Radioisotope production at LARAMED

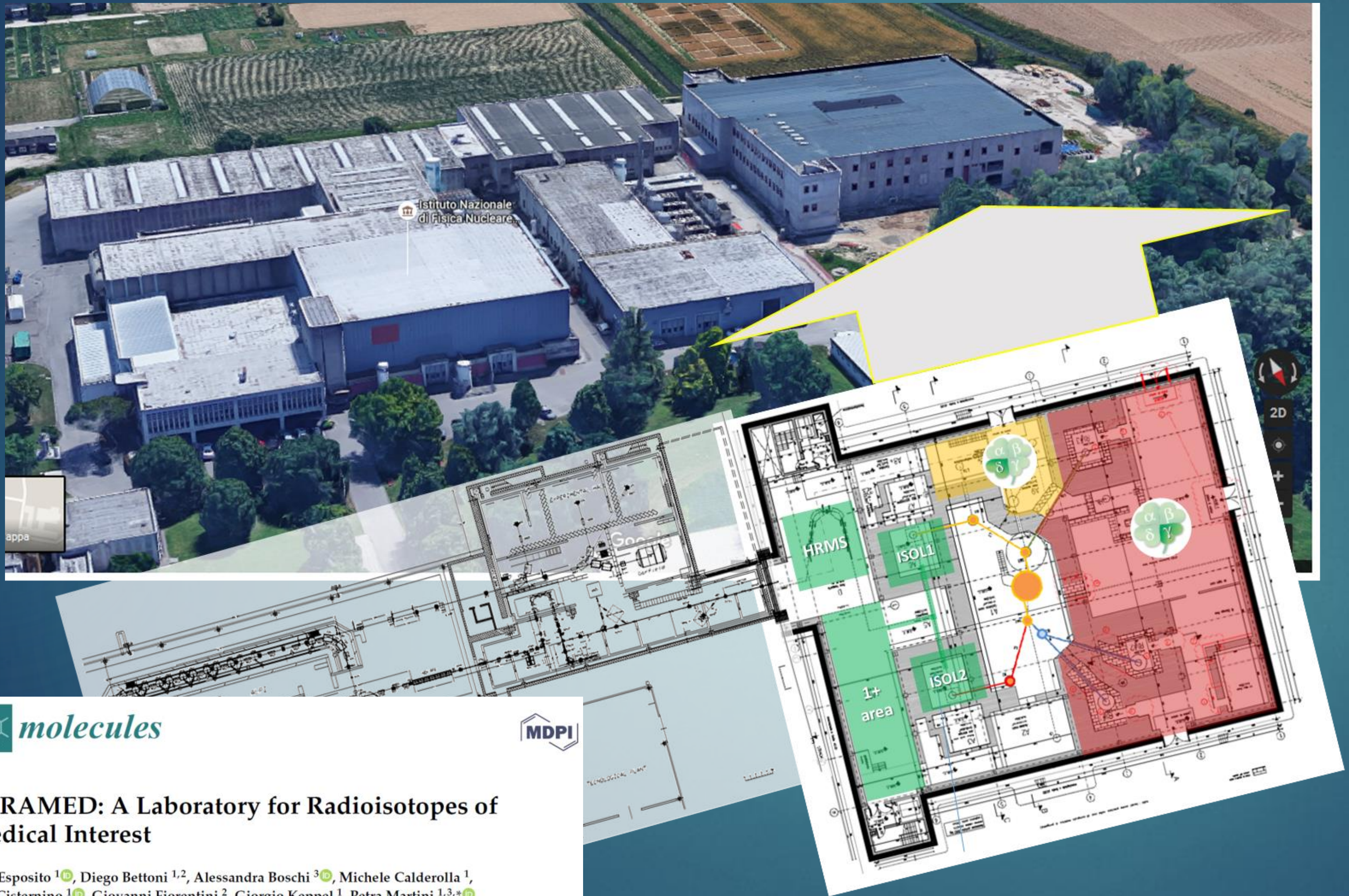
GAIA PUPILLO

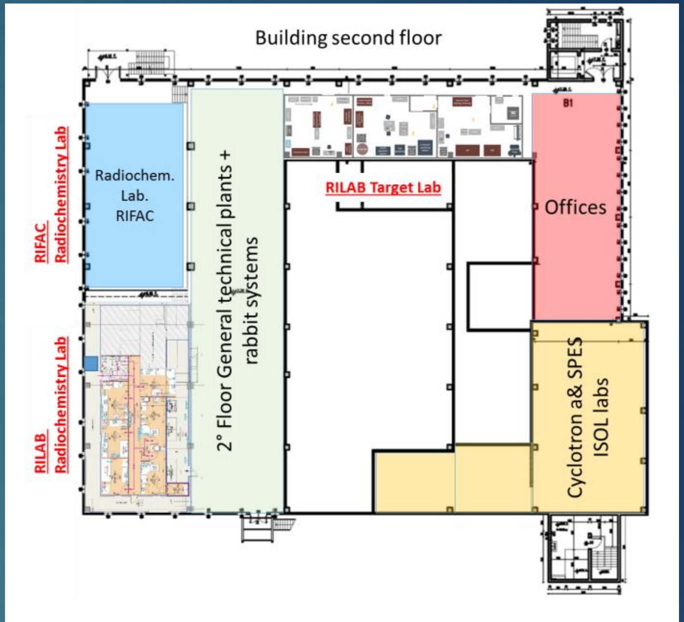
INFN-LNL (LEGNARO, PADUA, ITALY)

Interdisciplinary aspects and applications related to the SPES project

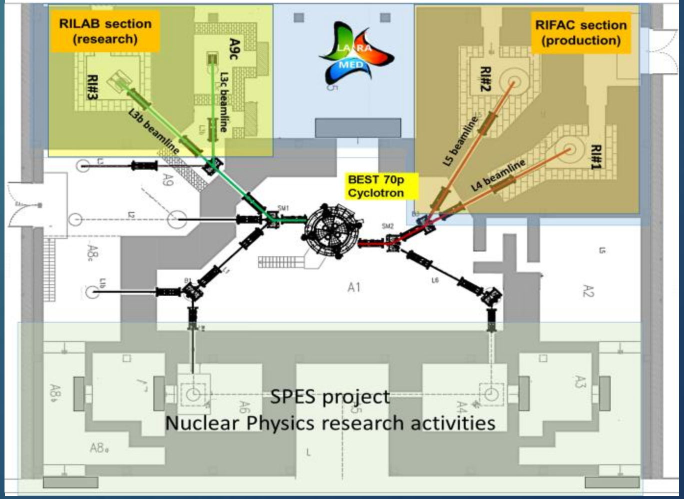
Ferrara, 29-30 January 2019

SPES/LARAMED INFRASTRUCTURE





Radioisotopes research area
(LARAMED)



molecules

MDPI

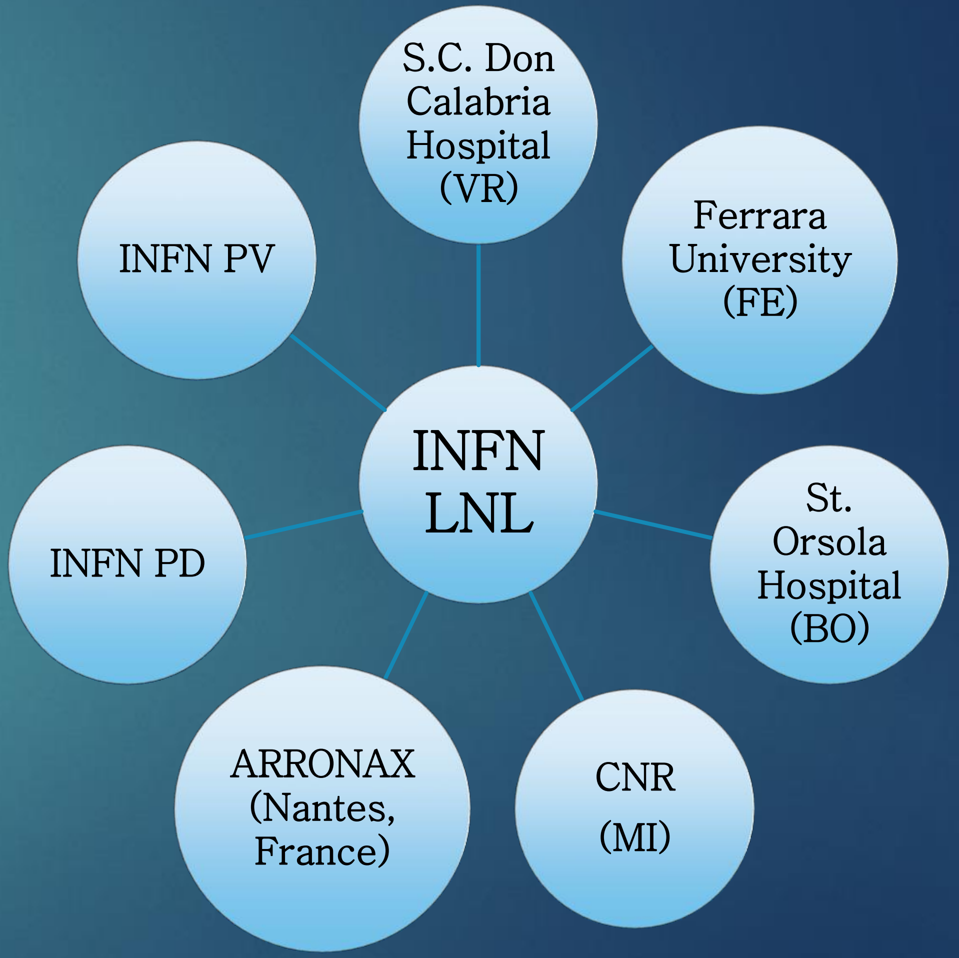
Letter

LARAMED: A Laboratory for Radioisotopes of Medical Interest

Juan Esposito [1], Diego Bettoni [1,2], Alessandra Boschi [3], Michele Calderolla [1], Sara Cisternino [1], Giovanni Fiorentini [2], Giorgio Keppel [1], Petra Martini [1,3,*], Mario Maggiore [1], Liliana Mou [1], Micòl Pasquali [1], Lorenzo Pranovi [1], Gaia Pupillo [1], Carlos Rossi Alvarez [1], Lucia Sarchiapone [1], Gabriele Sciacca [1], Hanna Skliarova [1], Paolo Favaron [1], Augusto Lombardi [1], Piergiorgio Antonini [1] and Adriano Duatti [1,4]

The LARAMED (net)work

INFN funded/running projects	Project name
Accelerator-Tc-99m alternative (direct) production route through hospital cyclotrons	APOTEMA (2012-2014) TECHNOSP (2015-2017)
CRP on"Alternative, non HEU-based, Tc-99m /Mo-99 supply"	IAEA CRP (2011-2015)
Alternative Cu-64/Cu-67 production for theranostic application	COME (2016)
Alternative Sc-47 production for theranostic application	PASTA (2017-2018)
CRP on "Radiopharmaceuticals Labelled with New Emerging Radionuclides" Cu-67, Re-186, Sc-47"	IAEA CRP (2016-2019)
High Power Target concepts R&D ($^{64/67}$Cu)	TERABIO (2016-2019)
High intensity vibrational powder plating	E_PLATE (2018-2019)
Multimodal pET/mRi Imaging with Cyclotron-produced Mn-52/51 and stable paramagnetic Mn iSotopes	METRICS (2018-2020)



Radionuclides of major interest for the LARAMED project

Tc-99m	Cu-67	Sc-47	Mn-52
Apotema/Techn-Osp	Come	Pasta	Metrics

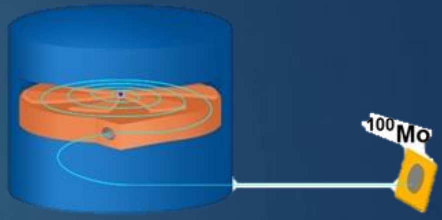
APOTEMA – CSN5 2012/2014

TECHN_OSP – CSN5 2015/2017

Direct ^{99m}Tc Cyclotron Production

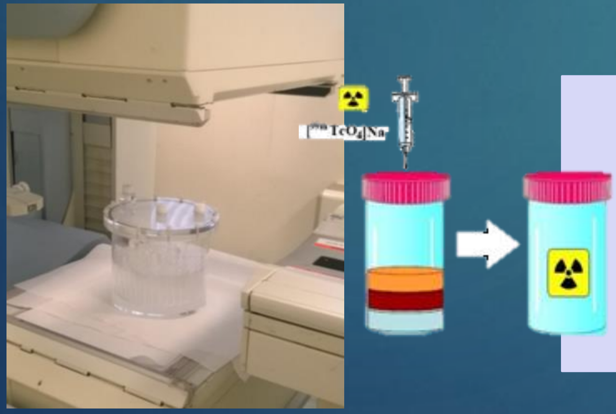
Target production

Cyclotron irradiation



Extraction
separation
purification

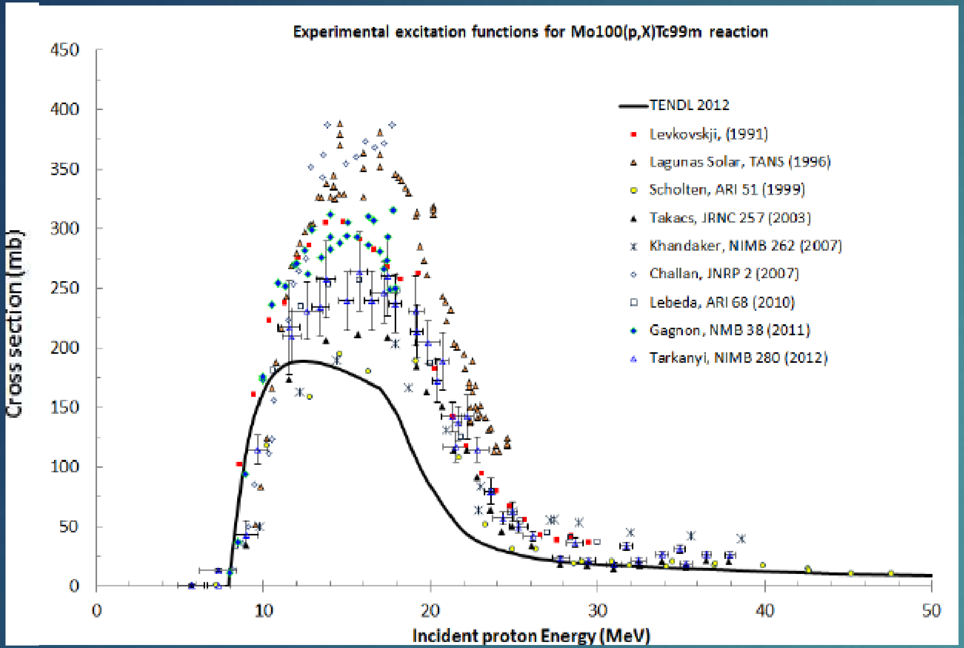
Radio-
pharmaceuticals,
QC, imaging



^{100}Mo recovery
techniques

$^{100}Mo(p,2n)^{99m}Tc$

$^{100}Mo(p,2n)^{99m}Tc$: Main physical data

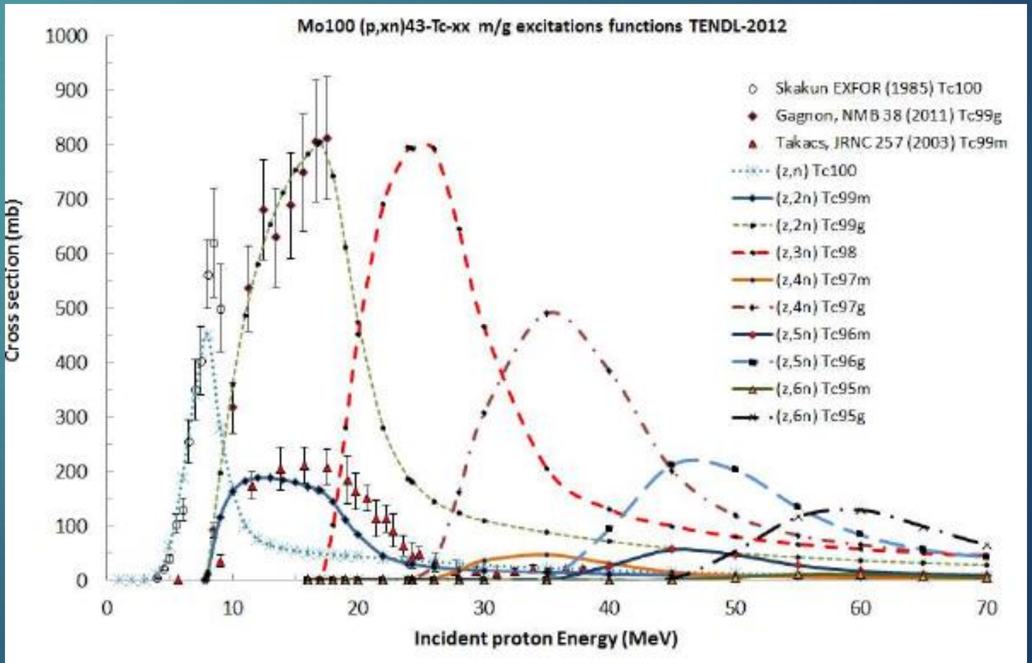


Irradiation Conditions	
Ep	18-20 MeV
Irr. Times	3-6 h
targets	^{100}Mo(>99%)

J. Esposito, Sci Tech of Nuc Inst, vol. 2013, Article ID 972381, 14 pages, 2013. doi:10.1155/2013/972381

Expected Tc-isotopes at EOB:

Isotopes	Half-life	Isotopes	Half-life
Tc-100	15.46 s	**Tc-95m**	61 d
Tc-99m	6.0067 h	**Tc-95g**	20.0 h
Tc-99g	$2.111 \cdot 10^5$y	**Tc-94m**	52.0 m
Tc-98	$4.2 \cdot 10^6$y	**Tc-94g**	293 m
Tc-97m	91.0 d	**Tc-93m**	43.5 m
Tc-97g	$4.21 \cdot 10^6$y	**Tc-93g**	2.75 h
Tc-96m	51.5 m	**Tc-92**	4.25 m
Tc-96g	4.28 d	**Tc-91g**	3.14 m

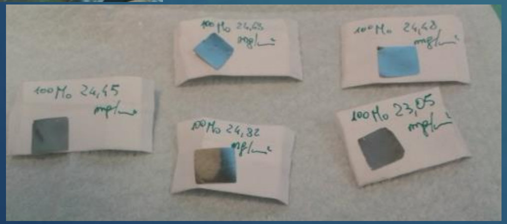


Direct ^{99m}Tc Cyclotron Production

Target production

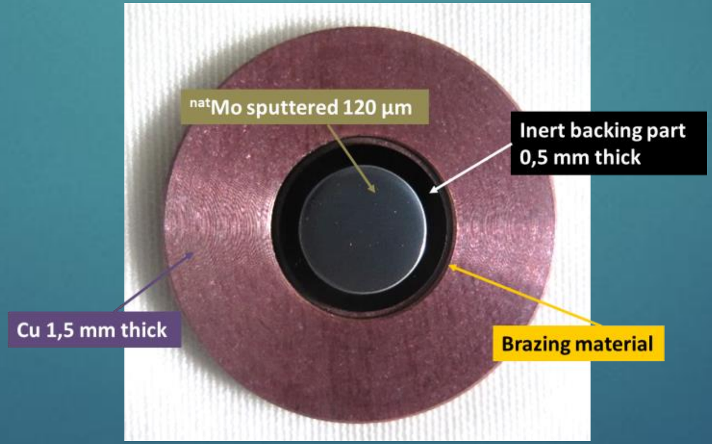
Isotopic composition (%)						
Mo-100	Mo-98	Mo-97	Mo-96	Mo-95	Mo-94	Mo-92
99,05	0,54	0,07	0,11	0,10	0,05	0,08

Lamination

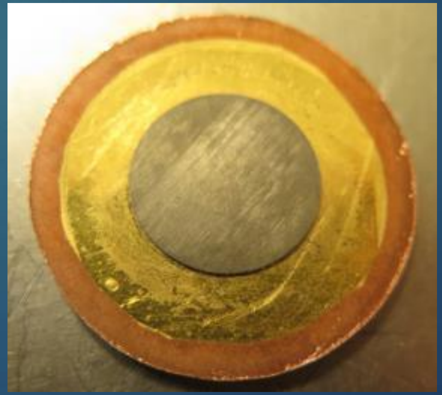


Sputtering on *chemically inert baseplate*

****patent N. 102017000102990****



Mo on an inert backing plate (SPS) Spark Plasma Sintering

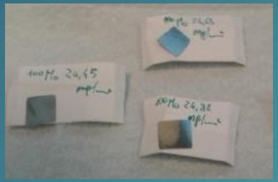


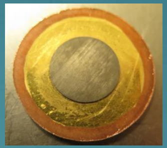
H. Skliarova , S. Cisternino , G. Cicoria , M. Marengo V. Palmieri"Innovative Target for Production of Technetium-99m by Biomedical Cyclotron"Molecules 2019, 24, 25; doi:10.3390/molecules24010025

Direct ^{99m}Tc Cyclotron Production

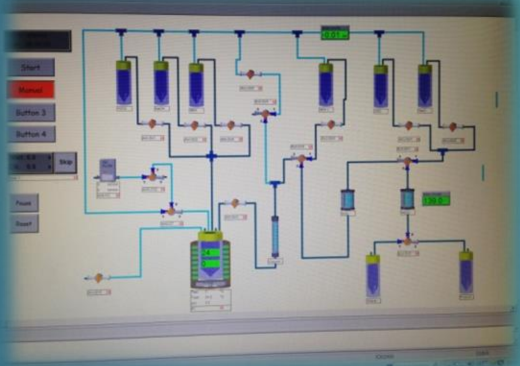
Extraction Separation Purification

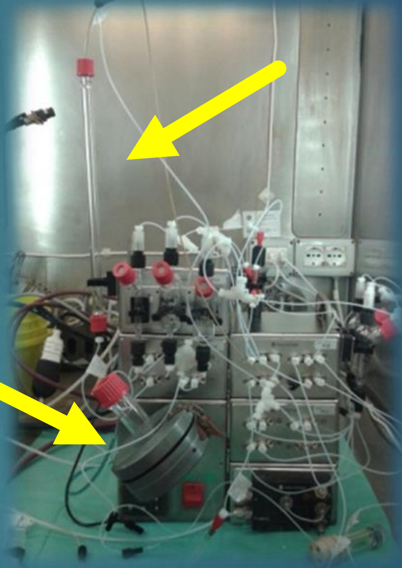
First automatic Prototype
(Unife/S. Orsola OspBO)





Second automatic Prototype
(Unife/S. Orsola OspBO)





Recovery Yield > 93%
Time: 60 min
Target mass: Up to 500 mg

ELSEVIER

Applied Radiation and Isotopes

Volume 118, December 2016, Pages 302–307

A solvent-extraction module for cyclotron production of high-purity technetium-99m

Petra Martini[a, b], Alessandra Boschi[a], Gianfranco Cicoria[c], Licia Uccelli[a], Micòl Pasquali[a], Adriano Duatti[b, d], Gaia Pupillo[b], Mario Marengo[c], Massimo Loriggiola[b], Juan Esposito[b]

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Contents lists available at ScienceDirect

ELSEVIER

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

In-house cyclotron production of high-purity Tc-99m and Tc-99m radiopharmaceuticals

Petra Martini[a,b,*,1], Alessandra Boschi[b,*,1], Gianfranco Cicoria[c], Federico Zagni[c], Andrea Corazza[c], Licia Uccelli[b], Micòl Pasquali[b], Gaia Pupillo[a], Mario Marengo[c], Massimo Loriggiola[a], Hanna Skliarova[a], Liliana Mou[a], Sara Cisternino[a], Sara Carturan[d], Laura Melendez-Alafort[e], Nikolay M. Uzunov[a], Michele Bello[d], Carlos Rossi Alvarez[a], Juan Esposito[a], Adriano Duatti[a,f]

Direct ^{99m}Tc Cyclotron Production

^{100}Mo Recovery Techniques

$^{100}Mo/^{99m}Tc$ separation module "waste":

$Na_2MoO_4\,(H_2O)_x$ + NaOH

$Na_2MoO_4 \rightarrow MoO_3$

Yield >90% MoO_3

$MoO_3(s) + H_2(g) = MoO_2(s) + H_2O(g)$ 450°C–750°C

$MoO_2(s) + 2H_2(g) = Mo(s) + 2H_2O(g)$ 750°C–950°C

Yield >95% Mo

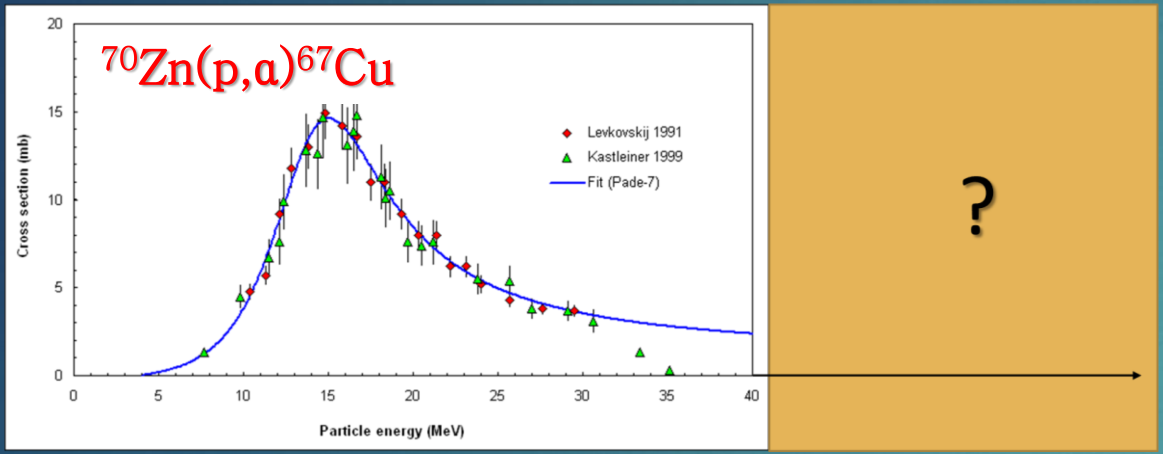
Reduction in a temperature controlled reactor in H_2 overpressure

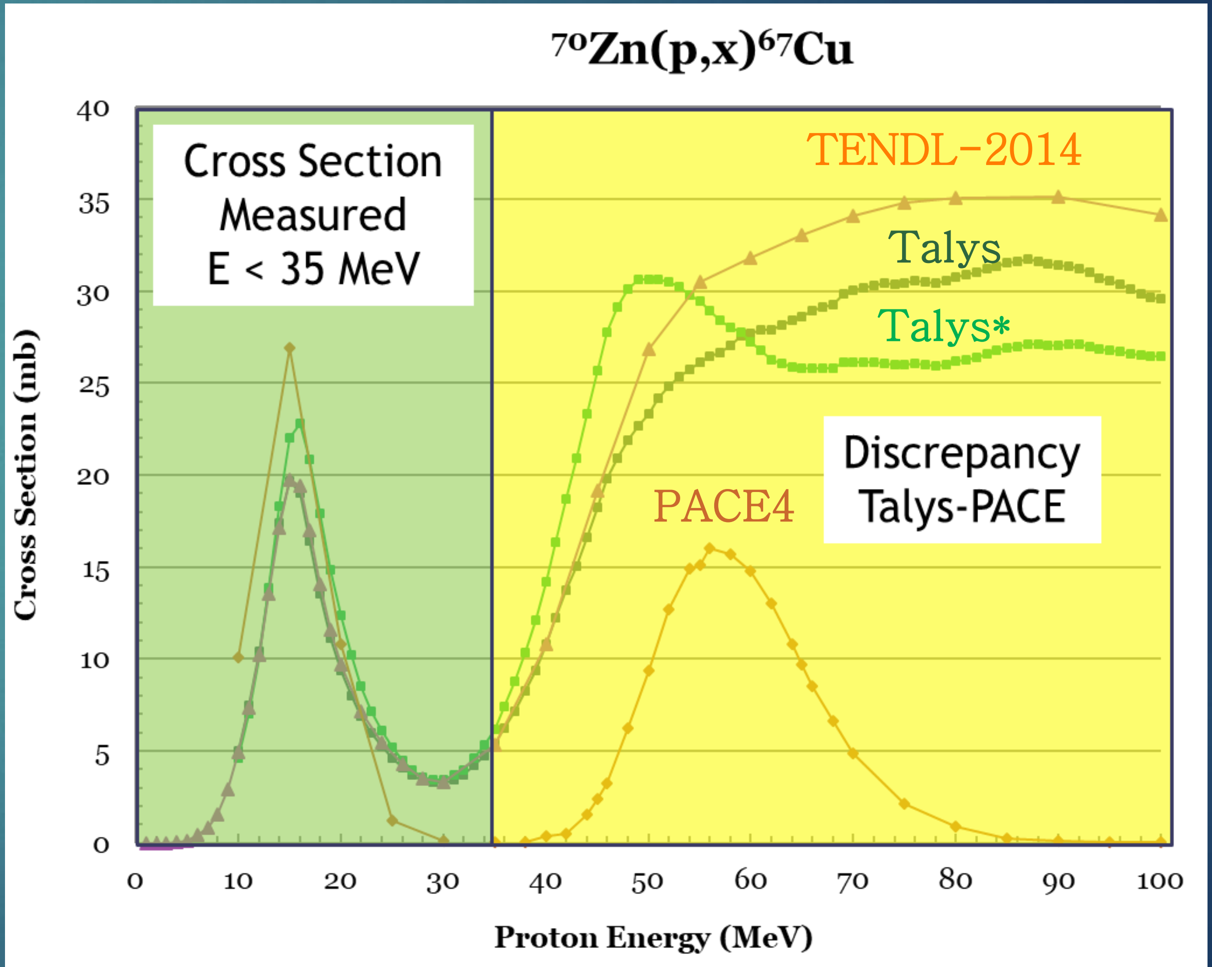
H. Skliarova, P. Buso, S. Carturan, C. R. Alvarez, S. Cisternino, P. Martini, A.Boschi, J. Esposito
"Recovery of Molybdenum Precursor Material in the Cyclotron-based Technetium-99m Production Cycle"
Instruments 2019 ***(under revision)***

COME – CSN3
2016

COpper MEasurement

^{67}Cu production: the $^{70}Zn(p,x)$ reaction



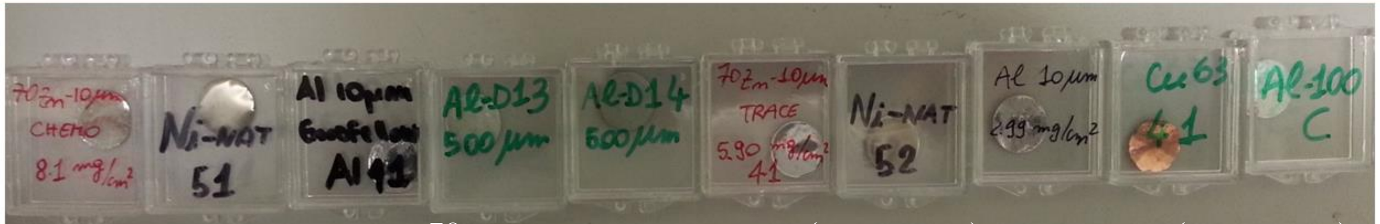


Collaboration with:

- ✓ **Arronax facility** to measure the nuclear cross section for $E_P > 35$ MeV
- ✓ **Experts in nuclear models** to describe and explain the trend of the reaction
  Mr Luciano Canton (INFN-PD)
  Mr Andrea Fontana (INFN-PV)

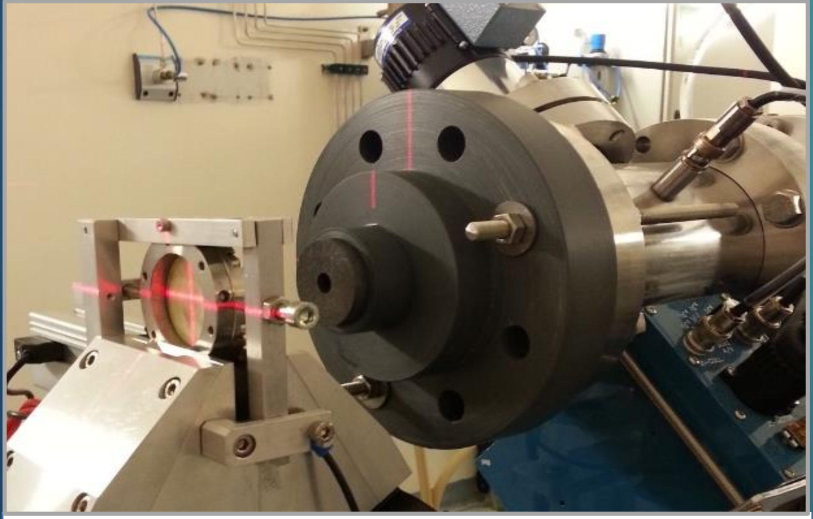
^{67}Cu production: the ^{70}Zn(p,x) reaction Measurement at the Arronax facility

Beam	Energy [MeV]	Intensity [µA]
Proton	30–70	< 350 (x2)
Deuteron	15–35	50
Alpha	68	< 35



Enriched powder of ^{70}Zn: Chemotrade (95.42%) – Trace (95.47%)

Target-foils (highly pure natural material) or enriched isotopes; produced by lamination @ LNL



Alignment of collimator and target-holder on the beam-line @ Arronax

Stacked-foils target structure with monitor foils

- Target (enriched ^{70}Zn)
- Monitor & Catcher (^{nat}Al)
- Degrader (Aluminium)
- Source of Cu-61 (^{63}Cu)

^{67}Cu production: the ^{70}Zn(p,x) reaction Measurement at the Arronax facility

Energy [keV]	Cu-67 Intensity	Ga-67 Intensity
91.266 5	7.0 1	3.11 4
93.311 5	16.1 2	38.81 3
184.577 10	**48.7 3**	**21.41 1**
208.951 10	0.115 5	2.46 1
300.219 10	**0.797 11**	**16.64 12**
393.529 10	0.220 8	4.56 24
494.166 15		0.0684 14
703.106 15		0.0105 9
794.381 15		0.0540 18
887.688 15		0.148 3

Co-production of ^{67}Ga during ^{70}Zn irradiation:

- ^{67}Cu and ^{67}Ga both decay to ^{67}Zn → same ɣ rays
- ^{67}Cu ^{67}Ga similar half-lives:

^{67}Cu (61.83 h)
^{67}Ga (78.24 h)

A chemical separation Cu/Ga is mandatory !!

Tracer: Cu-61 and Ga-66

Radiochemical procedure aimed at Cu/Ga/Zn separation

Petra Martini, PhD
Micòl Pasquali, PhD

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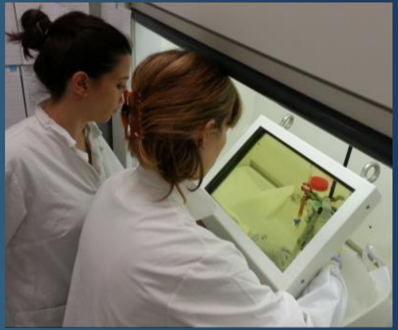
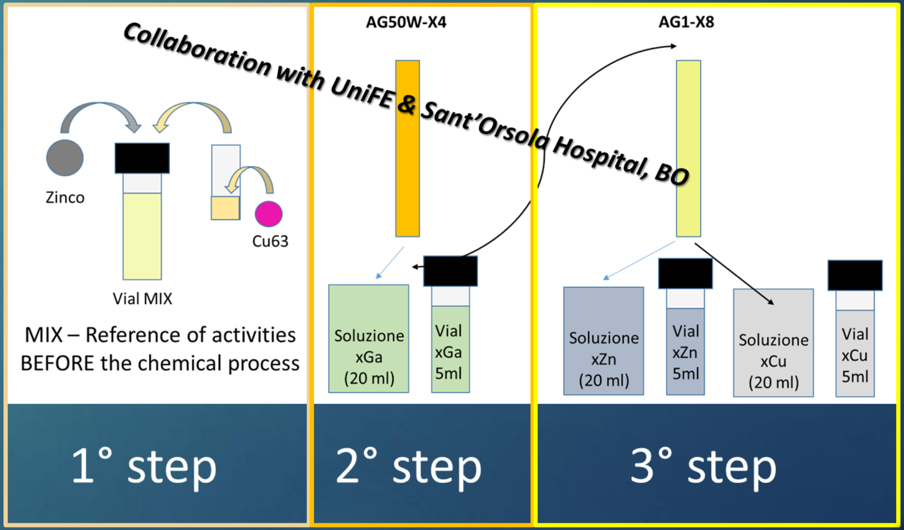




PASTA – CSN5 2017/2018

Production with Accelerator of Sc-47 for Theranostic Applications

^{47}Sc production: the PASTA project

Grant INFN 2017-2018

^{47}Sc theranostic radionuclide of great interest also for RAIT (long half-life) and possible use also in pair with ^{44}Sc (β^+ emitter, PET)
→ Ongoing CRP (F22053) on ^{67}Cu, ^{47}Sc and ^{186}Re

Sc-47 3.3492 d 6	γ-ray [keV]	γ-ray [%]	β- [keV]	β- [%]
β- : 100% (Ti-47)	159.381 15	68.3 % 4	142.6 7 203.9 8	68.4 % 6 31.6 % 6
			Mean β- energy 162.0 keV 21 ; total β- int. 100.0% 8	

Isotope	half-life
^{43}Sc	3.891 h 12
^{44g}Sc	3.97 h 4
^{44m}Sc	58.61 h 10
^{45}Sc	stable
^{46}Sc	83.79 d 4
^{46m}Sc	18.75 s 4
^{47}Sc	3.3492 d 6
^{48}Sc	43.67 h 9
^{49}Sc	57.18 m 13
^{47}Ca	4.536 d 3

Contaminants of major concern are:

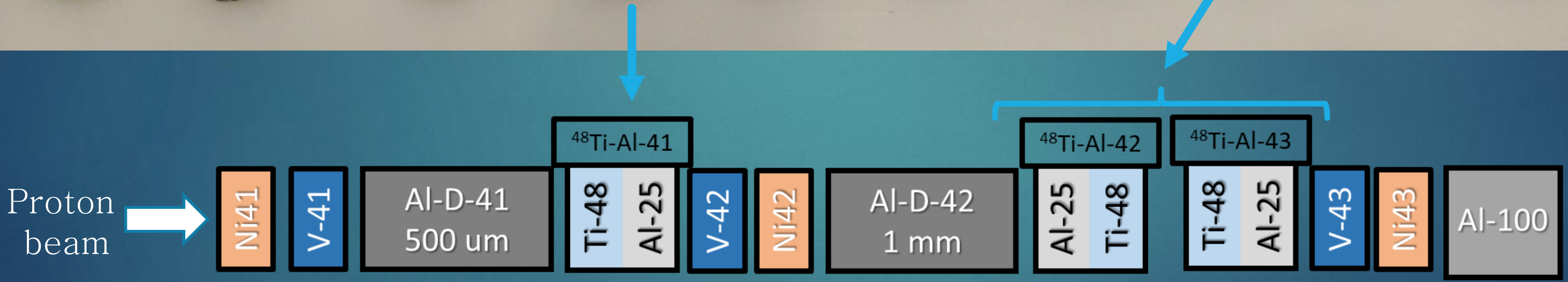
^{44m}Sc (58.61 h, IT ^{44}Sc 98.80%; ε ^{44}Ca 1.20%);

^{44}Sc (3.97 h, β^+); ^{46}Sc (83.79 d, β^-)

Nuclear data extracted from NuDat 2.7 – https://www.nndc.bnl.gov/nudat2/

^{47}Sc production: stacked-foils target

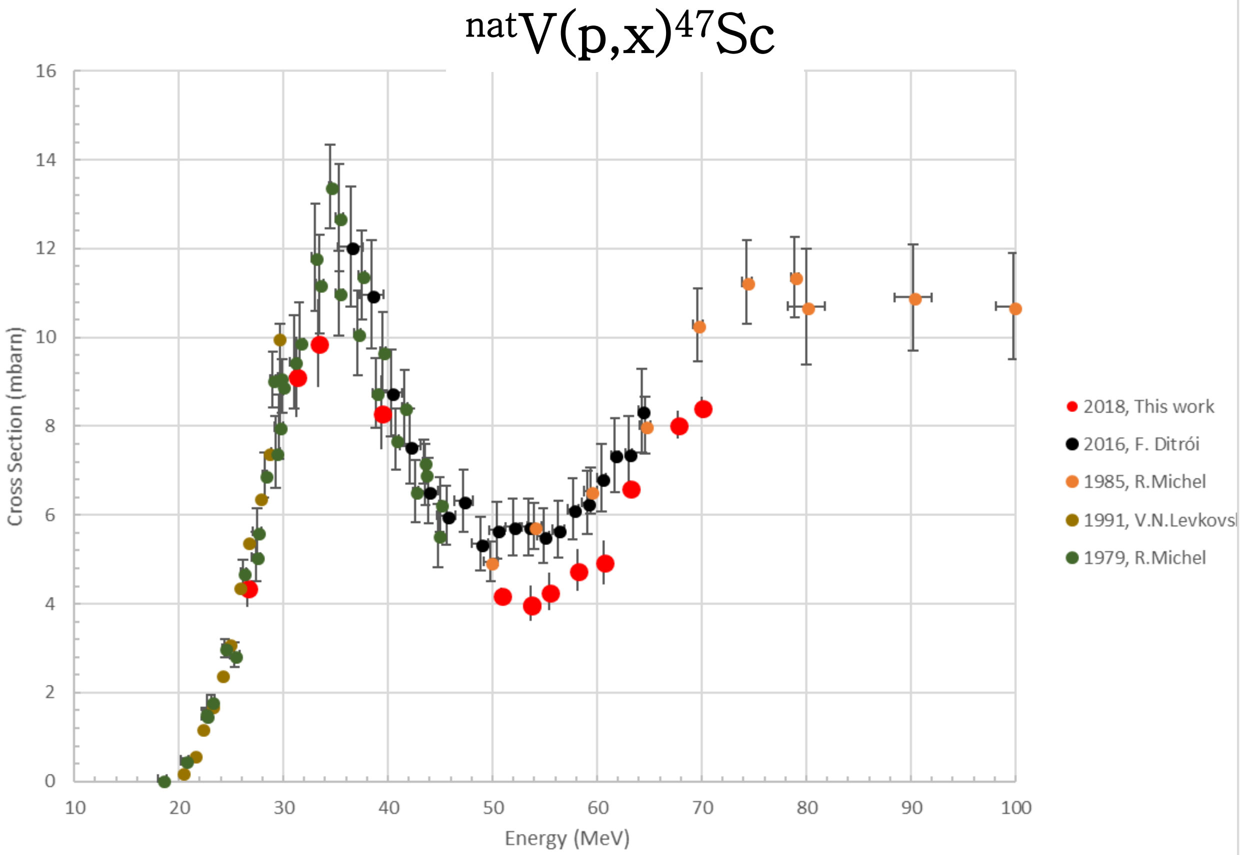
The enriched ^{48}Ti powder (99.32% purchased by TraceScience) has been deposited by HIVIPP method*
(Ms Hanna Skliarova and Ms Sara Cisternino, E_PLATE project @ INFN-LNL)

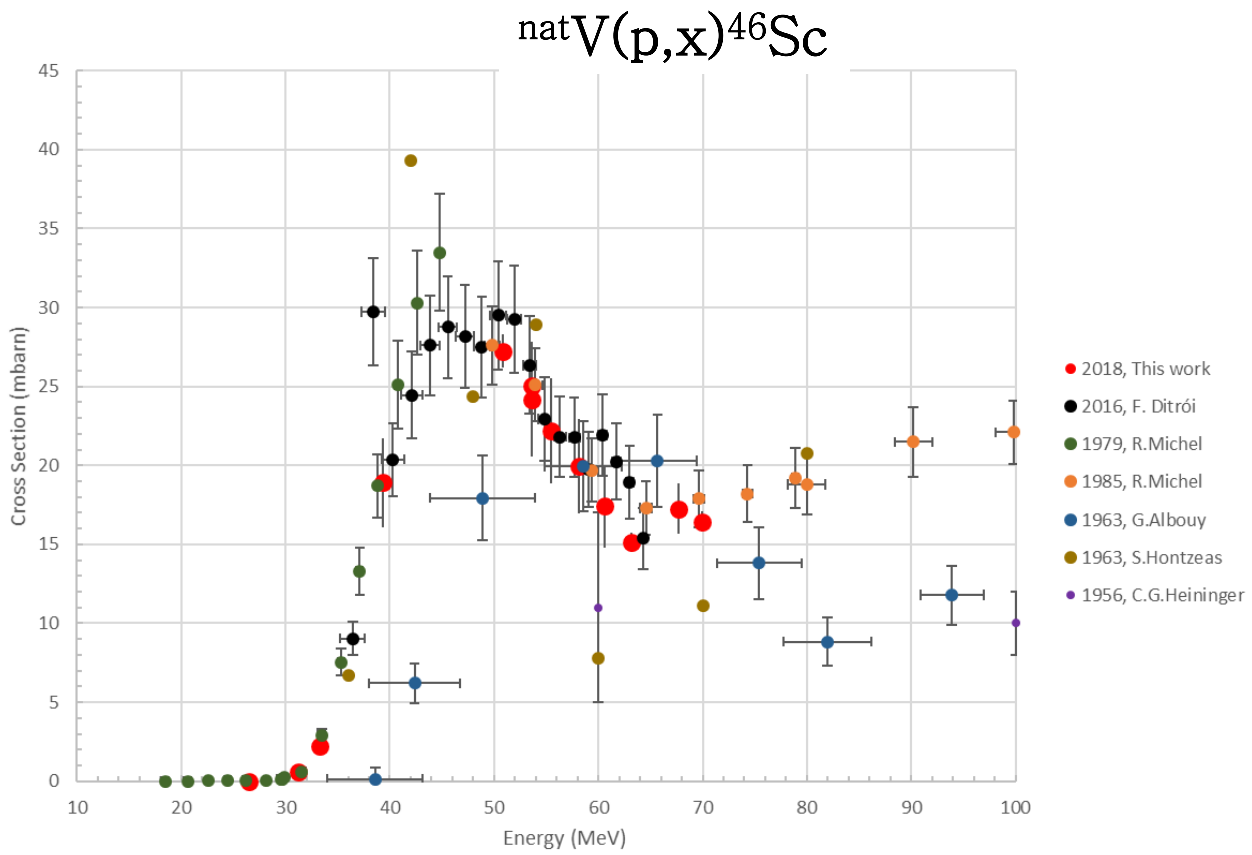


- Ti-48 - deposited target
- Al-nat 25 μm - support
- V-nat 20 μm (99.8%)
- Ni-nat 20 μm (99.9%)
- Al-nat 500 μm - degrader
- Al-nat 100 μm - support

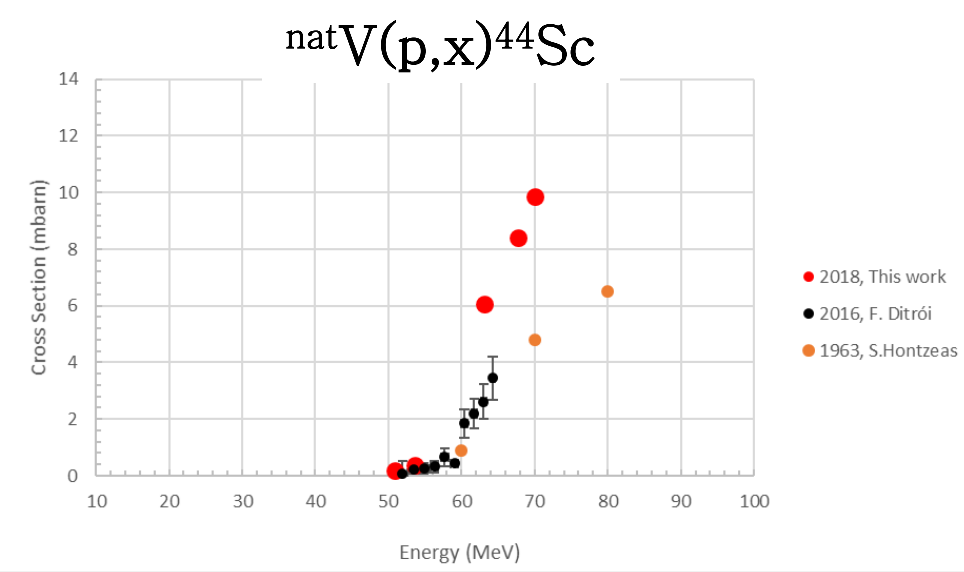
*An application of a new type deposition method to nuclear target preparation, Isao Sugai

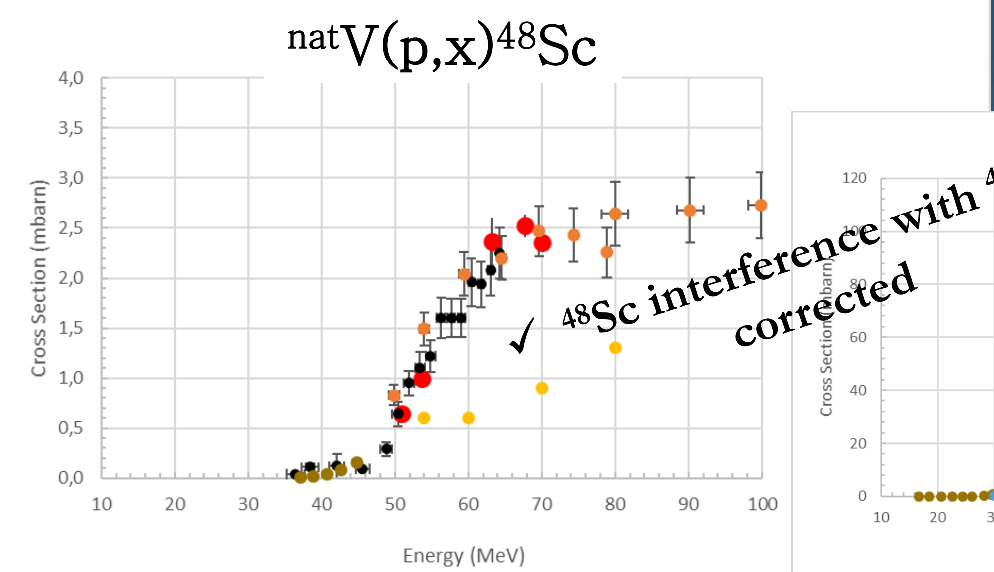
^{47}Sc: Preliminary results with ^{nat}V

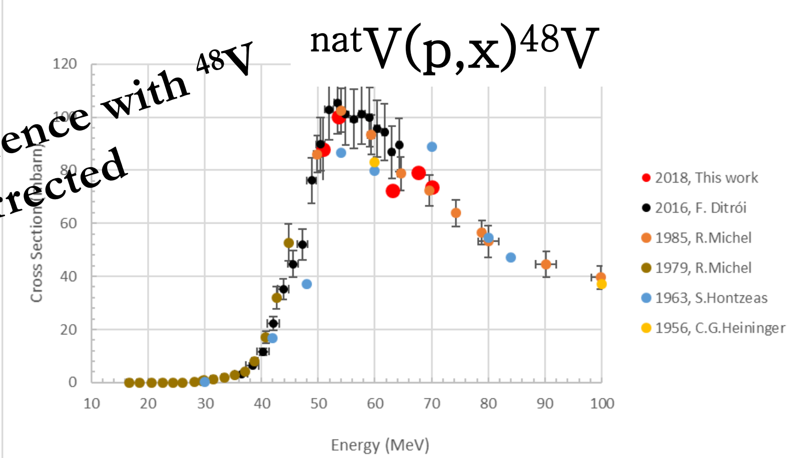


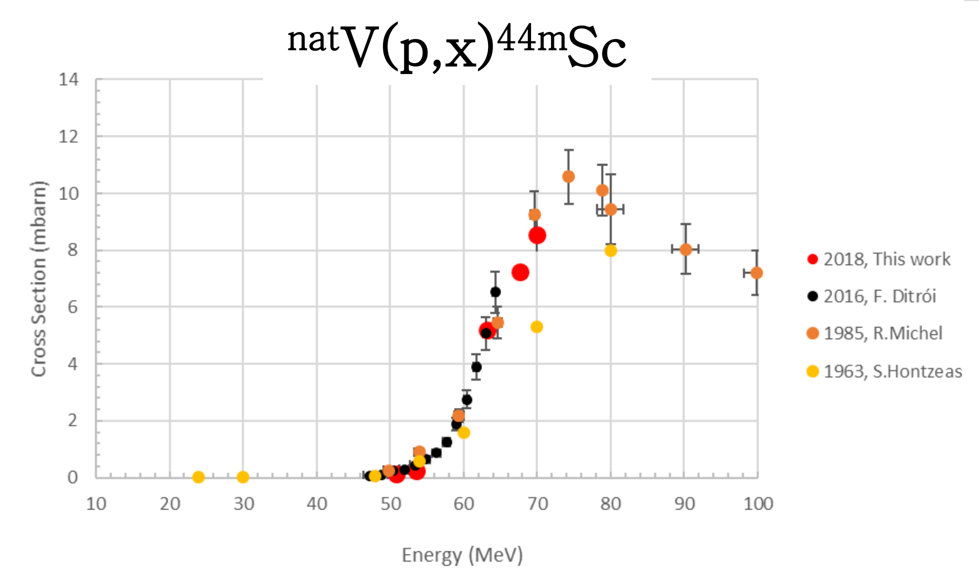


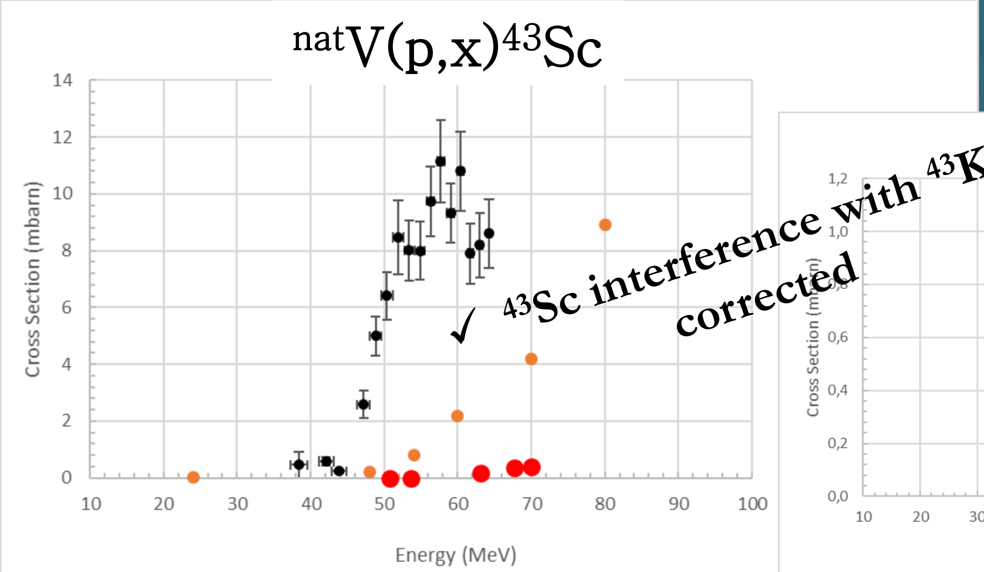
^{47}Sc: Preliminary results with ^{nat}V

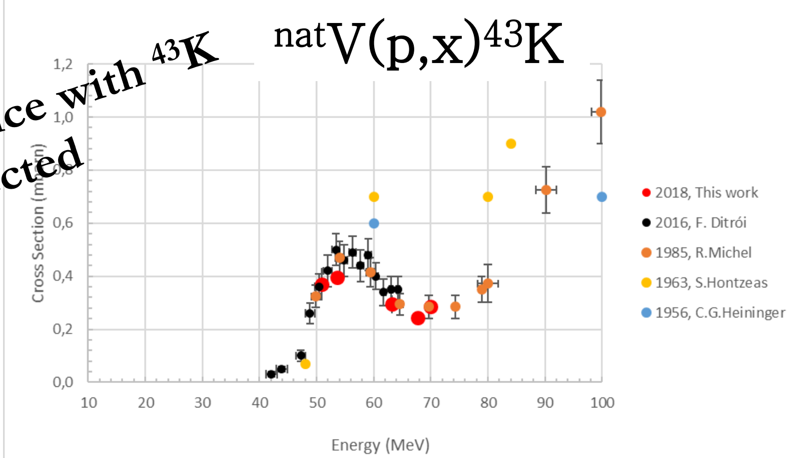








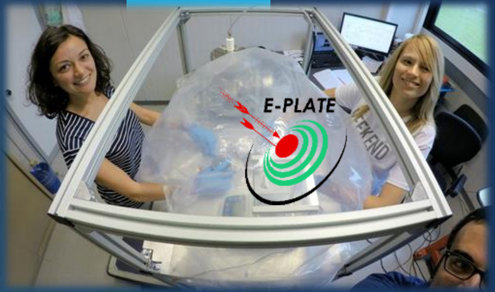




E_PLATE – CSN5
2018/2019

Electrostatic Powder pLating for Accelerator TargEts

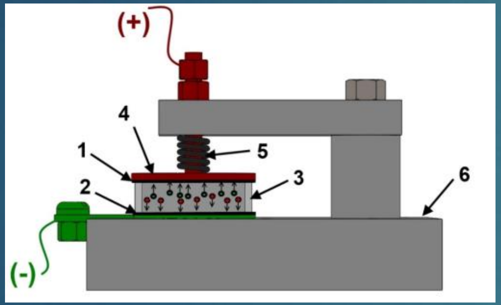
Realization of Enriched Titanium Metal Targets:
E_PLATE Project (Grant Giovani CSN5 2018-2019)



High intensity vibrational powder plating – HiViPP :

This deposition technique exploits the phenomenon of **vibrational motion** of metallic **particles in a static electric field** [1].

Experimental set up



1 – backing (upper electrode, anode)
2 – backing (lower electrode, cathode)
3 – quartz or glass cylinder
4 – pressing plate
5 – spring
6 – insulator holder

Target deposition homogeneity and surface mass density measured with RBS technique @ INFN-LNL

Advantages:

- Two targets are deposited simultaneously
- High Efficiency: 95-98%!
- High uniformity
- Small amount of starting material (≈50mg)

a. ^{nat}Mo on Al (1mm)
b. ^{nat}Mo on Cu (250µm)
c. ^{48}Ti on Al (25µm)

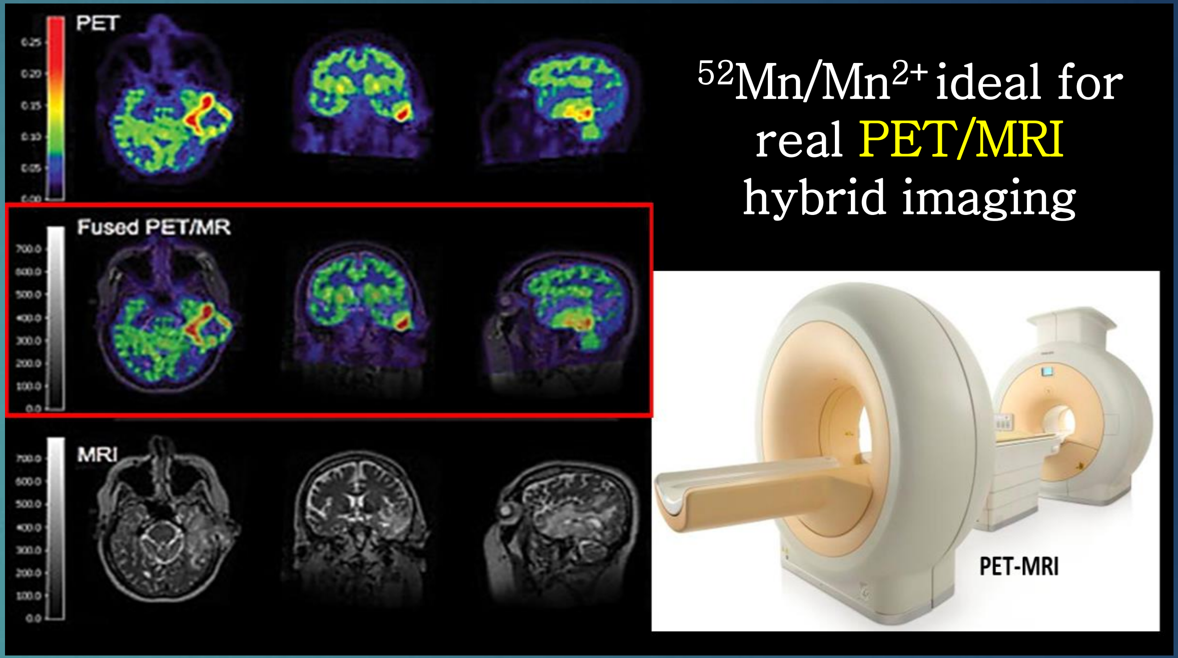
[1] An *application* of a new type deposition method to nuclear target preparation, Isao Sugai

METRICS – CSN5 2018/2020

Multimodal pET/mRi Imaging with Cyclotron-produced $^{52/51}$Mn and stable paramagnetic Mn iSotopes

AIM: To achieve a genuine fusion between PET and MRI, having chemically identical contrast and radioactive agents

Multi Modality Imaging MMI	
PET/SPECT	CT/MR
functional imaging	anatomical imaging
radiolabeled tracer	contrast agent
e.g. ^{18}F–FDG for PET	e.g. Ba and I for CT
or ^{99m}Tc–HMPAO for SPECT	or Gd–OMNISCAN for MRI



^{52}Mn	E β+ $_{(avg)}$ ~250 keV	PET
^{51}Mn	E β+ $_{(avg)}$ ~960 keV	
Mn^{2+}	paramagnetic properties	MRI contrast agents

→Develop/optimize the ^{52}Mn cyclotron production and proper separation/purification method

→Establish stable Mn(II)/^{52}Mn– complexes

Thank you for your attention!