ISOLPHARM_EIRA

A new approach to create high purity radionuclides for nuclear medicine applications

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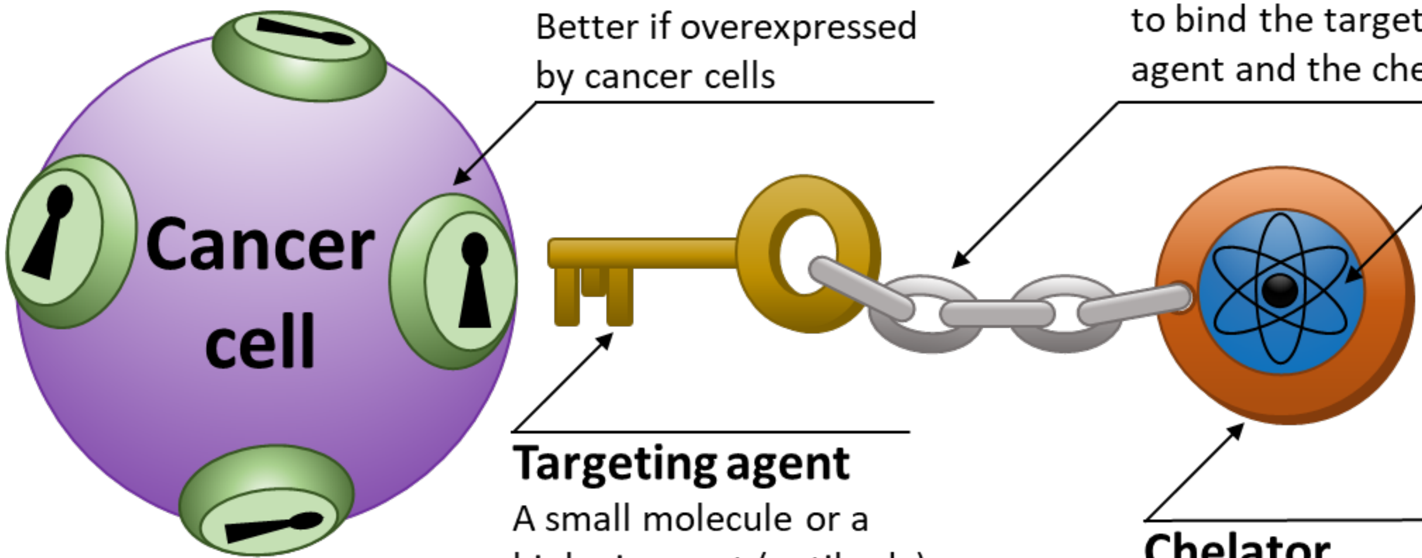
Radiopharmaceuticals



Cancer target
Better if overexpressed by cancer cells

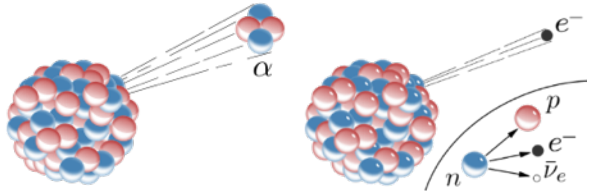
Linker/spacer
to bind the targeting agent and the chelator

Radioisotope
May be a diagnostic isotope for imaging and/or a therapeutic isotope for treatment

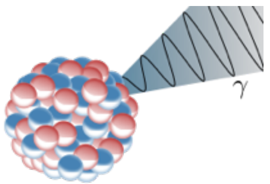
Targeting agent
A small molecule or a biologic agent (antibody)

Chelator
Molecule carrying the radioisotope

Therapeutic agents



Diagnostic agents



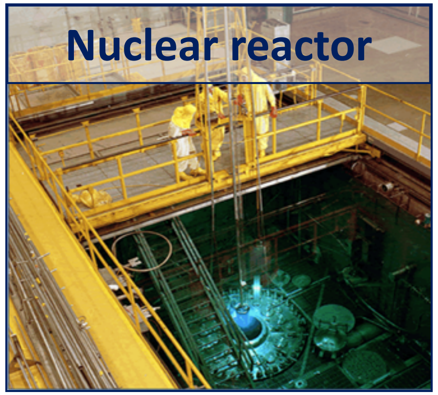
Radionuclides properties:

- Decay properties
- Half-life
- Chemical properties
- Production Feasibility

Specific activity →
$$\frac{\text{activity of the radioisotope (MBq)}}{\text{mass of the element (mg).}}$$

Radionuclidic purity →
$$\frac{\text{activity of the desired nuclei}}{\text{overall activity of the compound}}$$

Production methods



Radionuclides from traditional methods:

- High neutron/proton fluxes required
- Irradiation of targets of the same element
- Direct reaction methods -> A(p,x) or A(n,x)…
- Target with large activation levels
- Chemical separation required

→ Isotopic impurities (Low S.A.)

With the innovative ISOL technique:

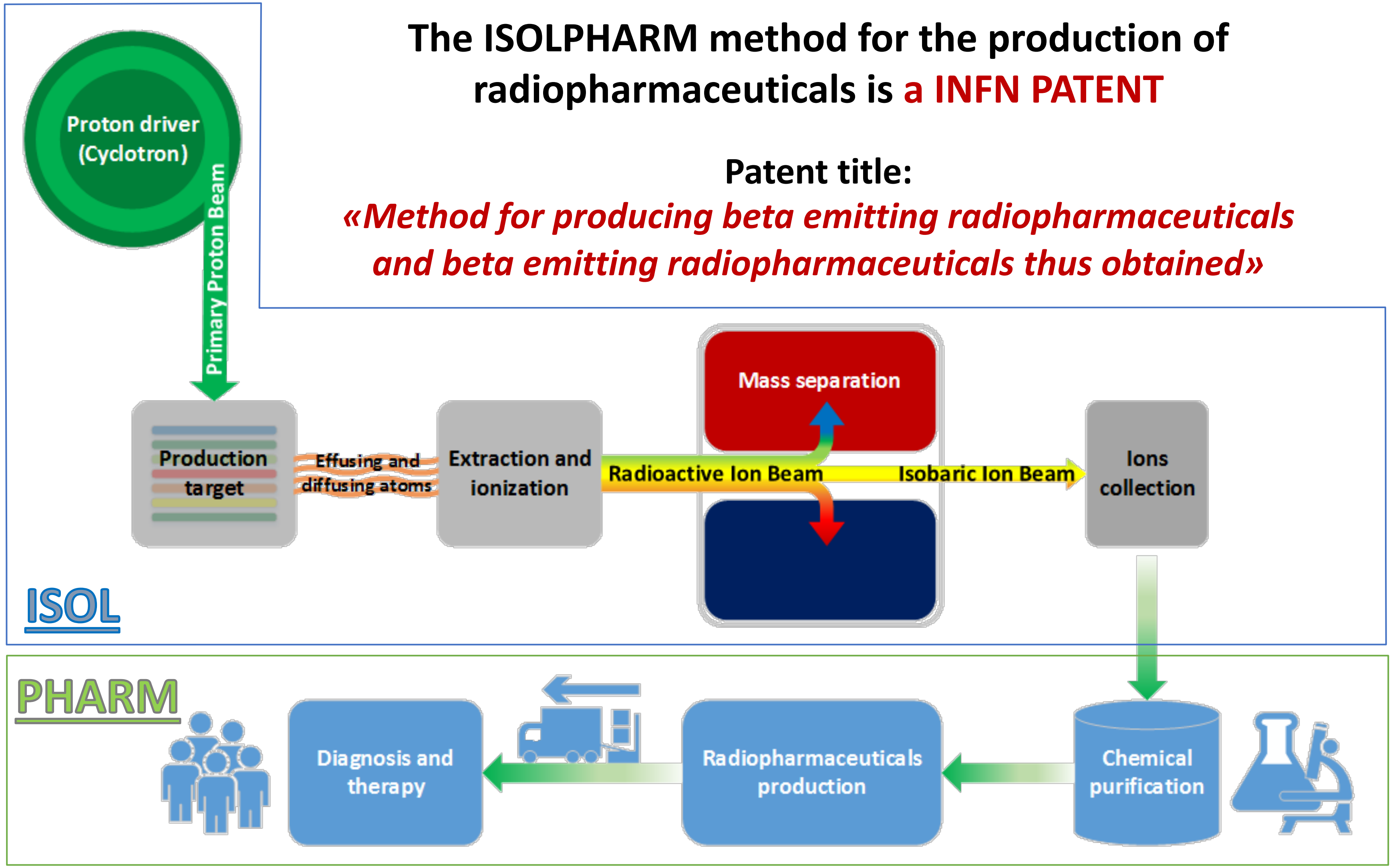
- **Radionuclides can be easily produced as carrier-free isotopes (Mass Separation)**
- **No nuclear reactor required for several beta-radionuclides**

The ISOLPHARM method

The ISOLPHARM method for the production of radiopharmaceuticals is a INFN PATENT

Patent title:

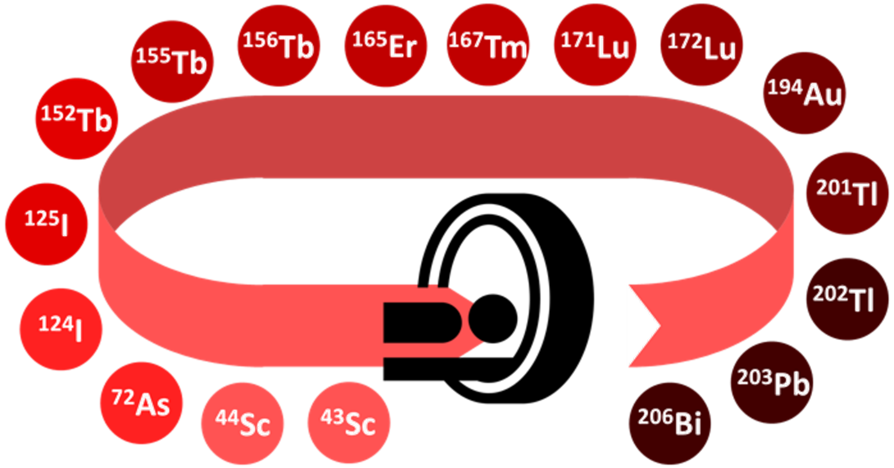
«Method for producing beta emitting radiopharmaceuticals and beta emitting radiopharmaceuticals thus obtained»



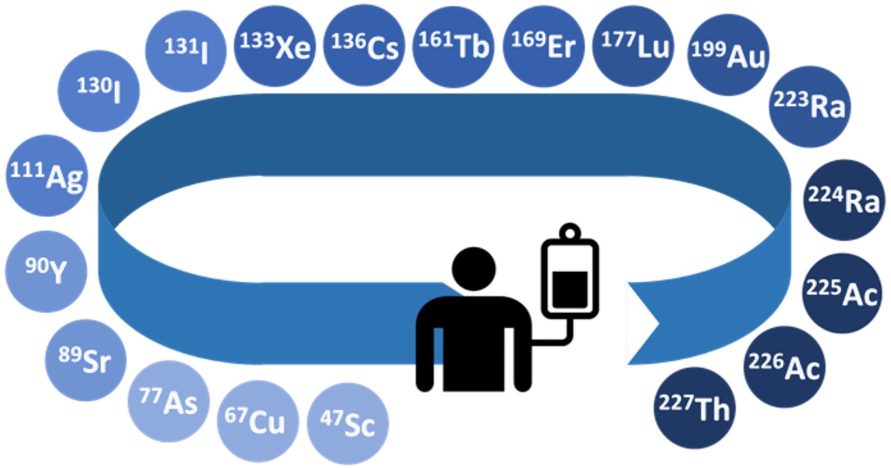
Flexible production, high specific activity & radionuclidic purity

Possible ISOL isotopes medical interest

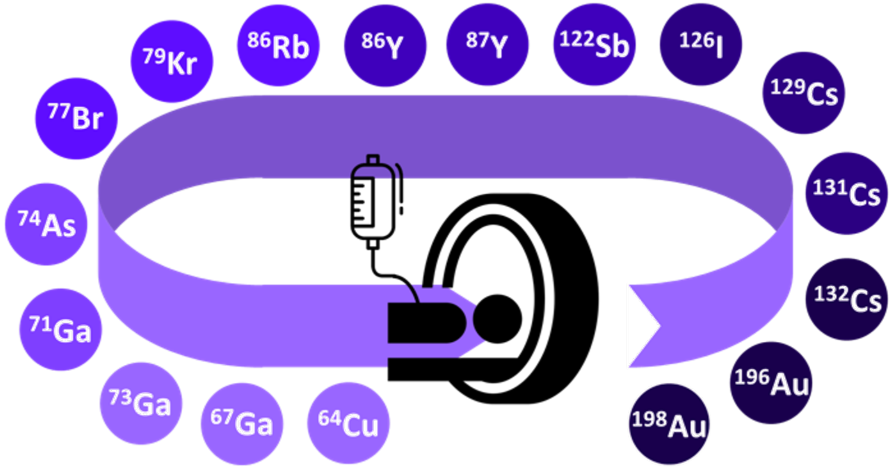
Diagnostic isotopes



Therapeutic isotopes



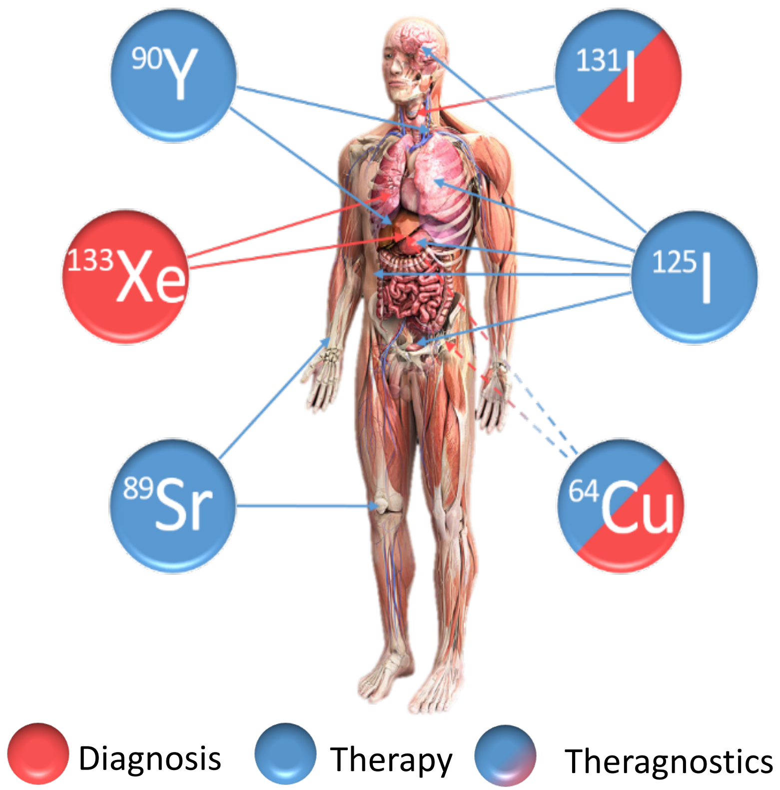
Theragnostic isotopes



Among the wide set of **ISOL producible nuclides**, almost **60** show relevant properties for medicine, in terms of **half-life**, **decay radiation** and **chemical behavior**

Possible ISOL isotopes medical interest

Early feasibility studies were focused on state-of-art radionuclides:



F. Borgna *et al.*, *Appl. Radiat. Isot.*, 2017

ISOLPHARM true potential can be expressed if innovative/less available nuclides are considered

^{111}Ag
- $t_{½}$: 7.45 d
- 100% β- (360 keV av.)

^{64}Cu pair ^{67}Cu

^{64}Cu:
- $t_{½}$: 12.701 h
- 38,5% β- (191 keV av.)
- 61,5% β+ (PET)

^{67}Cu:
- $t_{½}$: 2.58 d
- 100% β- (162 keV av.)

^{43}Sc pair ^{47}Sc

^{43}Sc:
- $t_{½}$: 233 min
- 100% β+/ϵ (PET)

^{47}Sc:
- $t_{½}$: 3.4 d
- 100% β- (162 keV av.)

^{152}Tb pair ^{149}Tb pair ^{155}Tb

^{152}Tb:
- $t_{½}$: 17.5 h
- 100% β+/ϵ (PET)

^{149}Tb:
- $t_{½}$: 4.12 h
- 16.7% α (3.97 MeV)

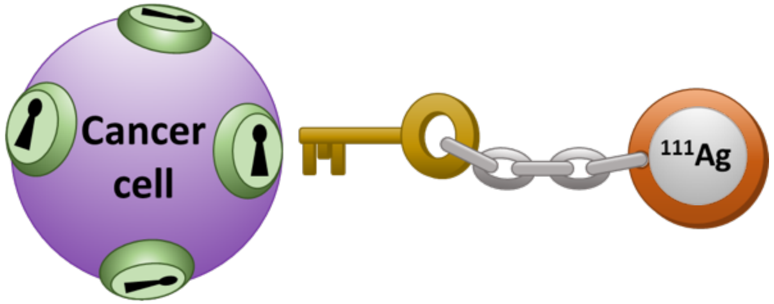
^{155}Tb:
- $t_{½}$: 5.32 d
- 100% β+/ϵ (SPECT)

Main goal of ISOLPHARM_EIRA

To **go beyond the results of ISOLPHARM_Ag** and further promote the research on a ^{111}Ag based radiopharmaceutical by:

1. Producing the first batches of radioactive ^{111}Ag via neutron irradiation at the existing TRIGA Mark II research reactor at LENA.

2. Testing *in-vitro* and *in-vivo* the first ^{111}Ag radiolabeled compounds



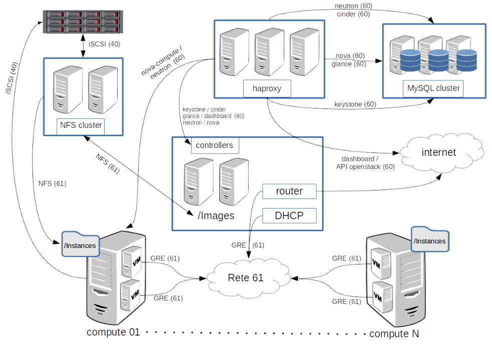
Infrastructures and Laboratories

^{111}Ag

Task 1: Physics

INFN LNL · INFN PADOVA · INFN PAVIA

MC simulations: CloudVeneto



cloudveneto

Legnaro National Laboratory

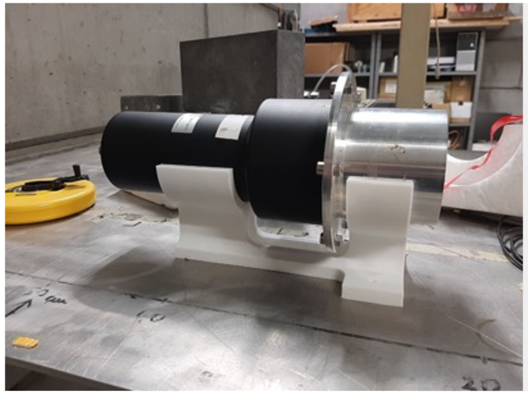
^{111}Ag production and quality control: LENA

Università degli Studi di Padova · Dipartimento di Fisica e Astronomia Galileo Galilei · Università di Pavia · L.E.N.A. · Università degli Studi di Brescia · DIMI

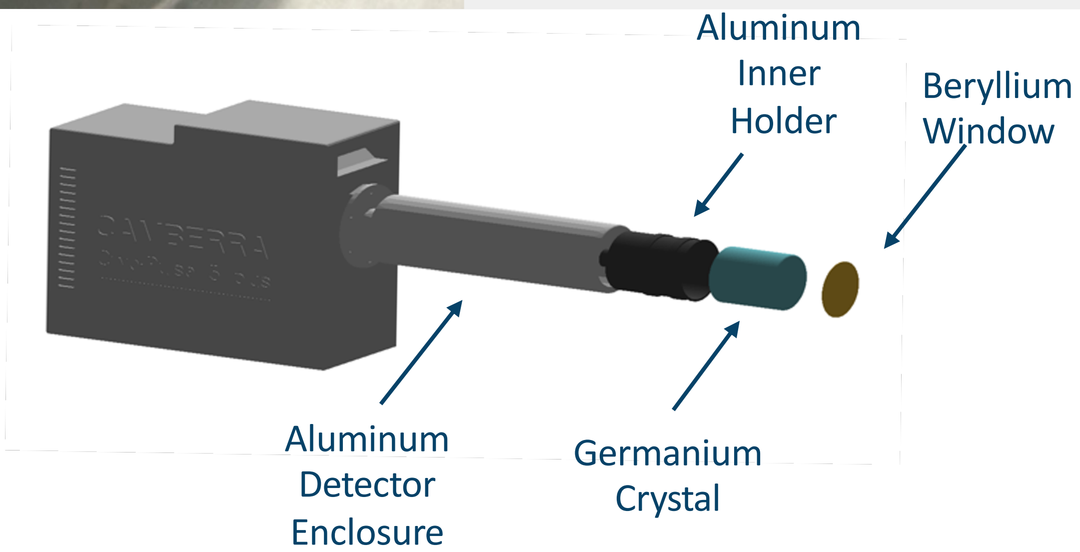
Spectroscopic system for ^{111}Ag characterization

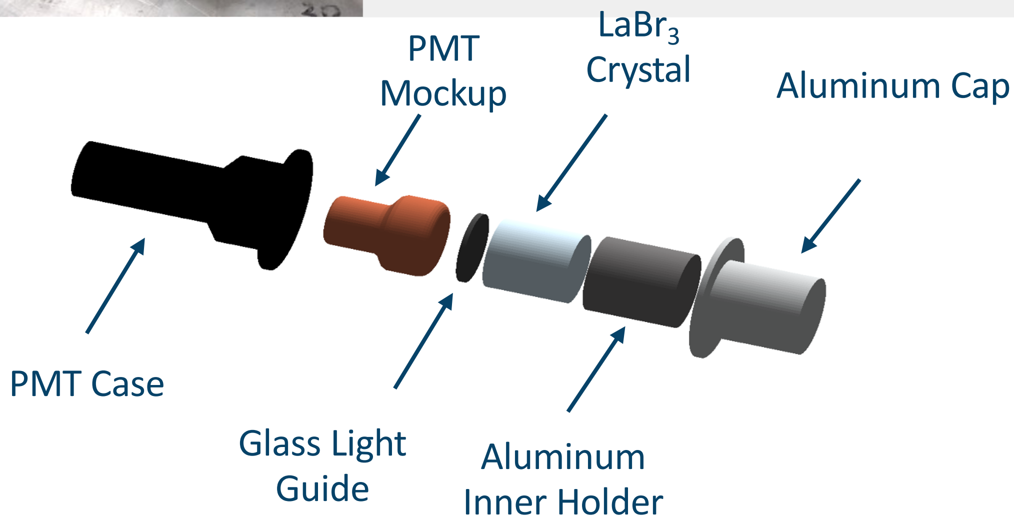
The spectroscopic system consists of two detectors: a germanium detector and a lanthanum bromide scintillator. The system has been characterized offline and compared with Monte Carlo simulations.

- Very good energy resolution: 2 keV at 1.3 MeV.
- Slow preamplified signal (~ 100 μs).
- Typical acquisition rate < 10 kcps.

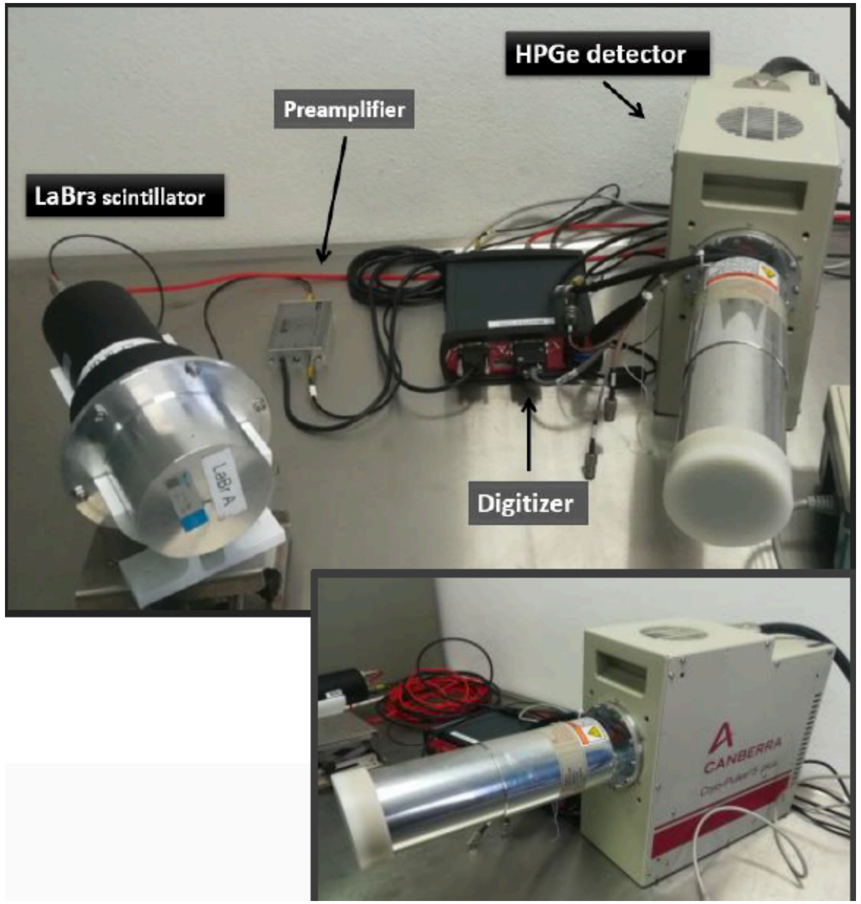


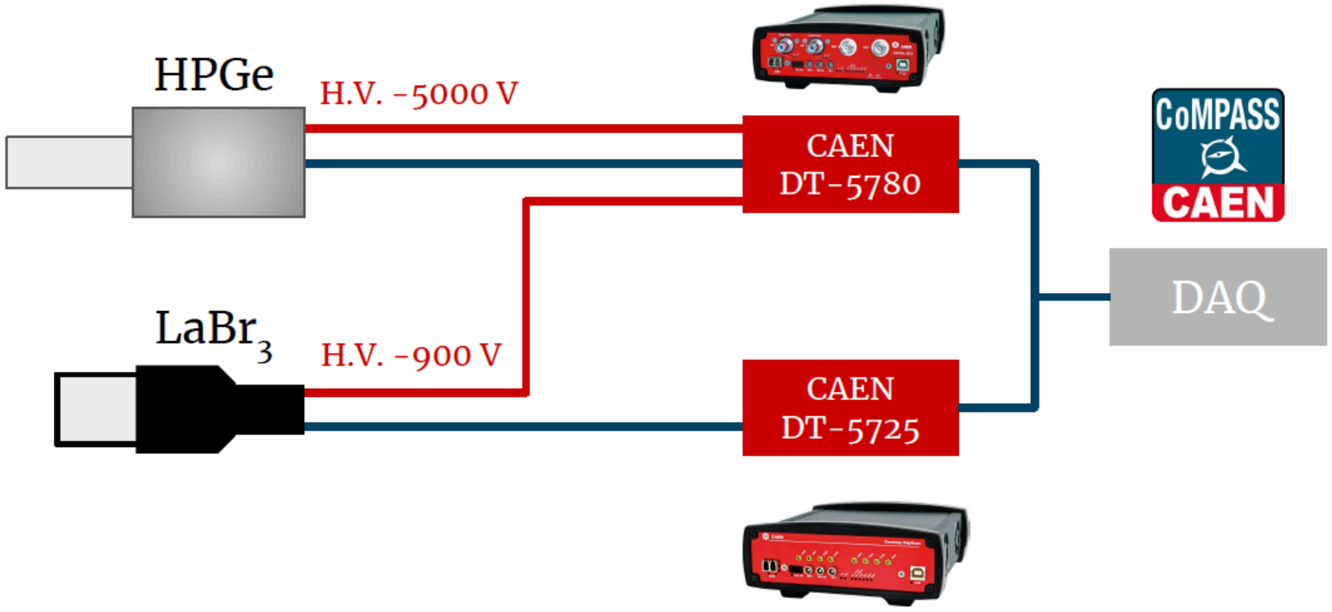
- Fair energy resolution < 30 keV at 1.3 MeV.
- Fast anode signal ~100ns.
- Fast acquisition rate up to 500 kcps
- Significant intrinsic background to be considered (~ 1 kHz)





Spectroscopic system for ^{111}Ag characterization





Irradiation Experiments at L.E.N.A.

28/10/2020 First Experiment

1. Irradiation time 1 hour between 11:22- 12:22
2. ^{nat}Pd sample mass: 55.5 mg

Data acquisition between 28/10 and 02/11 with the $LaBr_3$ detector and DT5725 digitizer.

10/11/2020 Second Experiment

1. Irradiation time 1 hour between 8:50 - 9:50
2. ^{nat}Pd sample mass: 42.1 mg

Data acquisition between 10/11 and 17/11 with both $LaBr_3$ and HPGe.

^{nat}Pd

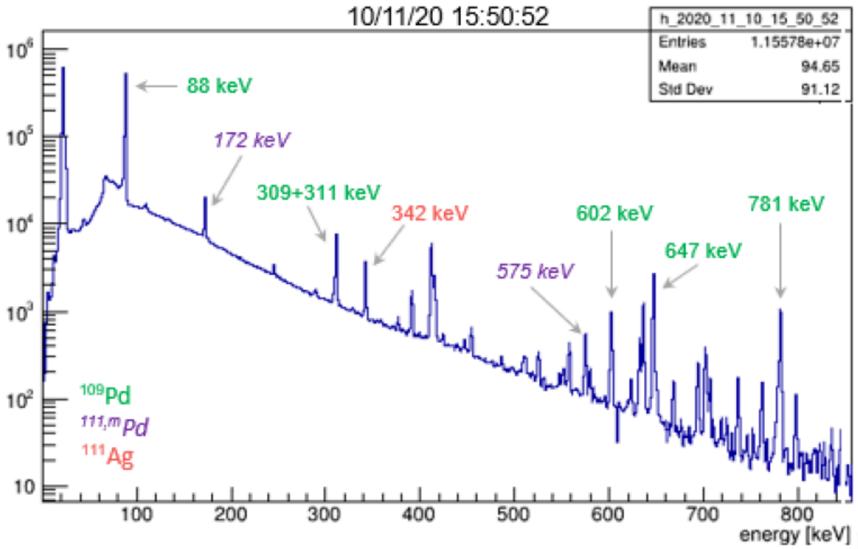
09/02/2021 Third Experiment

1. Irradiation time 1 hour between 11:28 - 12:28
2. ^{110}Pd sample mass: 62.7 mg

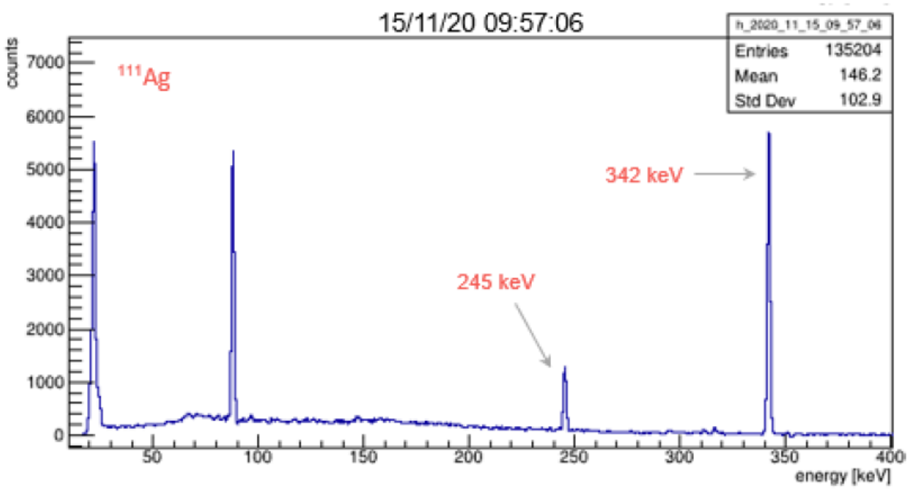
Data acquisition between 09/02 and 17/02 with both $LaBr_3$ and HPGe.

^{110}Pd

Spectroscopic analysis of irradiated samples



Spettro dopo 7 h dall'inizio dell'irraggiamento



Spettro dopo 5 d dall'inizio dell'irraggiamento

^{111m}Pd $T_{1/2}$ 5.5(1) h

E [keV]	Y[%]
➢ 575.0(1)	46(5)

transizione γ che segue
^{111m}Pd → ^{111}Ag + β−

E [keV]	Y[%]
➢ 172.18(8)	3.3(4)

transizione che segue il decadimento al ground state

^{111}Ag $T_{1/2}$ 7.45(1) d

E [keV]	Y[%]
➢ 245.40(2)	1.24(9)
➢ 342.13(2)	6.7(3)

transizioni γ analizzate seguono il decadimento
^{111}Ag → ^{111}Cd + β−

^{109}Pd $T_{1/2}$ 13.58(12) h

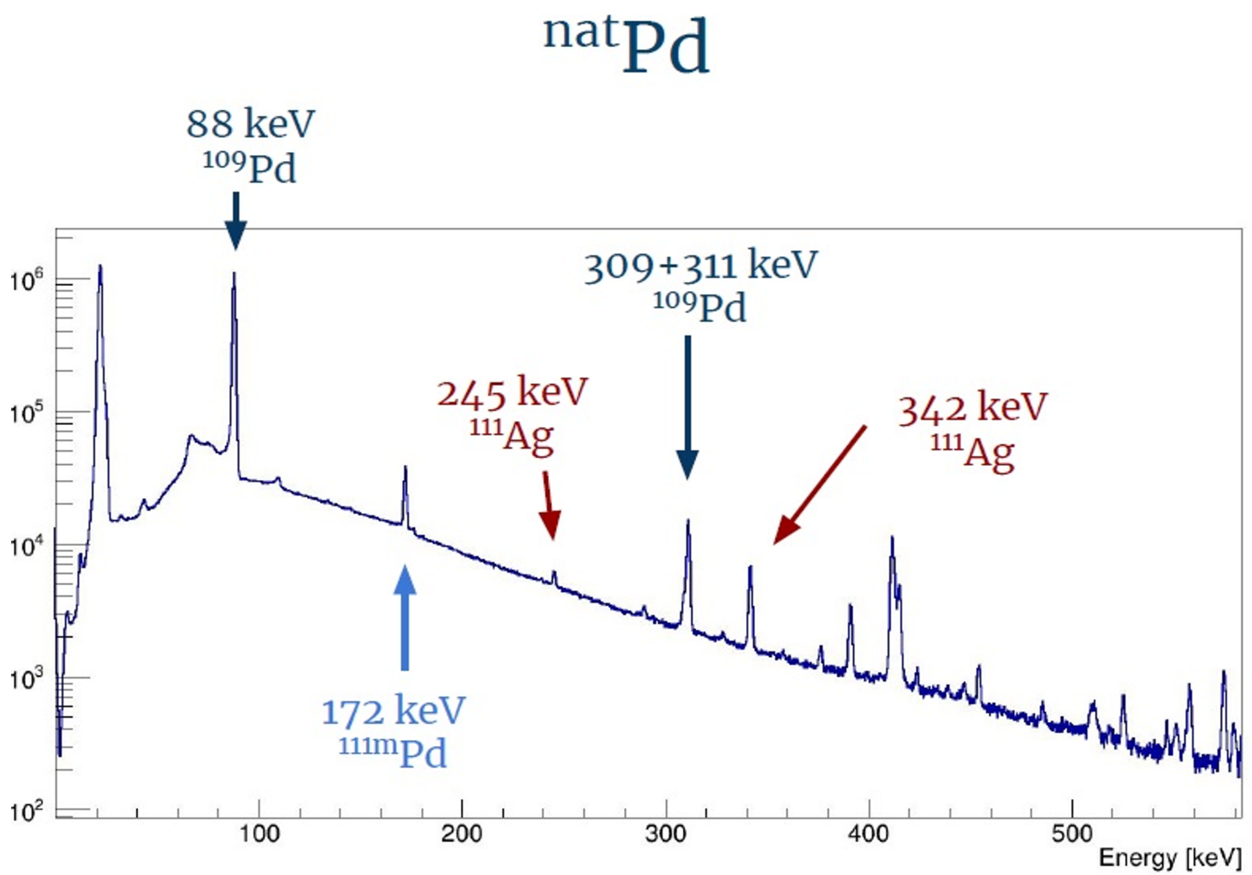
E [keV]	Y[%]
➢ 88.03360(103)	3.66(6)
➢ 311.4(1)	0.0314(21)
➢ 602.6(2)	0.0086(6)
➢ 647.3(1)	0.0252(14)
➢ 781.4(1)	0.0123(9)

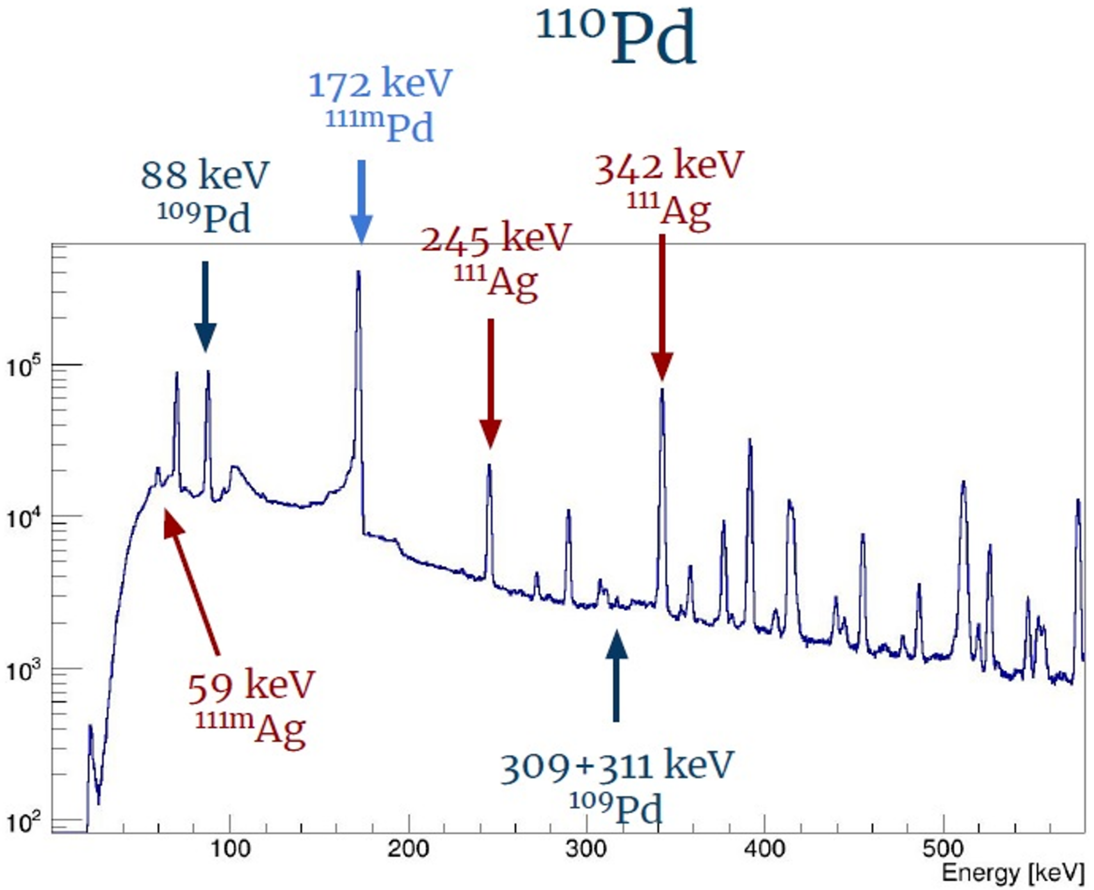
transizioni γ analizzate che seguono il decadimento
^{109}Pd → ^{109}Ag + β−

ISOLPHARM
SPES exotic beams for medicine

Spectroscopic analysis of irradiated samples for yield analysis

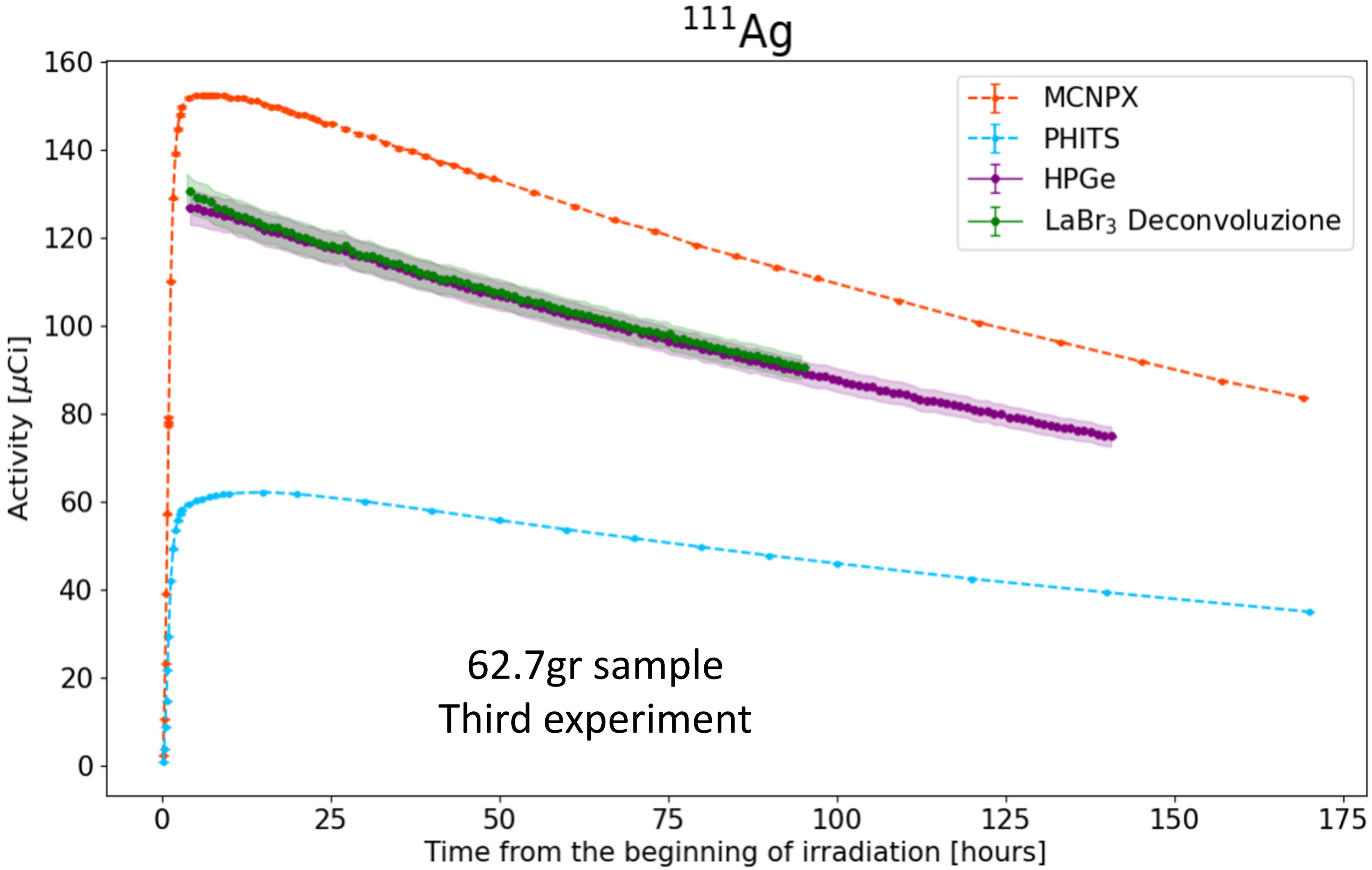
6 hours after the end of irradiation (taken with HPGe detector)





^{110}Pd Irradiation - ^{111}Ag

- ^{111}Ag yields measured with HPGe and $LaBr_3$ are compatible with each other.
- MCNPX seems to overestimate the activity of ^{111}Ag (~20%)
- PHITS underestimate the value from measurements (~90 %)



Final result

We can produce 2 mCi of ^{111}Ag starting from 100µCi of ^{110}Pd after 3 days of irradiation (6 hours per days).

What's next?

- Further simulation with MCNPX for understand the overstimation
- Customization of PHITS with new cross section
- Carrying on a detailed analysis of ^{111}Ag γ-lines.
- Analyzing data taken with $LaBr_3$ + DT5725 for comparison.
- Analyzing γ-γ coincidence data taken with DT5780.