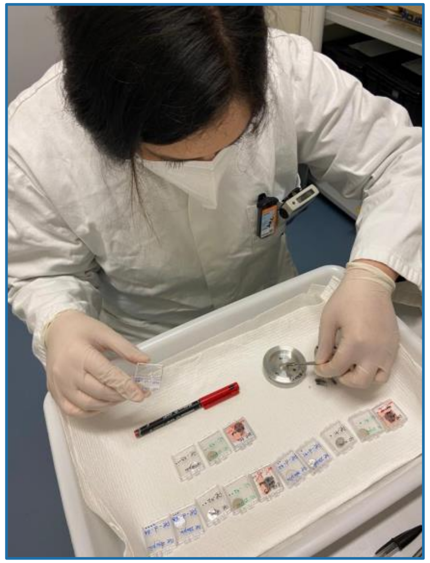
TARGET IRRADIATIONS @ ARRONAX



Arronax Nantes

Targets are assembled following the stacked-foils technique.

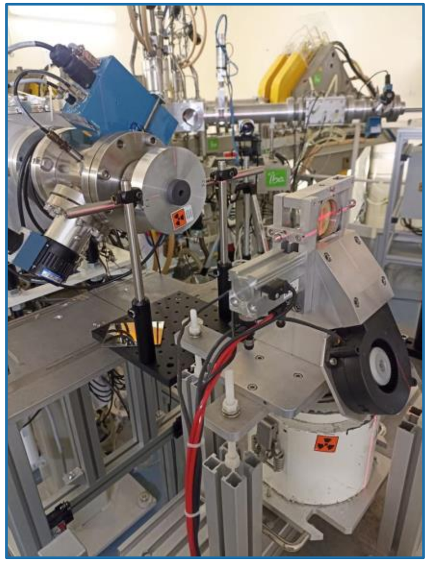
Material foil	Function
^{xx}Ti	^{47}Sc production
^{nat}Al (25μm)	Support for deposition
^{nat}Ni (10/25 μm)	Beam current monitor foil
^{nat}Al (10 μm)	Collect recoil from Ni foils
^{nat}Al (250/500 μm)	Degrade beam energy to bombard more Ti targets in one irradiation run at different energies



Target assembly.

Beam	Energy (MeV)	Intensity (μA)
Protons	**30-70**	**<350**
Deuterons	15-35	50
Alpha	68	<35

IBA cyclotron @ ARRONAX and alignment procedure.



TARGET IRRADIATIONS @ ARRONAX

PASTA ^{nat}V targets irradiated					
Run #	Date	Target foils #	Proton energy (MeV)	Irradiation time (min)	Current (nA)
1	11/04/2017	3	70.3	90	100
2	27/06/2017	3	54	90	100
3	04/07/2017	3	61	90	100
4	10/10/2017	3	34	90	120
5	22/11/2017	1	40	50	130
6	17/04/2018	1	34	90	100

REMIX ^{49}Ti targets irradiated					
Run #	Date	Target foils #	Proton energy (MeV)	Irradiation time (min)	Current (nA)
1	26/10/2021	3	70	60	110
2		3	40	90	112
3	01/03/2022	3	50	90	100
4		3	58	75	120

PASTA

tot ^{nat}V foils = 14.

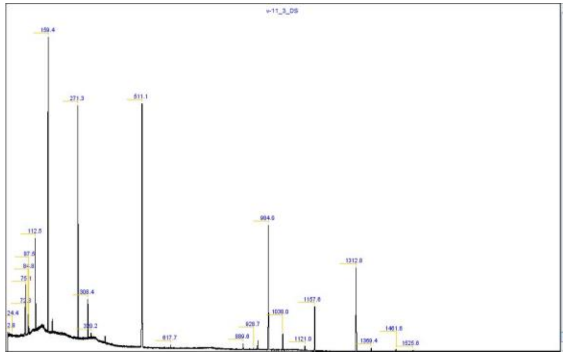
REMIX

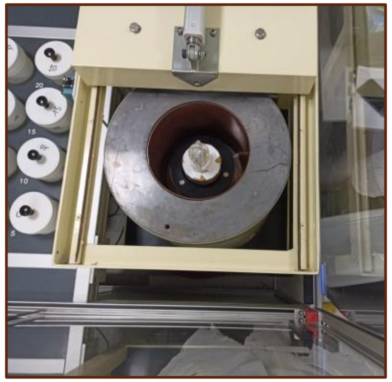
tot ^{49}Ti foils = 12.

Analysis in progress.

γ-SPECTROSCOPY @ ARRONAX

HPGe detectors for the acquisition of γ-spectra.





- First fast acquisition of each target soon after the EOB (End Of Bombardment) → to measure also the short-lived radioisotopes.
- Several other acquisitions in the following 5 days (up to 5 or 6 spectra for each foil) → to follow the decay of the produced radioisotopes and check interferences in γ-lines.
- One more long acquisition of each target about 30 days after EOB → to measure the long-lived radionuclides.

Data analysis is performed in parallel by me and Liliana Mou.

DATA ANALYSIS @ LNL

From γ-spectra → data analysis

Cross section calculations as*:

$$\sigma_x = \sigma_r \frac{C_x n_r \epsilon_r I_r f_r}{C_r n_x \epsilon_x I_x f_x}$$

- C = number of counts in the γ-line
- $n = \frac{\rho P x N_A}{A}$ number of atoms per area in the target
- ϵ = efficiency of the detector at the energy of the γ-line
- I = intensity of the γ-line
- $f = (1 - e^{-\lambda t_i}) e^{-\lambda t_c} (1 - e^{-\lambda t_m})/\lambda$ time correction factor
- r = quantities referred to monitor radionuclide
- x = quantities of the radionuclide of interest

*"*Uncertainty propagation in activtion cross section measurements*"

N. Otuka, et al., Radiat. Phys. Chem. 140, 502-510 (2017).

All the produced radionuclides are considered:

^{43}Sc, ^{44m}Sc, ^{44g}Sc, **^{46}Sc**, **^{47}Sc**, ^{48}Sc, ^{48}V, ^{48}Cr, ^{49}Cr, ^{51}Cr, ^{42}K, ^{43}K

<u>They are able to contribute to the dose delivered to a patient.</u>

^{46}Sc is the main contaminant since:

- It cannot be chemically separated (Sc-isotope).
- Its half-life is longer than the ^{47}Sc one.

Radioisotope	Half-life (d)	γ-emission		β-emission	
		Energy (keV)	Intensity (%)	Mean Energy (keV)	Intensity (%)
^{47}Sc	3.3492	159.381	68.3	142.6 203.9	68.4 31.6
^{46}Sc	83.79	889.277 1120.545	99.9840 99.9870	111.8 580.8	99.9964 0.0036

PASTA RESULTS: ^{NAT}V TARGETS

An energy interval where the production of ^{46}Sc is almost negligible has been individuated.

E_p < 30 MeV.

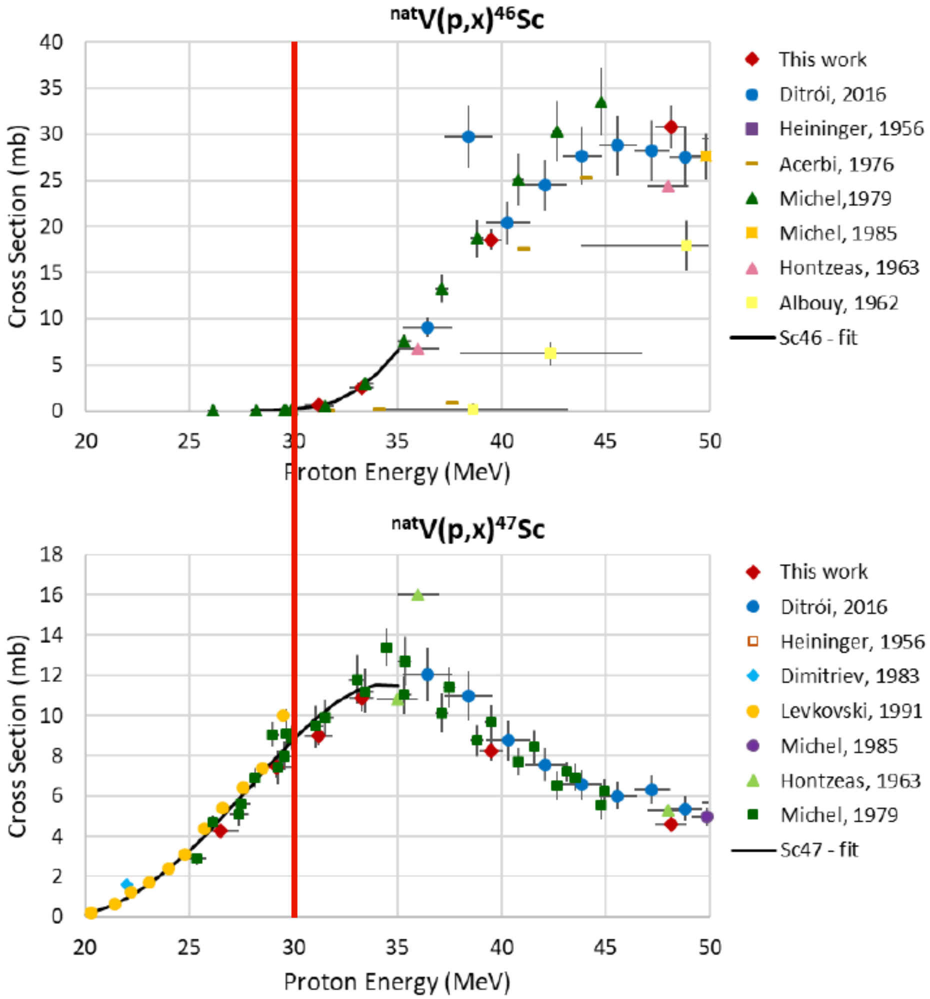
"New results on proton-induced reactions on vanadium for ^{47}Sc production and the impact of level densities on theoretical cross sections"

F. Barbaro, et al., Phys Rev C 104, 044619 (2021).

Dosimetric studies have extended this energy interval up to 35 MeV.

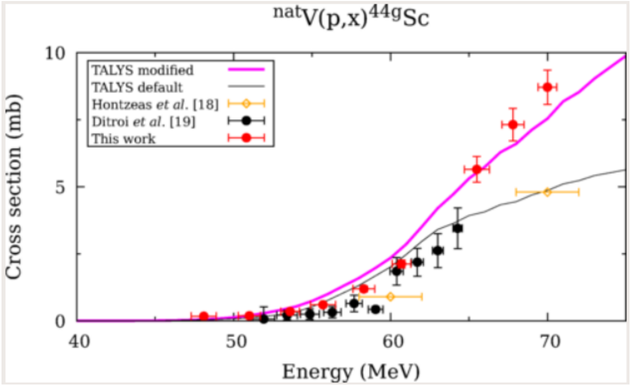
"Preliminary dosimetric analysis of DOTA-folate radiopharmaceutical radiolabelled with ^{47}Sc produced through ^{nat}V(p,x)^{47}Sc cyclotron irradiation"

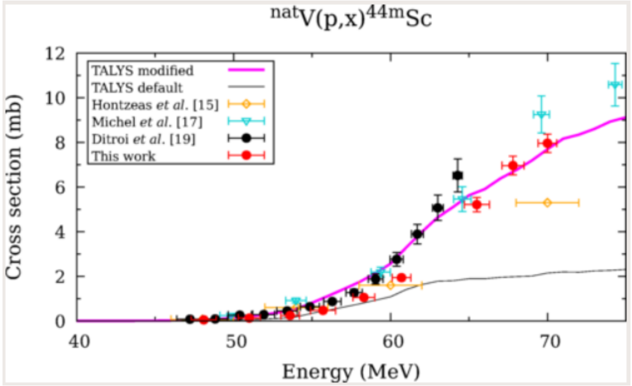
De Nardo L *et al.*, Phys. Med. Biol. 66, 025003, (2021).

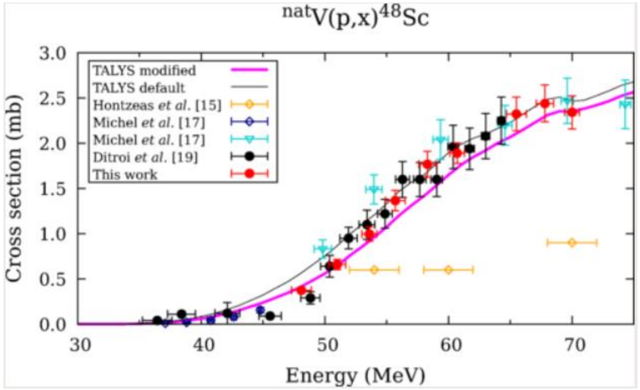


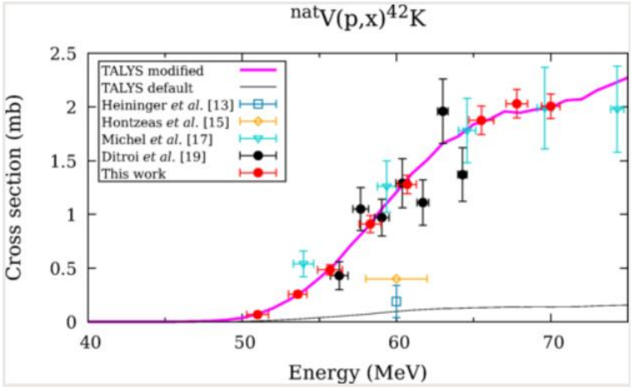
PASTA RESULTS: ^{NAT}V TARGETS

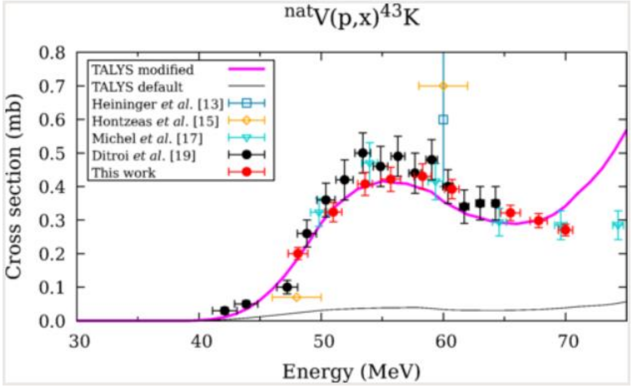
F. Barbaro, et al., Phys Rev C 104, 044619 (2021).

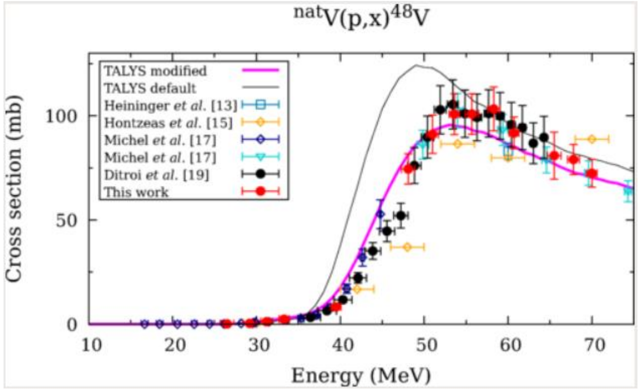


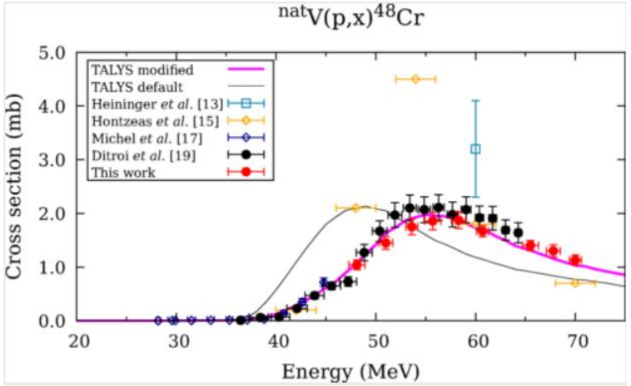


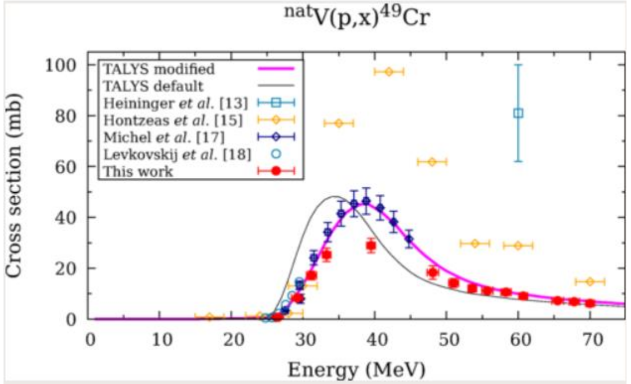


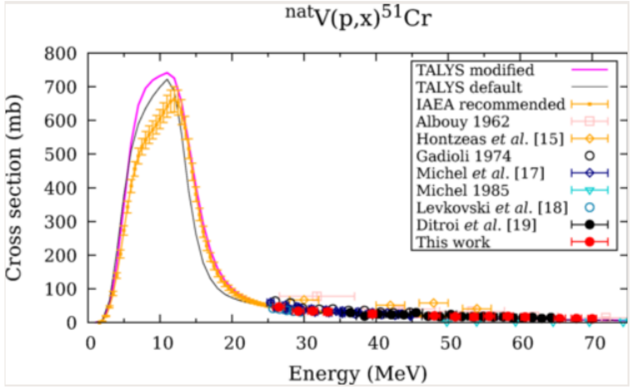






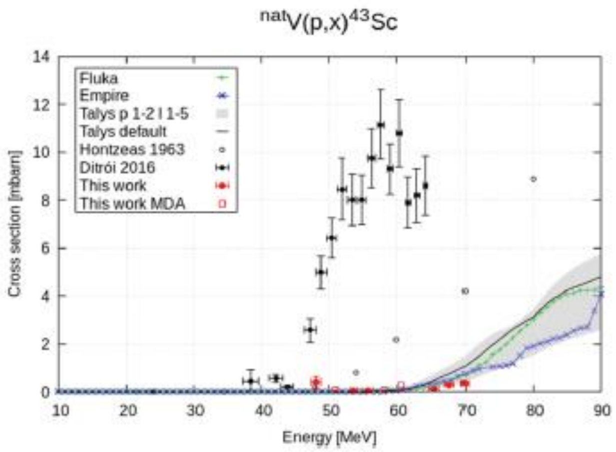


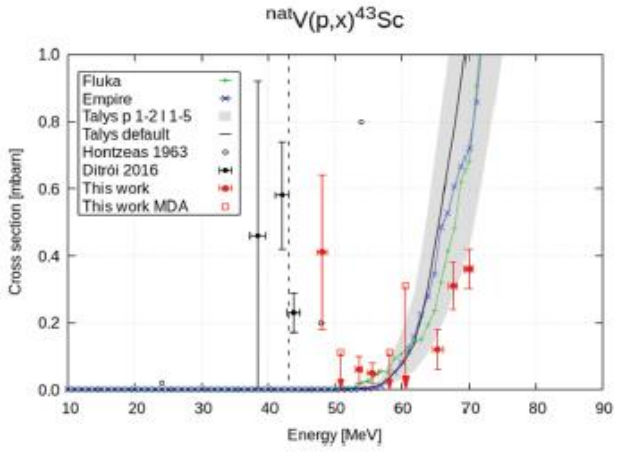




PASTA RESULTS: ^{NAT}V TARGETS

A discrepancy with previous data has been found in the case of ^{43}Sc production.





"New results on the $^{nat}V(p,x)^{43}Sc$ cross section: Analysis of the discrepancy with previous data"

G. Pupillo et al., Nuclear Inst. and Methods in Physics Research B 464, 32–35, (2020).

Theoretical simulations with TALYS, FLUKA, and EMPIRE codes supported our new results.

The discrepancy is due to the lack of correction in the counts of 373 keV γ-peak from the 617 keV ^{43}K peak activity in the previous data.

Radioisotope	Half-life (h)	γ-emission	
		Energy (keV)	Intensity (%)
^{43}Sc	3.891	**372.9**	22.5
^{43}K	22.3	**372.760** 617.490	86.80 79.2

→ Interference in the 373 keV γ-line!

REMIX PRELIMINARY RESULTS: ^{49}Ti TARGETS

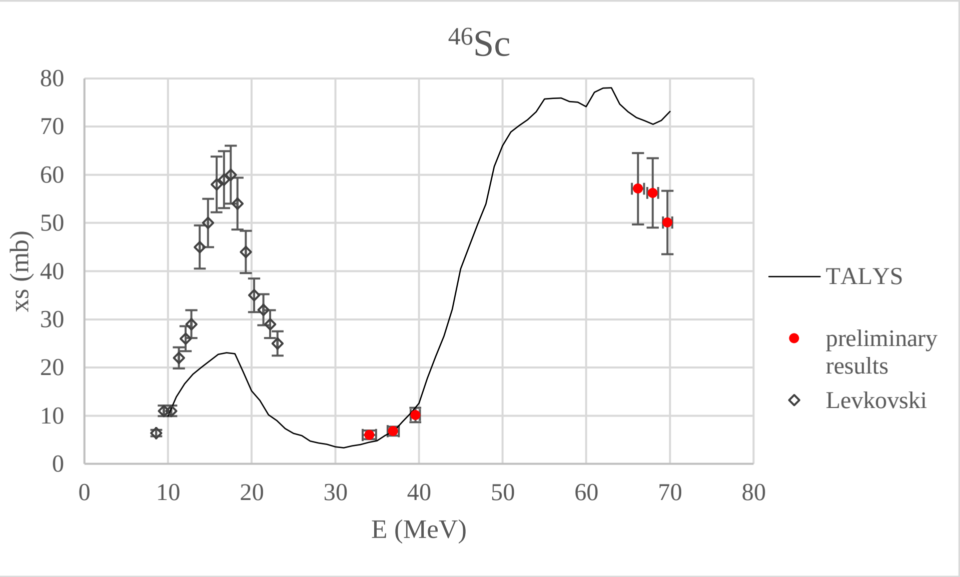
PRELIMINARY: Targets thicknesses analysis is ongoing.

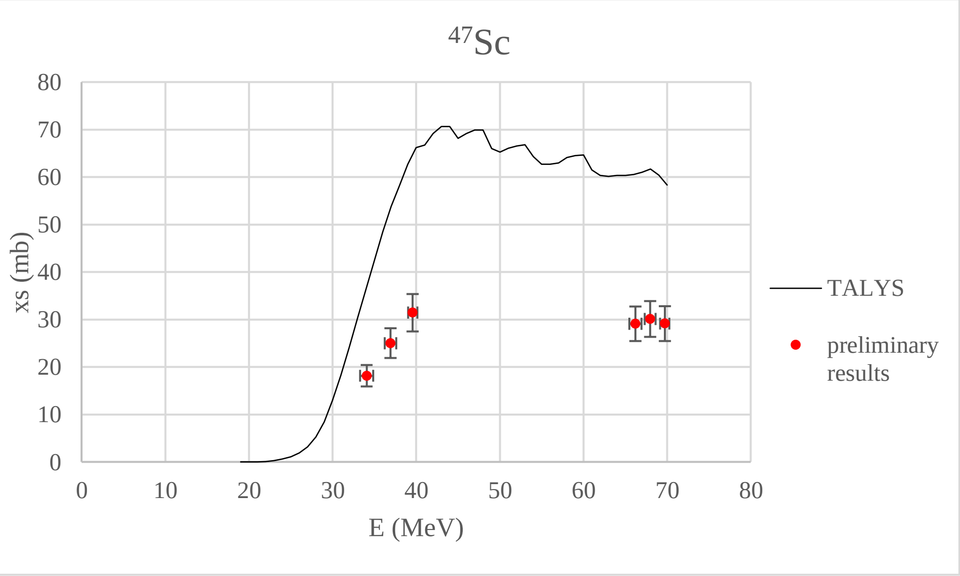
Interesting nuclear reactions because few data [^{49}Ti(p,x)^{46}Sc] or <u>no data</u> [^{49}Ti(p,x)^{47}Sc] are available in literature.

(Comparison only with TALYS default simulations).

No energy interval with negligible ^{46}Sc production can be found till now.

Future dosimetric studies will tell if an energy interval around 40 MeV can be exploited for ^{47}Sc production.



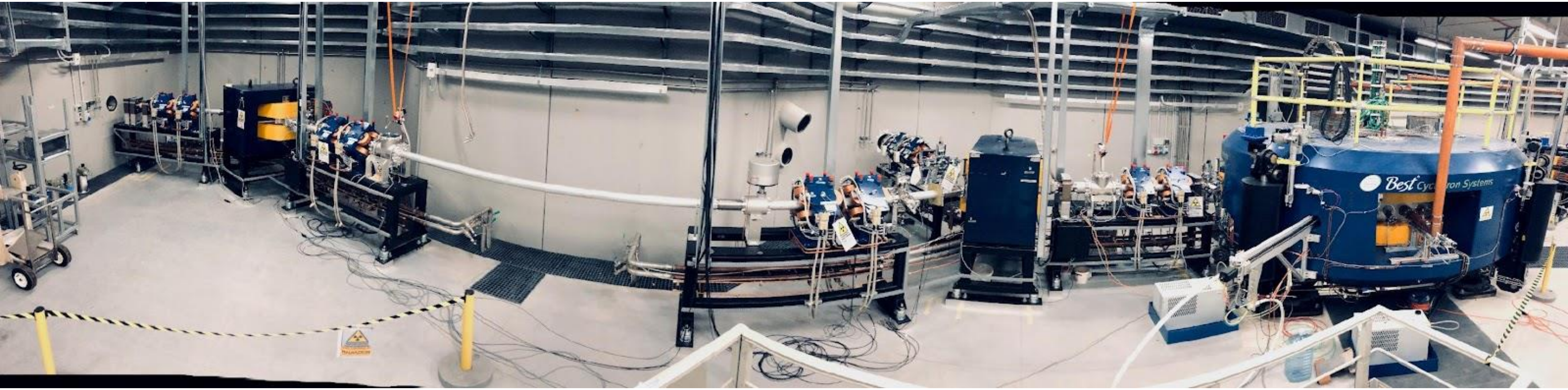


CONCLUSIONS

Production through the $^{nat}V(p,x)^{47}Sc$ nuclear reaction below 35 MeV is promising but the production is low so also other production routes are investigated:

- Calculations of the production using ^{48}Ti targets are going to be concluded.
- Data of the last two ^{49}Ti targets bombardments are under analysis → the proton energy range between 40 and 60 MeV was investigated to complete the production cross section curves.
- Irradiation runs involving ^{50}Ti targets will be performed this summer → targets have already been manufactured and will be subjected to the IBA.

THANK YOU FOR YOUR ATTENTION



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