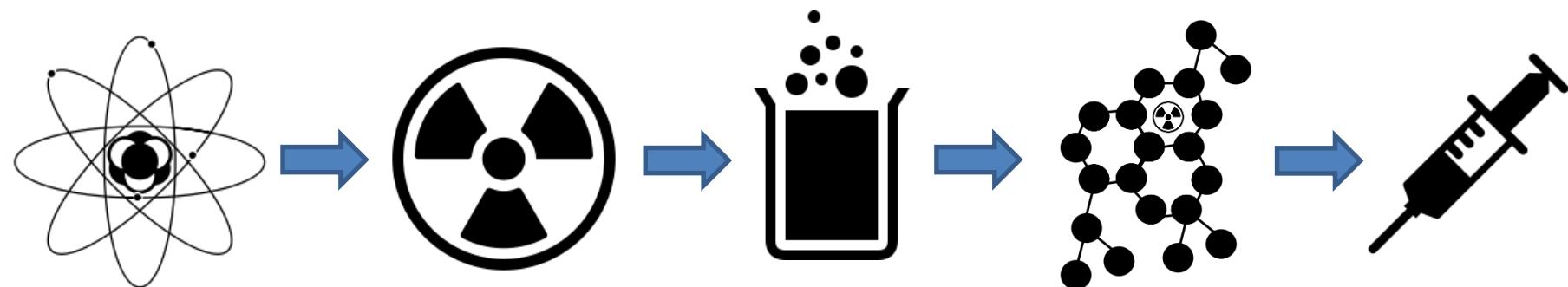


# The ISOLPHARM project: ISOL beams for medicine



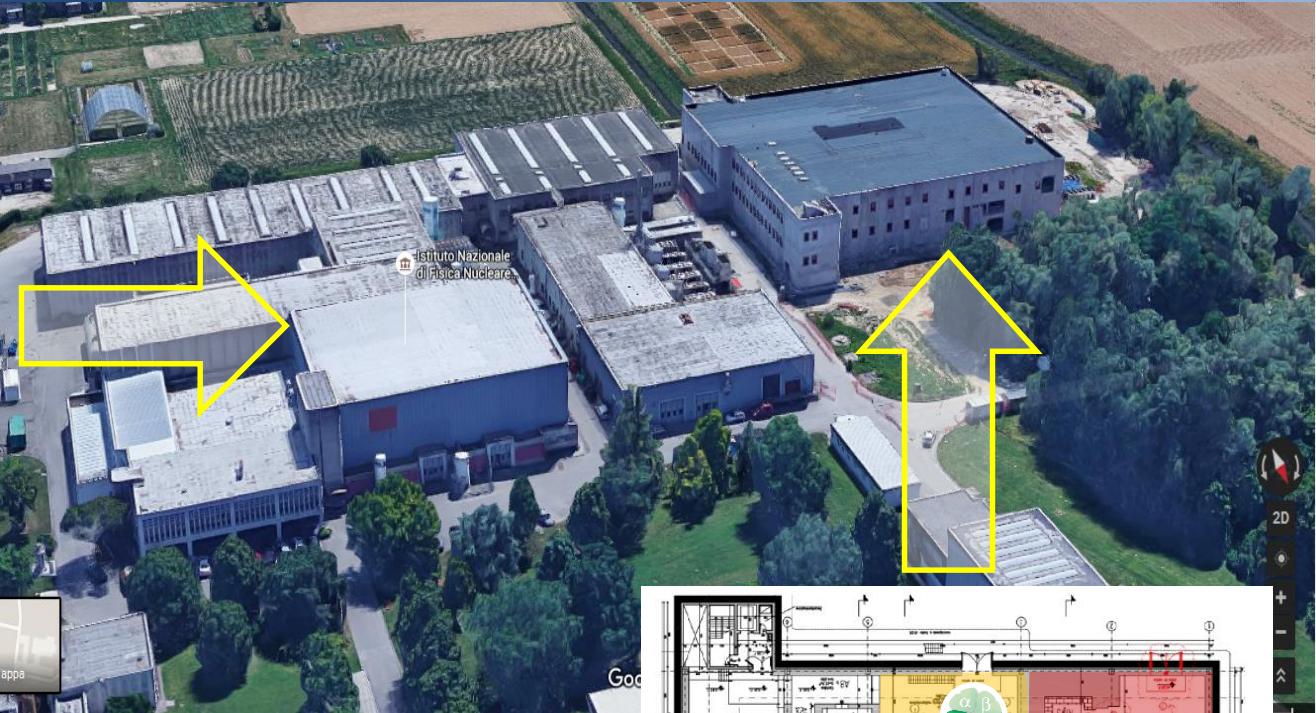
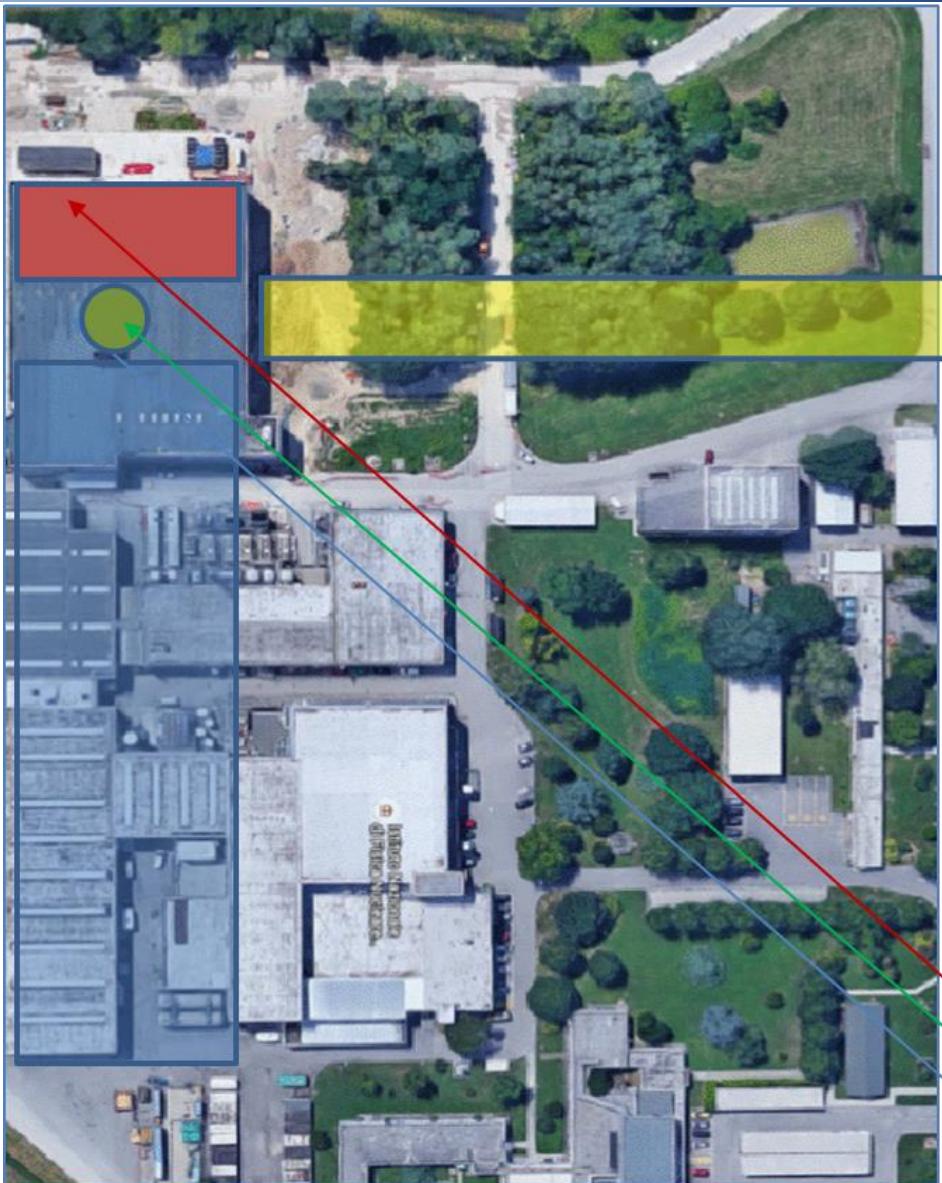
Alberto Andrigetto

Istituto Nazionale di Fisica Nucleare – Laboratori Nazionali di Legnaro - Legnaro (Italy)

- The SPES project a LNL: RIB for NP and applications
- SPES radionuclides for medicine: the ISOLPHARM project
- ISOLPHARM R&D activities
- ISOLPHARM\_Ag: a case study
- Summary



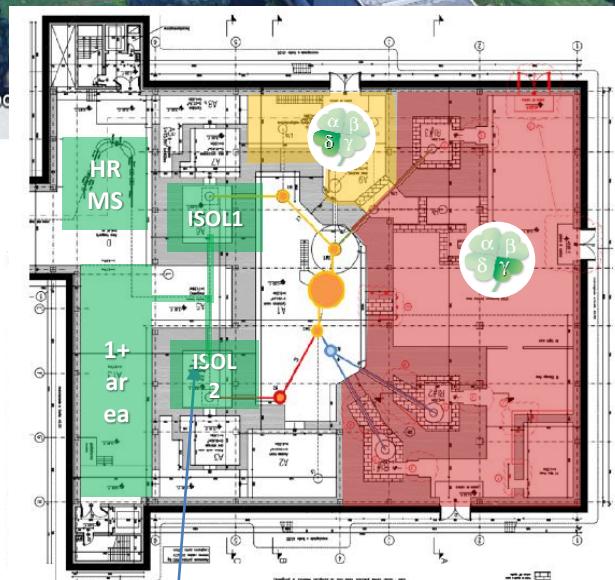
# The SPES project at LNL

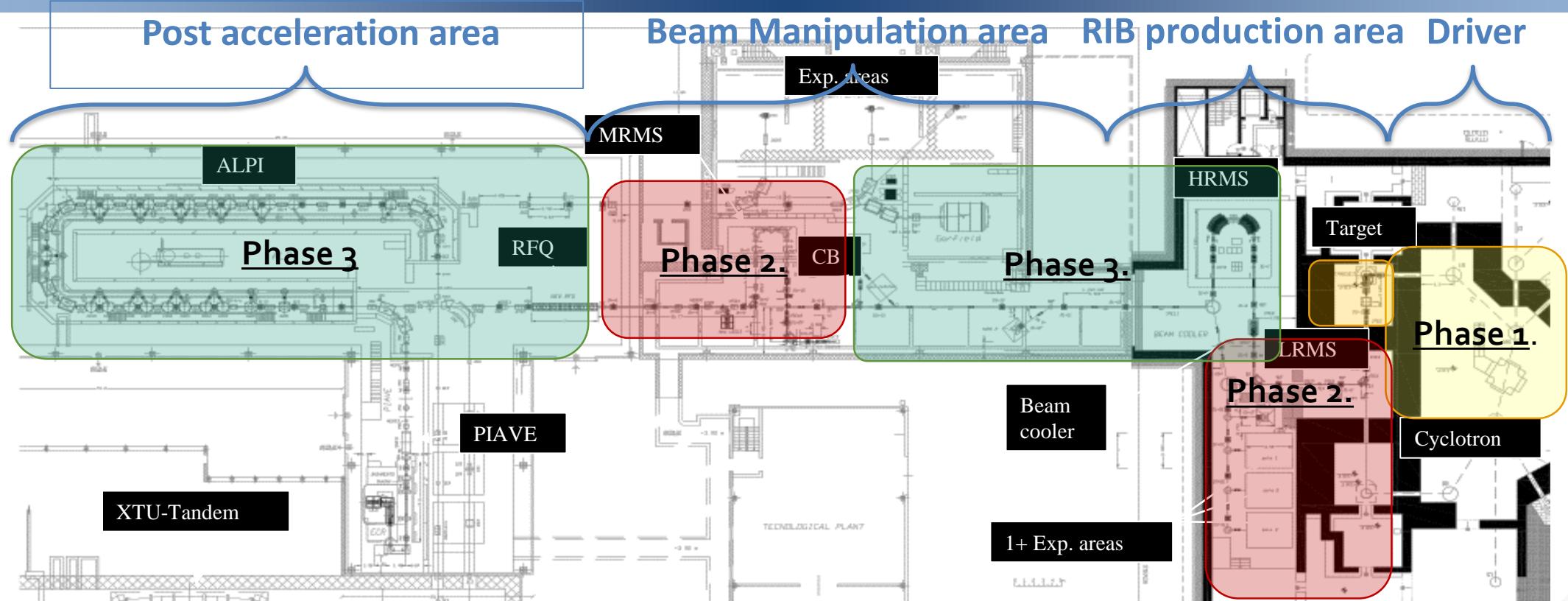


Project financed by INFN

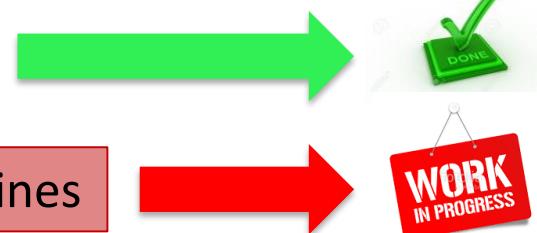
New infrastructure for:

- Application Facility
- Cyclotron
- RIB facility (2th generation ISOL)

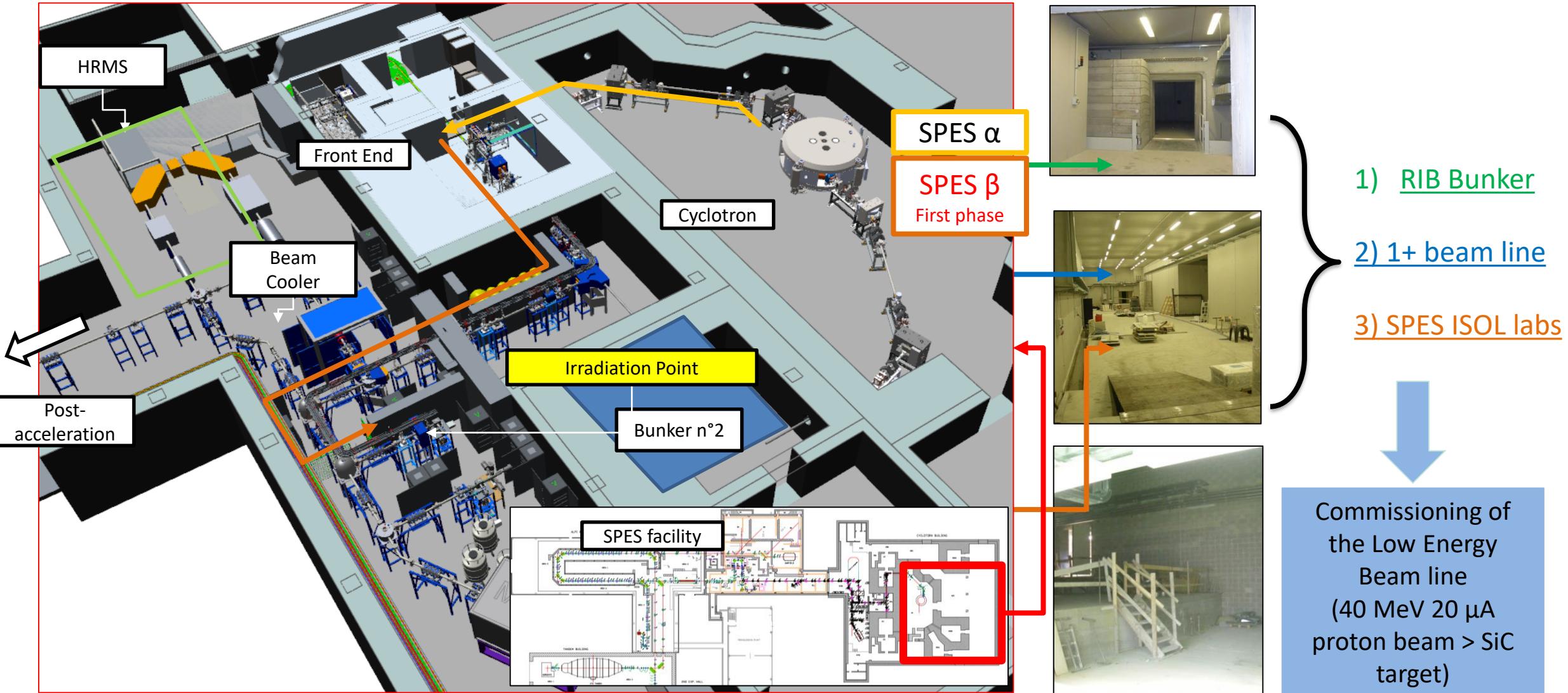




- **Phase 1.** - Building + First operation with the cyclotron
- **Phase 2.** - From C.B. to RFQ + SPES target, LRMS, 1+ Beam Lines
- **Phase 3.** - From the LRMS to the CB + rom RFQ to ALPI

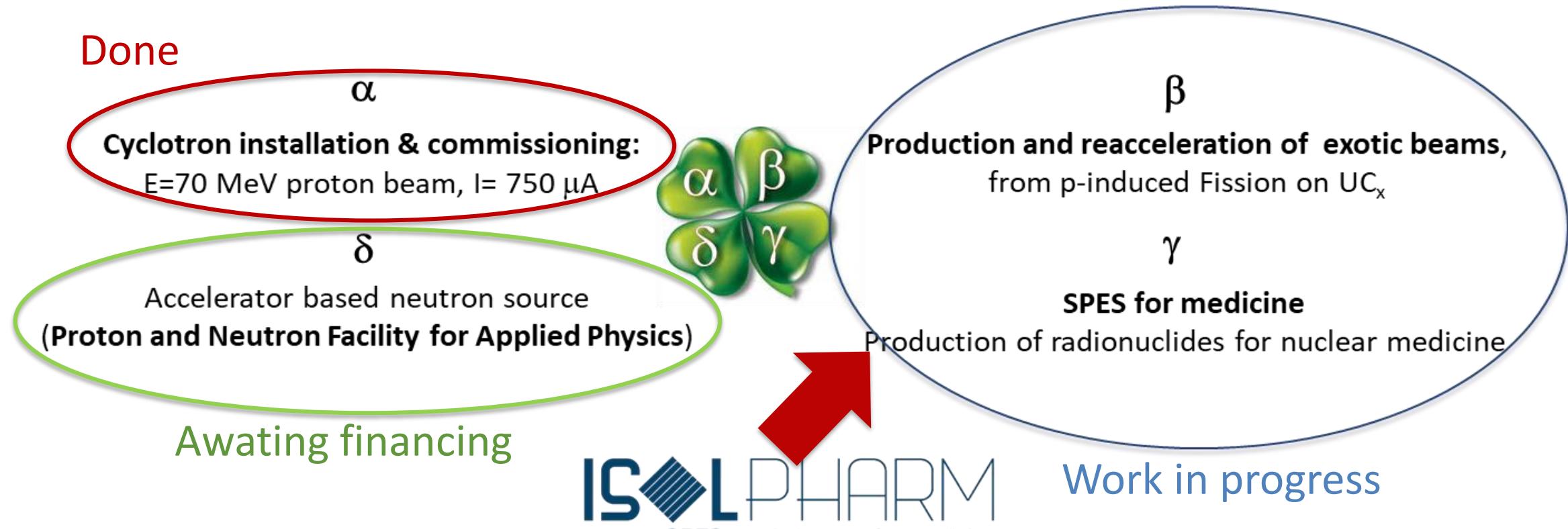


# The SPES beta: The 1+ RIB line



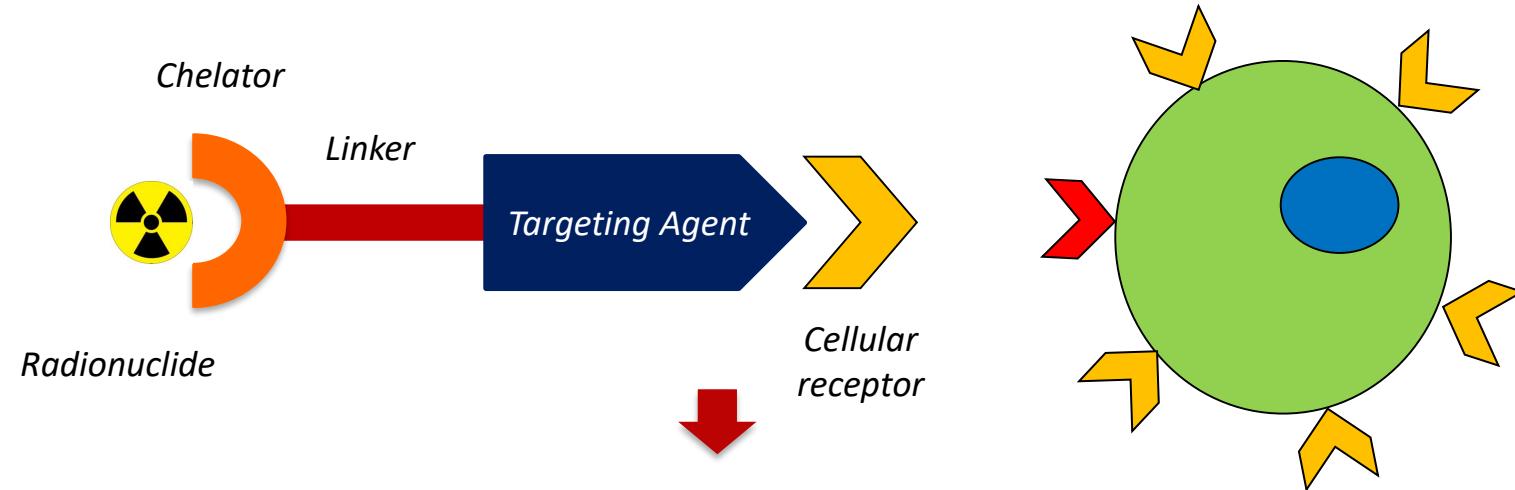
## ISOLPHARM:

Between the  $\beta$  and  $\gamma$  phase of the SPES project



**ISOLPHARM**  
SPES exotic beams for medicine

The main objective of the ISOLPHARM project is the production of carrier-free radionuclides for radiolabeling of bioactive molecules



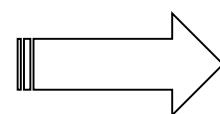
The radionuclide: Depending on the production method:



:

Radioisotopes present in pure form, free of dilution by stable isotope carriers

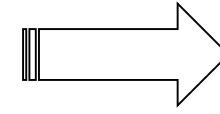
*Carrier-free radionuclides*



(high specific activity).

Radioisotopes diluted by non therapeutic atoms of the same element

*Carrier-added radionuclides*



(low specific activity).

**1 Cyclotrons**

- ✓ Radionuclides can be produced in big amounts
- ✓ Some High specific activity radionuclides can be produced if enriched targets are used, which are often very expensive
- ✗ Highly activated targets are produced and require processing for purification

**(3 Generators)****2 Nuclear reactors**

- ✓ Radionuclides for therapy can be produced in big amounts
- ✓ Parent nuclides for generators can be produced
- ✗ Radionuclides produced by direct reactions are often carrier added

Using accelerators, ISOL Methods:

**ISOLPHARM**

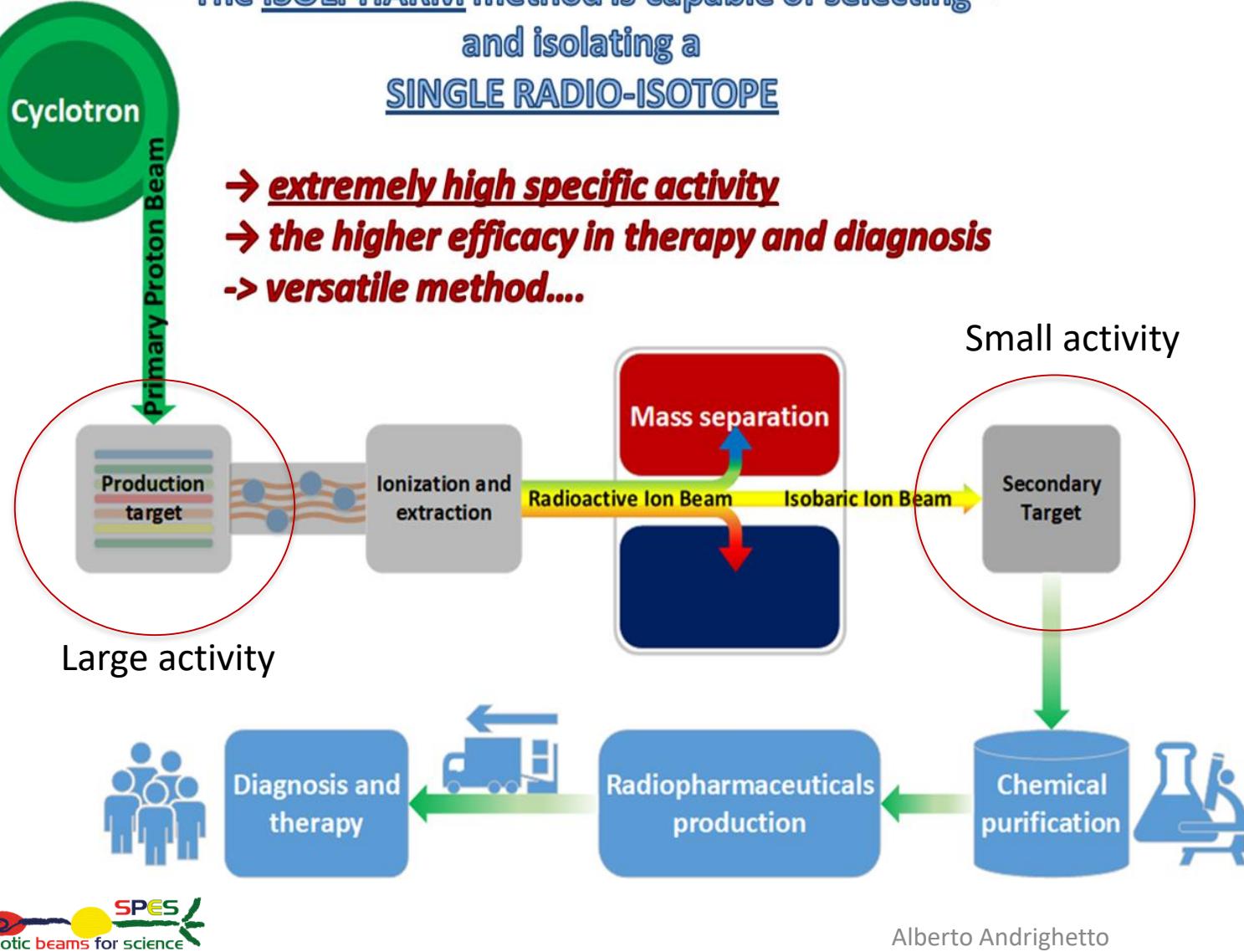


- ✓ Instrinsecally carrier-free radionuclides can be produced (**carrier free production**)
- ✓ Several radionuclides can be produced only by changing the mass separator settings (**versatility**)
- ✓ Designing specific targets a wide range of radionuclides can be produced (**new radionuclide for medicine application...**)
- ✗ Production yields are lower than those of cyclotrons and nuclear reactors

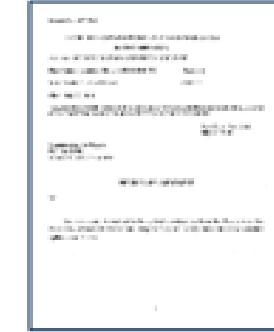
# The ISOLPHARM method

The ISOLPHARM method is capable of selecting  
and isolating a  
SINGLE RADIO-ISOTOPE

- extremely high specific activity
- the higher efficacy in therapy and diagnosis
- > versatile method....



### INFN PATENT



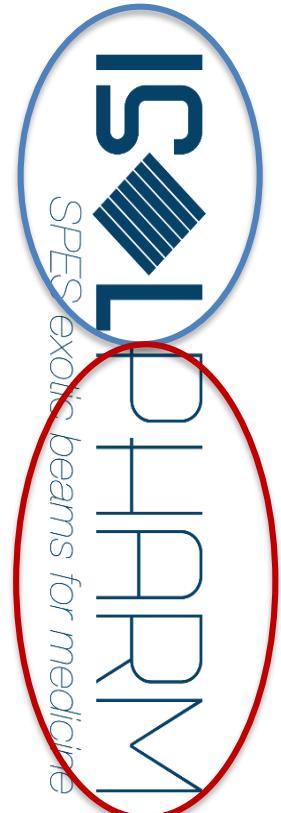
INFN PATENT	
Acknowledgement of receipt	
We hereby acknowledge receipt of the form for entry into the European phase (EPO as designated or elected Office) as follows:	
Submission number	452873
PCT application number	PCT/IB2014/067293
EP application number	14833237.2
Date of invent	28 July 2016
Examining Office	European Patent Office, The Hague
Your reference	IPI251EP00
Appln.	
Country	
Documents submitted	package-data.xml application-body.xml AMISPECPO-1.pdf/PCT/IB2014/067293-Extended claims sheet-0001.pdf (2 p.) CLMS-HWA.pdf/IPI251EP00_20160722_Amended claims sheet-0002.pdf (2 p.) CLMS-HWA-1.pdf/IPI251EP00_20160722_Amended claims Marked up.pdf (3 p.)
Submitted by	CH-Antonio Di Mandre 27529
Method of submission	Online
Date and time message received	28 July 2016, 14:05 (CEST)
Message Digest	D3FE0825204815ED01C51276A34D9B774A8
Acknowledgement of receipt - application number PCT/IB2014/067293	
Page 1 of 2	

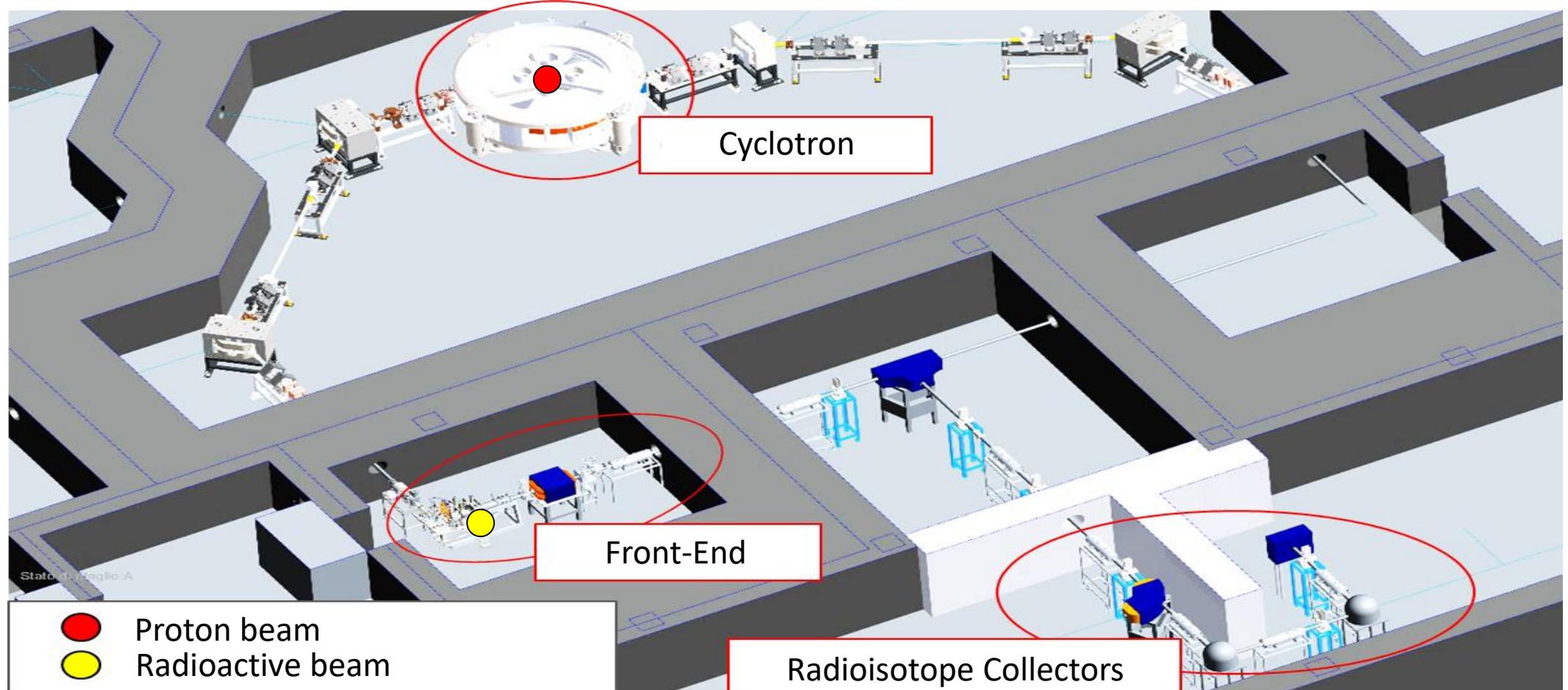
### PUBLISHED PAPERS



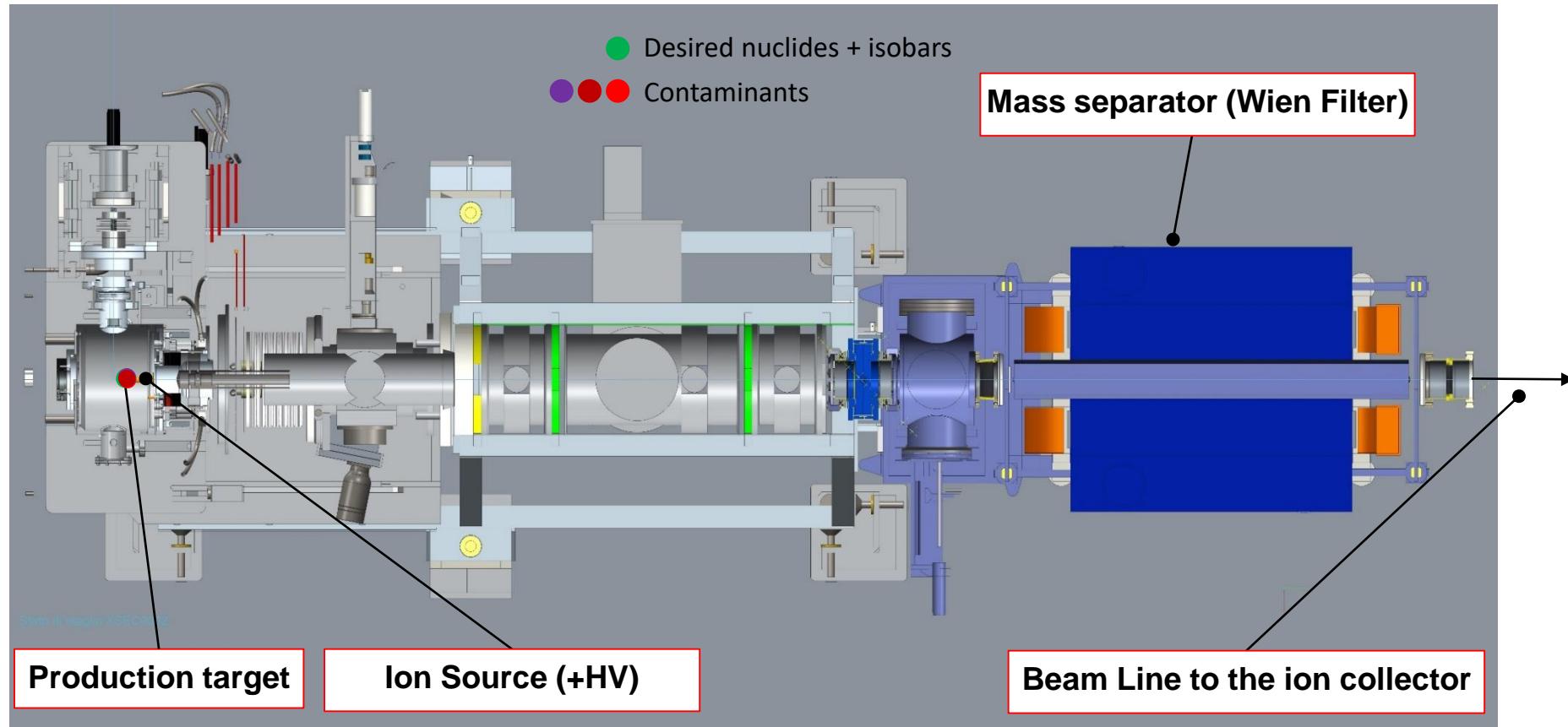
molecules

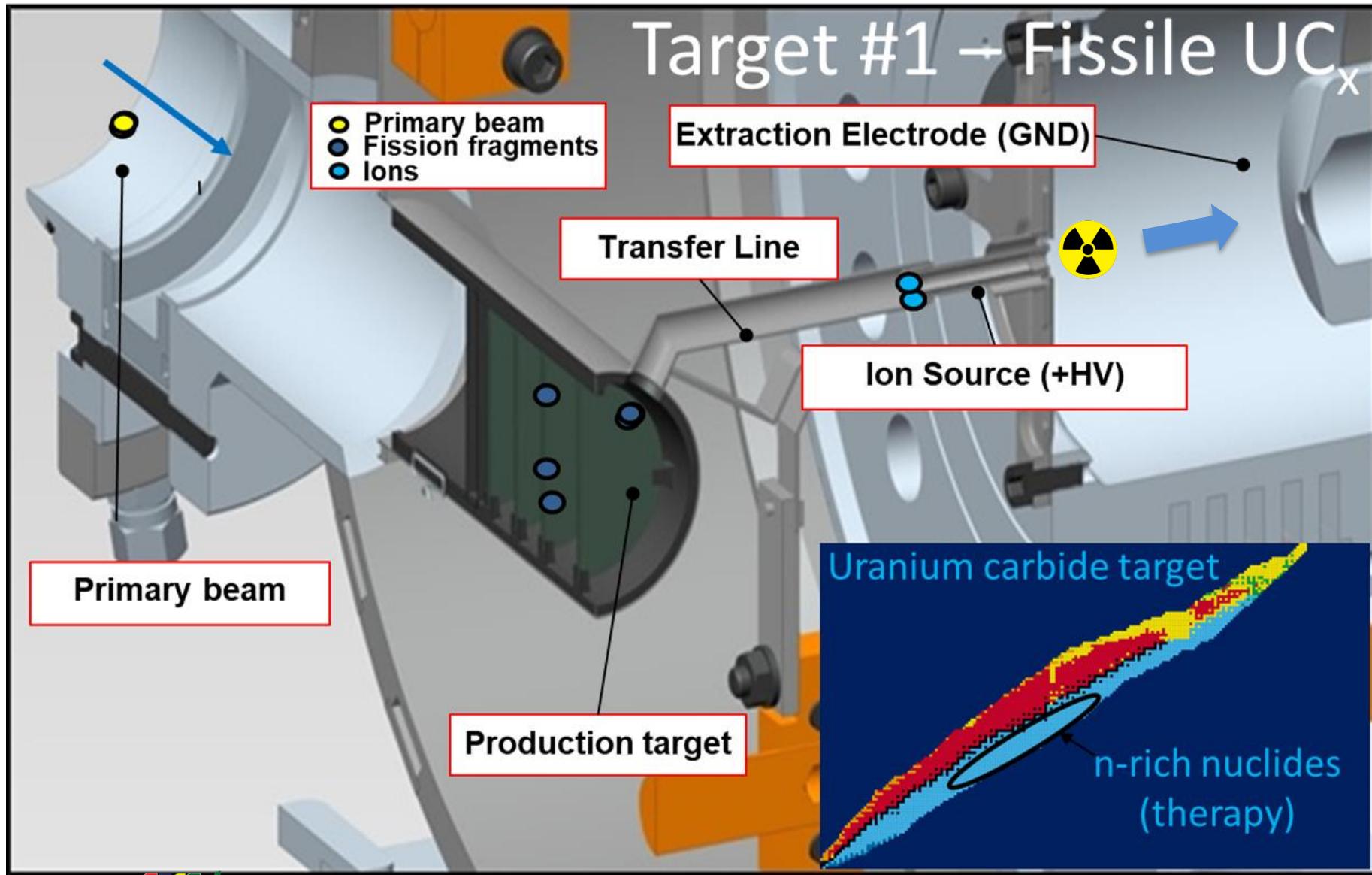
Early Evaluation of Copper Radioisotope Production at ISOLPHARM  
Francesca Benga <sup>1,2</sup>, Michele Ballal <sup>1,2</sup>, Chiara Favaretto <sup>1</sup>, Matteo Siviero <sup>1,2</sup>,  
Matteo Tocino <sup>1,2</sup>, Michele Caruso <sup>1,2</sup>, Stefano Corradi <sup>1</sup>, Alberto Andrigetto <sup>1</sup>,  
Valeria Di Marco <sup>1,2</sup>, Giovanna Mazzoni <sup>1,2</sup> and Nicola Rovida <sup>1</sup>

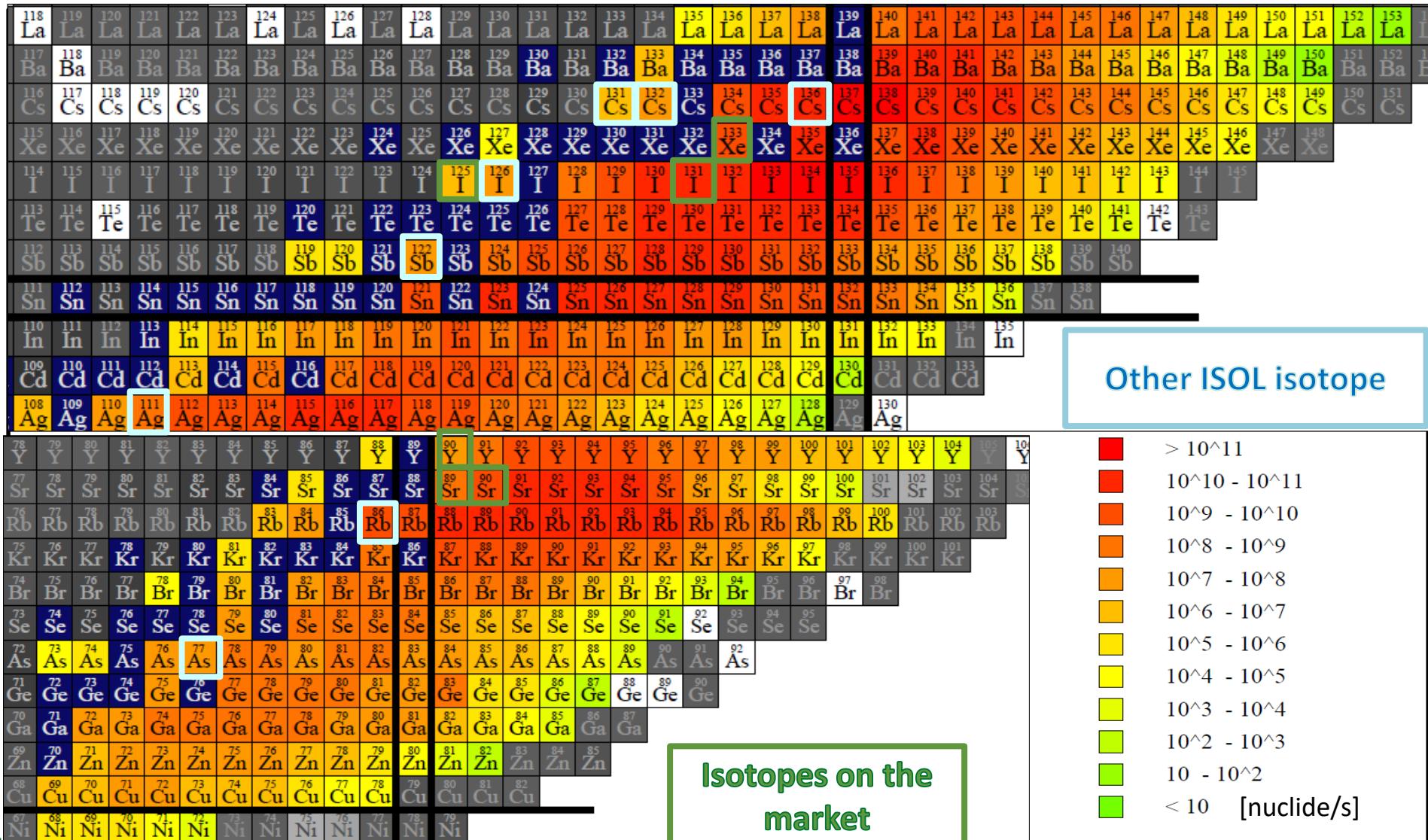


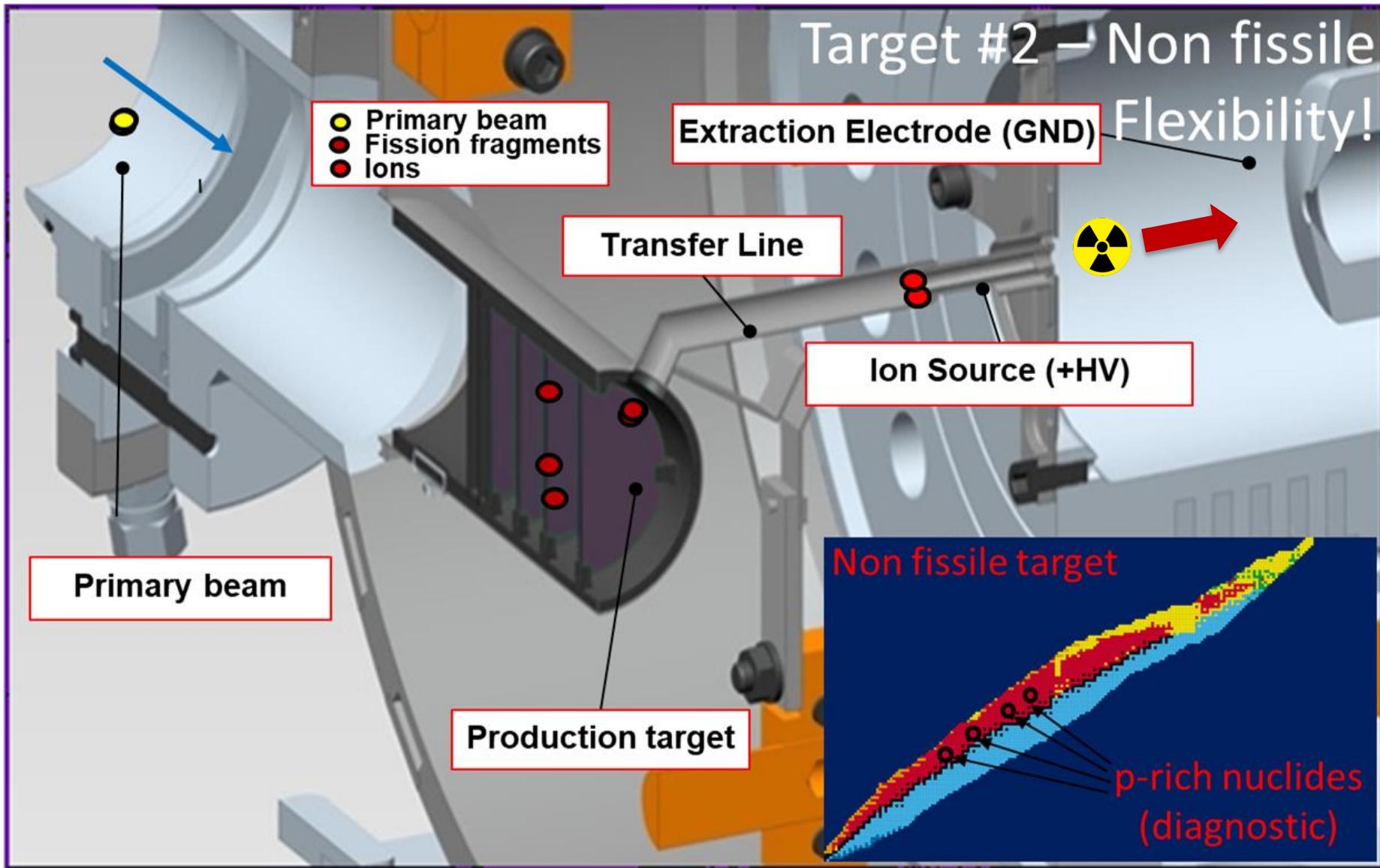


# Mass separation



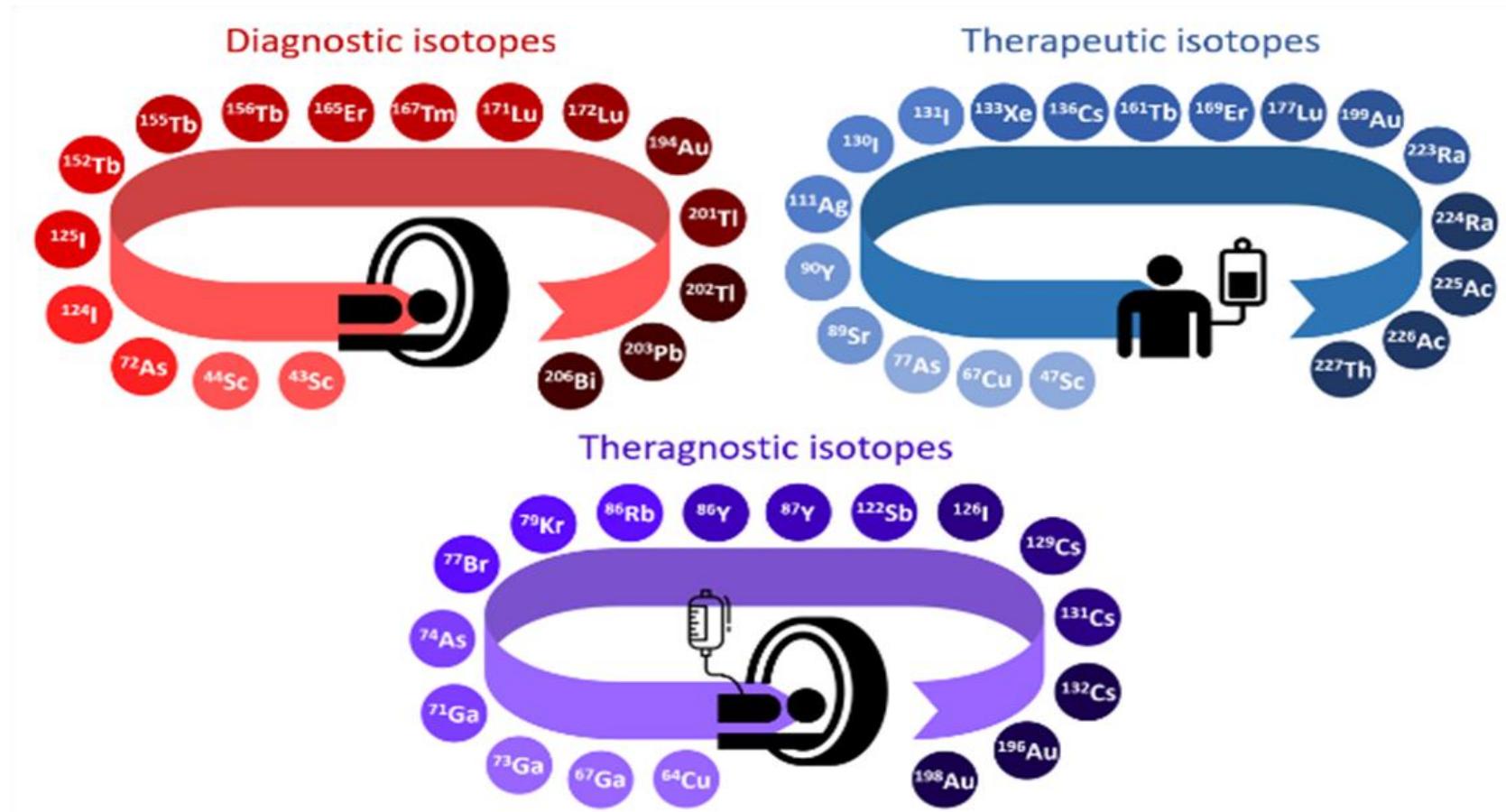






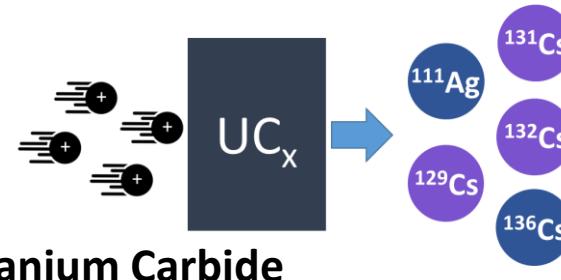
# ISOLPHARM:

## Radionuclides that could be produced at LNL



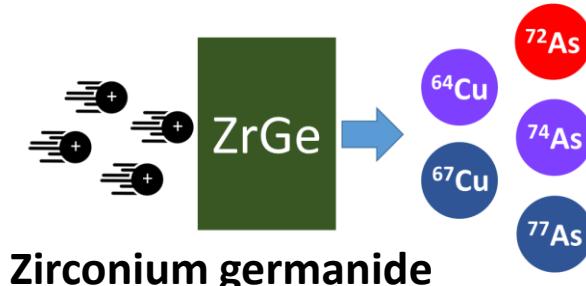
## Target concepts currently under investigation and related innovative isotope production:

### $\text{UC}_x$ target (Operation temperature: 2200°C)



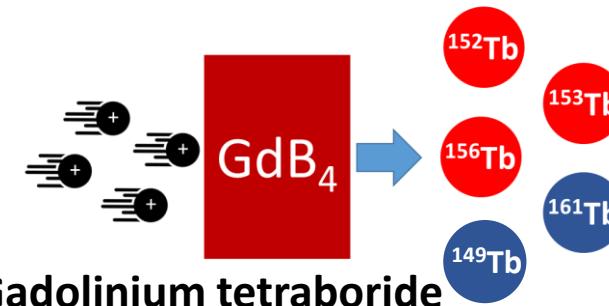
Nuclear reactions studied	Designed	Tested

### $\text{ZrGe}$ target (Operation temperature: 1800°C)



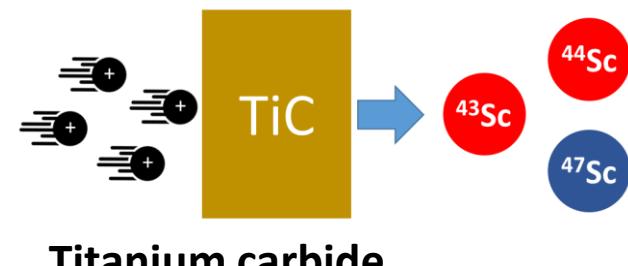
Nuclear reactions studied	Designed	Tested

### $\text{GdB}_4$ target (Operation temperature: 2000°C)



Nuclear reactions studied	Designed	Tested

### $\text{TiC}$ target (Operation temperature: 2000°C)

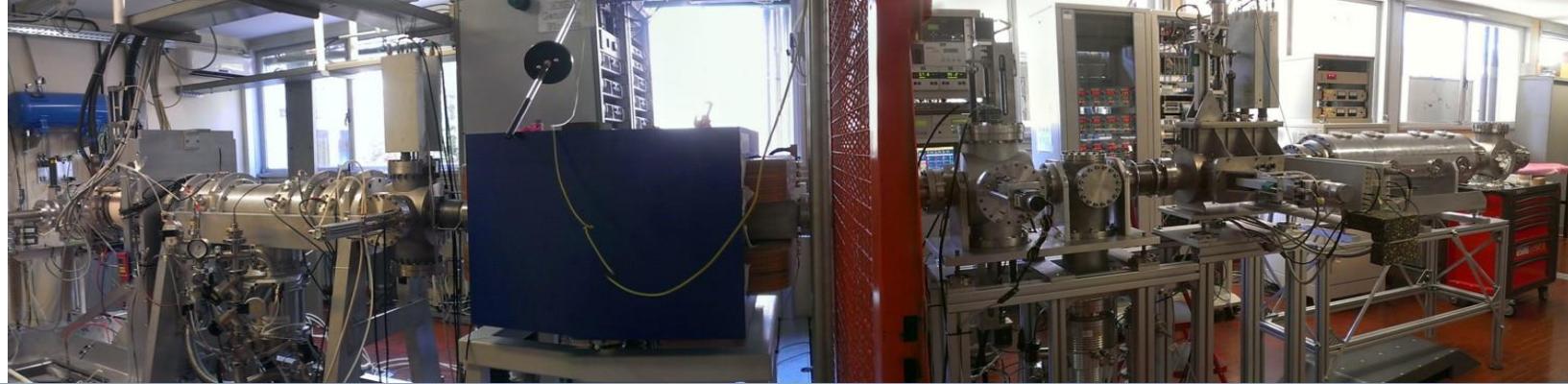


Nuclear reactions studied	Designed	Tested

# The ISOLPHARM R&D (so far...)

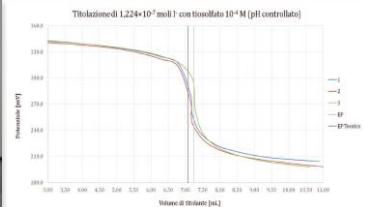
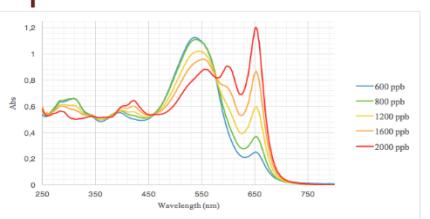
## Beam deposition @ LNL

Simulation of the process using stable ion beams thanks to the SPES test bench (front-end off-line)

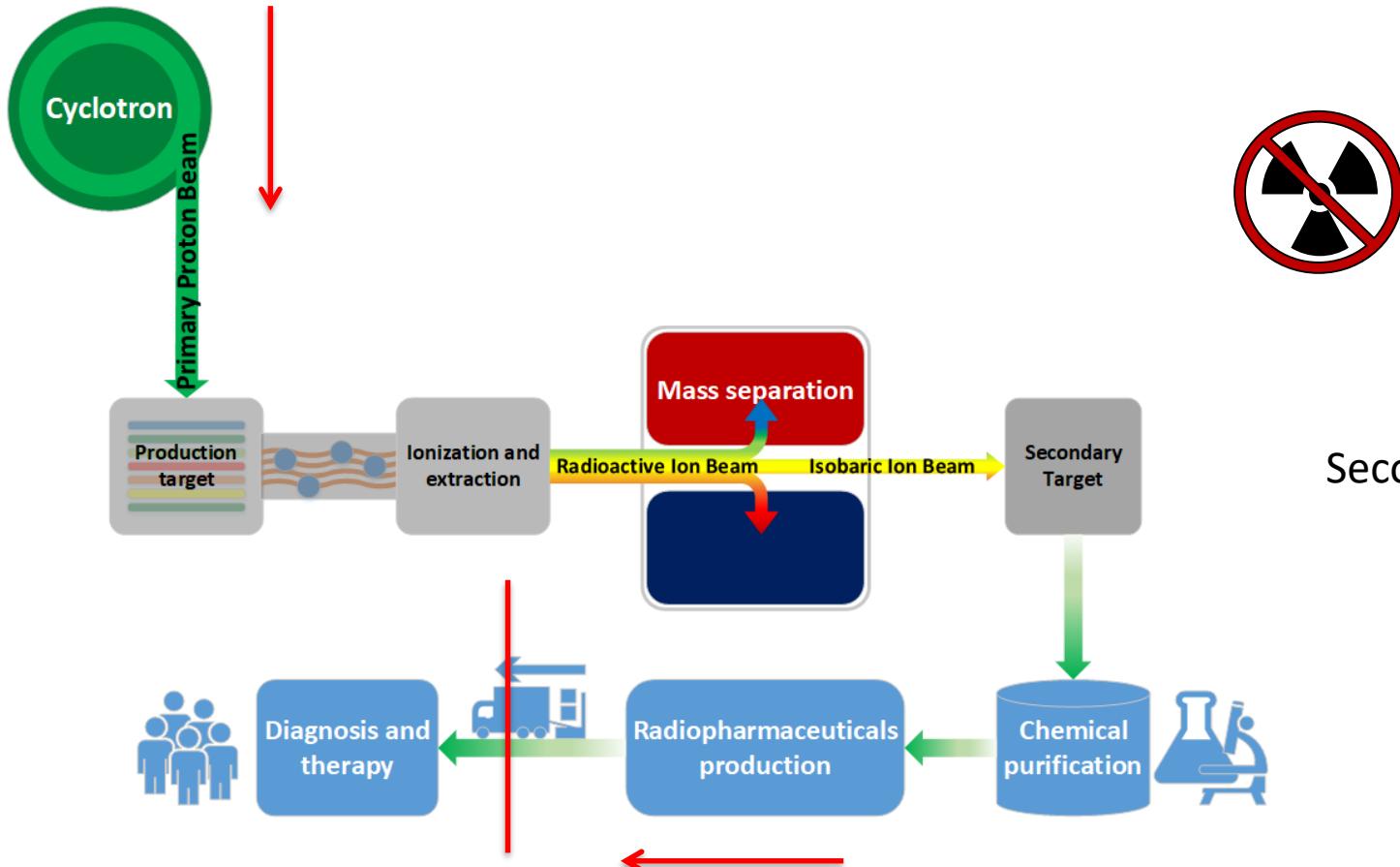


## Activities @ UNIPD-DSF-DSC

Extraction from the substrate, quantification and chemical separation of the deposited element



# Experimental activities: overview



## Step 1

The cyclotron commissioning

## Step 2

Production targets development

## Step 3

Ion beams production

## Step 4

Secondary targets development and ions recovery

## Step 5

Purification processes development

## Step 6

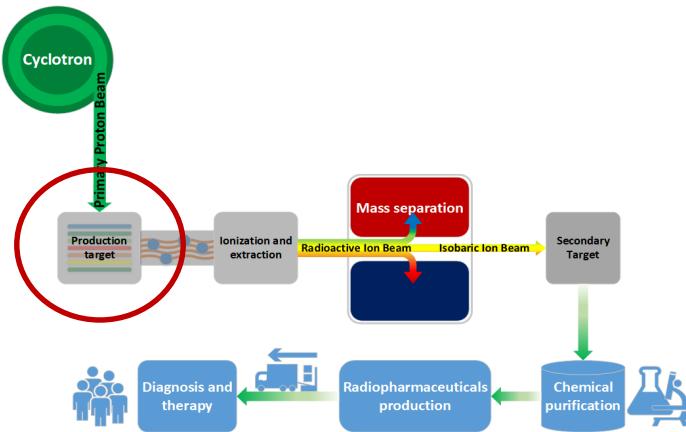
Radiolabeling studies



# The primary target

## The production targets

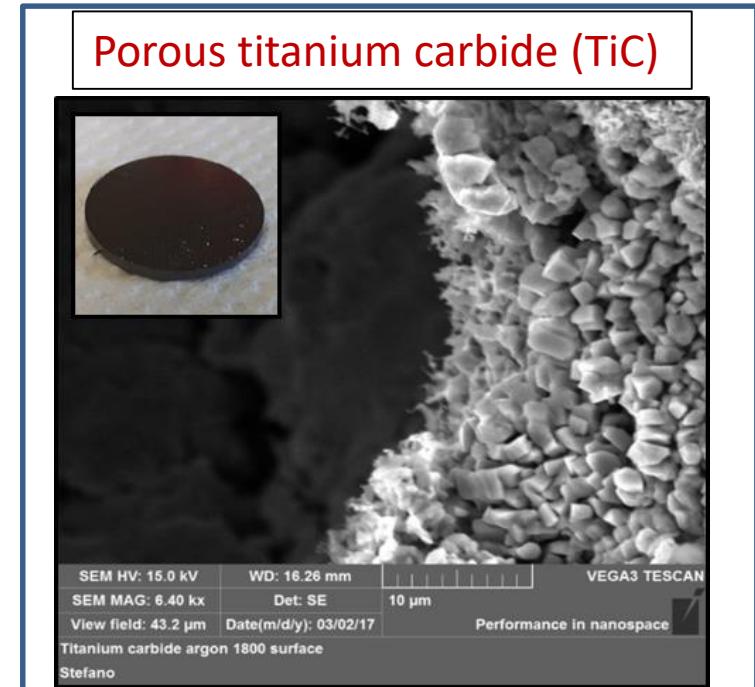
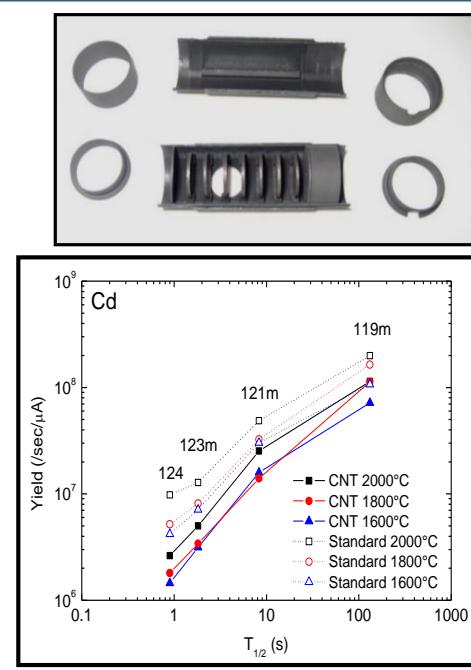
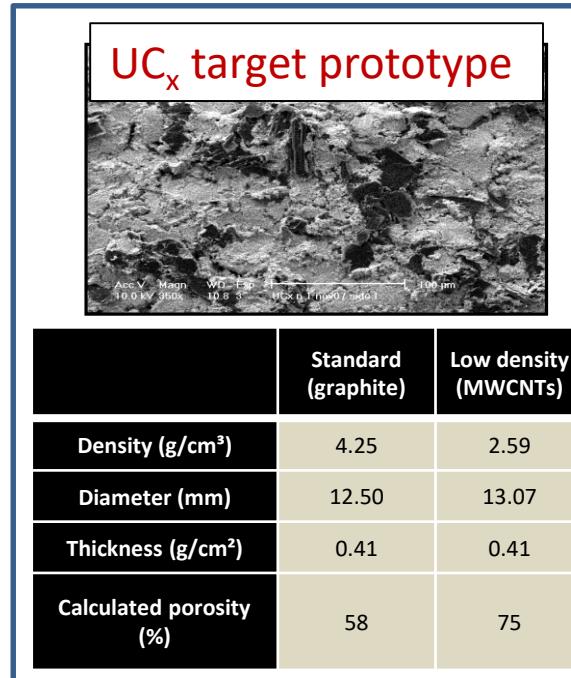
UC<sub>x</sub> target already developed and tested on-line!



Other targets under development for specific radionuclides production:

ZrGe: <sup>64</sup>Cu, <sup>67</sup>Cu

TiC: <sup>43</sup>Sc, <sup>44</sup>Sc, <sup>47</sup>Sc



SPES UC <sub>x</sub> target production, 40 MeV 200 μA PPB										
	<sup>111</sup> Ag		<sup>129</sup> Cs		<sup>131</sup> Cs		<sup>132</sup> Cs		<sup>136</sup> Cs	
Time	Produced activity		Produced activity		Produced activity		Produced activity		Produced activity	
[days]	[Bq]	[Ci]	[Bq]	[mCi]	[Bq]	[mCi]	[Bq]	[mCi]	[Bq]	[mCi]
0.5	9.46E+09	0.26	1.14E+06	0.03	4.30E+06	0.12	2.69E+07	0.73	1.30E+09	35.22
1	1.92E+10	0.52	2.02E+06	0.05	8.45E+06	0.23	5.24E+07	1.42	2.57E+09	69.52
1.5	2.85E+10	0.77	2.70E+06	0.07	1.24E+07	0.34	7.66E+07	2.07	3.81E+09	102.94
2	3.74E+10	1.01	3.22E+06	0.09	1.63E+07	0.44	9.96E+07	2.69	5.01E+09	135.49
3	5.40E+10	1.46	3.94E+06	0.11	2.36E+07	0.64	1.42E+08	3.83	7.33E+09	198.07
4	6.92E+10	1.87	4.37E+06	0.12	3.04E+07	0.82	1.80E+08	4.86	9.53E+09	257.44
5	8.29E+10	2.24	4.62E+06	0.12	3.68E+07	0.99	2.14E+08	5.79	1.16E+10	313.75

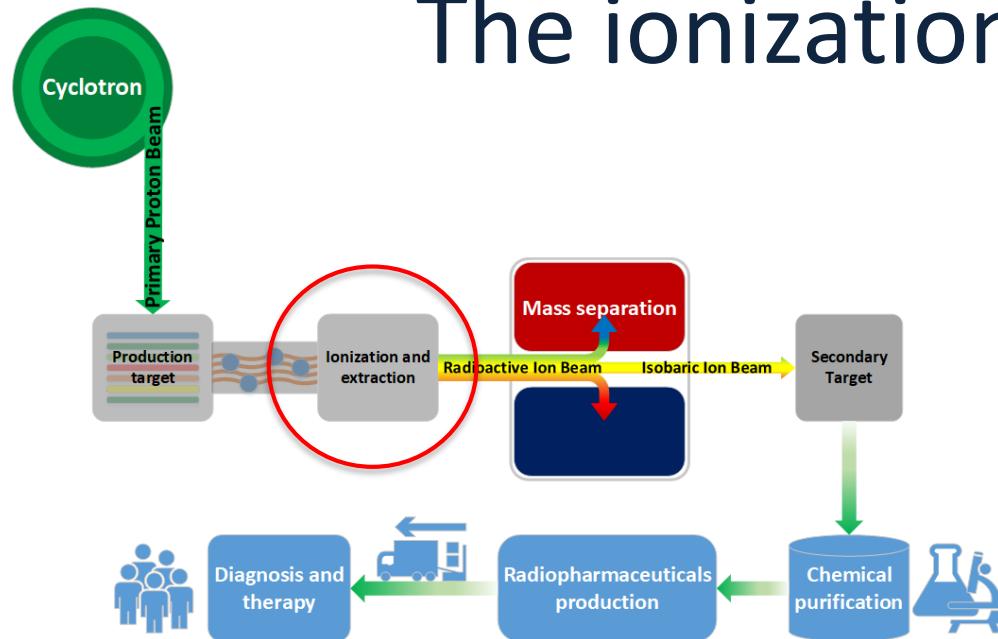
ZrGe target (100 μA, 70 MeV protons)										
	<sup>64</sup> Cu production (t <sub>1/2</sub> : 61,83 h)					<sup>67</sup> Cu production (t <sub>1/2</sub> : 61,83 h)				
Time	Activity			Nuclei		Activity			Nuclei	
[days]	[Bq]	[Ci]	[#]	[#]	[#]	[Bq]	[Ci]	[#]	[Bq]	[mCi]
0.5	2.66E+10	0.72	1.75E+15	2.37E+08	6.40	7.61E+13				
1	4.03E+10	1.09	2.66E+15	4.44E+08	11.99	1.43E+14				
1.5	4.75E+10	1.28	3.13E+15	6.24E+08	16.87	2.01E+14				
2	5.12E+10	1.38	3.38E+15	7.82E+08	21.15	2.52E+14				
3	5.42E+10	1.46	3.57E+15	1.04E+09	28.14	3.35E+14				
4	5.50E+10	1.49	3.62E+15	1.24E+09	33.49	3.99E+14				
5	5.52E+10	1.49	3.64E+15	1.39E+09	37.58	4.47E+14				

GdB <sub>4</sub> target (100 μA 70 MeV PPB)										
	<sup>149</sup> Tb production (t <sub>1/2</sub> : 4.12 h)		<sup>152</sup> Tb production (t <sub>1/2</sub> : 17.5)		<sup>155</sup> Tb production (t <sub>1/2</sub> : 5.32 d)		<sup>161</sup> Tb production (t <sub>1/2</sub> : 6.91d)			
Time	Activity		Nuclei		Activity		Nuclei		Activity	
[days]	[Bq]	[Ci]	[#]	[Bq]	[Ci]	[#]	[Bq]	[Ci]	[#]	[#]
0.5	3.16E+10	0.85	6.76E+14	4.26E+11	11.51	3.87E+16	1.43E+11	3.86	9.48E+16	8.46E+08
1	3.58E+10	0.97	7.67E+14	6.92E+11	18.70	6.29E+16	2.77E+11	7.49	1.84E+17	1.66E+09
1.5	3.64E+10	0.98	7.79E+14	8.57E+11	23.17	7.79E+16	4.02E+11	10.88	2.67E+17	2.43E+09
2	3.65E+10	0.99	7.80E+14	9.60E+11	25.95	8.73E+16	5.20E+11	14.06	3.45E+17	3.16E+09
3	3.65E+10	0.99	7.81E+14	1.06E+12	28.75	9.67E+16	7.33E+11	19.82	4.86E+17	4.52E+09
4	3.65E+10	0.99	7.81E+14	1.10E+12	29.83	1.00E+17	9.21E+11	24.89	6.11E+17	5.75E+09
5	3.65E+10	0.99	7.81E+14	1.12E+12	30.25	1.02E+17	1.09E+12	29.33	7.20E+17	6.86E+09

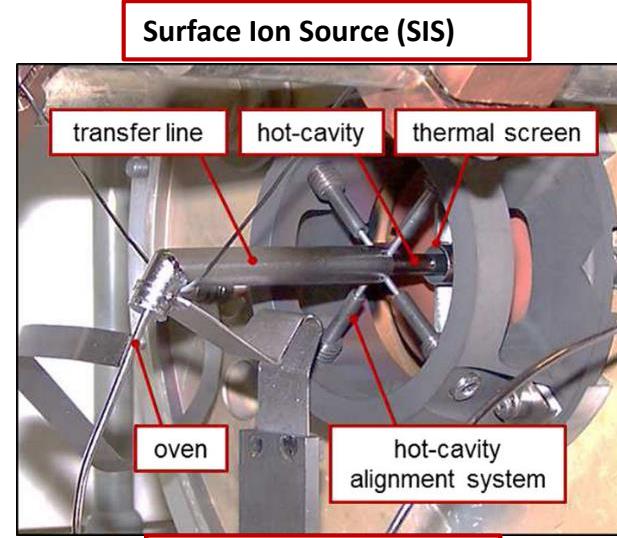
TiC target (200 μA 40 MeV PPB)												
	<sup>43</sup> Sc production (t <sub>1/2</sub> : 3.89 h)					<sup>44</sup> Sc production (t <sub>1/2</sub> : 3.97 h)					<sup>47</sup> Sc production (t <sub>1/2</sub> : 3.35 d)	
Time	Activity			Nuclei		Activity			Nuclei		Activity	
[days]	[Bq]	[Ci]	[#]	[#]	[#]	[Bq]	[Ci]	[#]	[#]	[#]	[Bq]	[Ci]
0.5	5.70E+10	1.54	1.15E+15	2.64E+11	7.14	5.37E+15	2.48E+10	0.67	1.04E+16			
1	6.37E+10	1.72	1.29E+15	3.25E+11	8.78	6.61E+15	4.72E+10	1.28	1.97E+16			
1.5	6.45E+10	1.74	1.30E+15	3.57E+11	9.65	7.26E+15	6.74E+10	1.82	2.81E+16			
2	6.46E+10	1.75	1.30E+15	3.83E+11	10.34	7.79E+15	8.56E+10	2.31	3.57E+16			
3	6.46E+10	1.75	1.31E+15	4.24E+11	11.45	8.62E+15	1.17E+11	3.16	4.87E+16			
4	6.46E+10	1.75	1.31E+15	4.55E+11	12.28	9.25E+15	1.42E+11	3.84	5.93E+16			
5	6.46E+10	1.75	1.31E+15	4.78E+11	12.91	9.72E+15	1.63E+11	4.40	6.78E+16			

Calculations performed with FLUKA (compared also with other models such as BIC, BERT etc..)

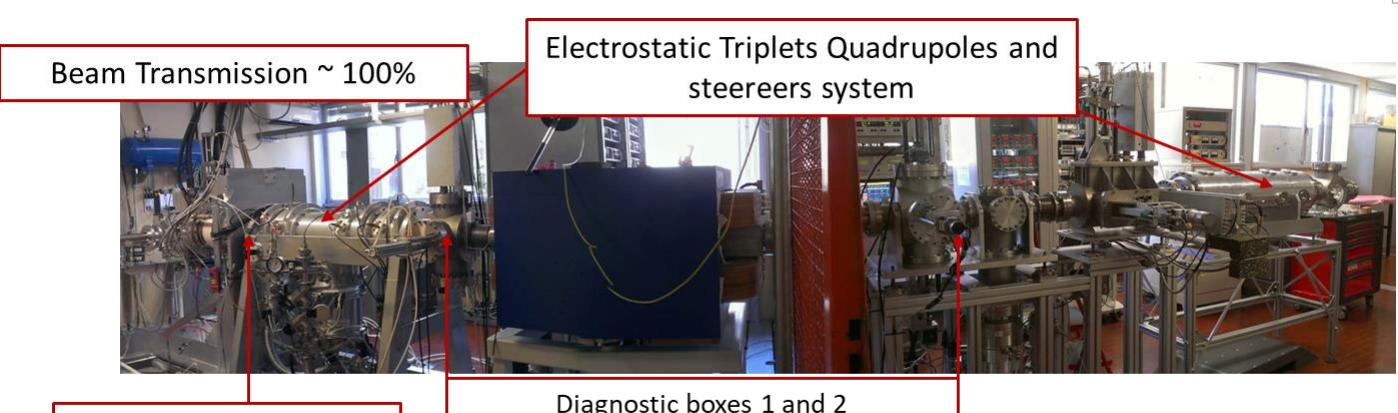
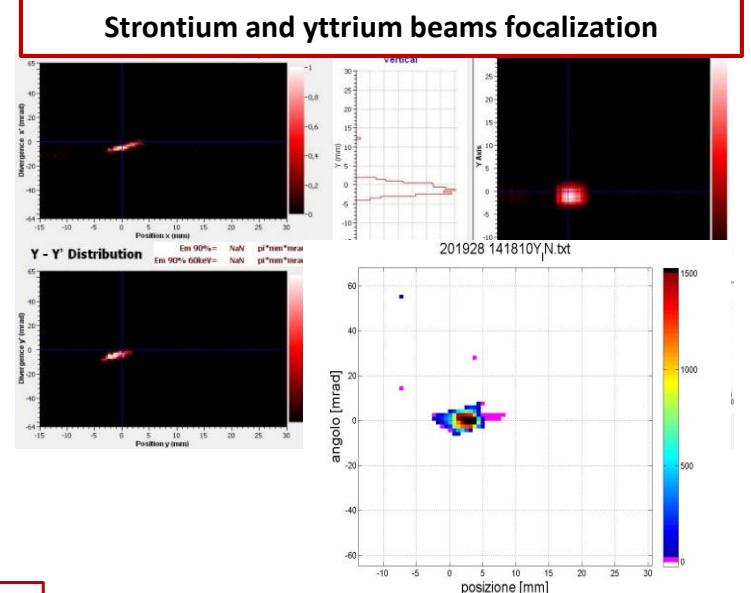
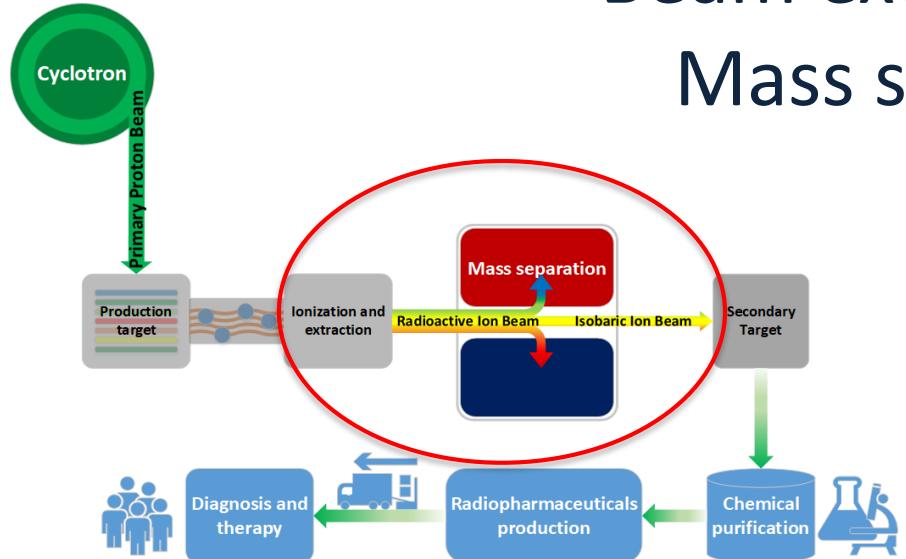
## The ionization source

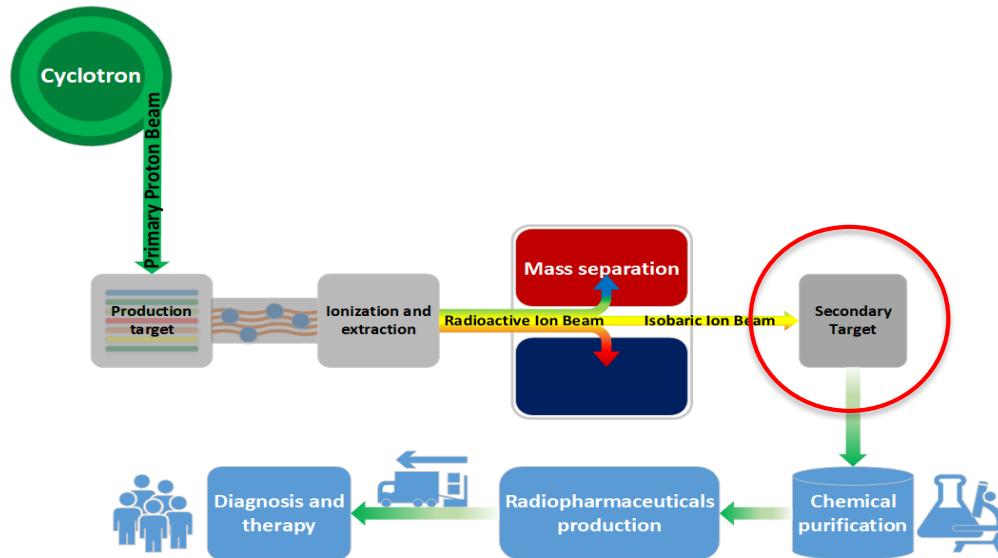


Ionized element	Desired radionuclide	Ionization source	Efficiency
Sr	$^{89}\text{Sr}$ , $^{90}\text{Sr}/^{90}\text{Y}$	SIS	~ 20 %
Y	$^{90}\text{Y}$	PIS	~ 1 %
I	$^{125}\text{I}$ , $^{126}\text{I}$ and $^{131}\text{I}$	PIS	~ 20 %
Cu	$^{64}\text{Cu}$ , $^{67}\text{Cu}$	PIS	~ 10 %
Ag	$^{111}\text{Ag}$	PIS	~ 15 %



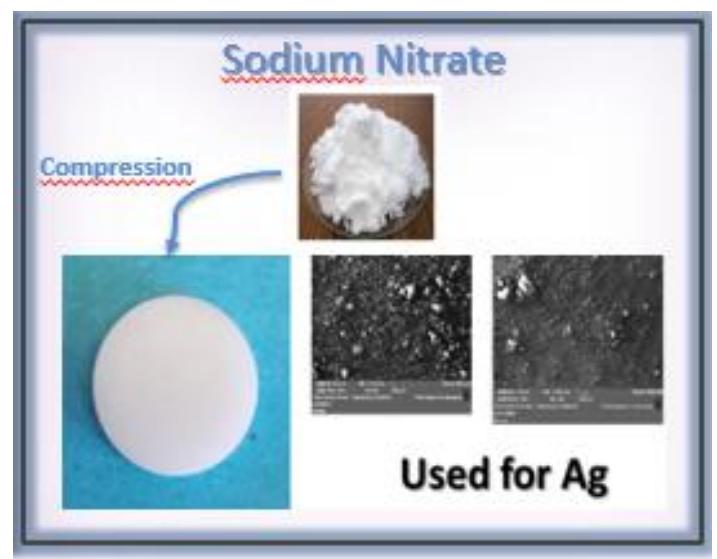
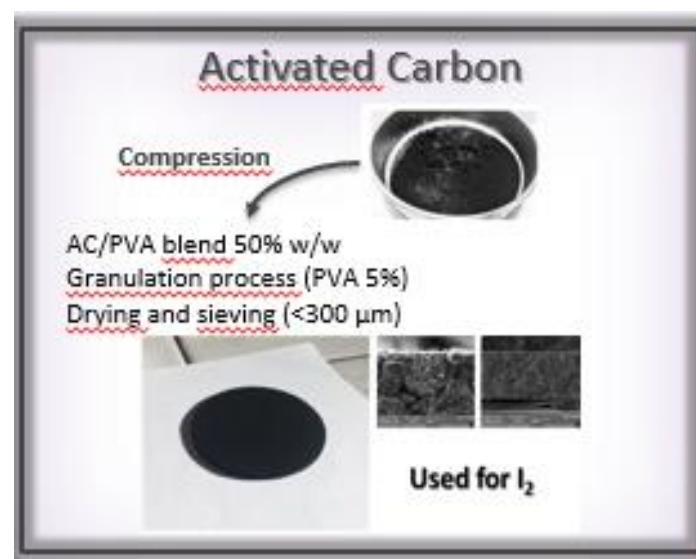
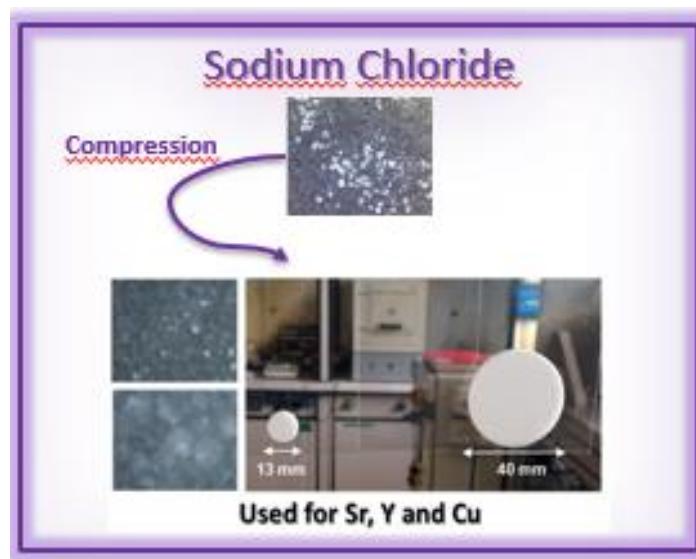
## Beam extraction and Mass separation



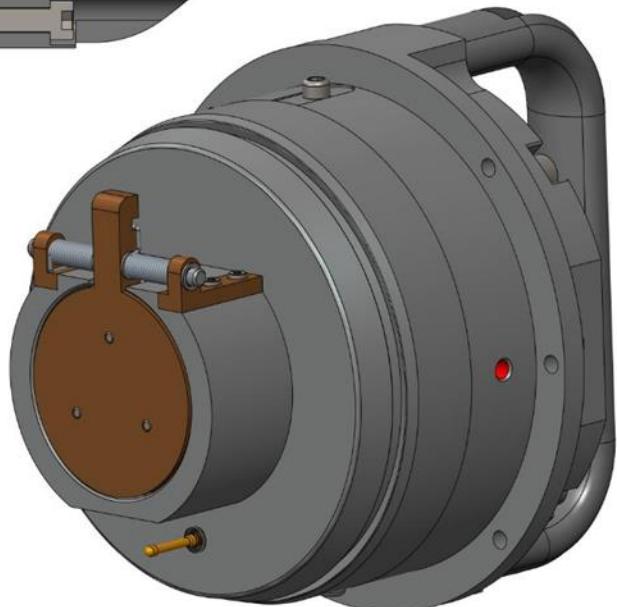
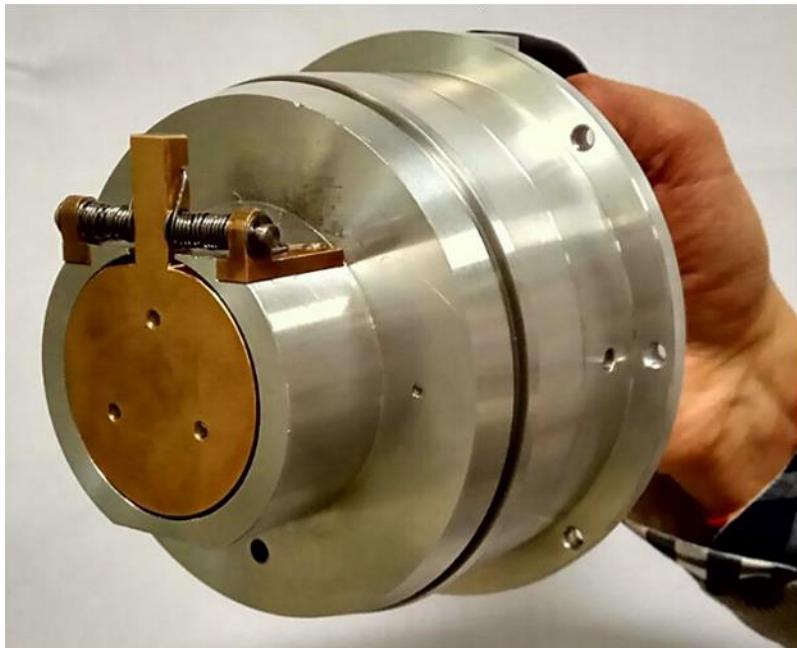
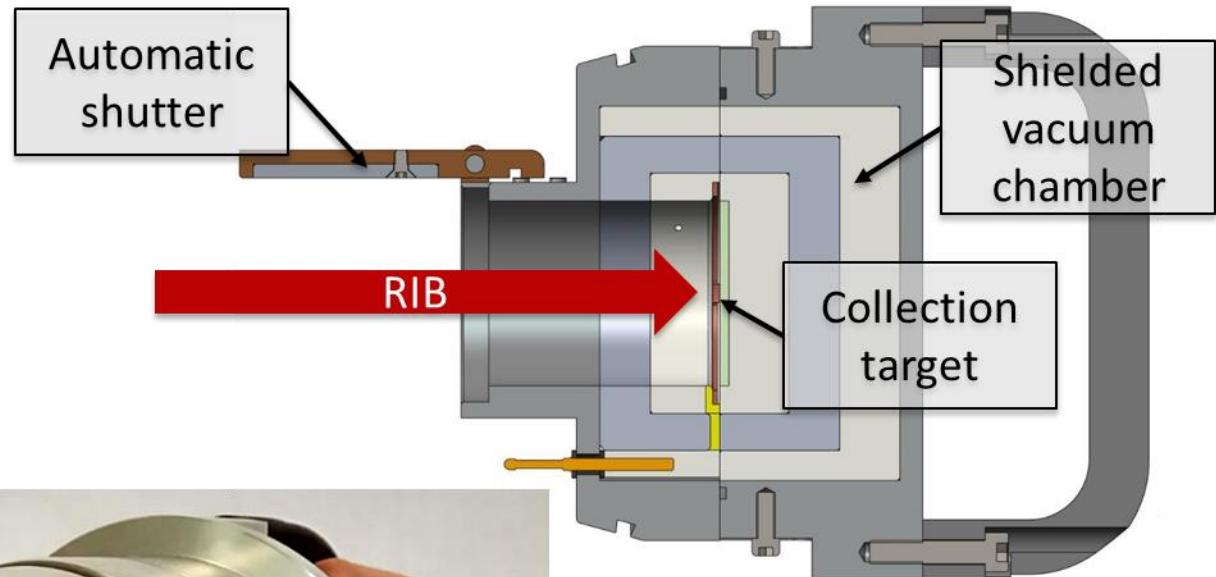


## Secondary target requirements:

1. Chemical compatibility with the element
2. Absence of metal contaminants
3. No incompatibilities with the production of a radiopharmaceutical for human administration
4. No interference with purification processes

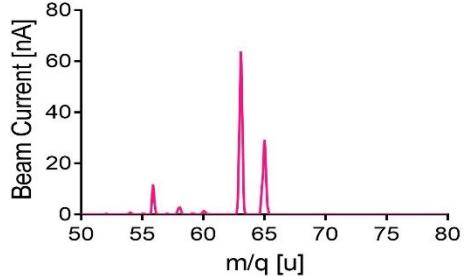


# The *ion collector*

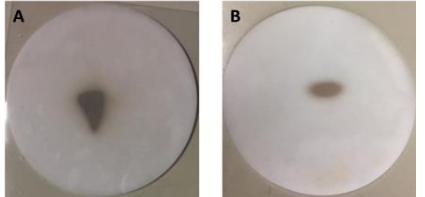
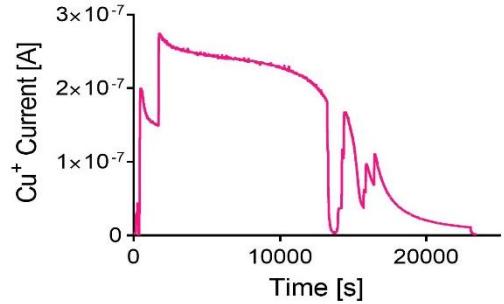


## Copper beams

**1)  $^{63}\text{Cu}$  and  $^{65}\text{Cu}$  identification  
(69.17% and 30.83%)**

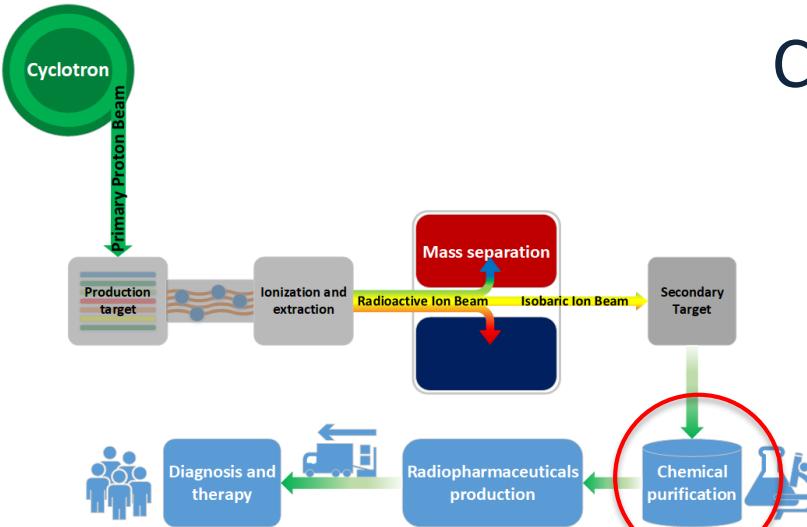


**2)  $^{63}\text{Cu}$  deposition**

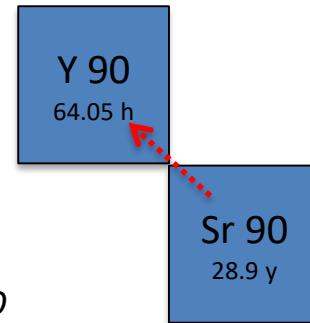
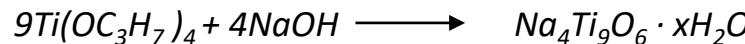
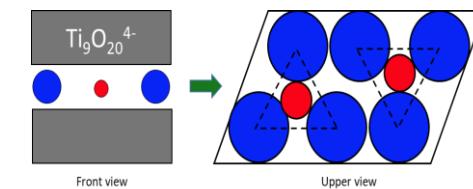


Ionization efficiency: 10%

	Copper (current) measured in FC2 and integrated in time [ $\mu\text{g}$ ]	Copper measured via GF-AAS [ $\mu\text{g}$ ]	
<b>1<sup>st</sup> deposition</b>	9.94	1.46	Target dissolved in $\text{HNO}_3$ 0.5 M, mild heating
<b>2<sup>nd</sup> deposition</b>	5.21	1.09	Target dissolved in $\text{HNO}_3$ 0.5 M, mild heating
<b>3<sup>rd</sup> deposition</b>	1.12	0.54	Target dissolved in concentrated $\text{HNO}_3$ , 180 °C for 20 min
<b>4<sup>th</sup> deposition</b>	0.94	0.50	Target dissolved in concentrated $\text{HNO}_3$ , 180 °C for 20 min



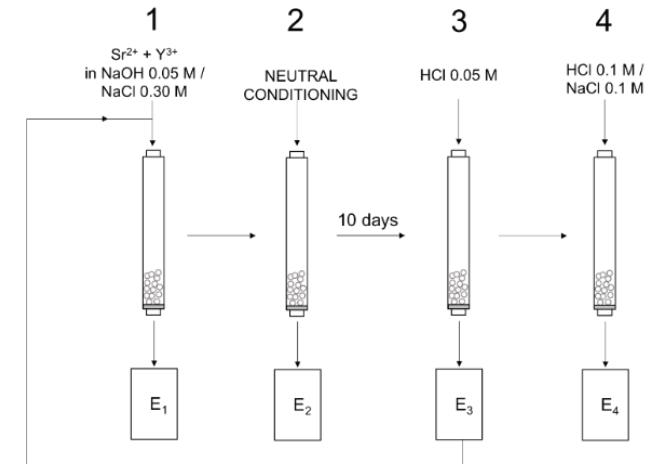
## Chemical purification



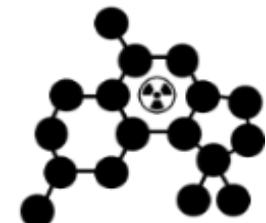
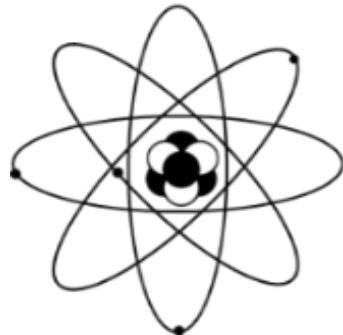
### The case of $^{90}\text{Y}$

$^{90}\text{Sr}$  main contaminant, but a source of  $^{90}\text{Y}$  as well

$^{90}\text{Y}$  directly produced +  
the  $^{90}\text{Y}$  from the decay of  $^{90}\text{Sr}$



# ISOLPHARM\_Ag: a case study



Istituto Nazionale  
di Fisica Nucleare  
Sezione di Padova



UNIVERSITÀ  
DEGLI STUDI  
DI PADOVA



UNIVERSITÀ DEGLI STUDI  
DI TRENTO



Istituto Nazionale  
di Fisica Nucleare  
Laboratori Nazionali di Legnaro



UNIVERSITÀ  
DEGLI STUDI  
DI PADOVA



Trento Institute for  
Fundamental Physics  
and Applications

BIOtech  
BIOtecp  
Biomedical Technologies

$^{111}\text{Ag}$ 

Promising radionuclide for therapy:

- $\beta^-$  emitter (average energy 360 keV)
- Low percentage of associated  $\gamma$ -emission (342 keV, 6.7%)
- $t_{1/2}$ : 7.45 days



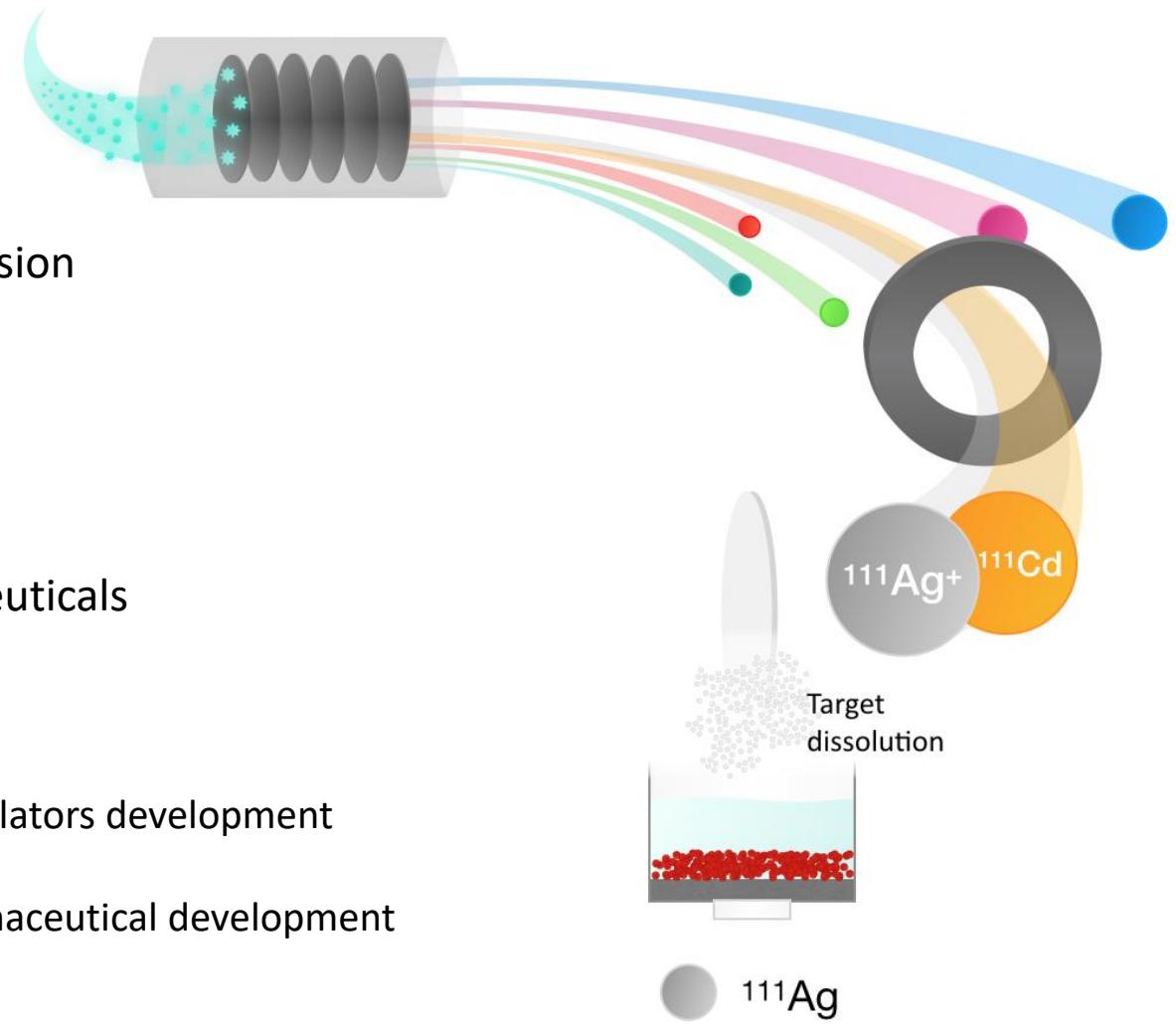
Development of Ag-based radiopharmaceuticals

Task 1: physics and computing

Task 2: production of  $\text{Ag}^+$ , purification and chelators development

Task 3: cellular targets studies and radiopharmaceutical development

## ISOLPHARM\_Ag



## UC<sub>x</sub> target Production of <sup>111</sup>Ag

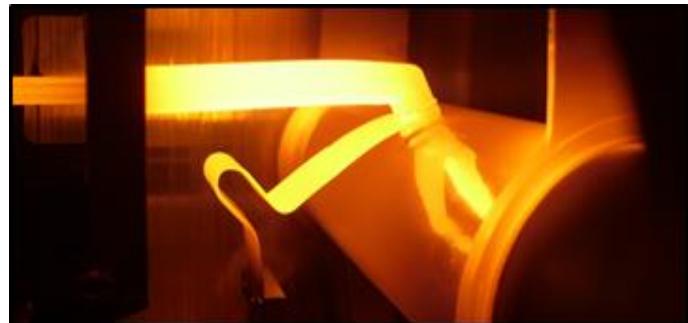
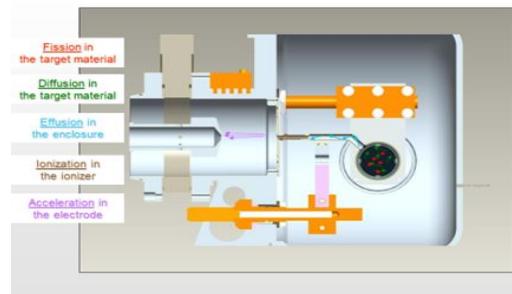
SPES UC <sub>x</sub> isotope production (200 μA 40 MeV PPB, 5 irradiation days)												
Isotope	Half-life	Decay radiations						Produced activity		Notes		
		t <sub>1/2</sub>	β-		β+/ε		γ		Auger	[MBq]	[mCi]	
<sup>77</sup> As	38,83 h	100%	0,683 MeV	/	/	1,59%	239 keV	0,06%	(9,67 keV)	2,21E+03	59,73	
<sup>86</sup> Rb	18,642 d	99,99%	1,776 MeV	0,01%	ε	8,64%	1077 keV	0,01%	(10,8 keV)	6,06E+01	1,64	
<sup>89</sup> Sr	50,53 d	100%	1,5 MeV	/	/	/	/	/	/	8,85E+03	239,15	
<sup>90</sup> Sr	28,9 y	NR	NR	NR	NR	NR	NR	NR	NR	5,16E+01	1,39	<sup>90</sup> Y generator
<sup>90</sup> Y	64.053 h	100%	2,28 MeV	/	/	/	/	0,00%	(13,4 keV)	1,88E+02	5,08	
<sup>111</sup> Ag	7,45 d	100%	1,036 MeV	/	/	6,70%	342 keV	0,04%	(19,3 keV)	8,29E+04	2241,85	
<sup>122</sup> Sb	2,7238 d	97,59%	1,984 MeV	2,41%	β+	70,67%	564 keV	0,29%	(21 keV)	1,32E+03	35,80	
<sup>125</sup> I	59,407 d	/	/	100%	ε	6,68%	35,49 keV	19,80%	22,7 keV	1,70E+00	0,05	
<sup>126</sup> I	12,93 d	47,30%	1,258 MeV	52,70%	β+	32,90%	666,33 keV	5,53%	22,7 keV	3,65E+01	0,99	
<sup>130</sup> I	12,36 h	100%	2,949 MeV	/	/	11,30%	1157 keV	0,19%	(24,6 keV)	2,82E+04	760,84	
<sup>131</sup> I	8,0252 d	100%	0,970 MeV	/	/	81,50%	364 keV	0,68%	(24,6 keV)	6,57E+04	1774,77	
<sup>133</sup> Xe	5,2475 d	100%	0,427 MeV	/	/	36,90%	80,99 keV	5,67%	25,5 keV	8,59E+04	2320,76	
<sup>129</sup> Cs	32,06 h	/	/	100,00%	β+	30,60%	371,92 keV	13,10%	24,6 keV	4,62E+00	0,12	Many Auger e <sup>-</sup> emissions
<sup>131</sup> Cs	9,689 d	/	/	100,00%	ε	/	/	9,30%	24,6 keV	3,68E+01	0,99	Many Auger e <sup>-</sup> emissions
<sup>132</sup> Cs	6,480 d	2%	1,279 MeV	98,13%	β+	1,58%	464 keV	9,40%	24,6 keV	2,14E+02	5,79	Many Auger e <sup>-</sup> emissions
<sup>136</sup> Cs	13,04 d	100%	2,548 MeV	/	/	80,00%	1048 keV	1,24%	26,4 keV	1,16E+04	313,75	
<sup>161</sup> Tb	6,89 d	100%	0,593 MeV	/	/	10,20%	75 keV	1,46%	37,2 keV	1,73E+02	4,67	
<sup>169</sup> Er	9,392 d	100%	0,351 MeV	/	/	0,00%	109,77 keV	0,00%	(5,67 keV)	1,54E+00	0,04	

The computing task can be divided into two different case studies, where cloud computing can be an extremely useful tool to perform fast and efficient simulations, related to both the target production and release of radionuclides of interest

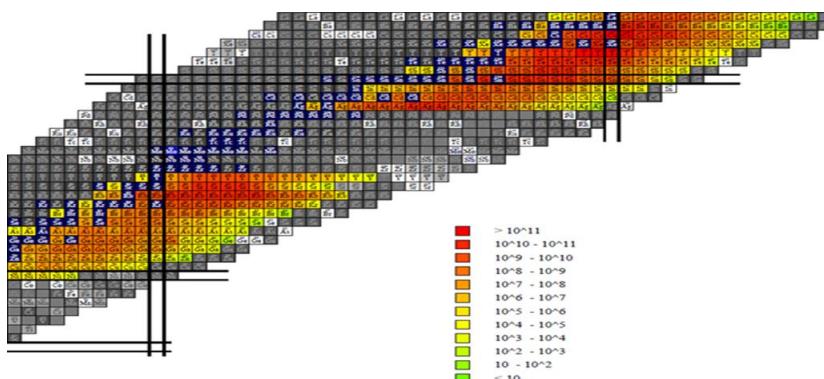
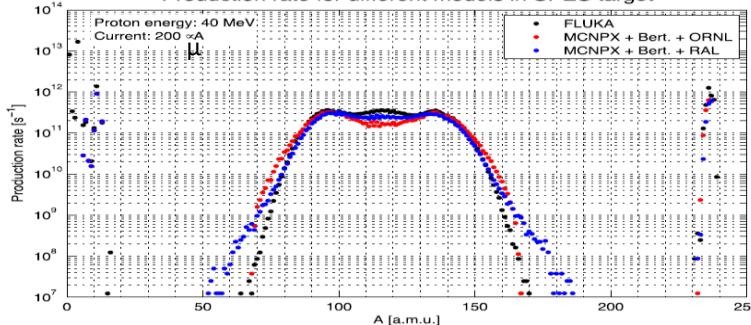
### Activities of this task:

1. Simulation of radionuclides production in the Isolpharm target
2. Simulation of radionuclides release from the Isolpharm target

ISOL Target: Production Method



Production rate for different models in SPES target



## Task 2:

### activities at LNL, DSF and DSC

- 1) Ionization and acceleration of  $\text{Ag}^+$  using the SPES Front End in off-line modality, the production of the secondary targets for  $\text{Ag}^+$  deposition and the deposition studies

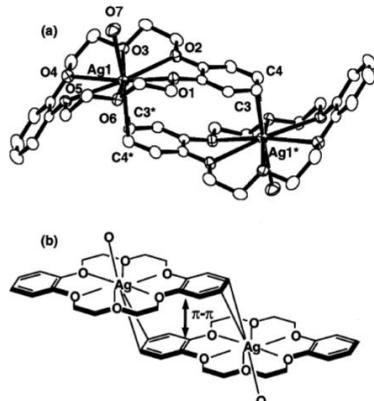
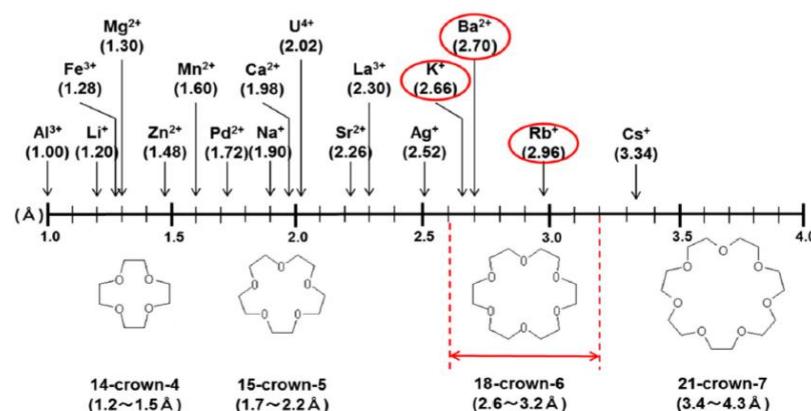


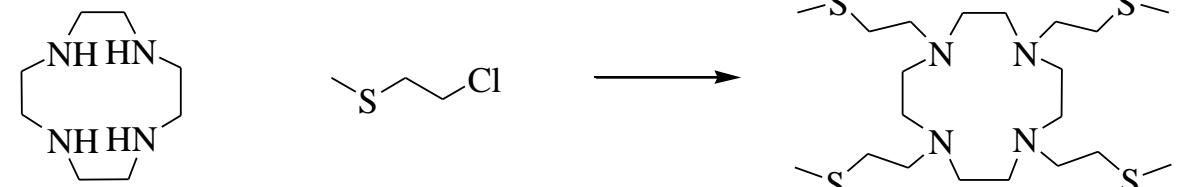
Fig. 1. Partial labelling (a) and schematic view (b) of silver(I)-DB[18]C6 dinuclear unit.

- 2) Synthesis of a resin for  $^{111}\text{Ag}^+$  purification from  $^{111}\text{Cd}^{2+}$

Fig. 6 Relationship between of crown ether pore sizes and metal ion diameters



- 3) Development of chelators for  $\text{Ag}^+$  based on DOTATE and analogues



Alberto Andriggetto

**$^{111}\text{Ag}/^{111}\text{Cd}$  purification**

Uptake and release under development

**30-09-2018**  
**MS5: Ionizzazione e deposito di Ag stabile presso FE SPES**

Deposito  $\text{Ag}^+$  su target da 40 mm di  $\text{NaNO}_3$

Target secondari (40 mm)

First Deposition      Second Deposition      Third Deposition

Deposito su target da 13 mm

Target secondari (13 mm)

Alberto Andriguetto

**31-12-2018**  
**MS6: Sintesi di una gamma di complessi a base Ag**

Condizioni di reazione:  
 • solvente: ACN  
 • Base:  $\text{K}_2\text{CO}_3$   
 • Rapporto cyclen: 2 – cloroetilmetilsulfuro 1:8  
 • Termostata a  $40^\circ\text{C}$  per 6 giorni

Purificazione mediante colonna cromatografica (eluente  $\text{CHCl}_3/\text{MeOH}$  9/1)

Condizioni di reazione:  
 • solvente: ACN  
 • Base:  $\text{K}_2\text{CO}_3$   
 • Rapporto cyclen: 2 – cloroetilmetilsulfuro 1:3  
 • Termostata a  $40^\circ\text{C}$  per 5 giorni

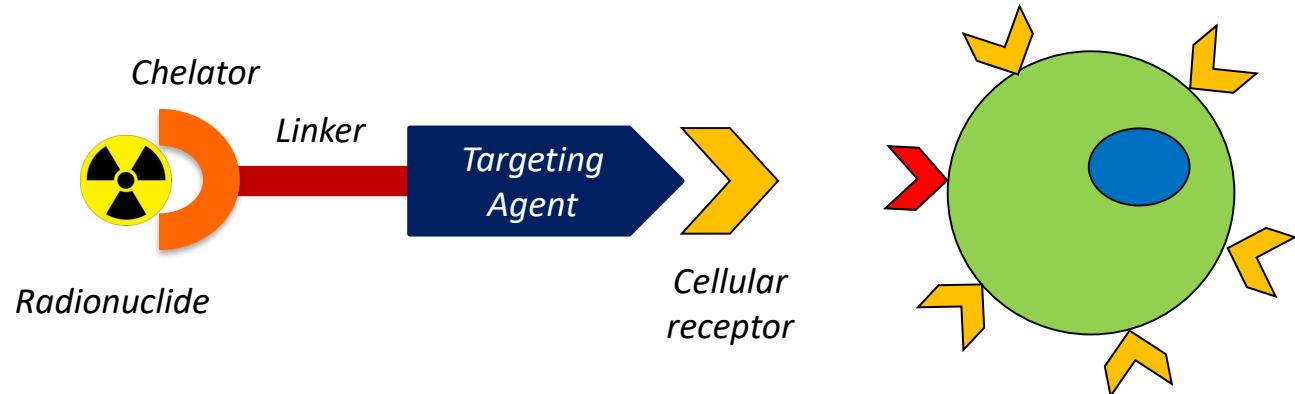
1

2

3

SPES exotic beams for science

### Pharmacology activities



#### 1) Cholecystokinin receptor (CCK2R and CCK2i4svR)

- objective: development of small molecule-based ligands.
- Targeting agent: synthesis ongoing
  - Linker moiety
  - Chelator

#### 2) Calreticulin (CRT): a potential target for proton therapy combined with targeted radionuclide therapy

- objective: development of a targeting agent for CRT

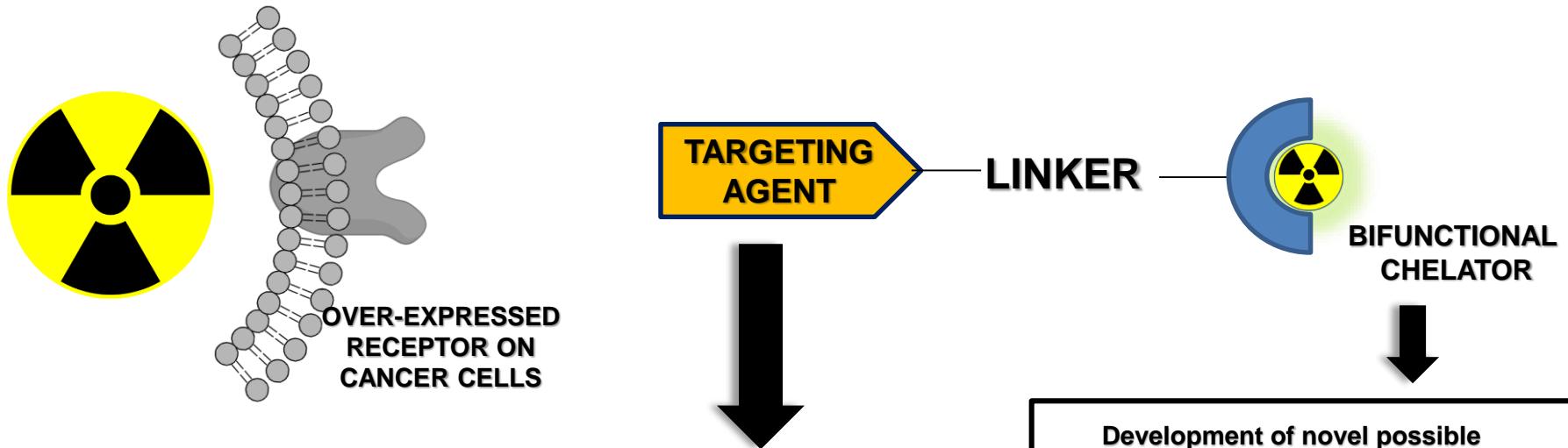


SERVIZIO SANITARIO REGIONALE  
EMILIA-ROMAGNA

Azienda Unità Sanitaria Locale di Reggio Emilia  
Azienda Ospedaliera di Reggio Emilia  
Arcispedale S. Maria Nuova  
Istituto in tecnologie avanzate e modelli assistenziali in oncologia  
Istituto di ricovero e cura a carattere scientifico



UNIVERSITÀ DEGLI STUDI  
DI TRENTO



**Development of targeting agent for Calreticulin and CCK2R**

Three chemical structures of targeting agents are shown:

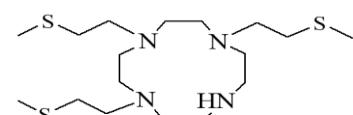
- A complex molecule containing a benzimidazole ring, a cyclohexyl group, and a carboxylic acid side chain.
- A long-chain molecule consisting of a benzimidazole core linked via amide groups to a poly(ethylene glycol) (PEG) chain, which is further linked to a carboxylic acid.
- A similar PEG-linked benzimidazole derivative with a different side chain.

**BIOtech at BIOtecn** Biomedical Technologies  
 UNIVERSITY OF TRENTO - Italy

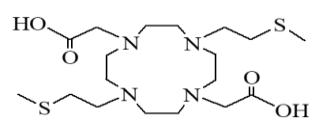
TIFPA Trento Institute for Fundamental Physics and Applications

dsf

Development of novel possible bifunctional chelators for  $^{111}\text{Ag}$  at Dept. of Chemical Sciences (UNIPD)



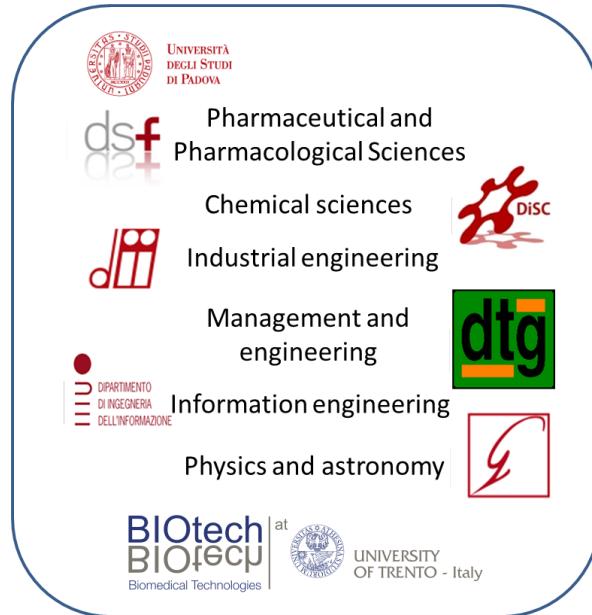
DOT3



DOT2( $\text{CH}_2\text{COOH}$ )<sub>2</sub>

# Summary

## The Italian Network



## The International Network



**DEMOKRITOS**  
NATIONAL CENTER FOR SCIENTIFIC RESEARCH

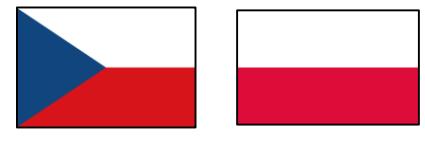
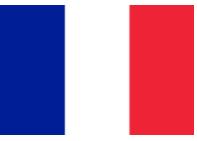
PAUL SCHERRER INSTITUT



INFN is the coordinator of a new JRA in the framework of the ERINS (IA) in Horizon Europe

### MAIA (MedicAI Isotopes from Accelerators)

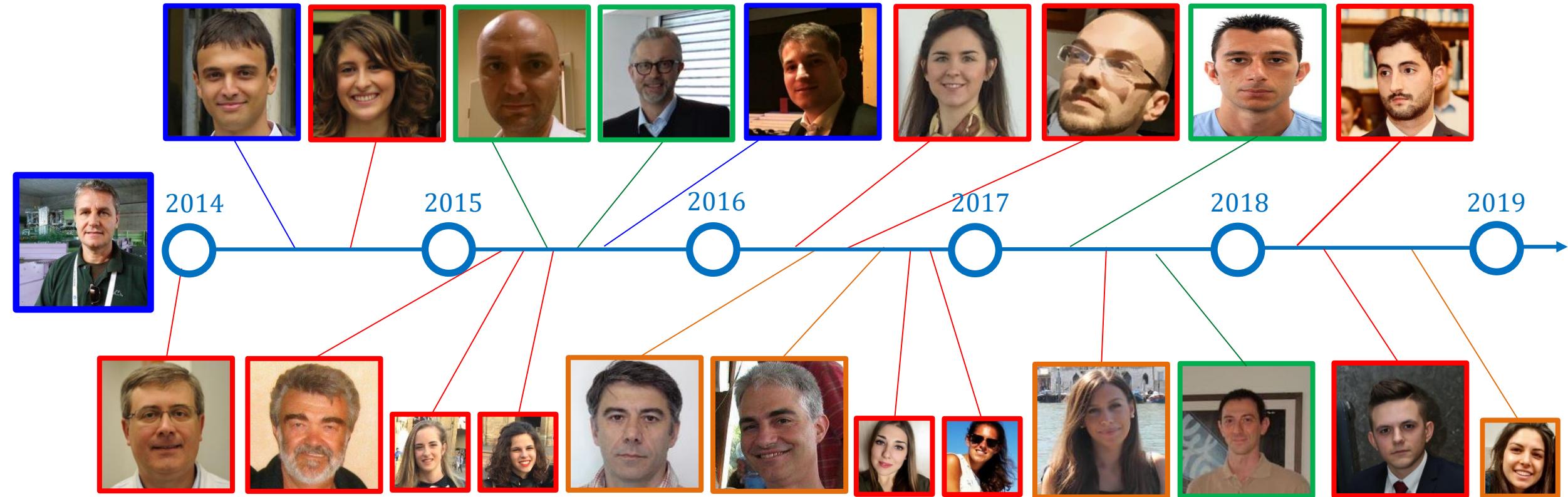
Involved institutions: INFN, [CEA & GANIL & ARRONAX/SUBATECH](#), USC& CSIC-I3M , [ELI-NP/IFIN-HH](#), NPI, [HIL](#)



Aim: study and develop new techniques for the production of radioisotopes of medical interest using accelerators

**Three different aspects will be part of the project:**

- New production methods
- Innovative target design, production and characterization
- From targets to isotopes: purification and processing



### ISOLPHARM needs a structure composed of competences in:

- Nuclear physics, for the generation and collection of nuclides
- Radiochemistry, for the chemical separation and complexation of the collected nuclides
- Radiopharmacy, for the performance of radiolabeling and in vitro/in vivo studies
- Nuclear medicine, for GMP development and possible clinical studies

## PhD theses (2)

**Head Office: Università degli Studi di Padova**  
Department of Chemical Sciences

**DOTTORATO DI RICERCA IN "FISICA"**  
CICLO XXXI

**COORDINATORE**  
Prof. Guido Vincenzo

**Ph.D. COURSE IN MOLECULAR SCIENCES**  
CURRICULUM PHARMACEUTICAL SCIENCES  
XXX SERIES

**PHARMACEUTICAL DEVELOPMENT OF THE ISOL TECHNIQUE FOR THE PRODUCTION OF RADIONUCLIDES AND THEIR APPLICATIONS IN TARGETED RADIONUCLIDE THERAPY**

**Development of targets for the production of radionuclides of medical interest according to the ISOL technique**

**Settore Scientifico Disciplinare FIS/07**

**Dottorando**  
Dott. Ballan Michele

**Tutore**  
Prof. Duatti Adriano

**Coordinator:** Ch.mo Prof. Leonard Prins  
**Supervisor:** Ch.mo Prof. Nicola Realdon  
**Co-Supervisor:** Dr. Alberto Andrigetto

**Ph.D. student:** Francesca Borgna

Anno 2015/2018

## Master theses in chemistry and industrial engineering (6)

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**Dipartimento di Ingegneria Industriale**  
Corso di Laurea Magistrale in Ingegneria Meccanica

**TESI DI LAUREA**  
ANALISI E PROGETTAZIONE DI UN SISTEMA DI CONTENIMENTO E MOTIVAMENTO DI UN'IMPIANTO PER LA RACCOLTA DI ISOTIPI RADIOATTIVI DI INTERESSE MEDICO

**Relatore:** Prof. GIOVANNI MENEGHETTI  
**Correlatore:** Dott. ALBERTO ANDRIGHETTO<sup>1</sup>  
Ing. MICHELE BALLAN<sup>2</sup>

**Istituto Nazionale di Fisica Nucleare di Legnaro<sup>3</sup>**

**Laurende:** SERGEI POPA  
Matricola: 115442

**ANNO ACCADEMICO 2016-2017**

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI TECNICA E GESTIONE DEI SISTEMI INDUSTRIALI**  
CORSO DI LAUREA MAGISTRALE IN INGENIERIA DELL'INNOVAZIONE DEL PRODOTTO

**TESI DI LAUREA**

**Sviluppo di un set-up sperimentale per la misura della conduttività termica di carburi di titanio per applicazioni in fisica e medicina nucleare.**

**Relatore:** Ch.mo Prof. LINA BIASITTO  
**Co-relatore:** Dott. ALBERTO ANDRIGHETTO  
Dott. STEFANO CORRADETTI  
Ing. MATTIA MANDARO

**Laurende:** PAOLO TODESCO  
Matricola: 112829

**ANNO ACCADEMICO 2016/2017**

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**FACOLTÀ DI INGEGNERIA**  
Corso di Laurea Magistrale in Ingegneria dei Materiali

**TESI DI LAUREA**  
TARGET CERAMIC POROSI PER LA PRODUZIONE DI FASCI RADIAZIONI IN FISICA E MEDICINA NUCLEARE

**Relatore:** Prof. Paolo Colombo  
**Co-relatore:** Dott. Alberto Andrigetto  
Dott. Stefano Corradetti  
Dott.ssa Giorgia Franchis

**Laurende:** Alberto Grivato  
Matricola: 112829

**ANNO ACCADEMICO 2016/2017**

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI INGEGNERIA INDUSTRIALE DI1**

**CORSO DI LAUREA MAGISTRALE IN INGEGNERIA DEI MATERIALI**

**TESI DI LAUREA**  
POROUS CERAMIC TARGET FOR THE PRODUCTION OF RADIACTIVE BEAMS FOR NUCLEAR PHYSICS AND MEDICINE

**Relatore:** Prof. Paolo Colombo  
**Co-relatore:** Dott. Alberto Andrigetto  
Dott. Stefano Corradetti  
Dott.ssa Giorgia Franchis

**Laurende:** Federico Gobbo D'Inca  
Matricola: 112829

**ANNO ACCADEMICO 2017/2018**

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**FACOLTÀ DI INGEGNERIA**  
Corso di Laurea Magistrale in Ingegneria dei Materiali

**TESI DI LAUREA**  
Sviluppo di un target refrattario mesoporous in carburo di titanio per applicazioni in fisica e medicina nucleare

**Relatore:** Prof. Paolo Colombo  
**Co-relatore:** Dott. Alberto Andrigetto  
Dott. Stefano Corradetti  
Dott.ssa Giorgia Franchis

**Laurende:** Daniela Negrelli  
Matricola: 112829

**ANNO ACCADEMICO 2017/2018**

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE CHIMICHE**

**CORSO DI LAUREA MAGISTRALE IN CHIMICA**

**TESI DI LAUREA**  
SENTESI E STUDIO TERMODINAMICO DI NUOVI POSSIBILI CIEHLANTI BIUNIZIONALI PER LA TARGETED RADIONUCLIDE THERAPY CON  $^{113}\text{Ag}$  (PROGETTO ISOLPHARM-Ap)

**Relatore:** Ch.mo Prof. VALERIO DI MARCO  
**Co-relatore:** Ch.mo Prof. GIOVANNI MARZARO  
**Controrelatore:** Ch.mo Prof. GIUSEPPE ZAGGIO

**Laurende:** Marianna Tosato

**ANNO ACCADEMICO 2017/2018**

## Master theses in pharmacy (9)

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE DEL FARMACO**

**CORSO DI LAUREA MAGISTRALE IN FARMACIA**

**TESI DI LAUREA**  
POTENZIALITÀ DELLA TECNOLOGIA ISOTOPE SEPARATION ON-LINE (ISOL) PER LA REALIZZAZIONE DI UN RADIODIFARMACO A BASE di  $^{90}\text{Sr}$  E PRELIMINARE SVILUPPO TECNOLOGICO DELLA FORMA FARMACEUTICA

**Relatore:** Ch.mo PROF. NICOLA REALDON  
**Co-Relatore:** DOTT. ALBERTO ANDRIGHETTO<sup>1</sup>  
DOTT. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**SVILUPPO PRELIMINARE DI UNA PREPARAZIONE RADIODIFARMACEUTICA CONTENENTE  $^{90}\text{YCl}_3$  MEDIANTE TECNOLOGIA ISOTOPE SEPARATION ON-LINE (ISOL)**

**Relatore:** Ch.mo PROF. NICOLA REALDON  
**Co-Relatore:** DOTT. ALBERTO ANDRIGHETTO<sup>1</sup>  
DOTT. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE DEL FARMACO**

**CORSO DI LAUREA MAGISTRALE IN FARMACIA**

**TESI DI LAUREA**  
SVILUPPO DI UN PROCESSO FARMACEUTICO PER LA PRODUZIONE DI  $^{131}\text{I}$  E  $^{125}\text{I}$  CON TECNOLOGIA ISOL (ISOTOPE SEPARATION ON-LINE)

**Relatore:** Ch.mo Prof. NICOLA REALDON  
**Co-Relatore:** DOTT. ALBERTO ANDRIGHETTO<sup>1</sup>  
DOTT. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE DEL FARMACO**

**CORSO DI LAUREA MAGISTRALE IN FARMACIA**

**TESI DI LAUREA**  
SVILUPPO TECNOLOGICO DI UN PROTOTIPO DI GENERATORE  $^{90}\text{Sr}/\text{Y}$  E DETERMINAZIONE DELL'EFFICIENZA DI DEPOSIZIONE DI  $^{90}\text{Sr}$  PER RADIONUCLIDI PRODOTTI CON TECNOLOGIA ISOL

**Relatore:** Ch.mo Prof. NICOLA REALDON  
**Co-Relatore:** DOTT. ALBERTO ANDRIGHETTO<sup>1</sup>  
DOTT. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE DEL FARMACO**

**CORSO DI LAUREA MAGISTRALE IN FARMACIA**

**TESI DI LAUREA**  
Ricerca di un metodo di purificazione dello  $^{113}\text{Ag}$  dal suo contaminante  $^{110}\text{Ag}$  per lo sviluppo tecnologico di un radiofarmaco per l'ionizzazione dello  $^{113}\text{Ag}$  con la tecnologia ISOL

**Relatore:** Ch.mo Prof. NICOLA REALDON  
**Co-Relatore:** DOTT. ALBERTO ANDRIGHETTO<sup>1</sup>  
DOTT. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE DEL FARMACO**

**CORSO DI LAUREA MAGISTRALE IN FARMACIA**

**TESI DI LAUREA**  
PROGETTO ISOLPHARM-Ap: SVILUPPO TECNOLOGICO DI UN PROCESSO FARMACEUTICO PER LA PRODUZIONE DI  $^{113}\text{Ag}$  E DEPOSIZIONE E PURIFICAZIONE DELLO  $^{113}\text{Ag}$  PER LA PRODUZIONE DI RADIODIFARMACI AD USO TERAPEUTICO

**Relatore:** Ch.mo Prof. NICOLA REALDON  
**Co-Relatori:** Ch.mo Prof. GIOVANNI MARZARO  
Dott. ALBERTO ANDRIGHETTO<sup>1</sup>  
Dott. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE DEL FARMACO**

**CORSO DI LAUREA MAGISTRALE IN FARMACIA**

**TESI DI LAUREA**  
PROGETTO ISOLPHARM-Ap: SVILUPPO TECNOLOGICO DI UN PROCESSO FARMACEUTICO PER LA PRODUZIONE DI  $^{113}\text{Ag}$  E DEPOSIZIONE E PURIFICAZIONE DELLO  $^{113}\text{Ag}$  PER LA PRODUZIONE DI RADIODIFARMACI AD USO TERAPEUTICO

**Relatore:** Ch.mo Prof. NICOLA REALDON  
**Co-Relatori:** Ch.mo Prof. GIOVANNI MARZARO  
Dott. ALBERTO ANDRIGHETTO<sup>1</sup>  
Dott. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE DEL FARMACO**

**CORSO DI LAUREA MAGISTRALE IN FARMACIA**

**TESI DI LAUREA**  
SINTESI E CARATTERIZZAZIONE DI MOLECOLE PER IL TARGETING ATTIVO SUL RECEZTORE CCK2R

**Relatore:** Ch.mo Prof. GIOVANNI MARZARO  
**Co-Relatori:** Ch.mo Prof. NICOLA REALDON  
Dott. ALBERTO ANDRIGHETTO<sup>1</sup>  
Dott. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

**DIPARTIMENTO DI SCIENZE DEL FARMACO**

**CORSO DI LAUREA MAGISTRALE IN FARMACIA**

**TESI DI LAUREA**  
SINTESI E CARATTERIZZAZIONE DI MOLECOLE PER IL TARGETING ATTIVO SUL RECEZTORE CCK2R

**Relatore:** Ch.mo Prof. GIOVANNI MARZARO  
**Co-Relatori:** Ch.mo Prof. NICOLA REALDON  
Dott. ALBERTO ANDRIGHETTO<sup>1</sup>  
Dott. STEFANO CORRADETTI<sup>2</sup>

<sup>1</sup>Istituto Nazionale di Fisica Nucleare

**LAUREANDA:** CHIARA TODESCO

**ANNO ACCADEMICO 2013/2014**

**LAUREANDA:** CHIARA TODESCO

**ANNO ACCADEMICO 2015/2016**

**LAUREANDA:** ELISA VETTORATO

**ANNO ACCADEMICO 2015/2016**

**LAUREANDA:** CHIARA FAVARETTO

**ANNO ACCADEMICO 2016/2017**

**LAUREANDA:** MARTA PELLIZZOLA

**ANNO ACCADEMICO 2016/2017**

**LAUREANDA:** GIANANDREA QUAGGIOTTO

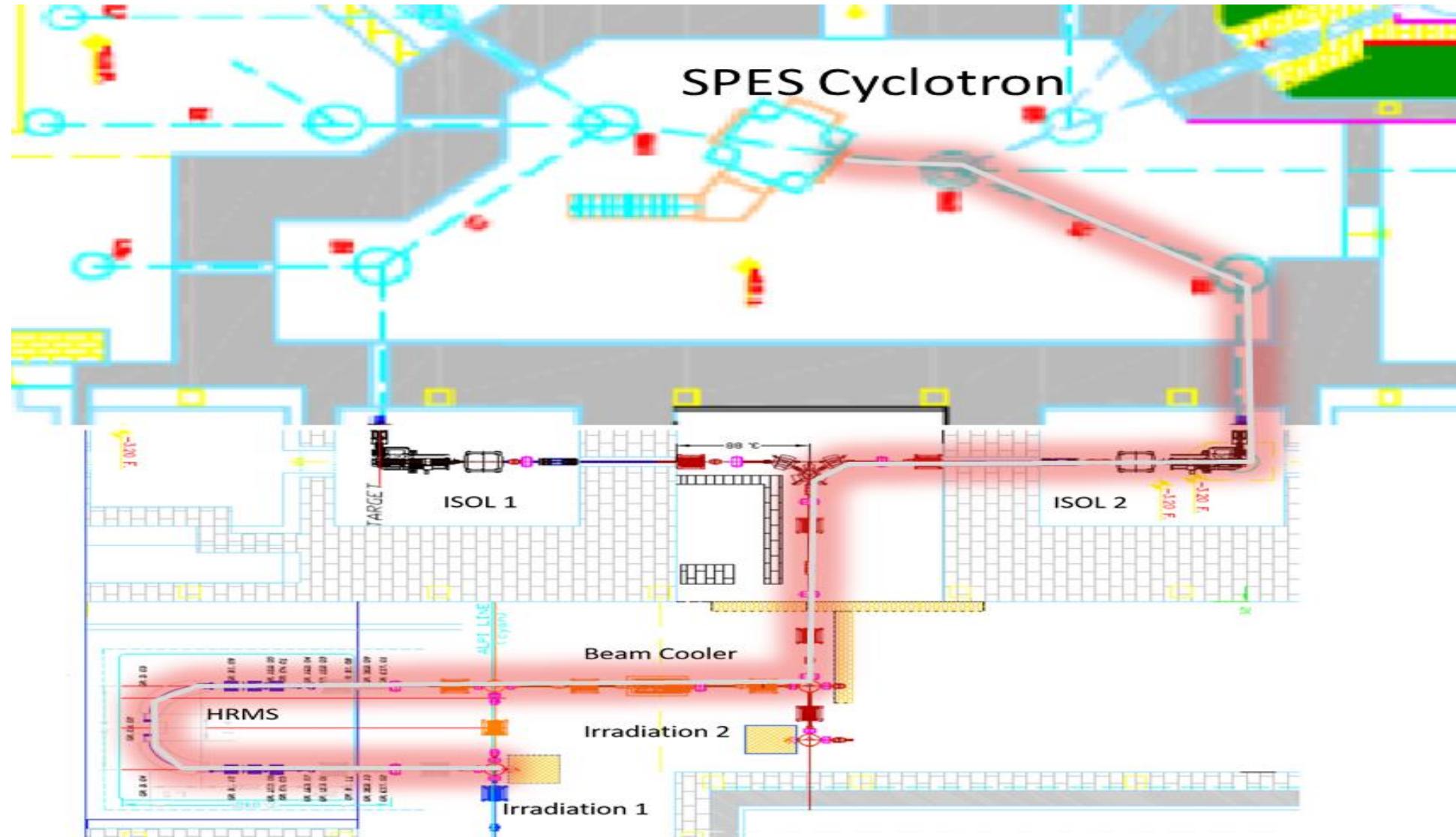
**ANNO ACCADEMICO 2017/2018**

**LAUREANDO:** MICHELE CAERAN

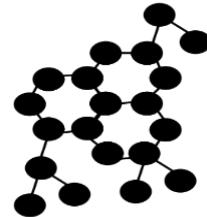
**ANNO ACCADEMICO 2017/2018**

**LAUREANDO:** MARCO VERONA

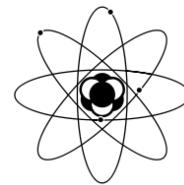
**ANNO ACCADEMICO 2017/2018**



At SPES it will be possible soon to **produce radionuclides for medical purposes** using the ISOL technique.



The ISOLPHARM method (patent deposited) is focused on the production of radiopharmaceutical precursors with **high specific activity** using a proton beam ad intermediate energies.



The ISOLPHARM collaboration has started 3 years ago. An increasing **experimental activity** is under development.



Some radionuclides (as  $^{111}\text{Ag}$ ,  $^{43}\text{Sc}$ , etc) are extremely interesting and could be used as precursors for **new radiopharmaceuticals**.



First step: to produce **first radionuclides of medical interest** for research (small quantities) when the first SPES RIB will be delivered.

