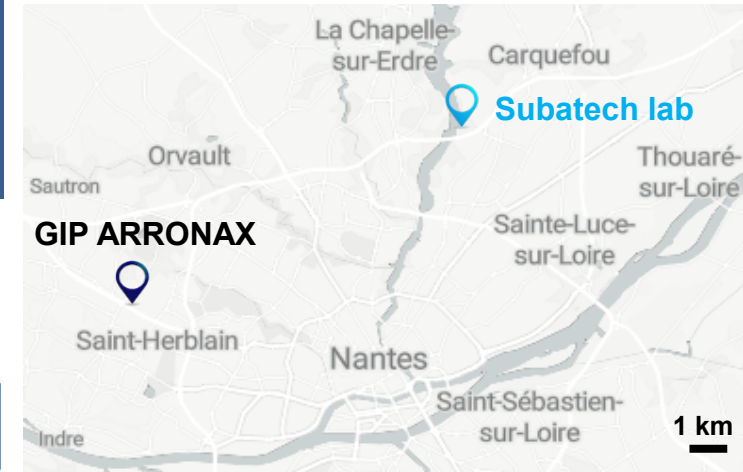




UNIVERSITÀ  
DEGLI STUDI  
DI MILANO



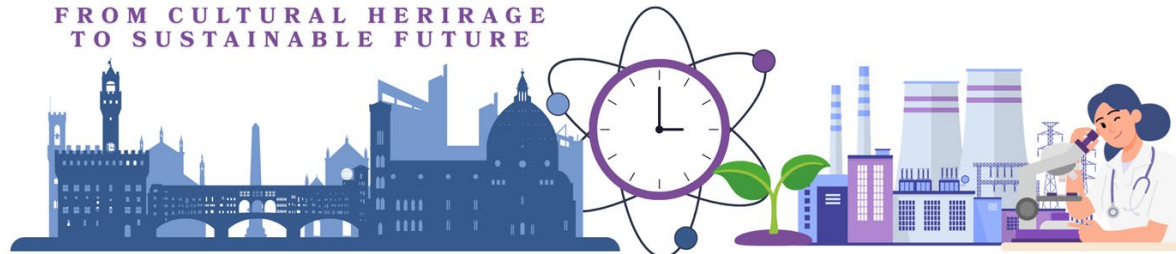
# Recent Advances In Nantes Around The ARRONAX Facility

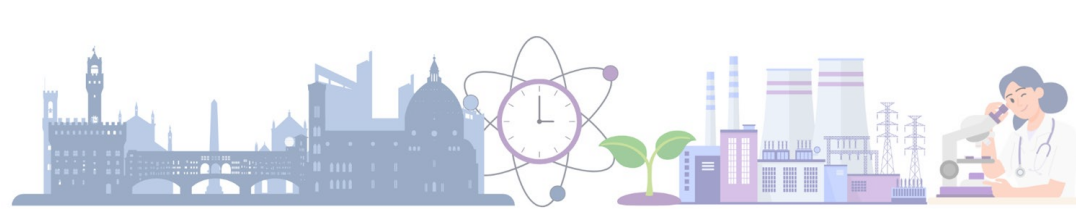


Arnaud Guertin et al. on behalf of PRISMA and GIP ARRONAX teams



**ISOTOPIC TIME MACHINE**  
FROM CULTURAL HERIRAGE  
TO SUSTAINABLE FUTURE





# PRISMA @ Subatech lab

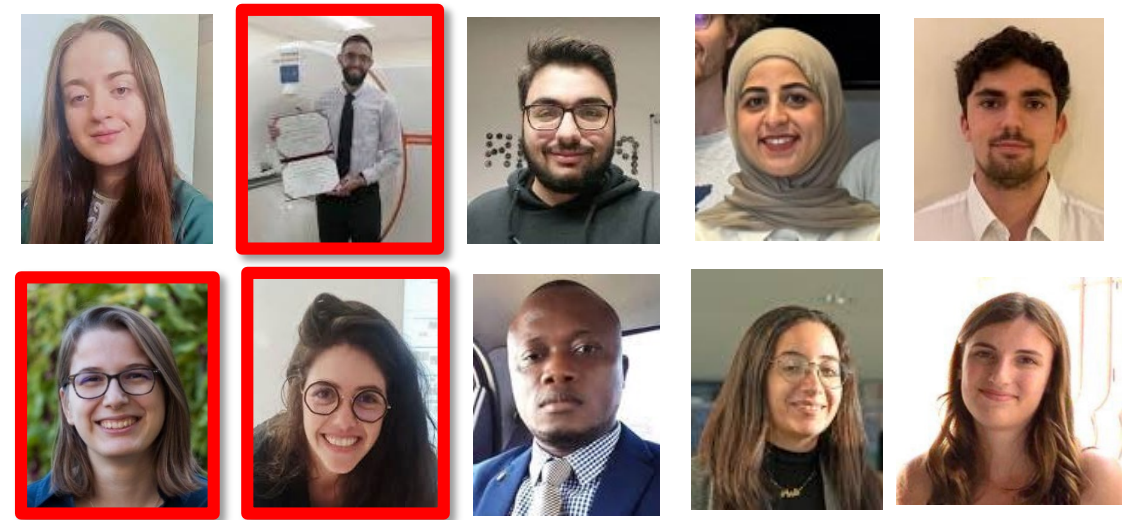
## Permanents

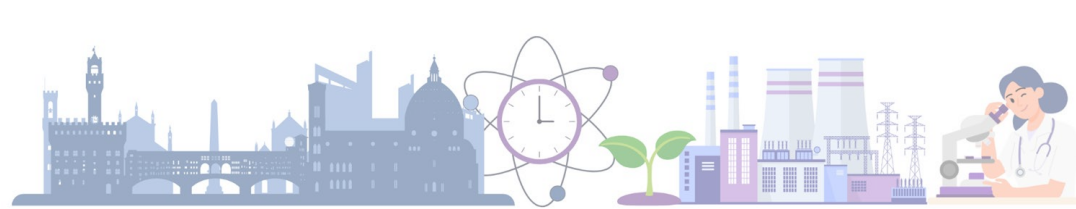


**PRISMA**

Physics of Radiation InteractionS with Matter and Applications

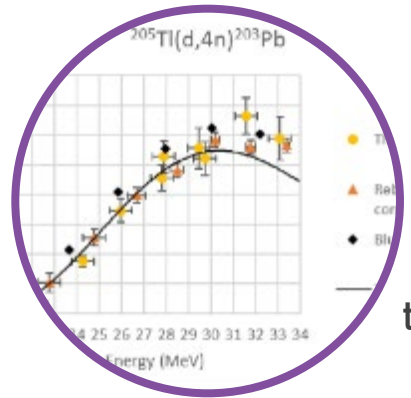
## PhD students





# PRISMA @ Subatech lab

**Isotopes for therapy and diagnosis**



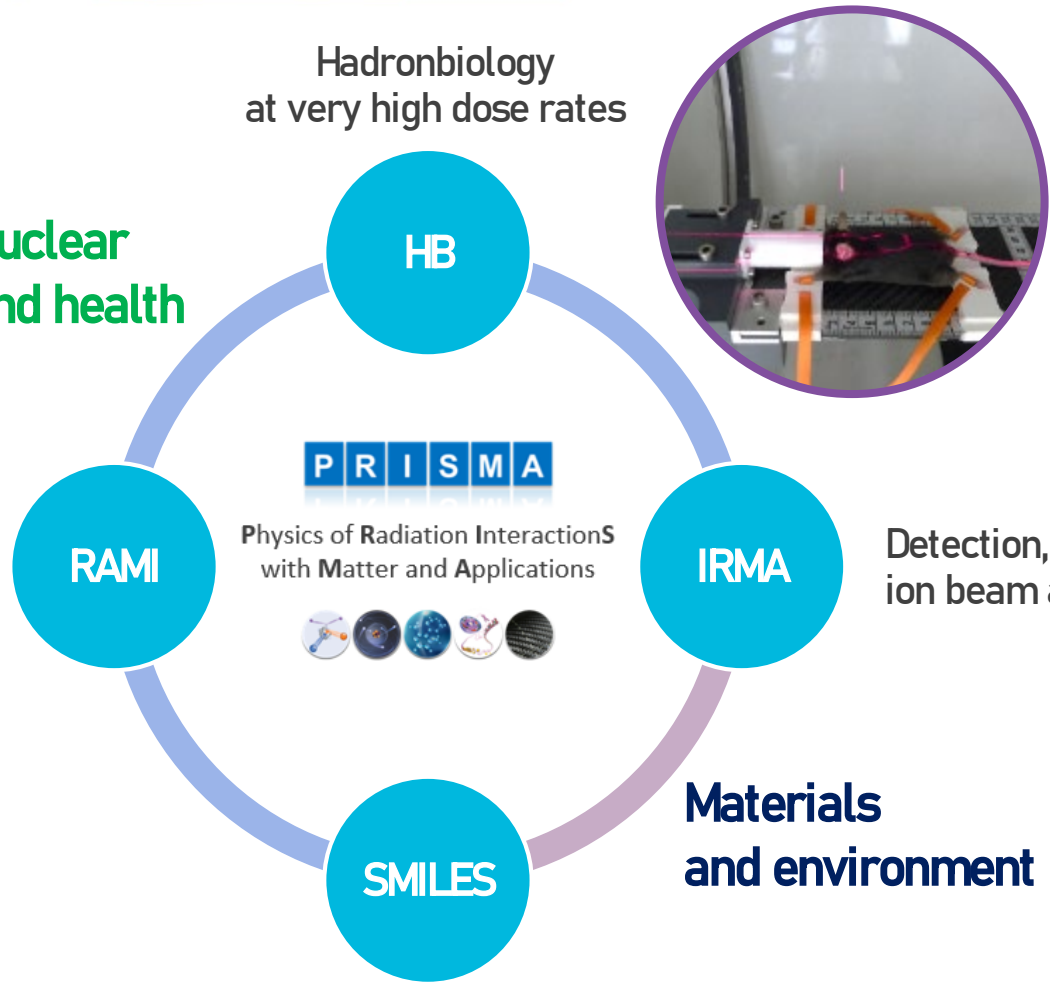
Which isotopes for tomorrow's nuclear medicine?

**Cross section measurements**



**Mass separation**

**Nuclear and health**



Hadronbiology at very high dose rates

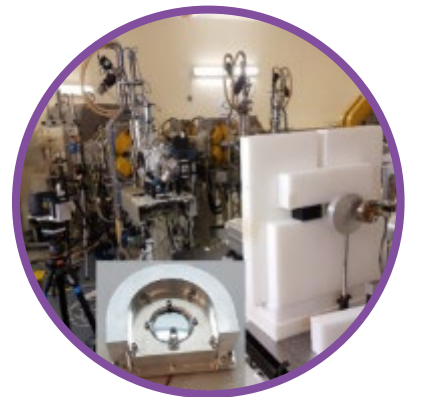


**Flash radiotherapy**

**Radiolysis**

Detection, ion beam analysis

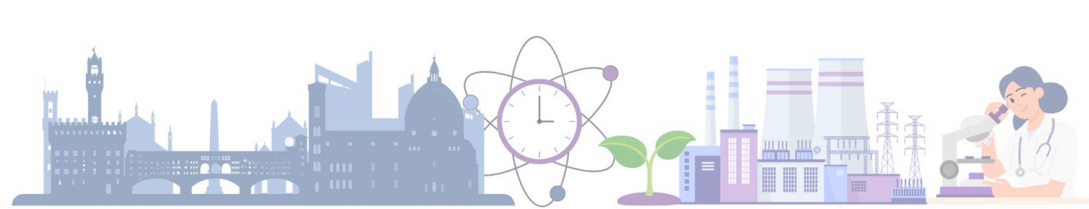
**Detector testing**



**Archeometry**

Mass separation coupled with laser ionisation

**Materials and environment**



# GIP ARRONAX

## Accelerator for Research in Radiochemistry and Oncology at Nantes Atlantix

3 main fields of investigations:

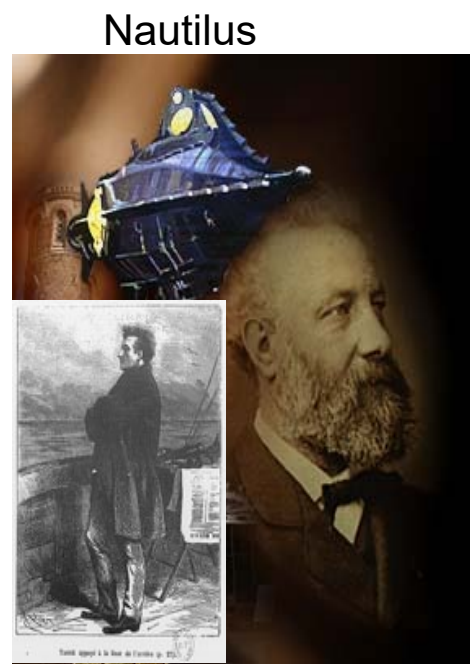
**Radionuclides** and **radiopharmaceuticals production** for nuclear medicine

**Research in related fields:** radiolysis, radiobiology, nuclear physics ...

**Training of students**

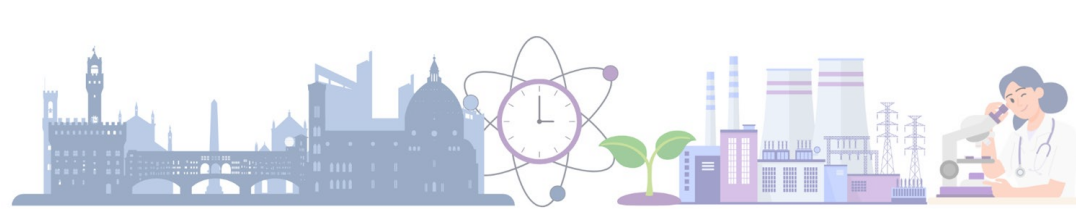
The name ARRONAX is a tribute to **Jules Verne, born in Nantes** in 1828.

**Aronnax** is the name of the main character of the novel «Twenty thousands leagues under the sea » published in 1870



Professor ARRONAX

Jules Verne



# ARRONAX Facility

## Key numbers:

- Creation **2008**, commissioned 2010
- **70 people** including students
- **C70XP** and **Kiube 180** coming soon

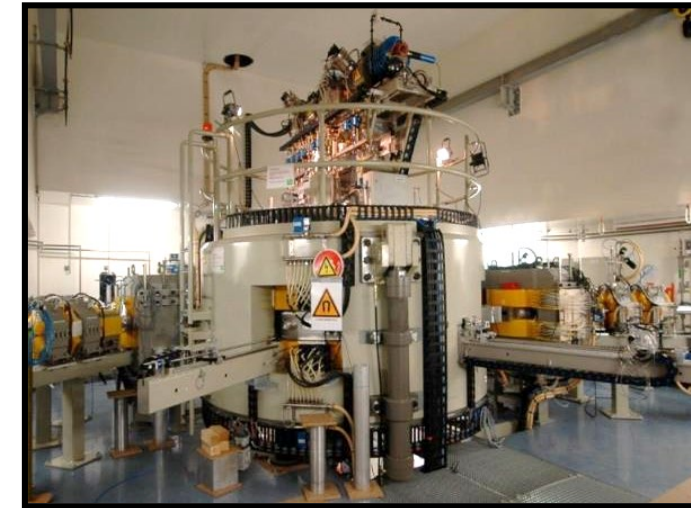
## Key features:

- **Multi-particles**
- **High energy**
- **High intensity**

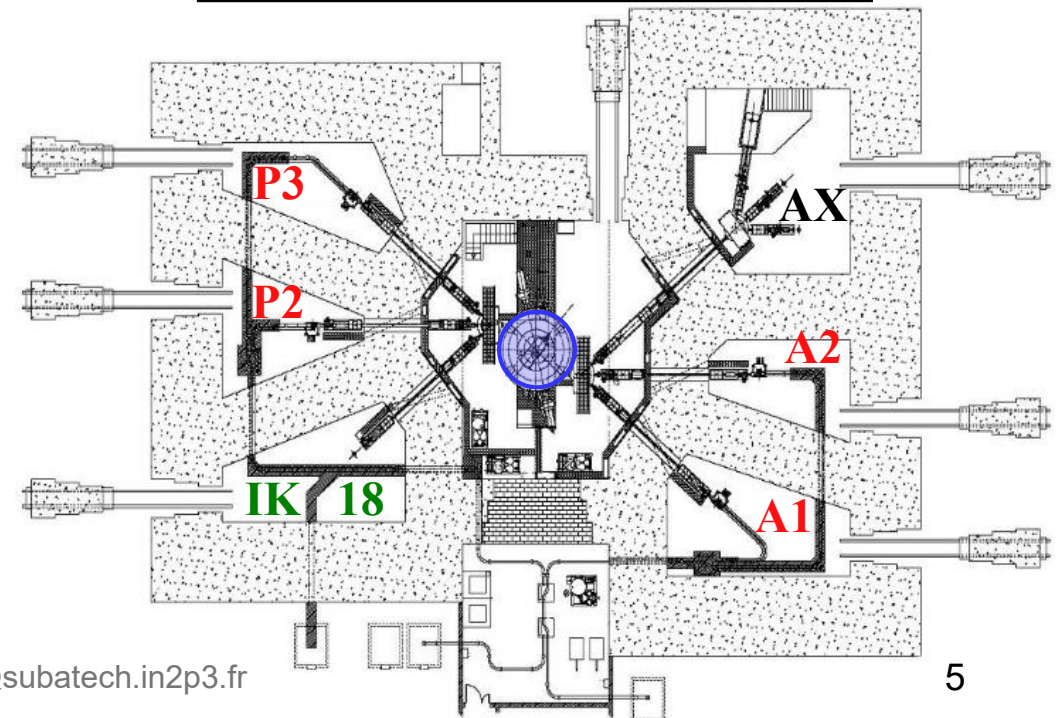
	Beam	Accelerated ions	Energy (MeV)	Intensity (eμA)	Dual beam
<b>C70XP</b>	<b>Proton</b>	H-	30- <b>70</b>	< <b>375</b>	<b>Yes</b>
		HH+	17	< 50	No
	<b>Deuteron</b>	D-	15-35	< 50	Yes
	<b>Alpha</b>	He++	<b>68</b>	< 70	No
<b>IK18</b>	<b>Proton</b>	H-	18	180	Yes

## A range of associated laboratories, 2000 m<sup>2</sup>:

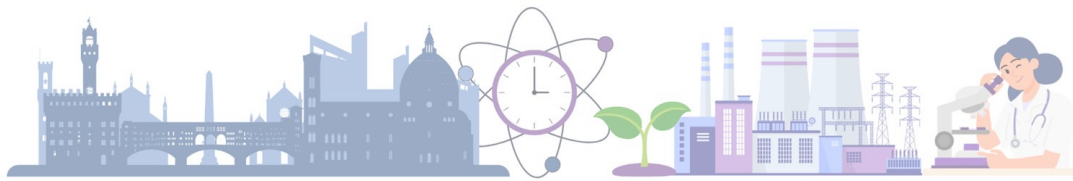
- radiochemistry, biochemistry, radiolabelling,
- cell culture, chemical analyses,
- nuclear metrology, quality control, etc.



C70XP cyclotron  
 @ GIP ARRONAX



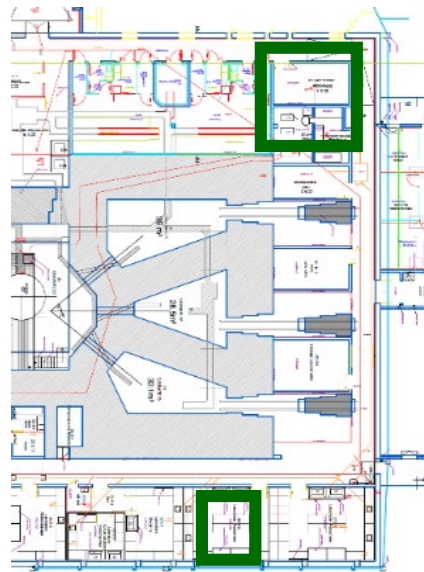
Cross-section view of the reaction casemates located around the C70XP



# Radiopharmacy

## Nantes University hospital/ GIP ARRONAX radiopharmacy

**Purpose:** production of radiopharmaceuticals for clinical trials in Europe



Good Manufacturing Practices

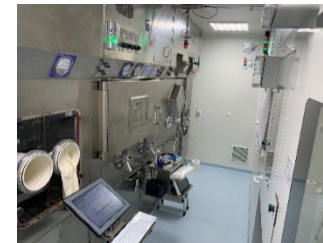
GMP S2



In use since 2018

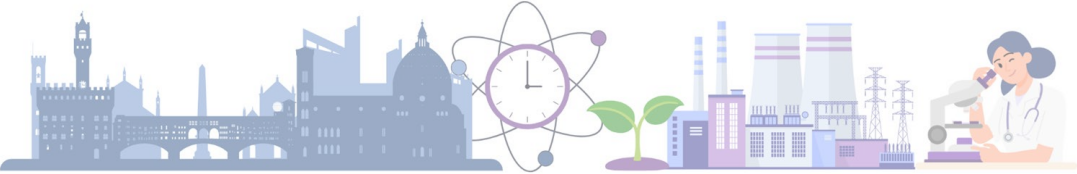


GMP S3



In use since 2023

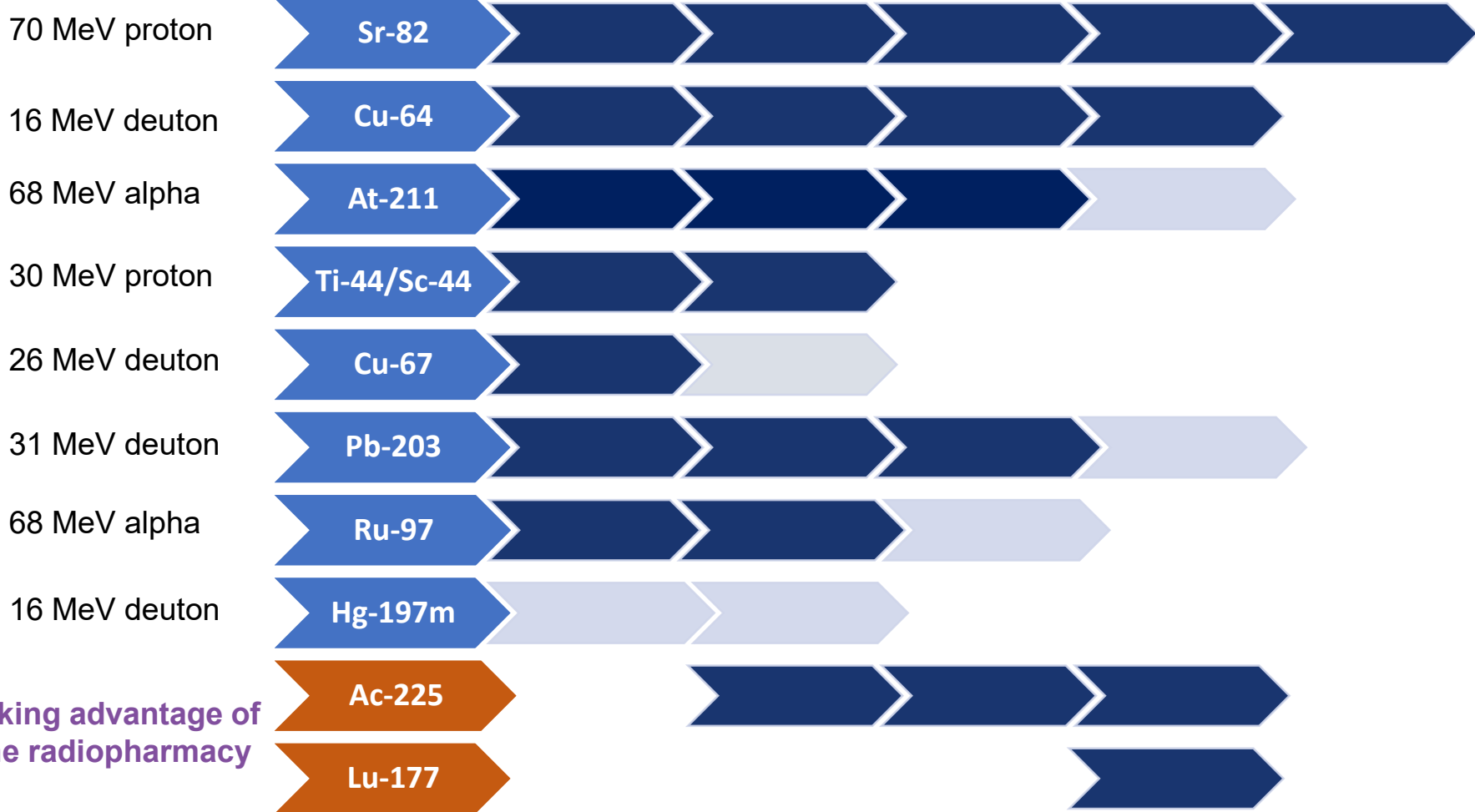
Several clinical trials performed using **Ac-225**, **Lu-177** and **Cu-64** and under preparation using **At-211**



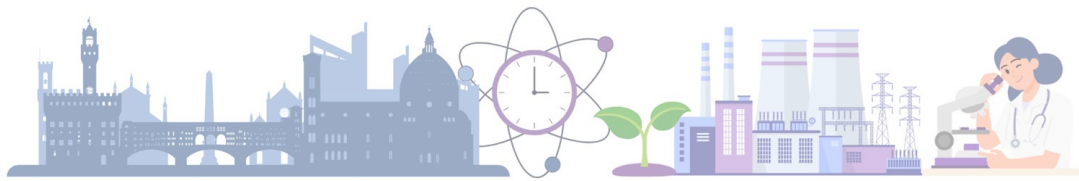
# Pipeline ARRONAX

Taking advantages of all beams available

**Physics**   **Chemistry**   **Pre clinical**   **Clinical trials**   **Clinical routine**



New developments on Auger emitters



## PRISMA and GIP ARRONAX

Cross section measurements and production of Tm-165 via the Ho-165( $\alpha$ ,4n) reaction: generator of a pure Auger electron emitter, **Er-165**

**E. Nigron** et al. 16/02 Africa Room 15h00

Molecular plating technique to prepare thin targets for production cross section measurement of the nat-Gd(p,x)**Tb-155** reaction

**V. Rhoden** et al. 16/02 Europa Room 15h00

Production cross section measurements of **Ag-111** with the reaction nat-Pd( $\alpha$ ,X)

**L. Puren** et al. 17/02 Africa Room 16h15

**Target developments** for research and production of radionuclides at GIP ARRONAX

**T. Sounalet** 17/02 Africa Room 11h20

Development of Ni electroplating for **Cu-61** and **Cu-64** production in clinical cyclotrons: Costa Rica case study

**J.D. Campos Mendez** 17/02 Africa Room 12h15

Radiolabelling of an octadentate bispidine ligand with theranostic pair of **scandium**

**T. Demartinécourt** 18/02 Europa Room 15h10

## Collaborators from INFN and GANIL

Cross section results about the Ti-49(d,x) reaction for the production of **Sc-47** and its contaminants

**L. De Dominicis** et al. 16/02 Africa Room 16h00

Optimization and validation of the indirect **Tb-155** production route in the Aphrodite-155 project

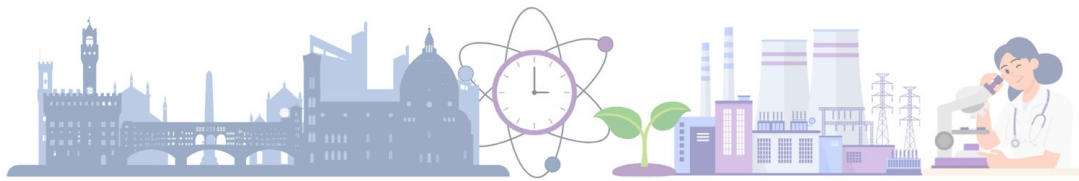
**M. Colluci** et al. 17/02 Asia Room 15h30

Data-driven optimization of **terbium** production via nat-Eu( $\alpha$ ,x) reactions: from experiments to NSGA-II modelling

**M. Colluci** et al. 17/02 Africa Room 17h30

First measurement of **At-210,211** cross sections using the GANIL SPIRAL2 LINAC

**A.M. Frelin** et al. 18/02 Africa Room 12h45



# At-211, what is it for ?

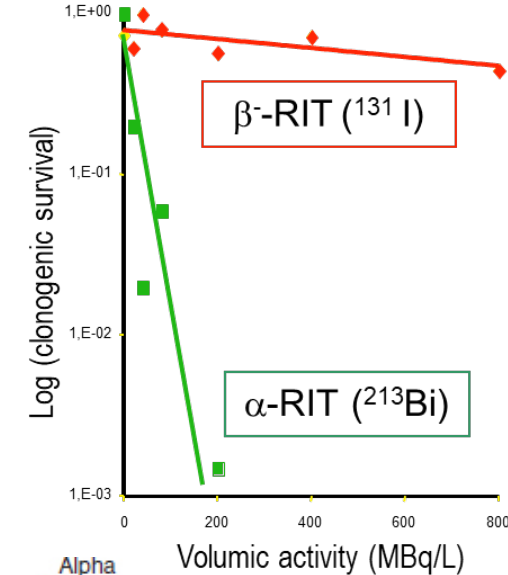
A limited number of alpha emitter candidates

Radionuclide	Half life	# $\alpha$ / decay	$E_\gamma$ (keV)
Tb-149	4,1 h	0,17 ( $\beta$ et $\epsilon$ )	165
<b>At-211</b>	<b>7,2 h</b>	<b>1</b>	<b>79</b>
Bi-212	1 h	1 ( $\beta$ )	727
Bi-213	45 m	1 ( $2\beta$ )	440
Ra-223	11,4 d	4 ( $2\beta$ )	269
Ac-225	10 d	4 ( $2\beta$ )	100
Th-226	31 m	4	111
Th-227	18,7 d	5 ( $2\beta$ )	256

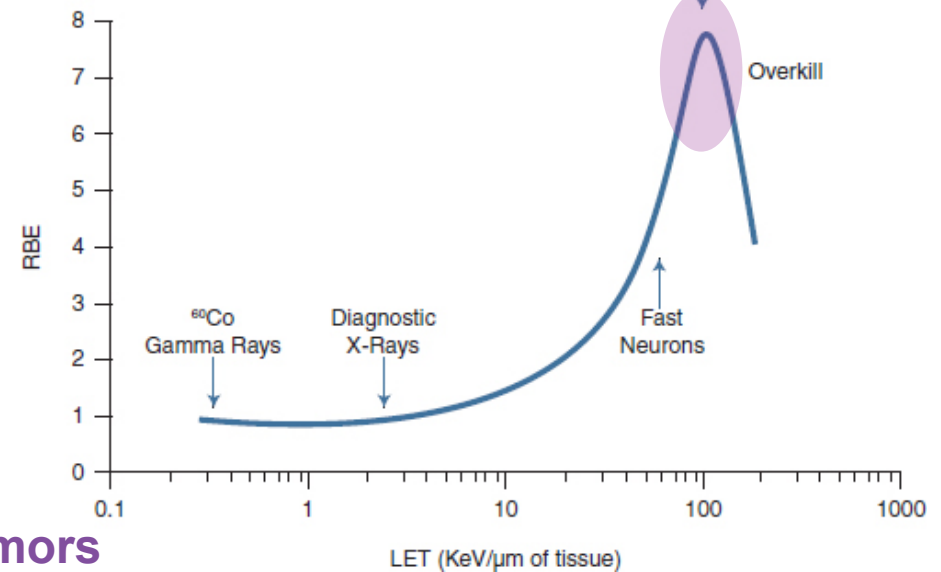
**Highly cytotoxic**,  $E_\alpha$  [5-9] MeV  
 potentially more than  $\beta$  radiation

Better preservation of healthy tissue,  
 range of 40 to 100  $\mu\text{m}$  in water,  
 a few cell's length

**High Relative Biological Efficacy**  
**High LET**,  $\sim 80 \text{ keV}/\mu\text{m}$

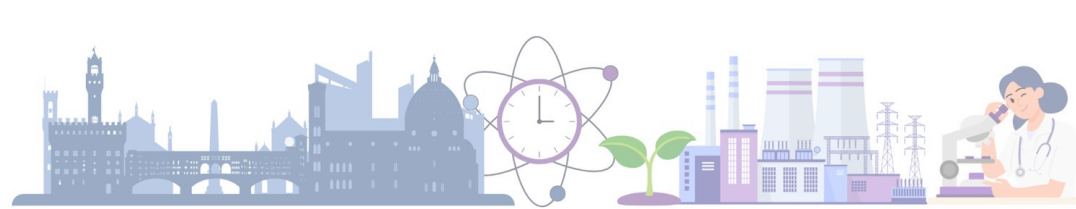


Supiot S. et al. Cancer 2002. 94: 1202-9

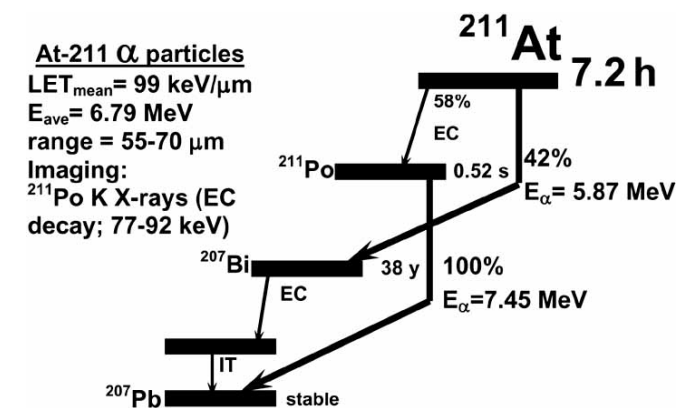


The essential Physics of Medical Imaging, Book, Bushberg et al., 2002

⇒ **To eradicate tumors**



# At-211



**At-211  $\alpha$  particles**  
 LET<sub>mean</sub> = 99 keV/ $\mu$ m  
 E<sub>ave</sub> = 6.79 MeV  
 range = 55-70  $\mu$ m  
**Imaging:**  
<sup>211</sup>Po K X-rays (EC decay; 77-92 keV)

■ **<sup>211</sup>At, main interests:**

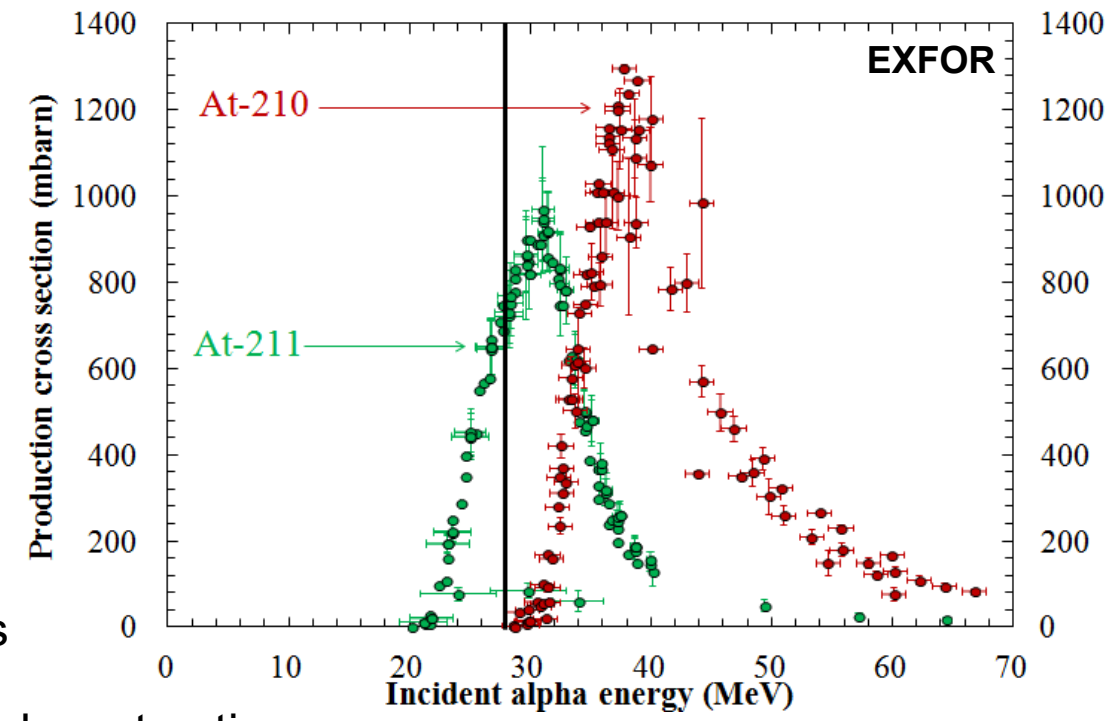
- **Half-life: 7.2 hours** - not too short, not too long
  - Suitable for **RadioPharmaceutical Therapy**
- **One alpha particle** per decay
  - Better **control of the deposited dose**
- **Accelerator** production
  - IBA : C30XP, multi-particules
  - ACSI : TR-ALPHA, 30 MeV "only alpha"

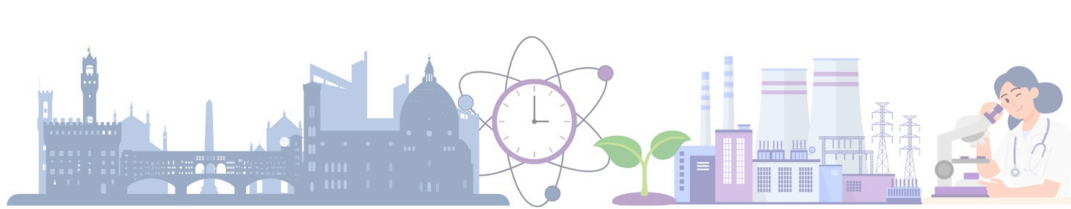
■ **Production route:** **Bi-209 +  $\alpha$   $\rightarrow$  At-211 + 2n**

■ **Keep in mind:**

- **Precise beam energy** adjustment
  - **Avoiding the production of At-210 - ( $\alpha,3n$ ) reaction**
- The At-210 begins to be produced above 28.613 MeV
  - Half-life 8.1 hours
  - 99.8% CE towards **Po-210** with a half-life of 138.4 days

■ **Production scheme:** **energy degrader**, home made target, dry extraction



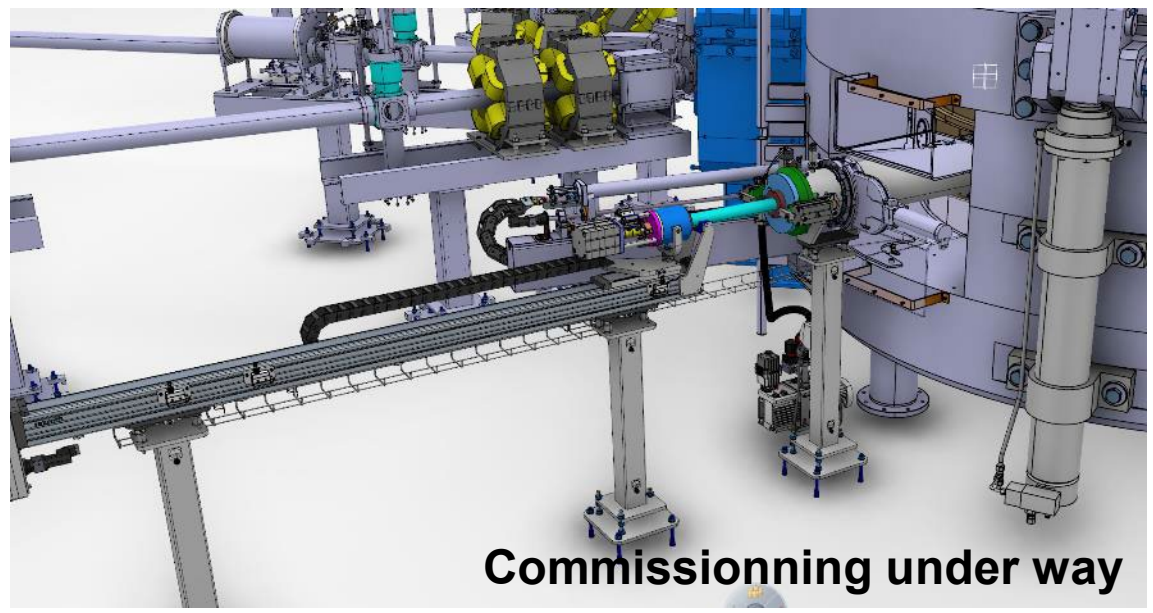


# Internal Target for At-211

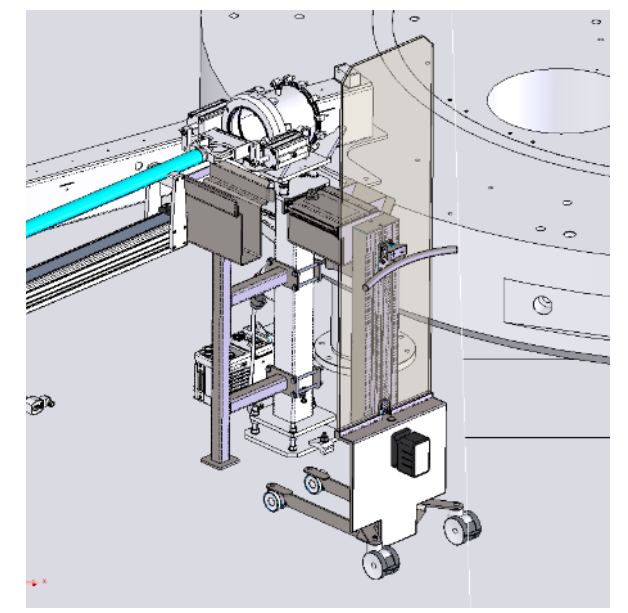
## How to improve the availability of At-211@ARRONAX?

**Upgrade of the machine:** development of an internal target to intercept the beam at the right energy (28-29 MeV)


- No more need to degrade the beam energy and better control of At-210 production
- Limitation will be now the target itself

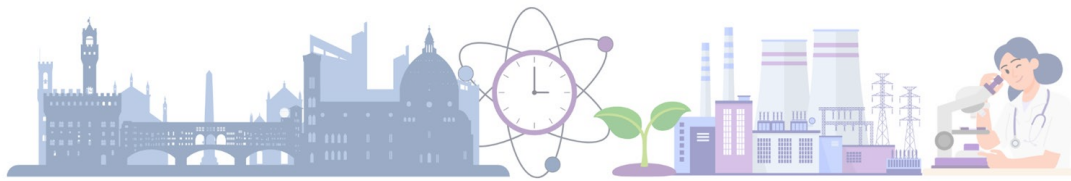


**Commissioning under way**



**Target handling after irradiation**

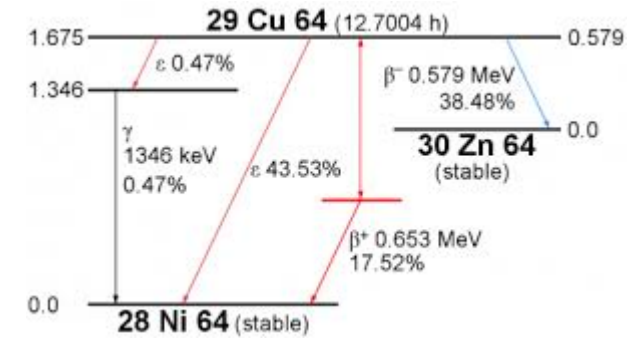
**Our goals:** improve both the quality and the quantities of the final product – participation to 



# Cu-64, what is it for?

## ■ Cu-64, main interests:

- **Half-life: 12.7 hours** - not too short, not too long
  - Suitable for **Positron Emission Tomography**
- **Theranostic pair** with Cu-67
  - **What you see is what you treat**
- **Applications**
  - PET imaging of NET - Detectnet (Curium Pharma)
    - FDA approval date: September 3, 2020

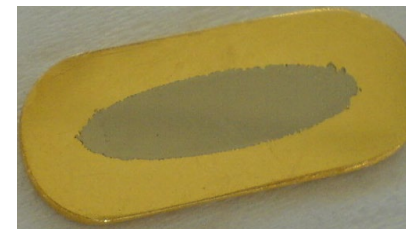
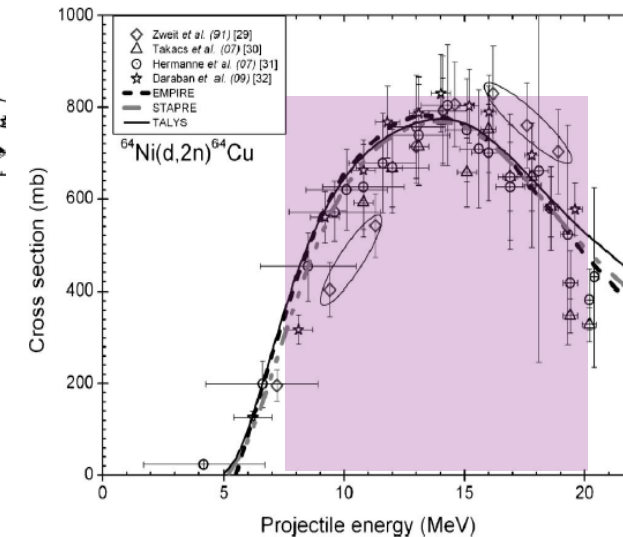
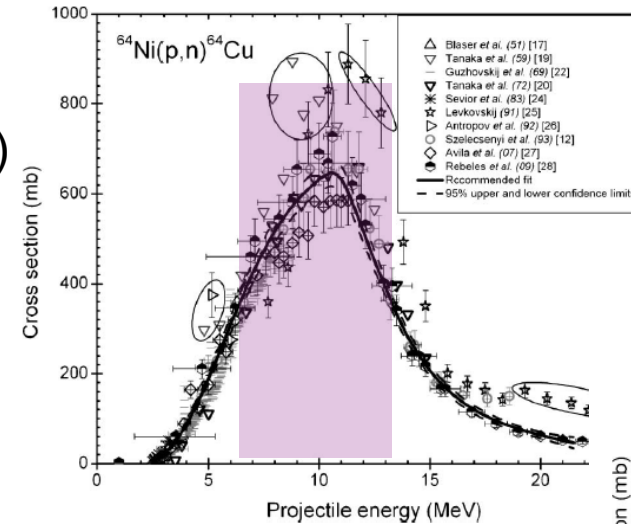


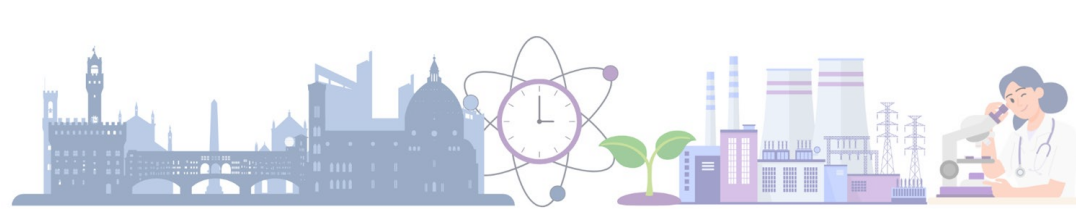
## ■ Production routes:

- **Main:** Ni-64 + p → Cu-64 + n
- **Alternative:** Ni-64 + d → Cu-64 + 2n

## ■ Production scheme:

- **Enriched Ni-64** electroplated on Au backing
- Monthly production of CuCl<sub>2</sub>

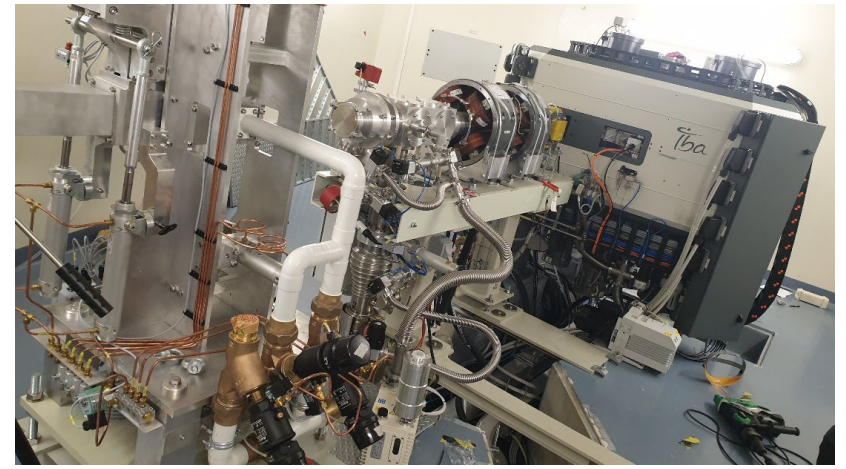
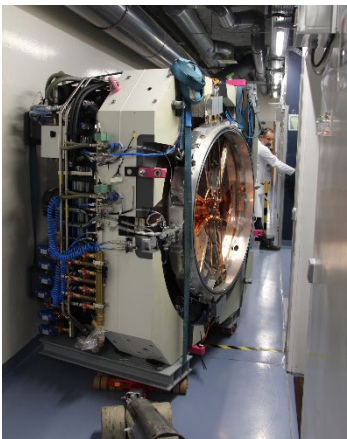
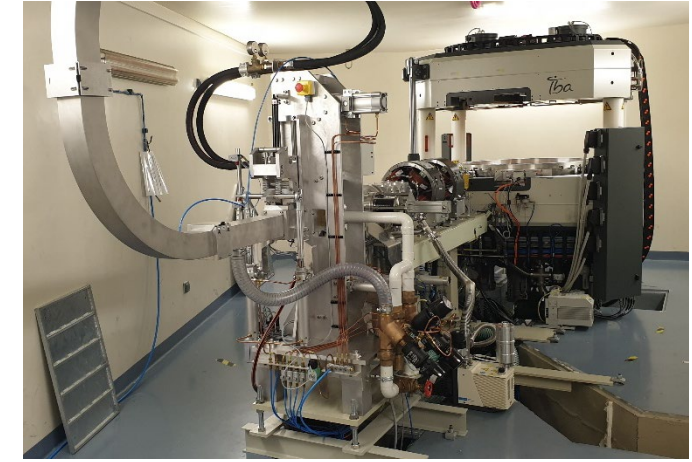
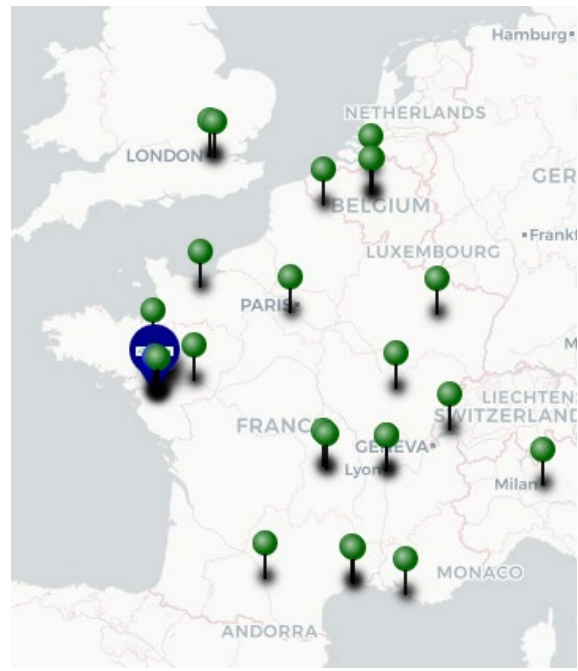
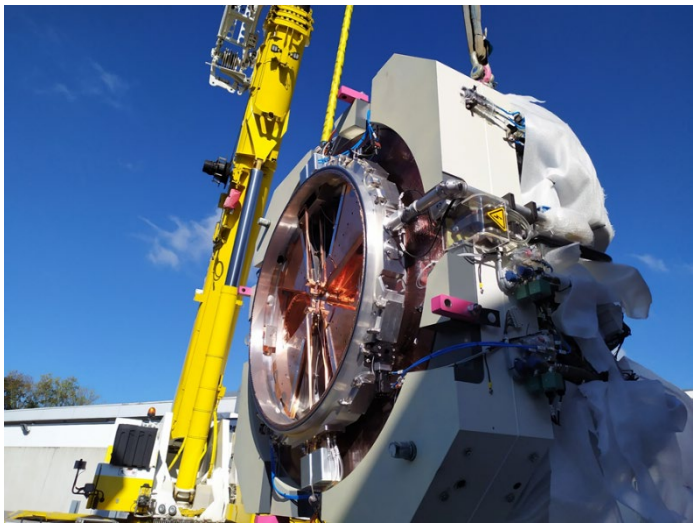


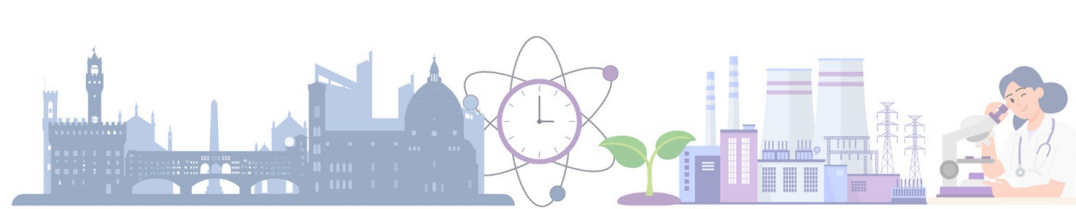


# Kiube 180 for Cu-64 (F-18)

## How to improve Cu-64 availability in France and neighbouring countries (current partners)

Installation of a 18 MeV cyclotron, IK18, IBA Kiube 180, with a solid target system customized to be connected to the existing one for C70XP





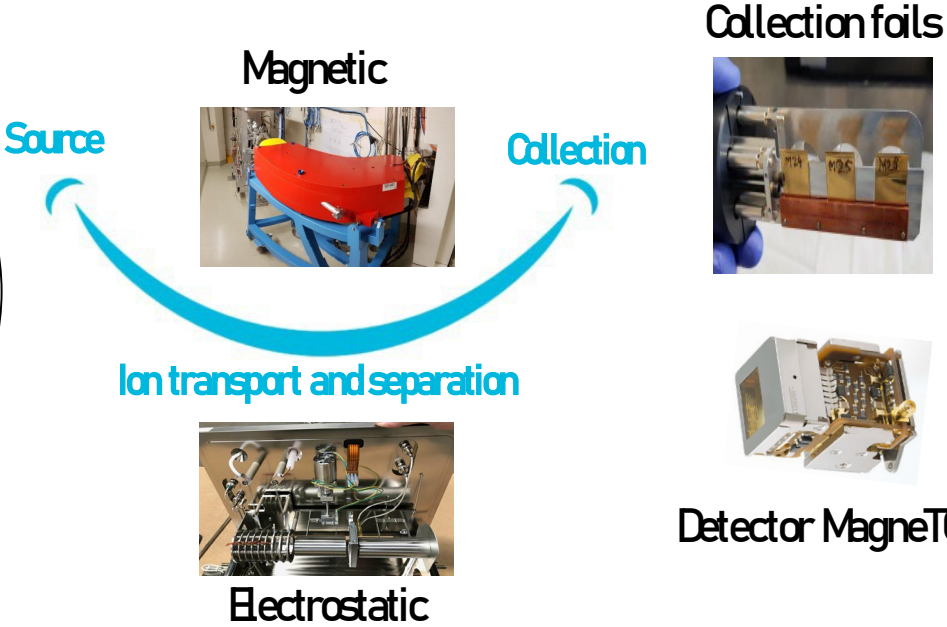
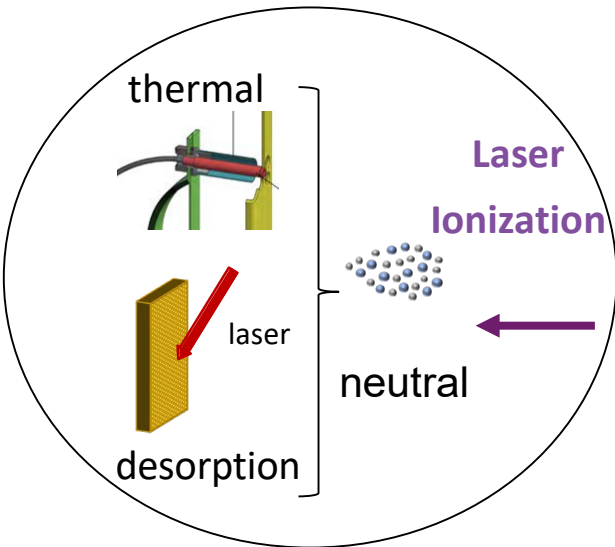
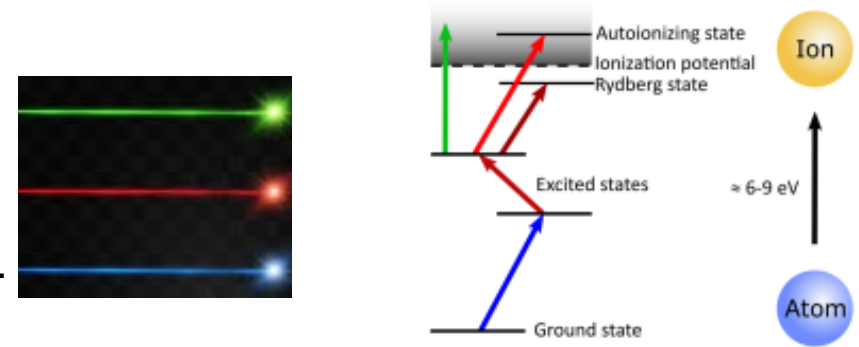
# SMILES project

## Mass separation coupled with laser ionization for environmental and health applications

Develop a mass separation device that includes resonant laser ionization:

- To perform analytical measurements on environmental sample.
- To build expertise on these techniques and on associated simulation tools.
- To prepare for an off-line mass separator for radionuclide production.

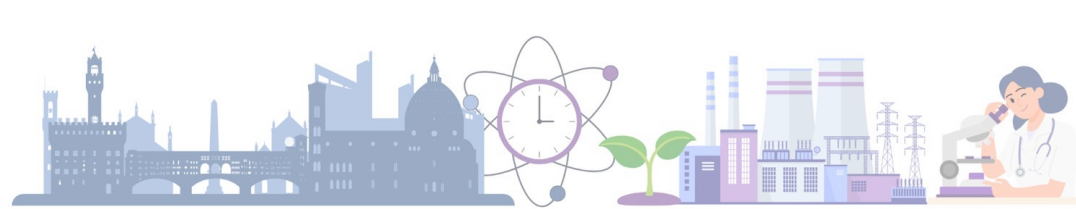
### Multistep Selective Laser Ionization



### Mass selection

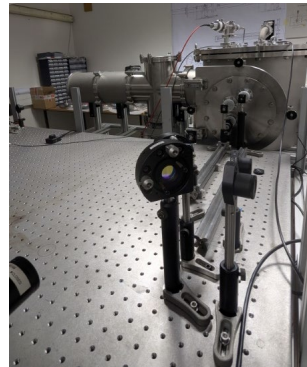
62Ga 116.48 MS ε: 100.00%	63Ga 32.4 S ε: 100.00%	64Ga 3.627 M ε: 100.00%	65Ga 15.2 M ε: 100.00%	66Ga 9.49 H ε: 100.00%	67Ga 3.2617 D ε: 100.00%	68Ga 67.71 M ε: 100.00%
61Zn 89.1 S ε: 100.00%	62Zn 9.186 H ε: 100.00%	63Zn 38.47 M ε: 100.00%	64Zn STABLE 46.63%	65Zn 243.66 D ε: 100.00%	66Zn STABLE 27.90%	67Zn STABLE 4.10%
60Cu 23.7 M ε: 100.00%	61Cu 3.333 H ε: 100.00%	62Cu 9.67 M ε: 100.00%	63Cu STABLE 69.17%	64Cu 12.701 H ε: 61.53% β-: 38.50%	65Cu STABLE 30.83%	66Cu 5.120 M β-: 100.00%
59Ni 7.6E+4 Y ε: 100.00%	60Ni STABLE 26.223%	61Ni STABLE 1.140%	62Ni STABLE 3.634%	63Ni 100.1 Y β-: 100.00%	64Ni STABLE 0.926%	65Ni 2.5172 H β-: 100.00%
58Co 70.86 D ε: 100.00%	59Co STABLE 100%	60Co 1925.28 D β-: 100.00%	61Co 1.650 H β-: 100.00%	62Co 1.50 M β-: 100.00%	63Co 27.4 S β-: 100.00%	64Co 0.30 S β-: 100.00%

Courtesy of N. Michel



# SMILES Project

- Operational linear TOF
- SMILES lab set-up in new building



2026

- Reception / installation of magnet
- Finalization of ion measurement system and species collection for magnetic separator



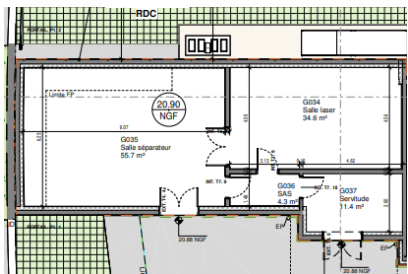
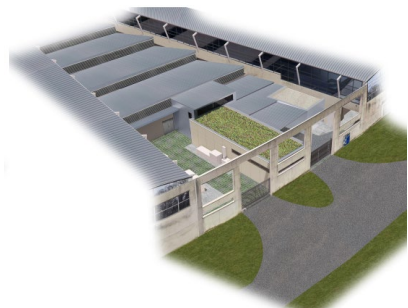
2028

- Creation of new research collaboration projects with external partners



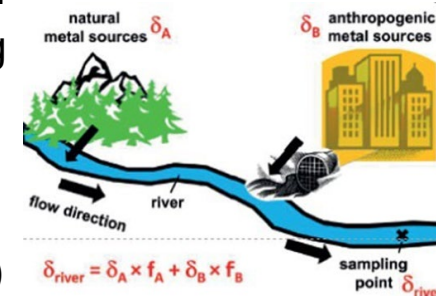
2025

- Magnet call for tenders
- Elaboration of magnetic separator transport line
- Copper and actinide isotopes analyses with TOF-R coupled with laser ionization and comparison with other techniques



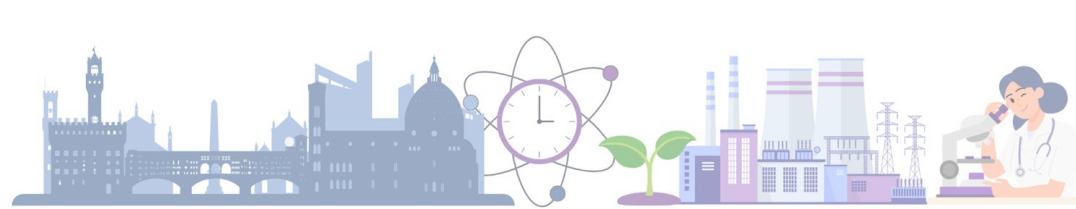
2027

- Cross section measurements of stable copper isotopes during Cu-61,64 or 67 productions
- Ra-226 and Ra-228 analysis in different radioecological samples (water, soils, diatoms..)



2029

Adapted from N. Michel



# Conclusions

**GIP ARRONAX** possesses 2 cyclotrons:

- a versatile C70XP cyclotron allowing a wide range of radionuclide production as well as irradiation research.
- a Kiube-180 cyclotron, IK18, under final commissioning

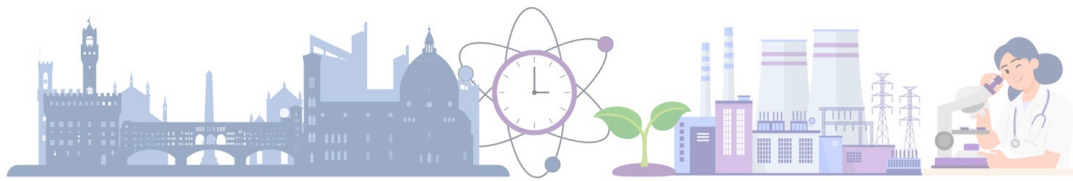
**GIP ARRONAX and PRISMA** are developing and producing radionuclides but also radiopharmaceuticals for research in nuclear medicine

**PRISMA** is also working on:

- Which isotopes for tomorrow's nuclear medicine?
- Hadronbiology at very high dose rates
- Detection, ion beam analysis
- Mass separation coupled with laser ionisation

These work can only be achieved through collective work at all scales (local, national and international) and with all partners (academia and industry)





# Conclusions

More than **500 000** patients have benefited of our Sr-82 in the **USA** since 2012  
More than **20 000** european patients have benefited of our Sr-82 since 2020  
More than **200** clinical doses for clinical trials produced in our radiopharmacy

## Thank you for your attention

The **ARRONAX** project is supported by:  
**Regional Council of Pays de la Loire**  
**Nantes Université**  
**French government (CNRS, INSERM)**  
**European Union.**

**Subatech laboratory** is supported by:  
**CNRS** Nucléaire et Particules  
**Nantes Université**  
**IMT Atlantique**

This work has been, in part, supported by a grant from the French National Agency for Research called "Investissements d'Avenir", Equipex Arronax-Plus noANR-11-EQPX-0004, Labex IRON no ANR-11-LABX-18-01, ISITE NEXt no ANR-16-IDEX-007, EU Horizon 2020 PRISMAP program n° 101008571, Accelerate.EU program n° 101173001.