Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro

CSN5 INFN new research project proposal
(2023-2025)

CUPRUM-TTD

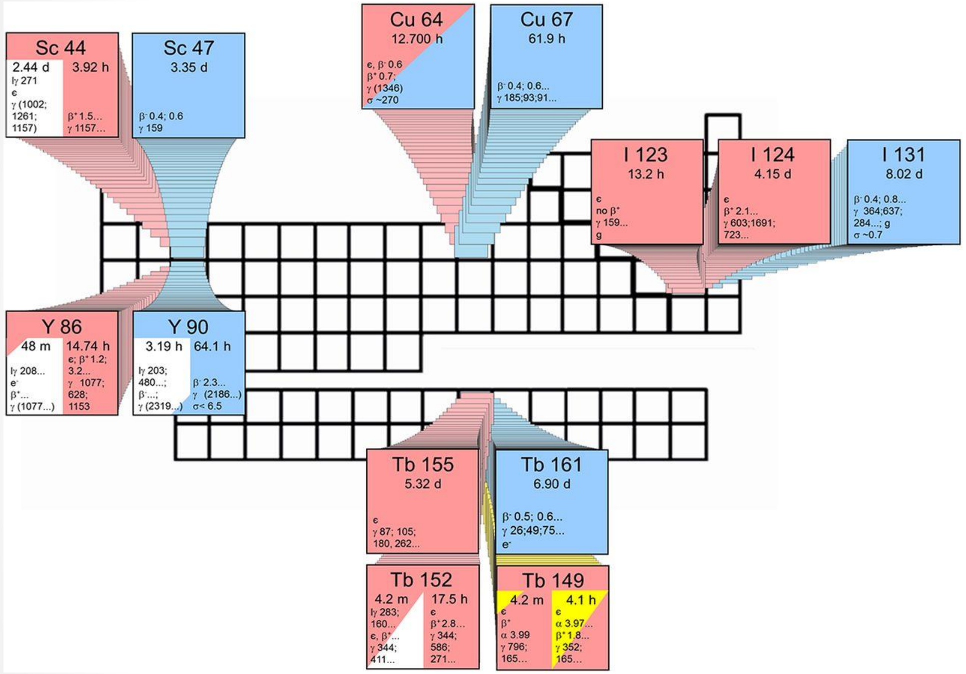
$^{67/64}$CU PRoduction and Use in Medicine – Target Technology Development

J. Esposito on behalf of INFN/UNIPD/UNIFE/SCDC Hospital (Negrar, VR)/IOV/Padua Hospital/ICMATE-CNR collaboration network

New research project proposal to CSN5 INFN, July 1st, 2022

^{67}Cu and ^{64}Cu: a theranostic pair

Real Theranostic pairs

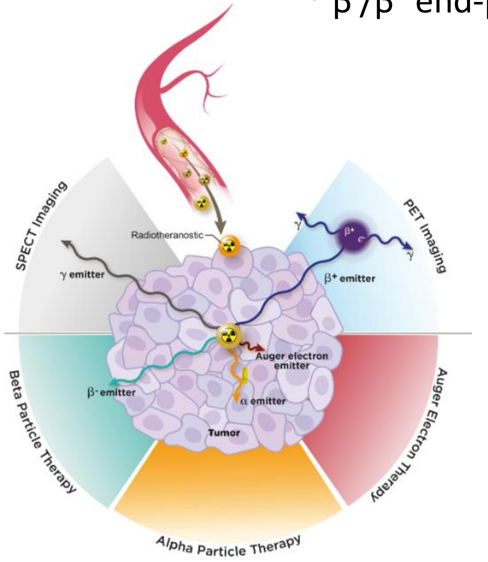


[C. Müller *et al.* J Nucl Med **2014**, 55:1658-64]

Radioisotope	Half-life [h]	Decay (%)	Main emissions (%) [KeV]
^{64}Cu	12.72	β^- (38.5%)	β^- 579 (38.5%)
		β^+ (17.5%)	β^+ 653 (17.5%)
		EC (44%)	γ 511 (35%) γ 1346 (0.5%)
^{67}Cu	61.83	β^- (100%)	β^- 562 (20%) β^- 468 (22%) β^- 377 (57%)
			γ 185 (49%) γ 91-93 (23%)

[NuDat 3.0]

* β^-/β^+ end-point energy



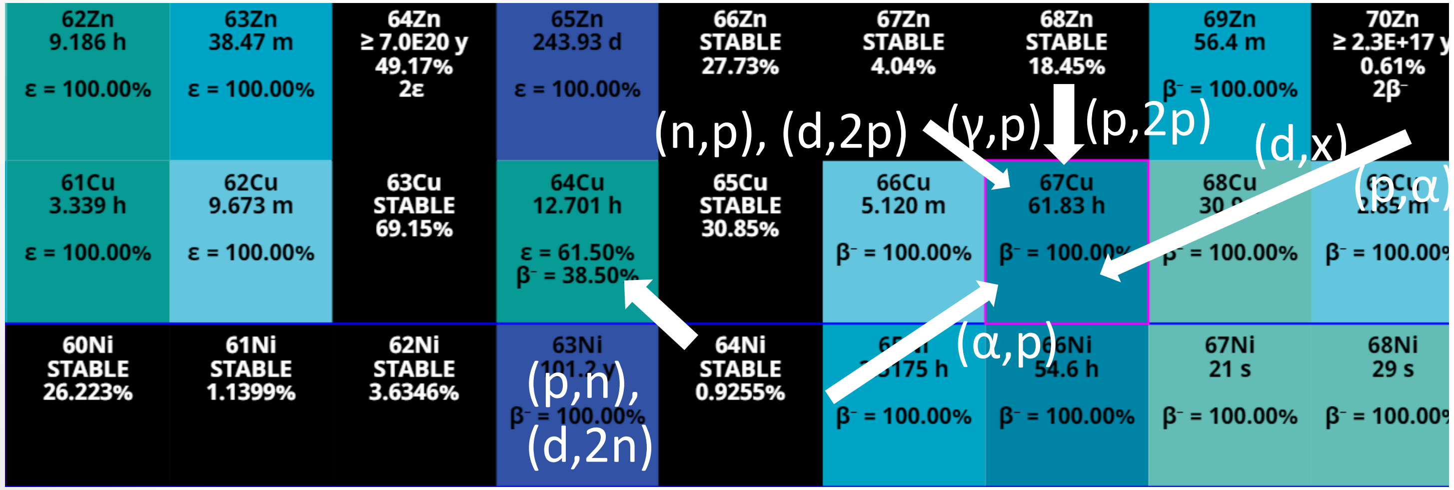
[N.Herrero Álvarez *et al*, ChemMedChem **2021**, 16: 2909 –2941]

- Imaging (PET, SPECT)
- Therapy

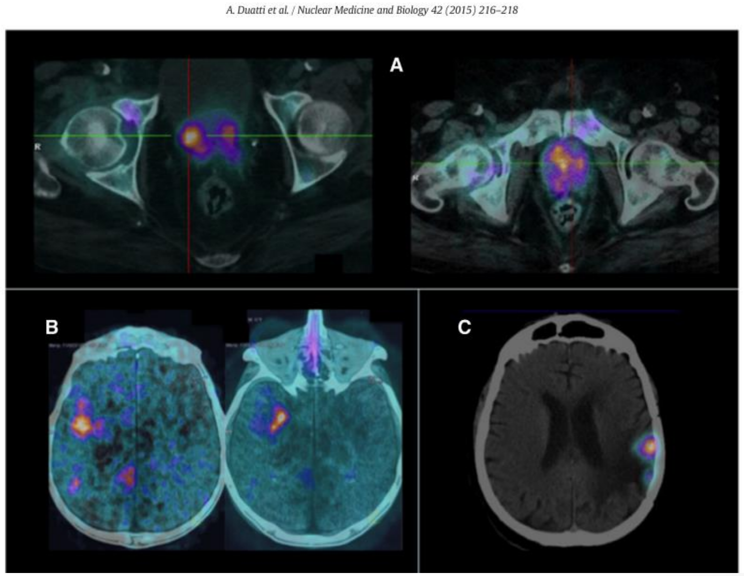
State of the art and background experience on Cu radiometals

- ^{64}Cu is ALREADY commercially available and used in nuclear medicine for PET
- ^{64}Cu seems to provide excellent results also in THERAPY (even under simple $^{64}CuCl_2$)
- **^{67}Cu is a promising radionuclide** for **Theranostic and Radioimmunotherapy,** as single isotope, or in pair with ^{64}Cu
- **^{67}Cu**'s limiting factor: still lacking a **REGULAR availability worldwide**
- Only recently become available in US in enough quantities for **medical research applications (DOE-IP)**
- Production capability upon request **(~ 1-2 Ci/batch,** 1 patient dose~100 mCi = 3.7 GBq) **@ ANL-LEAF via ^{68}Zn(γ,p) nuclear reaction (BNL through the ^{68}Zn(p,2p))**

➢ **^{67}Cu future supply in Europe: Goal both for ARRONAX and LARAMED**



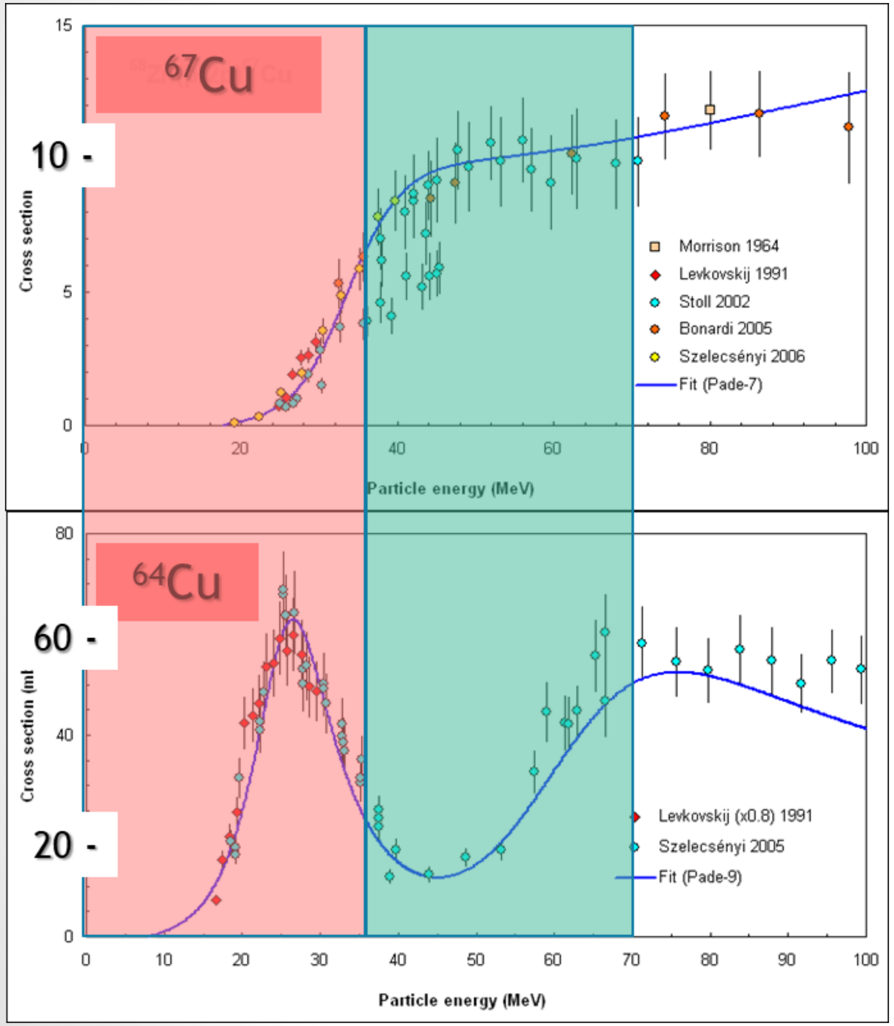
[https://www.nndc.bnl.gov/nudat3/]

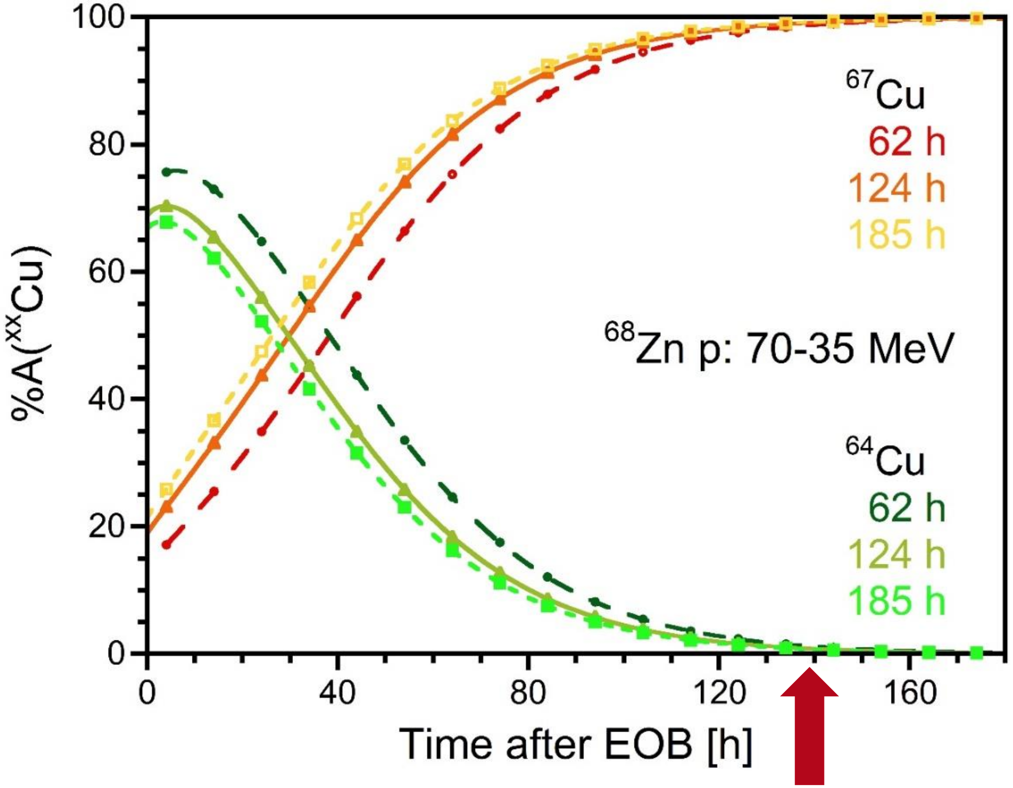


PET/CT images collected after i.v. injection of $^{64}CuCl_2$ in patients with (a) prostate cancer, (b) cerebral tumor, (c) glioma.

$^{68}Zn(p,2p)^{67}Cu$ reaction production route

IAEA *Technical Report Series No. 473* (2011)



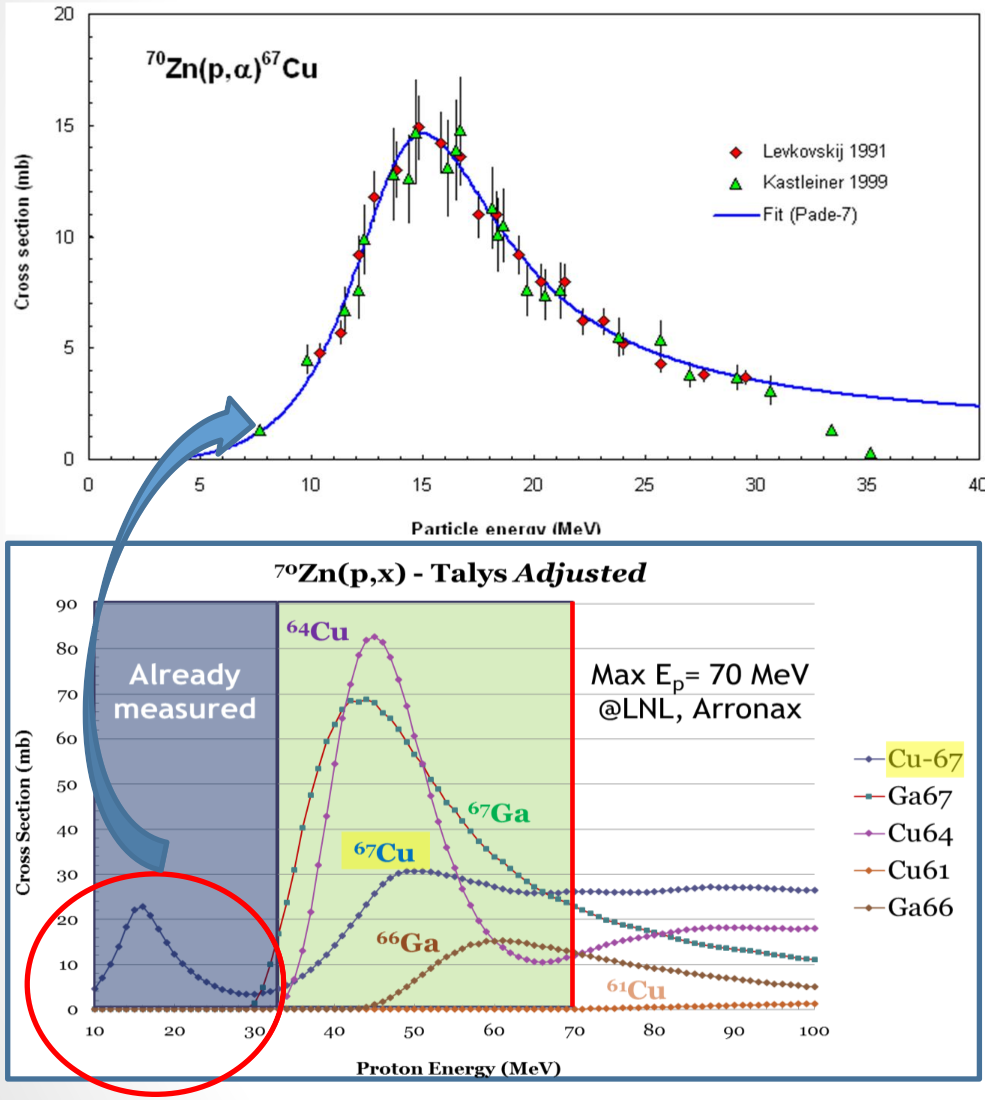


$t_{RNP \geq 99\%}$: 133-145 h

- In order to have a *pure* ^{67}Cu (RNP>99%) it is necessary to wait that ^{64}Cu decays → lose ≈ 80% of ^{67}Cu activity

^{67}Cu alternative production route: ^{70}Zn(p,α)^{67}Cu

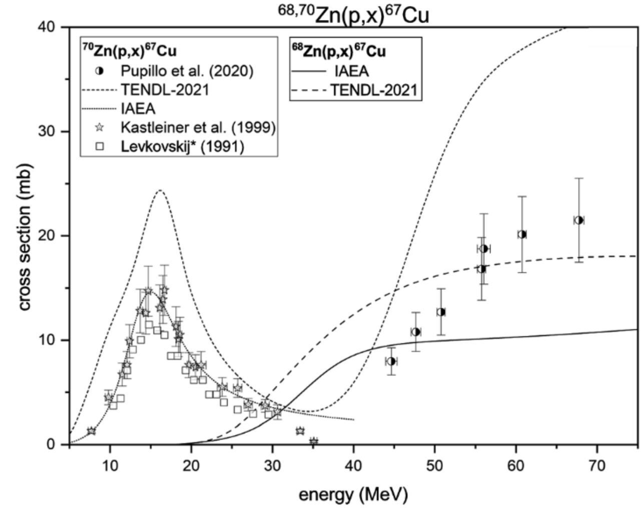
IAEA *Technical Report Series No. 473* (2011)

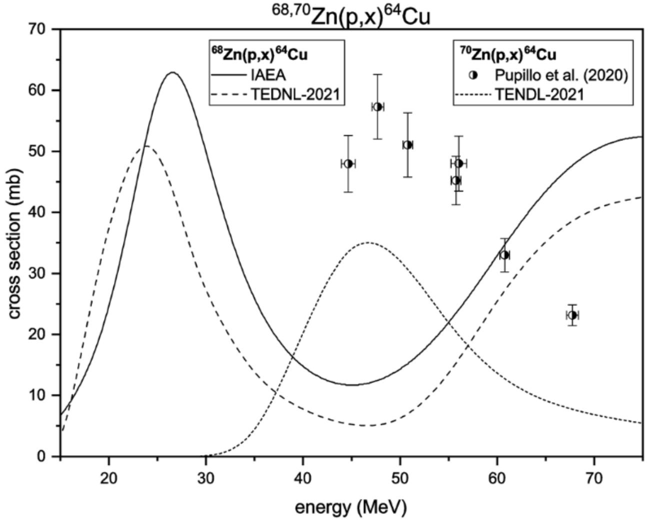


No experimental data available for E_p > 35 MeV

CoMe project (COpper xs MEasurement) : INFN funded (Dotazioni CSN3_2016)**:**

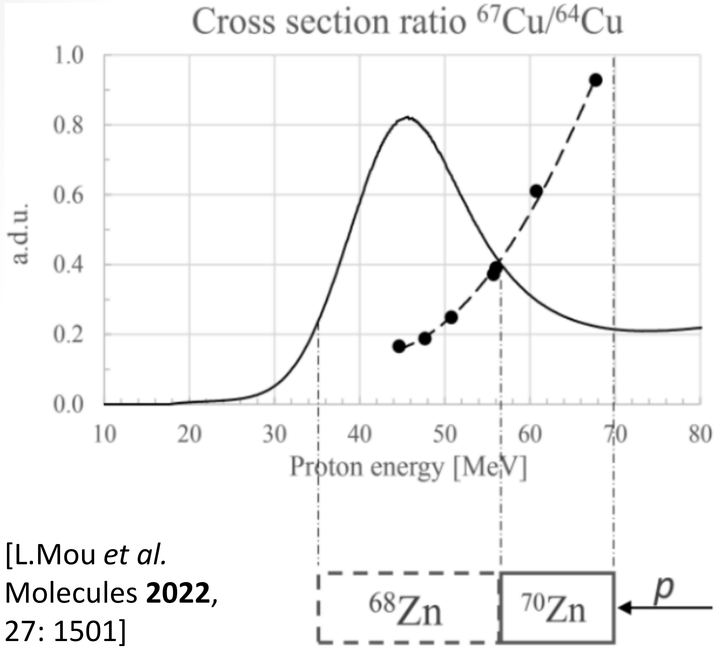
^{70}Zn(p,x)^{67,64}Cu xs measurements in 45-70 MeV range





[G. Pupillo Radiochim. Acta 2022]

Main achievement held by COME prj



[L.Mou *et al.* Molecules **2022**, 27: 1501]

"A method and a target for the production of ^{67}Cu"

Mou, Pupillo, Martini, Pasquali

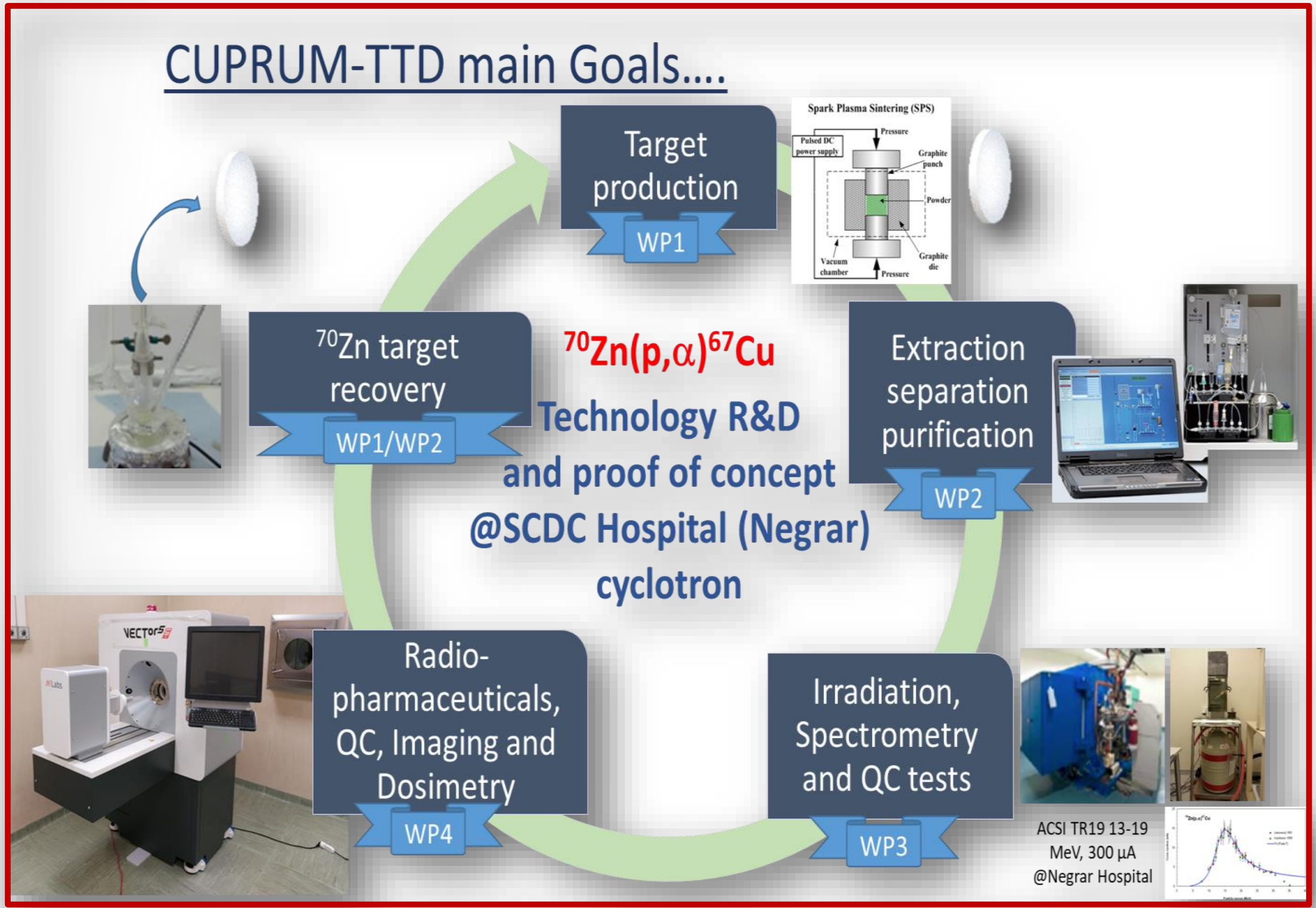
International Patent n° WO 2019/220224 A1

	Irr. time (h)	^{67}Cu at EOB (MBq/μA)	^{64}Cu at EOB (MBq/μA)	^{61}Cu at EOB (MBq/μA)	^{60}Cu at EOB (MBq/μA)	$t_{99\%}$ (h)	^{67}Cu at $t_{99\%}$ (MBq/μA)
^{68}Zn: 70–35 MeV	62	1240.1	6512.0	1140.1	26.5	145	244.1
	124	1859.4	6732.9	1140.1	26.5	136	404.8
	185	2165.2	6740.4	1140.1	26.5	133	487.5
^{70}Zn: 70–45 MeV	62	1751.7	7506.7	11.7	–	139	368.7
	124	2626.5	7761.4	11.7	–	131	604.8
	185	3058.5	7770.0	11.7	–	128	728.3
^{70}Zn: 70–55 MeV + ^{68}Zn: 55–35 MeV	62	1881.3	5825.0	40.0	0.0012	132	428.3
	124	2820.9	6022.6	40.0	0.0012	123	710.5
	185	3284.9	6029.3	40.0	0.0012	120	855.6

[De Nardo L. et al. Med Phys. 2022;1–16]

CUPRUM-TTD (2023-2025) research project

In view of the next preclinical/clincal applications the goal of the current research proposal is therefore to develop beforehand a reliable technology aimed at **producing clinical-grade batches of ^{67}Cu- ^{64}Cu, on a routine basis by small medical cyclotrons.**



Main project GOALS:

a) to acquire a **robust and reliable target manufacturing technology to produce ^{70}ZnO target** (and ^{nat}Ni targets for first ^{64}Cu yield batches from ^{64}Ni(p,n)^{64}Cu at a later stage);

b) to design and construct proper targets, able to sustain **beam power levels from medical cyclotrons (i.e. 18-20 MeV, 2/3 kW max)**;

c) to develop/optimize the **radiochemistry separation/purification methods: Zn→Cu** to achieve a clinical-grade **^{67}Cu radionuclide**;

d) Implementation of *in-vitro* survival studies;

e) Pre-clinical and clinical phantom imaging;

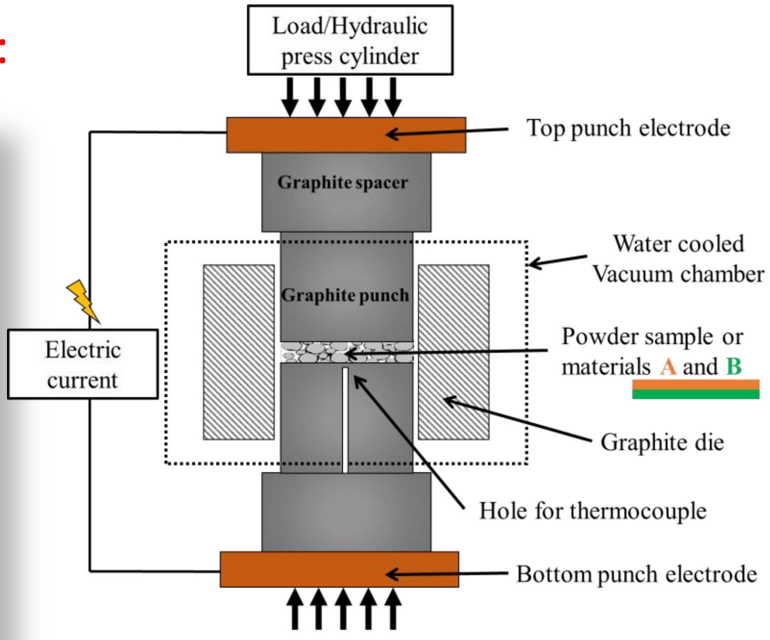
f) to develop /optimize technology for the **costly ^{70}Zn-enriched target material recovery.**

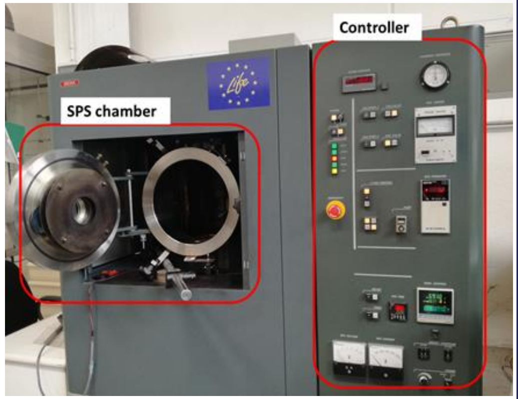
INFN –LNL Target technology development

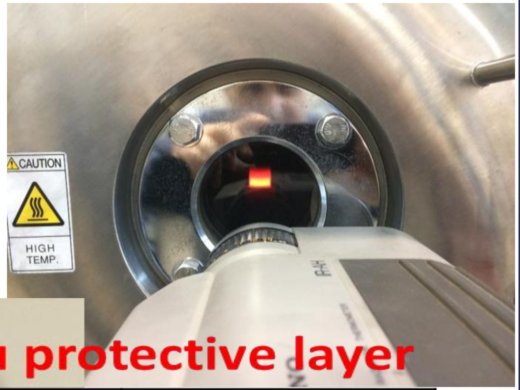
The starting point is the *know-how* gained for **metallic targets manufacturing** for medical cyclotrons (up to 1.0 kW/cm^2) successfully produced by a refined SPS (Spark Plasma Sintering) technique.

SPS (Spark Plasma Sintering) main advantages:

- ✓ Only **few minutes** for target fabrication compared to conventional sintering techniques
- ✓ Sintering of **high melting point materials** e.g metals Mo/Cr/Y or oxides
- ✓ **Bonding** between different materials (target material on backing) → no filler material in between
- ✓ Starting materials→ **powder or foil**
- ✓ **100% efficiency→ very negligible losses of isotope-enriched material** during manufacturing
- ✓ Possibility to produce easily **100-500 μm thickness pellet**



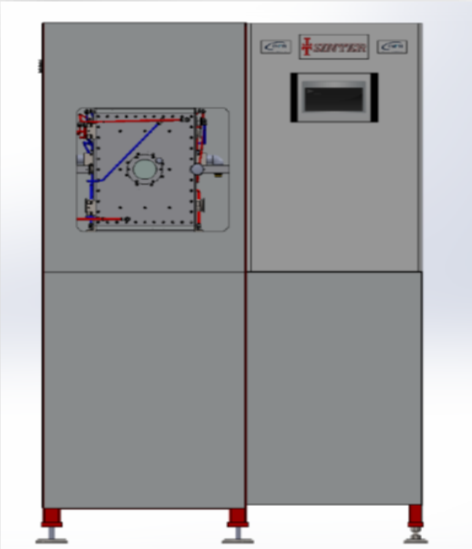


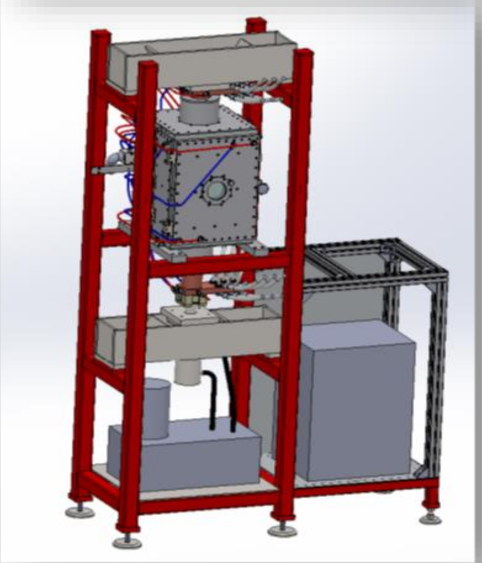


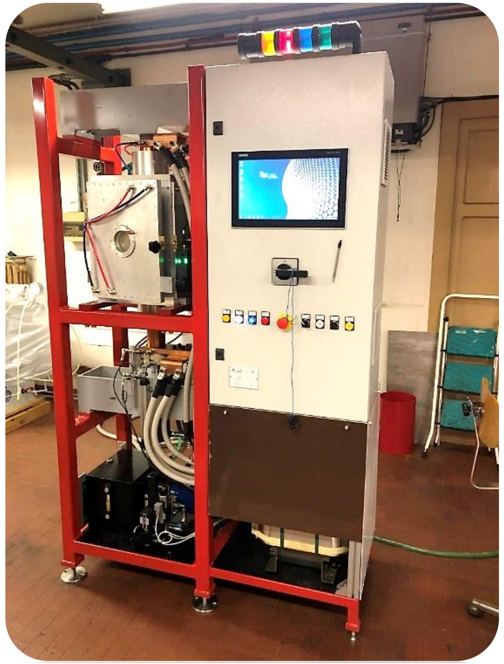
Au protective layer

Cr green pellet	D=10 mm, s=0.4mm (mass= ~200 mg)
Cu backing	D=23.7mm, s=1.7mm
Au protective layer in between (~25 μm) onto Cu disk	

The new SPS TT SINTER machine developed by INFN Pavia and PV University to be installed in the future LARAMED target laboratory

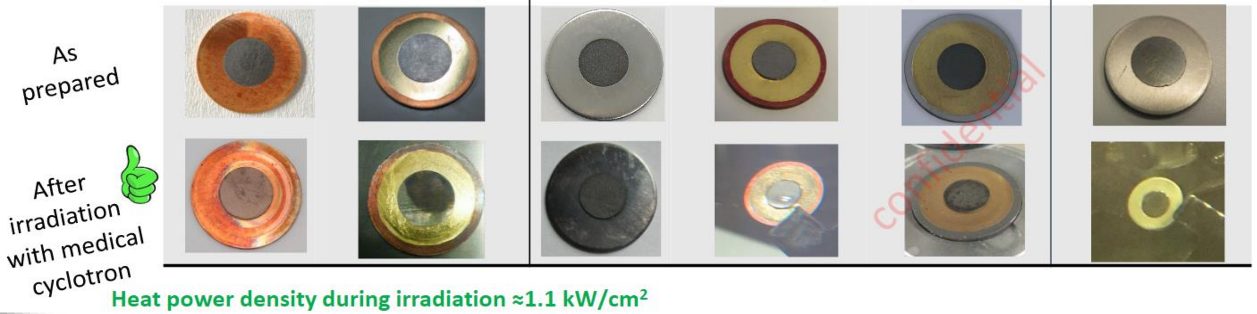






- machine design based upon LNL specifications

$^{100}Mo \rightarrow ^{99m}Tc$		$^{nat,52}Cr \rightarrow ^{52}Mn$			$Y \rightarrow ^{89}Zr$
^{nat}Mo pellet	^{100}Mo pellet	^{nat}Cr pellet	^{nat}Cr pellet	^{52}Cr pellet	^{nat}Y foil
Cu backing	Cu backing Au protective layer	Nb backing	Cu backing Au protective layer	Nb backing Au protective layer	Nb backing



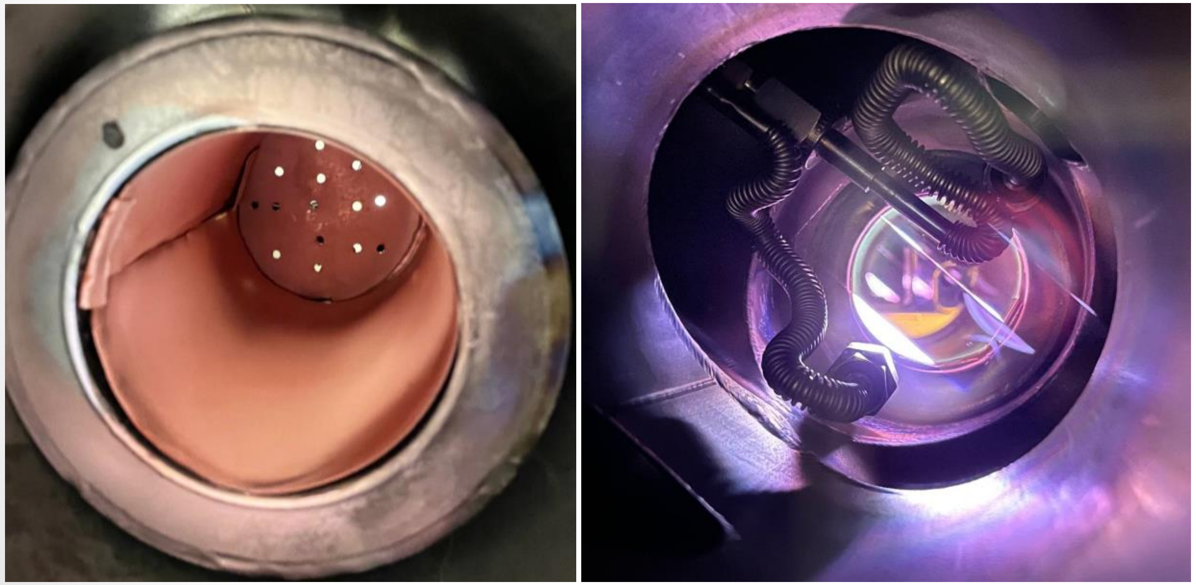
Heat power density during irradiation ≈1.1 kW/cm²

SPS technique: some past results

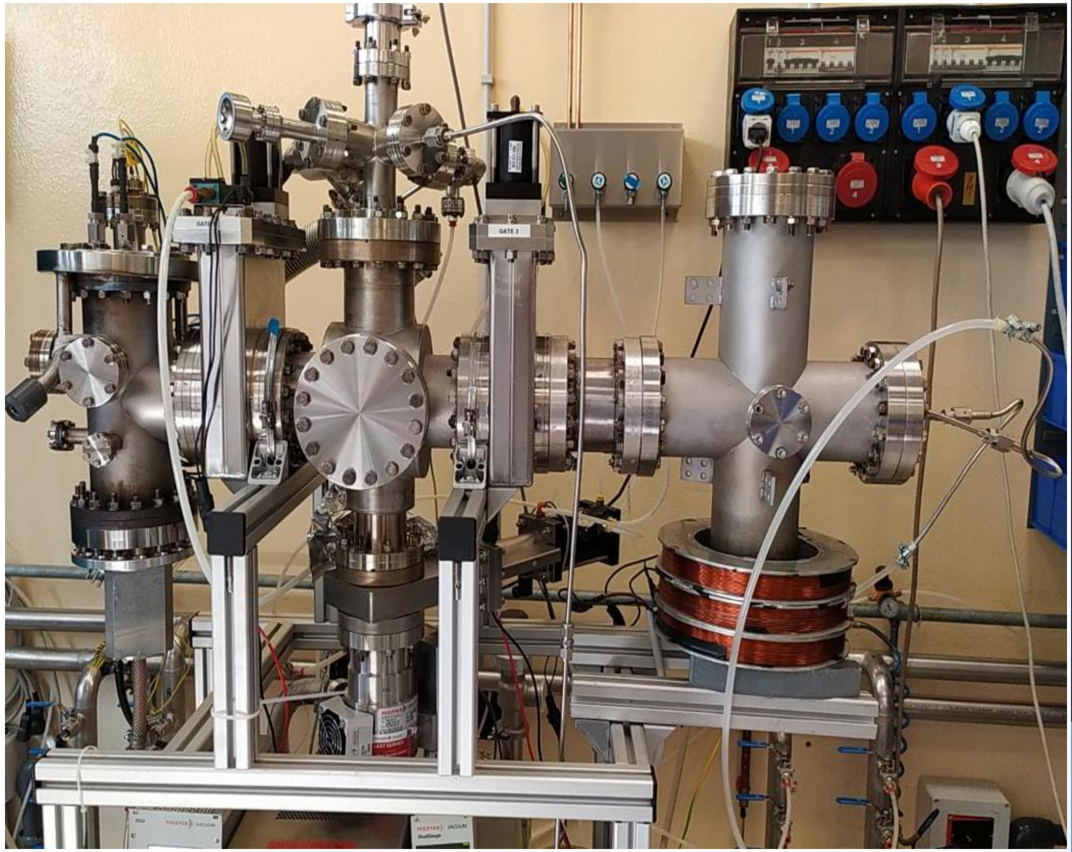
Inverted magnetron deposition system developed for solid target production

The new, optimized, and alternative magnetron deposition setup as developed in the framework of METRICS (CSN5 2017-2021) – INTEF_TOTEM (2021-2022) projects.

Main idea: combine the advantages of Magnetron Sputtering (MS) deposition, along with target material improved usage or/and high recovering level.



Inverted magnetron: target (left view) and plasma (right view)



The vacuum system dedicated for inverted magnetron deposition test and future target production

CUPRUM-TTD proposed approach

- Development of a robust and reliable **target manufacturing technology** suitable for **irradiations at small medical proton cyclotrons (e.g. up to 19 MeV like the ACSI TR19-300 of SCDCH - Negrar, VR)** by using **^{nat}ZnO material**.
  - **know-how acquisition to manufacture Zn oxides targets** (not metallic) in view of their **future use with higher power proton beams like the SPES cyclotron (Zn melting temp.: 1970 °C in oxide form, 419.5 °C in metal form).**

- Development of the **radiochemical procedure** for ^{nat}ZnO processing and extraction of the product ^{6x}Cu (semi-automatic/automatic module).

- **Irradiation test @ HSCDC TR19/300 cyclotron** with first **^{70}ZnO targets** produced and separation of ^{67}Cu product, QC studies, transport @ LNL and imaging @ LARIM lab (LNL), with the **micro-PET/SPECT/CT small animal scanner (collaboration with IOV).**

CUPRUM-TTD proposed approach for **phase 1 project:**

^{nat}ZnO target production for first irradiation tests @HSCDC

Study of the SPS process to obtain ^{nat}ZnO pellets;

- pellet main features **-> thickness 0.7 mm; mass about 500 mg**
- backing optimization (chemically resistant, high thermal conductivity):

Goal: max sustainable beam-on-target current determination

Bonding
Pellet+Backing mat.
(Possible approaches)

- (Nb, Ta, RG_C?) + Au : backing + coating; → **Spark Plasma Sintering (SPS) process**
- capsule holder (Al/Nb depending upon the needs) → **SPS process for ^{nat}ZnO pellet only**
- ZnO layer on selected backing → **Magnetron Sputtering**

Tests to be carried out :

- **^{nat}ZnO layer characterization** with different techniques @ LNL**:** SEM, Energy Dispersive X-ray Spectroscopy (EDS) and profilometer (Surf. Treat. Lab.);
- **^{nat}ZnO pellet mechanical resistance determination** (target upload/download from target station);
- **Thermomechanical tests resistance** (**19 MeV, 5-50 μA → ~0.1 – ~1.0 kW**)

Collaboration with : HSCDC (Negrar –VR)

INFN divisions involved: **LNL** (PV)

CUPRUM-TTD proposed approach for **phase 1 project:**

Target radiochemistry processing studies from ^{nat}ZnO targets @HSCDC

To develop the optimized ^{nat}ZnO targets dissolution/separation/purification system following the first irradiation tests

- **preliminary studies with ^{nat}ZnO pellets (cold tests)** to assess chemistry separation techniques (e.g. solvent-extraction, extraction chromatography etc.) – **(^{nat}Ni pellets at a later stage)**
- **design of the reactor system configuration** when first ^{nat}ZnO/ ^{nat}Ni pellets/targets will be available
- radiochemistry process optimization (and system semi-automation) once the **first target samples (pellet + backing)** will be available

Tests to be carried out :

- **ICP-OES analysis** (in collaboration with UniFE);
- **gamma-spectrometry measurements** and **QC assessment** (in collaboration UniFE, UniMI @ LASA and HSCDC, Negrar-VR)

Goal: Development of the semi-automated ^{6x}Cu isotopes separation/purification with minimum isotopic contaminants

Collaboration with : HSCDC (Negrar –VR)

INFN divisions involved: **LNL**, Fe, (PV), MI

CUPRUM-TTD proposed approach for phase 2 project:
first ^{70}ZnO-enriched targets beam tests and ^{67}Cu batches production @HSCDC

(^{70}Zn-enriched) ZnO first target samples manufacturing

a) selection of beam parameters suitable to yield small batches of ^{67}Cu based on theoretical calculations;

b) Irradiation @ SCDC TR19/300 cyclotron: **Emax = 19 MeV ; t_{irr} = ? ; I_{max} = ?**

- [thermomechanical tests]

c) Radiochemistry separation and purification tests of the **^{67}Cu** samples produced;

- [QC assessment]
- [labeling tests with selected pharmaceutical products]

Experimental activities with ^{67}Cu thus produced:

- **Pharmacology lab** @UNIFE available for cellular ***in-vitro*** studies and with $^{67}CuCl_2$; (1 transport Negrar-UNIFE about 200 €)
- **SPECT phantom** imaging studies with ^{67}Cu with **preclinical and clinical gamma-camera** (@ LARIM and Padua Univ. Hospital)
- Possible ***in-vivo* studies @LARIM (depending upon the completion of plants and re-starting activities)?**

Goal: First ^{67}Cu *in-vitro* (*in vivo*?) imaging studies with known (or new) carrier molecules.

Collaboration with : HSCDC (Negrar –VR) and IOV

INFN divisions involved: LNL, Fe, PD

CUPRUM-TTD proposed approach for **phase 2 project:** first ^{64}**Ni-enriched** targets production for ^{64}Cu batches @ HSCDC

- **(^{64}Ni-enriched) Ni first target samples manufacturing**

SPS process to obtain first ^{64}Ni-enriched and targets (Nb/Au/XX config.)

- **^{64}Cu**: ^{64}Ni(p,n)^{64}Cu → energy range 11.5 - 9 MeV → target: ~100 µm ^{64}Ni

To seek for alternative nuclear production routes…

^{67}Cu/ ^{64}Cu (^{61}Cu) **with alpha-induced reactions @ARRONAX– Milan contribution**

- **^{61}Cu**: ^{nat}Ni(alpha,pxn)^{61,64,67}Cu → energy range 70 – 8 MeV → target: ~20 µm ^{nat}Ni with the study of contaminants and the determination of RNP and SA
- **^{67}Cu**: ^{64}Ni(alpha,p)^{67}Cu → energy range 30 – 15 MeV → Thick Target Yield (TTY), using a thick target produced @LNL
- **^{61}Cu**: ^{59}Co(alpha,2n)^{61}Cu → energy range 70 – 8 MeV → target: ~20 µm ^{59}Co with the study of contaminants

Collaboration with : HSCDC (Negrar –VR) and ARRONAX center (Nantes- FRA)

INFN divisions involved: LNL, MI, PV, PD

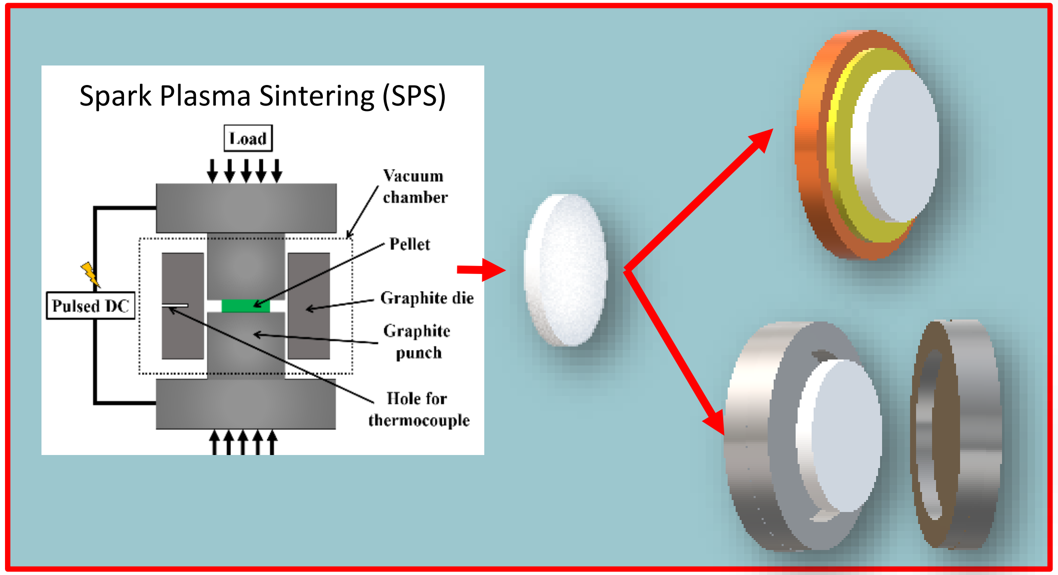
CUPRUM-TTD WP1: Target production and recovery

Target material

- ^{70}ZnO Tm=1975°C (25$/mg)
- 1 target 500mg → 4 target 41.6k€

Target production by SPS technique:

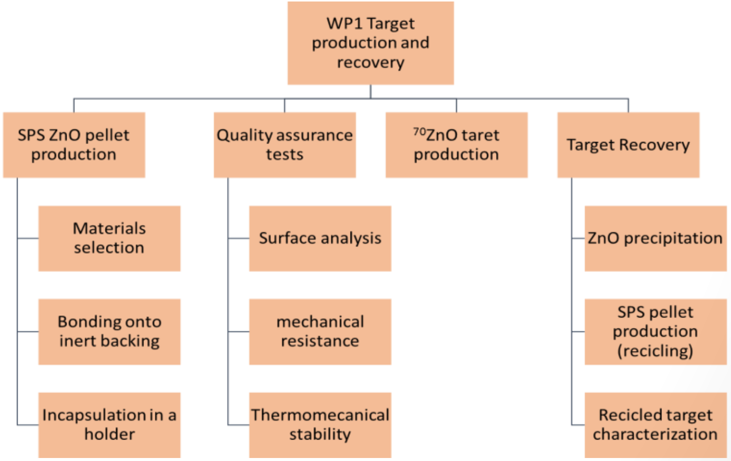
- Collaboration with Chem Dept UNIPV (ZnO +Ni pellet)
- Support/holder investigation
- Target recovery and recycling (SPS)



- Milestones and deliverables planned

WP1	
Sara Cisternino Gabriele Sciacca Juan Esposito Giorgio Keppel Oscar Azzolini Alisa Kotliarenko	LNL
Umberto A. Tamburini	UNIPV

M1: SPS technique development for ZnO target manufacturing (Nb/Au/ZnO kind); M2: recovery process development for ^{nat}ZnO, and material powders characterization (SEM, EDS, profilometer); M3: trial of target production with SPS technique starting from recovered ^{nat}ZnO; M4: SPS technique development for ^{nat}Ni target manufacturing (Nb/Au/Ni kind);
D1: 2/3 ZnO targets for surface analyses investigations (WP2); D2: 5 ZnO targets for cold test chemical processing optimization (WP2); D3: 2/3 ^{70}ZnO targets for production test; D4: recovered ^{nat}ZnO powders.

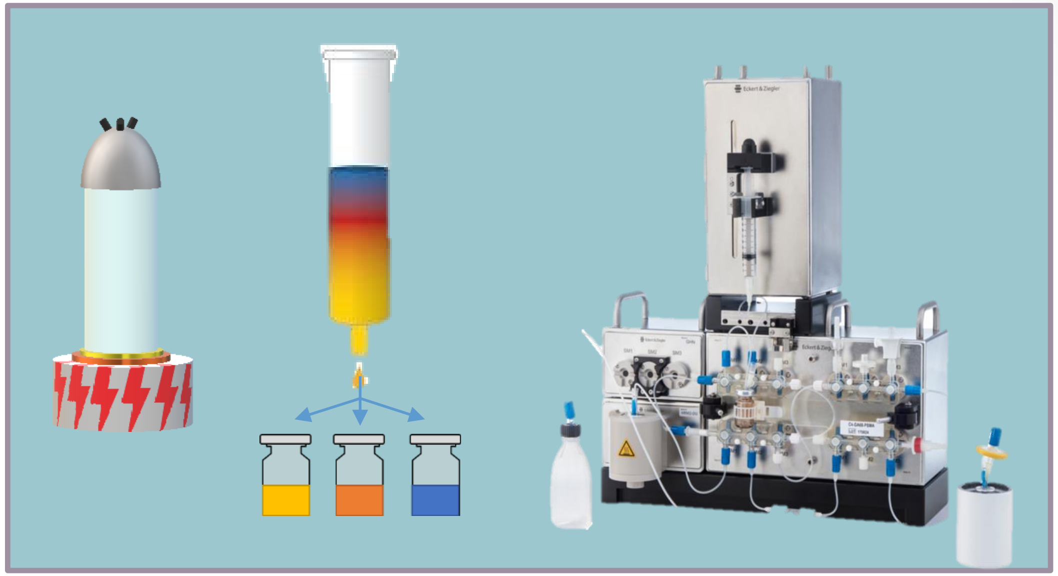


CUPRUM-TTD WP2: Target radiochemistry processing

Separation and purification procedure development:
- cold tests ^{nat}ZnO
- ICP(OES) characterization @UNIFE

Automated module prototype development
- Purchase of modular units
- Hot test ^{nat}ZnO

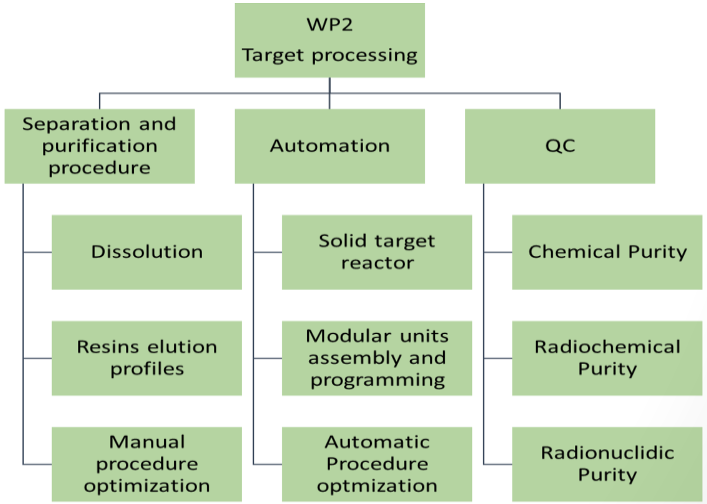
Quality Control (QC) assessment on RCP:
- Hot tests ^{70}ZnO



- Milestones and deliverables planned

WP2	
Petra Martini	
Alessandra Boschi	
Teresa Ghirardi	UNIFE
Licia Uccelli	
Lorenza Marvelli	
Emiliano Cazzola	HSCDC

M5: development of separation and purification procedure using cold targets of ^{nat}ZnO
M6: development of a semi-automatic system for the separation and purification of Zn/Cu
M7: optimization and automation of ^{6x}Cu separation
M8: productions tests of ^{67}Cu (^{64}Cu) by using enriched target and determination of the extraction yield and purity of the final product.
M9: QC analysis on ^{67}Cu (^{64}Cu) produced and isolated for pharmaceutical studies
D5: Zn/Cu separation and purification procedure
D6: semi-automatic module for the separation and purification of ^{67}Cu (^{64}Cu) from ZnO/Ni target
D7: ^{67}Cu (^{64}Cu) radiochemistry product quality assessment

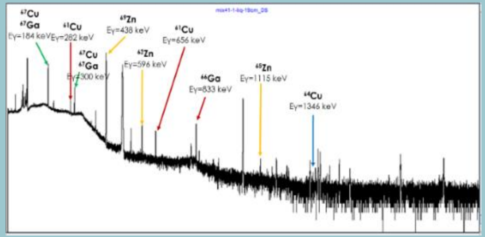


CUPRUM-TTD WP3: Irradiation, γ-spectrometry and QC test

Irradiation runs on $^{nat}ZnO/^{nat}Ni$ for targets and radiochemical separation optimization

- selection of beam parameters suitable to yield small batches of $^{67}Cu/^{64}Cu$ based on theoretical calculations;
- 3 irradiation runs on ^{70}ZnO for first batches of ^{67}Cu;
- 2 irradiations runs on ^{64}Ni for first batches of ^{64}Cu;
- 4 irradiations runs on ^{nat}Ni and ^{59}Co with alpha particles for $^{61,64,67}Cu$ optimization production (xs meas. @ARRONAX)
- **2 irradiations runs on thick target of ^{64}Ni for TTY**
- **γ-spectrometry analysis for yield and RNP determination**

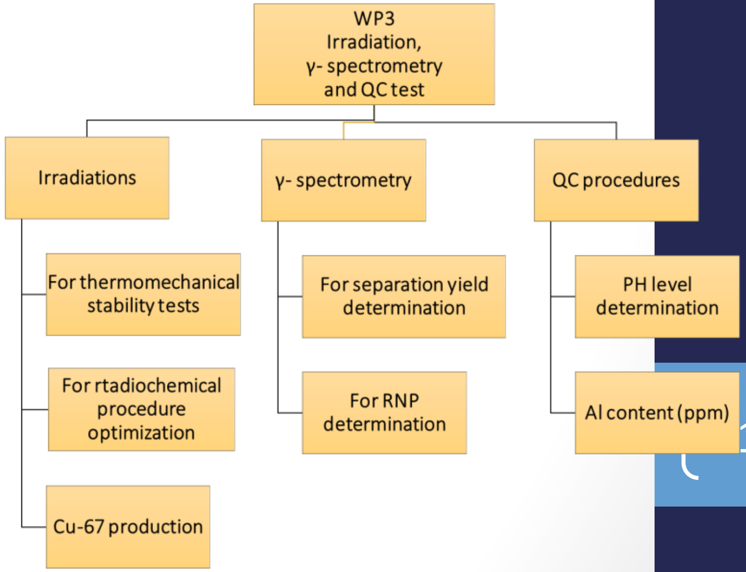

ACSI TR19 13-19 MeV, 300 μA @Negrar Hospital



WP3	
Liliana Mou	
Gaia Pupillo Carlos Rossi Alvarez Juan Esposito	LNL
Emiliano Cazzola Giancarlo Gorgoni	HSCDC
Luciano Canton Francesca Barbaro	INFN-PD
Simone Manenti Flavia Groppi Francesca Cagnetta	UNIMI (INFN-MI)

- Milestones and deliverables planned

M10: ^{nat}ZnO targets irradiation for thermomechanical stability tests M11: ^{nat}ZnO targets irradiations for radiochemical separation optimization procedure M12: 3 irradiations on ^{70}ZnO targets for ^{67}Cu batches production (2 irradiations on ^{64}Ni targets for ^{64}Cu). M13: γ-spectrometry meas. to determine radiochemical procedure efficiency ($^{nat}Zn/^{nat}Ni$ targets) M14: γ-spectrometry meas. to determine the activity and RNP of ^{67}Cu produced by irradiation of ^{70}Zn targets (^{64}Cu produced by ^{64}Ni targets and ^{61,64,67}**Cu** production by alpha beams **on $^{nat}Ni/^{64}Ni/^{59}Co$** for xs determination)
D8: RNP of the produced $^{67}Cu/^{64}Cu$ radionuclides from $^{70}ZnO/^{64}Ni$ D9: xs measurements with alpha beams



WP4: RPs development, cellular, dosimetry and Imaging studies

Bifunctional ligand synthesis @LARIM

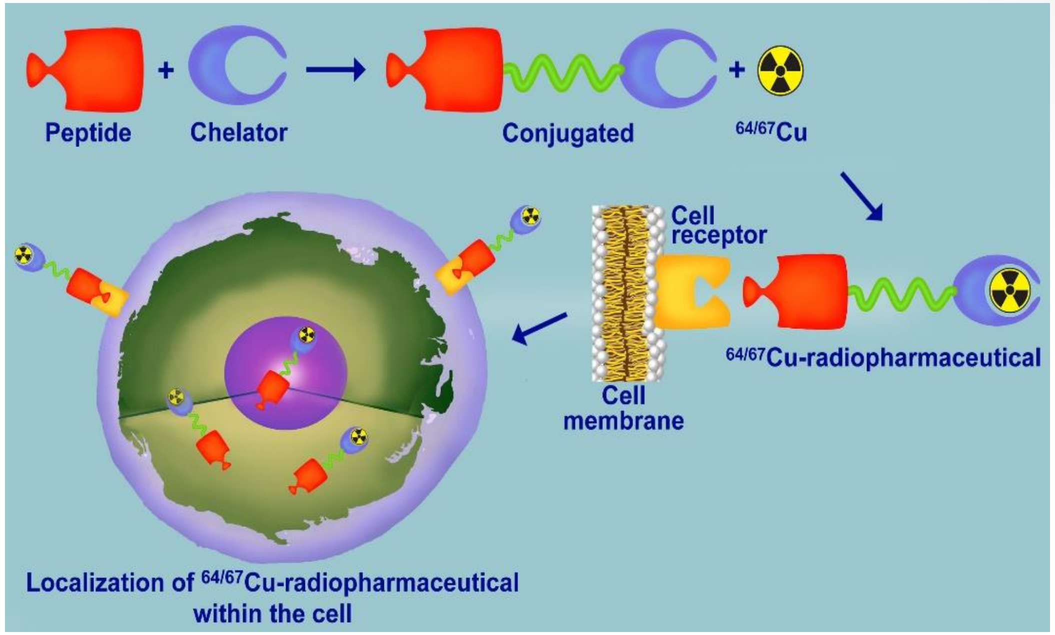
Radiolabeling with ^{xx}Cu @LARIM

Characterization and stability evaluation of ^{xx}Cu RPs @LARIM @ICMATE-CNR

Evaluation of specific uptake and internalization in both PSMA-positive and negative PCa cells

Cellular Dosimetry calculations @ INFN-PD

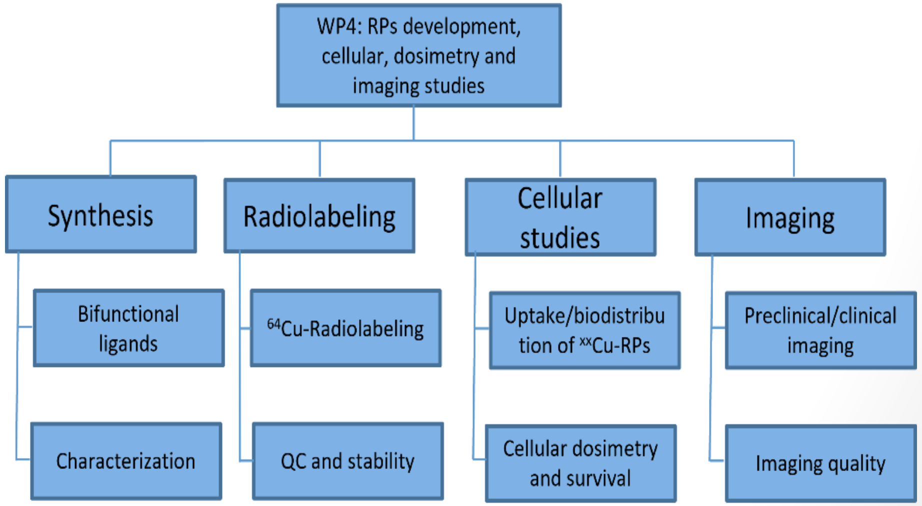
Preclinical and clinical Nuclear Imaging quality studies with ^{XX}Cu @LARIM @Padova Hospital



WP4	
Laura Melendez-A. Alessandra Zorz Marta Paiusco	IOV (INFN-LNL/Pd)
Laura De Nardo Michele Bello Diego Cecchin	UNIPD (INFN-Pd/LNL)
Cristina Bolzati	CNR (INFN-Pd)
Giov. Di Domenico Angelo Taibi	UNIFE (INFN-FE)

- Milestones and deliverables planned

M15: synthesis of new conjugates M16: Radiolabeling and stability studies M17: Cellular uptake and dosimetry/survival calculations M18: phantom imaging studies
D10: conjugates D11: method to obtain Cu-PSMA RPs with high radiochemical yield D12: Minimum activity and dimension of the tumor to obtain good imaging



Research units/collaborations taking part…

INFN
Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro

INFN
Istituto Nazionale di Fisica Nucleare

- Ferrara Branch
- Padua Branch
- Milan Branch

AZIENDA OSPEDALE UNIVERSITÀ PADOVA

I.O.V. Istituto Oncologico Veneto I.R.C.C.S.

Sacro Cuore Don Calabria Negrar - Verona
Ospedale Sacro Cuore Don Calabria
PRESIDIO OSPEDALIERO ACCREDITATO - REGIONE VENETO

Arronax Nantes

ICMATE
Istituto di Chimica della Materia Condensata e di Tecnologie per l'Energia

FERRARIAE UNIVERSITAS · 13 91 · EX LABORE FRUCTUS

UNIVERSITÀ DEGLI STUDI DI MILANO

UNIVERSITÀ DEGLI STUDI DI PADOVA
Dipartimento di Fisica e Astronomia Galileo Galilei

UNIVERSITÀ DI PAVIA

CUPRUM-TTD project 2023: FTE

Anagrafica LNL 2023	FTE: 4.8
Esposito J.	0.5
Pupillo G.	0.2
Mou L.	0.2
Sciacca G.	0.5
Cisternino S.	0.4
Melendez-Alafort L.	0.4
Bello M.	0.8
Kotliarenko A.	0.4
Keppel G.	0.1
Azzolini O.	0.1
Anselmi-Tamburini U.	0.2
Borsista***	1.0

Anagrafica INFN-PD 2023	FTE: 1.5
De Nardo L.	0.5
Canton L.	0.1
Barbaro F.	0.1
Zorz A.	0.2
Paiusco M.	0.2
Cecchin D.	0.2
Bolzati C.****	0.2

Anagrafica INFN-FE 2023	FTE: 4.0
Martini P.	0.6
Di Domenico G.	0.1
Taibi A.	0.1
Boschi A.	0.7
Uccelli L.	0.5
Marvelli L.*	1.0

Anagrafica INFN-MI 2023	FTE: 2.1
Groppi F.	0.4
Manenti S.	0.3
Cagnetta F.	0.4
Bolchini F.C.**	1.0

* associazione INFN-Fe da settembre 2022
** associazione INFN-Mi da settembre 2022
*** contratto da firmare a ottobre 2022
**** associazione INFN-Pd da gennaio 2023

TOTALE FTE 12.4

CUPRUM-TTD project
INFN-Padua

PLANNED ACTIVITIES for 2023 and budget quotation (12 K€)

Item	What is needed	Estimated cost K€
In vitro studies to determine the percent of specific uptake and internalization in cells	Refrigerated shaker for incubating biological cultures	**7.5**
	^{64}Cu to radiolabel the developed Radiopharmaceuticals (2x10mCi)	**3.0**
	Consumables for cellular studies	**1.0**
Travels	Domestic travels Padua-Legnaro	**0.5**
TOTAL		**12**

Nessuna richiesta di servizi in sezione

Summary overall budget request CUPRUM FY2023

Sezioni / Lab	Missioni	Consumo/ Altri consumo	Trasporti	Manutenzione	Inventario	apparati	Sp- servizi	Tot. per sez/lab	FTE previsto
LNL	10.0	27.0				26.0		**63.0**	**4.8**
Fe	2.5	18.0						**20.5**	**4.0**
Pd	0.5	4.0			7.5			**12.0**	**1.5**
Mi	8.5	5.0	7.5	4.0				**25.0**	**2.1**
TOTALE	**16.5**	**52.0**	**15.0**	**4.0**		**18.0**		**120.5**	**12.4**

Budget request outlook CUPRUM-TTD FY2024 ~ 180 kEuro (circa 110 kEuro modulo automatico)
FY2025 ~ 70 kEuro

TOTAL BUDGET request (3yrs) ~ 370 kEuro

GRAZIE

CUPRUM-TTD project INFN-LNL

Item	What is needed	Estimated cost K€
○ ZnO/Ni powder pellets production for target processing investigations ○ Preparation of samples with SPS technique @ PV university and first attempts with MS technique @LNL	Equipment for target manufacturing and raw materials	**5.0**
	Chemical products for ZnO/Ni radiochemical separation	**5.0**
Manufacturing of first prototype ZnO/Ni targets	Nb backing + capsule procurement	**5.0**
	Gold foil for Cu target protecting layer	**10.0**
Equipment (lab. Furniture)	Muffola for ZnO recovery	**3.0**
	Hydraulic press for pellets preparation	**7.5**
	Quartz/borosilicate/Peek reactor vessels procurement	**7.5**
Upgrade inverted MS system	- dedicated vacuum chamber - Dedicated magnetic coil for cylindrical MS - Zn/ZnO target material - Cathode body for sputtering	**3.0** **5.0** **1.0** **1.0**
Travels	Domestic travels Padua-Legnaro Padua-Ferrara, Padua-Pavia + presentations nat./intern. Congresses	**10.0**
	TOTAL	**63.0**

CUPRUM-TTD project
INFN-Ferrara

Item	What is needed	Estimated cost K€
Early experiments on the proper separation and purification procedure using cold targets of ^{nat}ZnO and ^{nat}Ni	Consumables: solvents, glassware, chemical products to optimize the radiochemistry method. Materials to assess the quality control of the extracted radionuclide.	**16.0**
Service	Chemical analyses: ICP(OES) characterization @UNIFE	**2.0**
Travels	Domestic travels for meetings and experimental activity at the SCDCH (Negrar –VR) cyclotron unit	**2.5**
	TOTAL	**20.5**

CUPRUM-TTD project
INFN-Milano

PLANNED ACTIVITIES for 2023 and budget quotation (25.0 k€)

Item	What is needed	Estimated cost k€
. ^{nat}Ni, ^{59}Co, ^{nat}Cu – commercially . ^{64}Ni targets produced by LNL/UNIPV for testing at ARRONAX facility with alpha beams Spectrometry analyses of $^{67/64/61}Cu$ thus produced at the LASA lab	Targets purchase Spectrometry lab components	**5.0**
Radioactive transport service	Nantes-MI; Pavia-Milano routes	**7.5**
Travels	Domestic travels: Milano, Legnaro, Pavia, Verona International travels: Milano-ARRONAX for irradiations (2/3)	**8.5**
Mantainace	Nitrogen; Radiochemical Lab.; Filters hoods	**4.0**
	TOTAL	**25.0**