

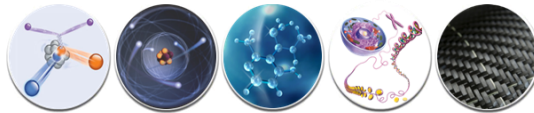
Projet BePAT :

BeaQuant, a digital autoradiograph for the production of radionuclides for nuclear medicine applications

Arthur Bongrand

Melissa Azzoune, Samuel Duval, Arnaud Guertin Julie Champion

Boulogne-Billancourt, 21 – 25 november



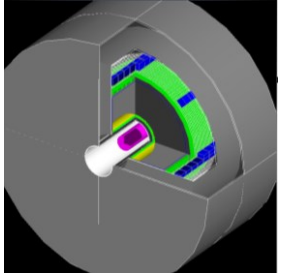
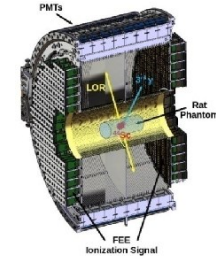
NEA
NUCLEAR ENERGY AGENCY

My career path

Master 2
Physique médicale



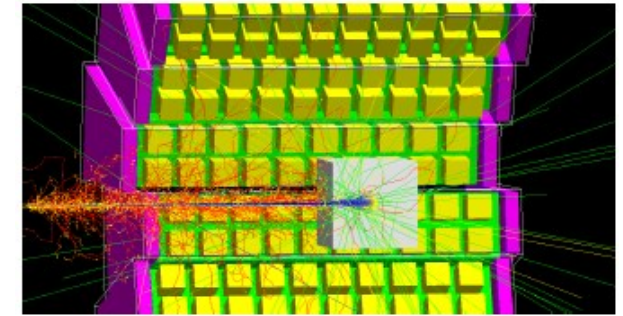
M2 Rayonnements Ionisants et Applications médicales (RIA)



PhD
2016-2019



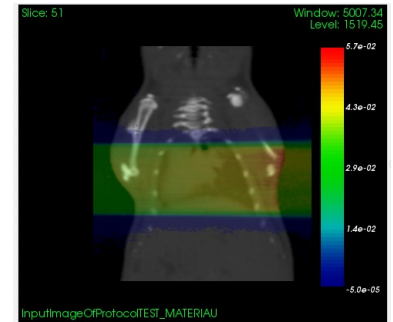
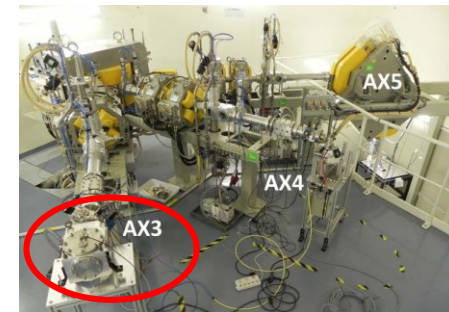
Studies of the performance of a detector dedicated to ballistic control during hadrontherapy treatments using Monte-Carlo simulation code



ICO – ARRONAX – NANTES
2019-2021



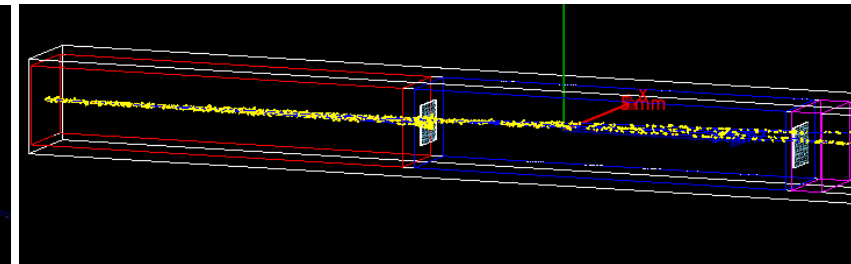
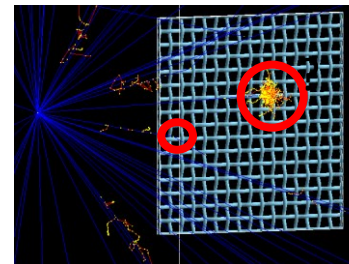
FLASH radiotherapy



Ai4R – SUBATECH
12/2021 - 12/2023



Projet BePAT



BeaQuant : real-time autoradiography system for “small” samples

Autoradiography

→ An **emission imaging technique** carried out from a radioactive source placed in contact with an emulsion, a photographic film or an adapted detector

→ Area of interest located at the surface ($\approx 10 \mu\text{m}$ deep)

Applications

→ Pre-clinical (oncology + drug discovery)

Visualization of molecules or fragments of molecules labeled with radioactive elements

→ Geology (study of uraniferous rocks, environmental pollution...)

Samples

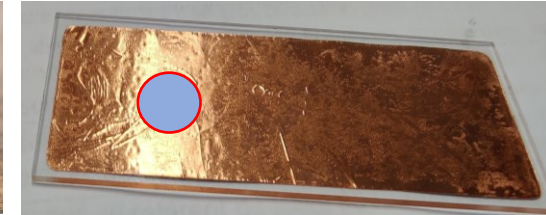
→ "Thin" (<1 cm thick) \approx size of a small sugar square

→ Can be electroplated on a glass slide, a “sugar” or a **metal foil (new)**

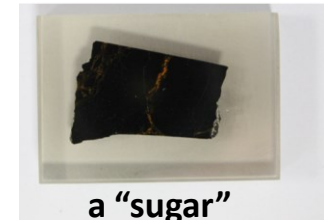
Specificities of the BeaQuant

→ Real-time direct counting

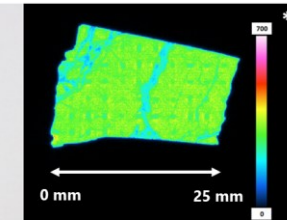
- ✓ Quantification
- ✓ Tracking



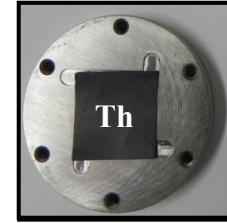
Glass slide



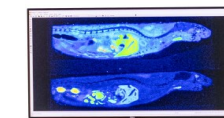
a “sugar”



Lefevre et al., under review NIMA



Metal foil



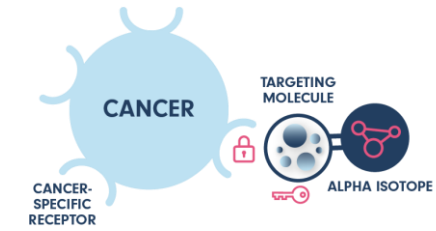
BeaQuant



Technology	Direct gaseous counter
Performance	<ul style="list-style-type: none"> •Spatial: Alpha 20 μm – Beta 20 μm – High energy β or β^+ 50 μm •Linearity over 5 orders of magnitude •Sensitivity: 0.0005 cpm/mm² (\approx mBq)
Markers	All radioisotopes

Radionuclide production scheme and expertise of PRISMA@Subatech

Most important factors
→ Purity & Quantity



Need identified in the clinic:
Advances in biology, oncology ...

Determine the optimal production path

High current

Extraction & Purification
Chemistry/Physics

Radioactive marker

Tracer



Identify the (best) candidate radionuclides

Nuclear data
Cross section

Develop targeting

Fundamental chemistry
Radiochemistry

Towards preclinical use

BePAT

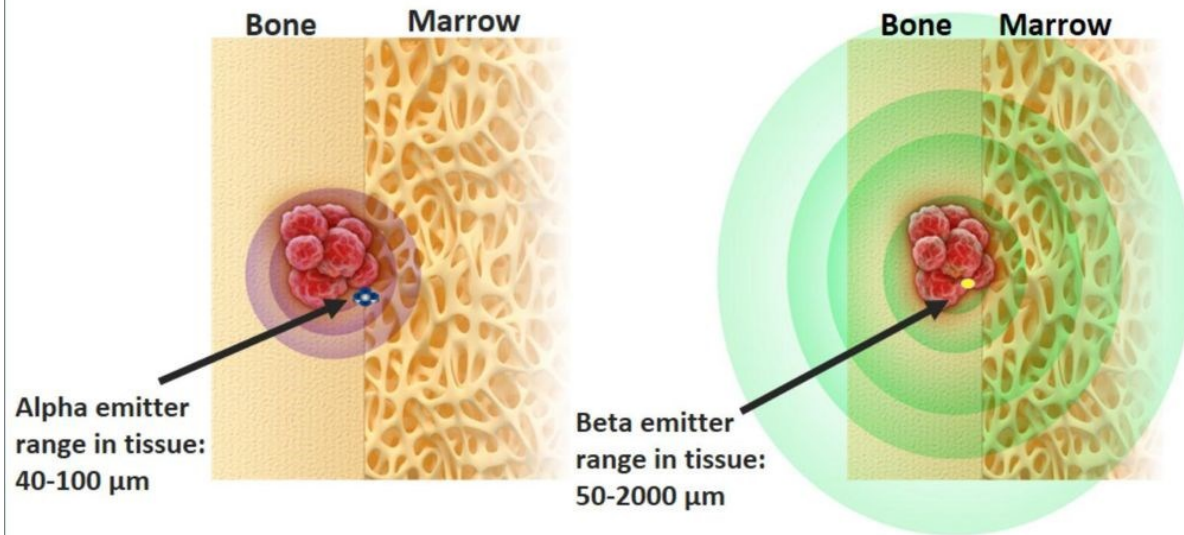
How autoradiography can be useful in the acquisition of nuclear data for the production of radionuclides for nuclear medicine applications ?



Extracted particles	Range of energies (MeV)	Highest beam intensity (μA)
H ⁺ (protons)	35 – 70	375 x 2
He ²⁺ (alpha)	68	70
HH ⁺	35	50
D ⁺ (deuteron)	15 – 35	50



Properties of Alpha- and Beta-Emitting Radionuclides



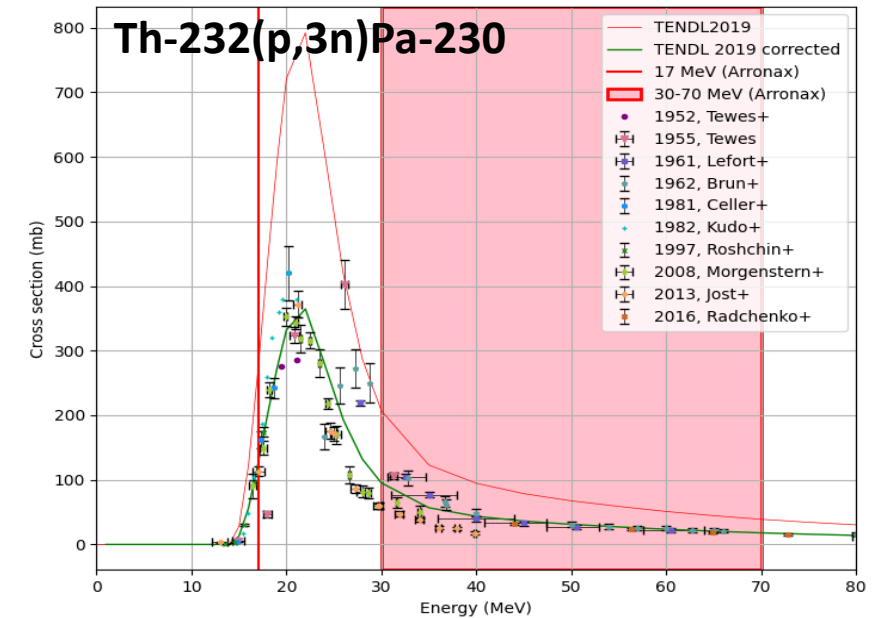
Henriksen G, et al. *Cancer Res.* 2002;62:3120-3125.
Speer TW. *Targeted Radionuclide Therapy.* 2011.

- α therapy benefit

- Short range in human tissues : $\approx 100\mu\text{m}$ (\approx cell diameter)
- High Linear Energy Transfer (LET) : 60-200 keV/ μm
- Great DNA damages \rightarrow no cell repair

- $^{230}\text{U}/^{226}\text{Th}$ from ^{230}Pa

considering Arronax's characteristics
17 and 30-70 MeV Proton beam



Moulin, 2021

Chemical separations of Pa-230 and U-230
after production

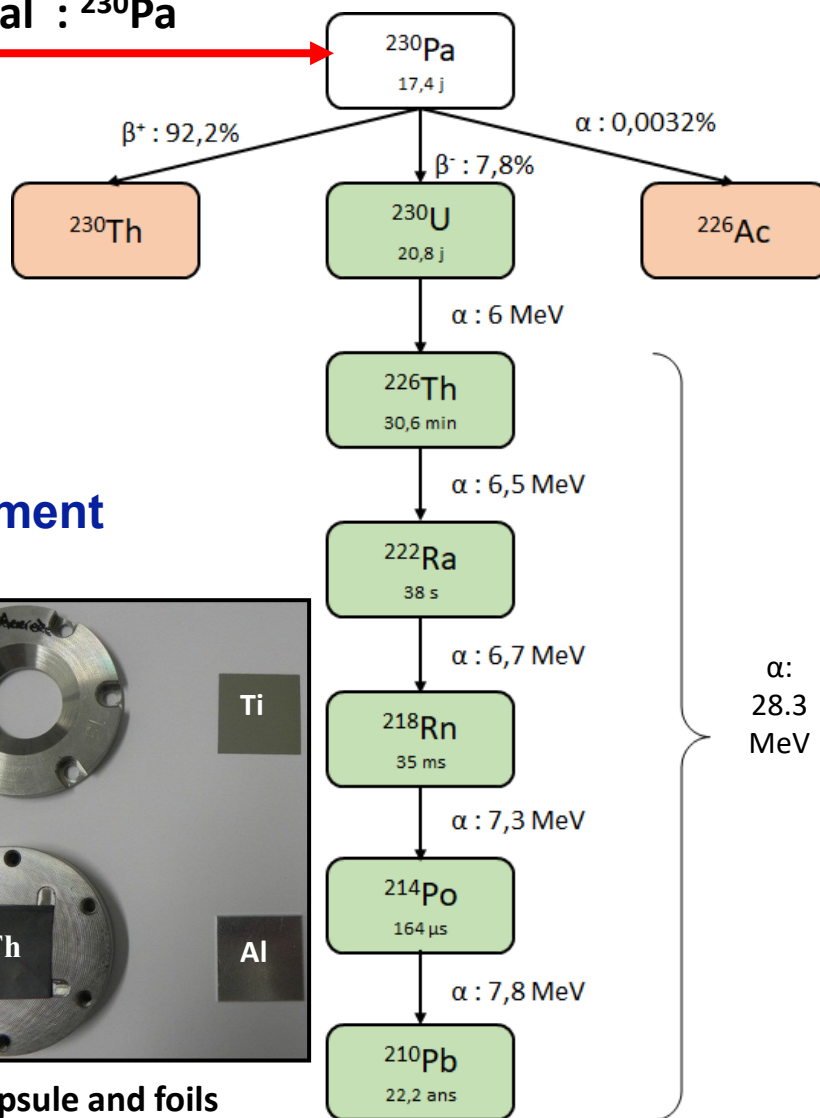
\rightarrow Contaminant :

^{233}Pa ($t_{1/2}$: 27j, β^-)

^{231}Pa ($t_{1/2}$: 104 ans, $\alpha \approx 5\text{MeV}$)

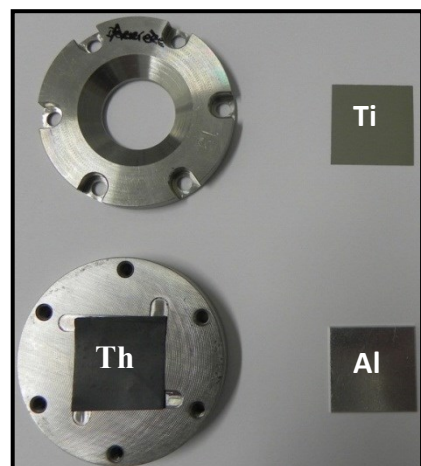
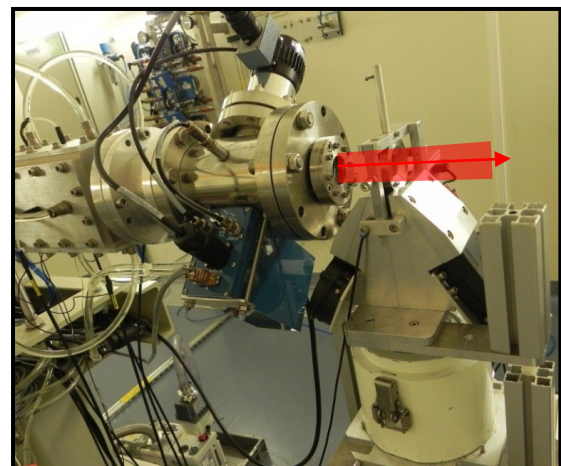


Goal : ^{230}Pa



Protons

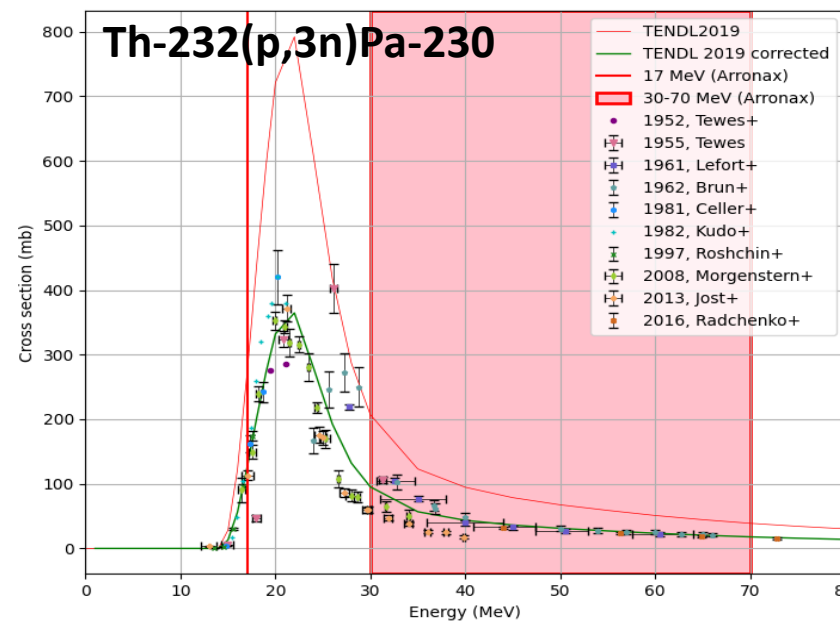
« Stacked foil » experiment



Irradiation station and beam line

Capsule and foils

- α therapy benefit
- Short range in human tissues : $\approx 100\mu\text{m}$ (\approx cell diameter)
- High Linear Energy Transfer (LET) : 60-200 keV/ μm
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- $^{230}\text{U}/^{226}\text{Th}$ from ^{230}Pa
considering Arronax's characteristics
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Moulin, 2021

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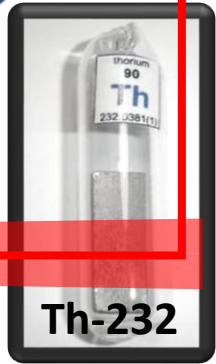
^{233}Pa ($t_{1/2}$: 27j, β^-)

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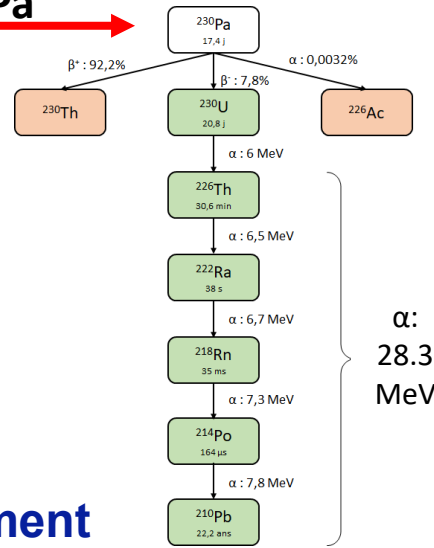
Application of BePAT



Goal : ^{230}Pa

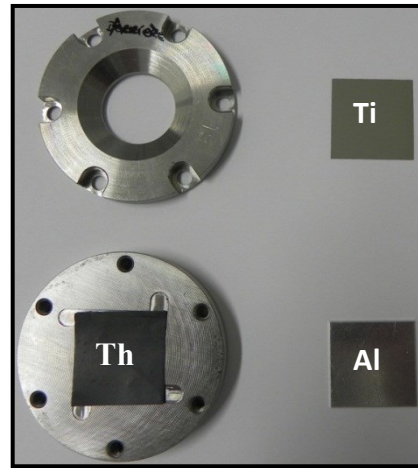
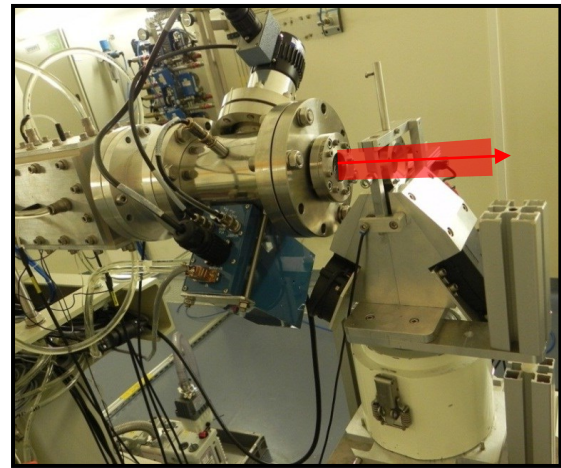


Th-232

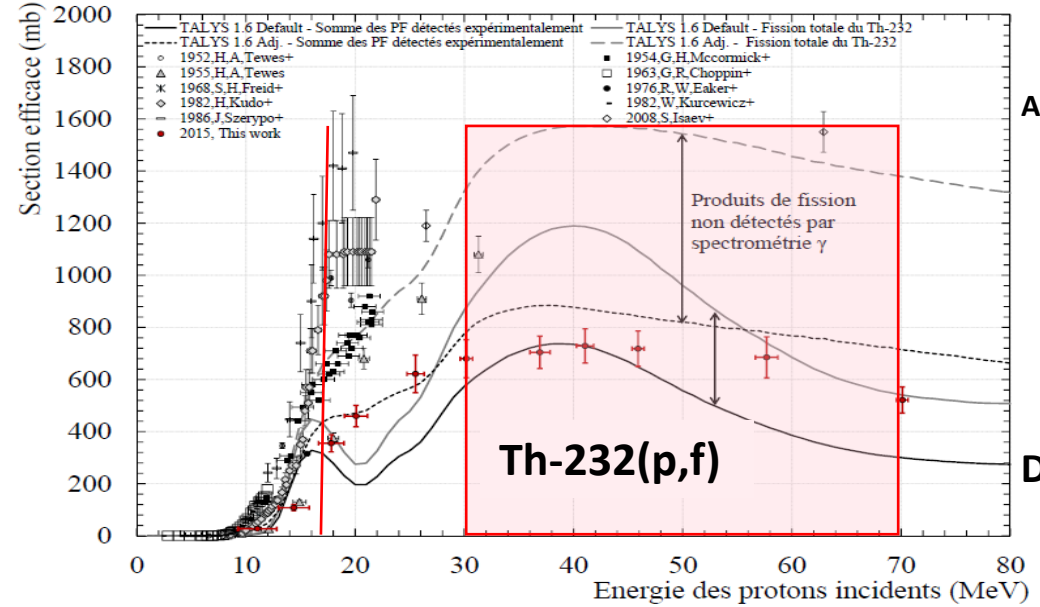


Protons

« Stacked-foil » experiment



Capsule and foils



Arronax 17, 30-70 MeV

Duchemin, 2015
tel-01220522

Contaminant

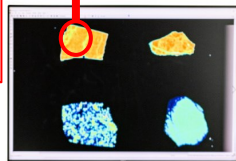
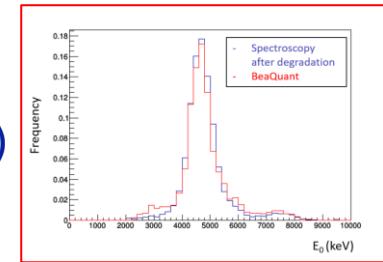
^{233}Pa ($t_{1/2}$: 27j, β^-)

^{231}Pa ($t_{1/2}$: 104 ans, $\alpha \approx 5\text{MeV}$)

In a nutshell

→ Large number of fission products not detected by γ spectroscopy

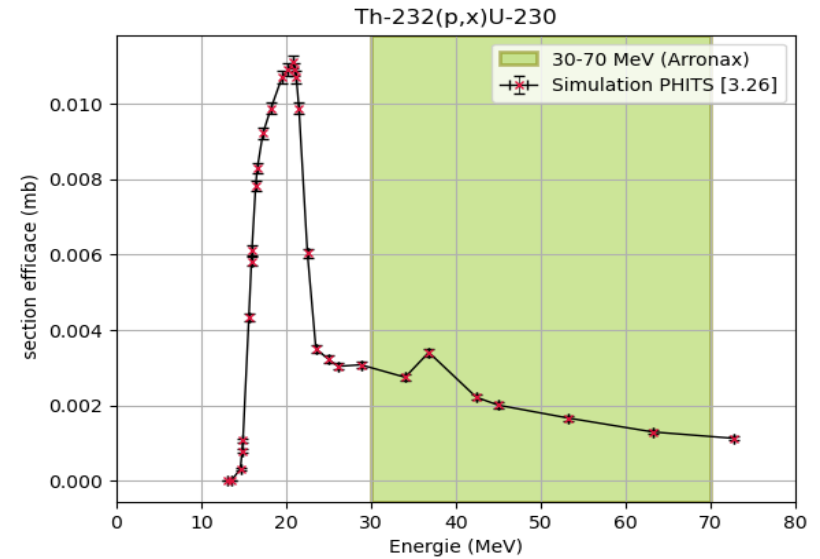
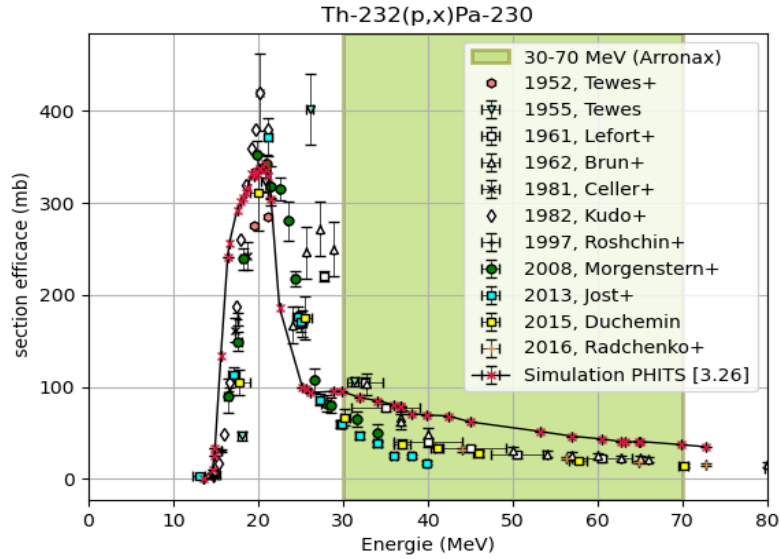
→ Need for α spectrometry !



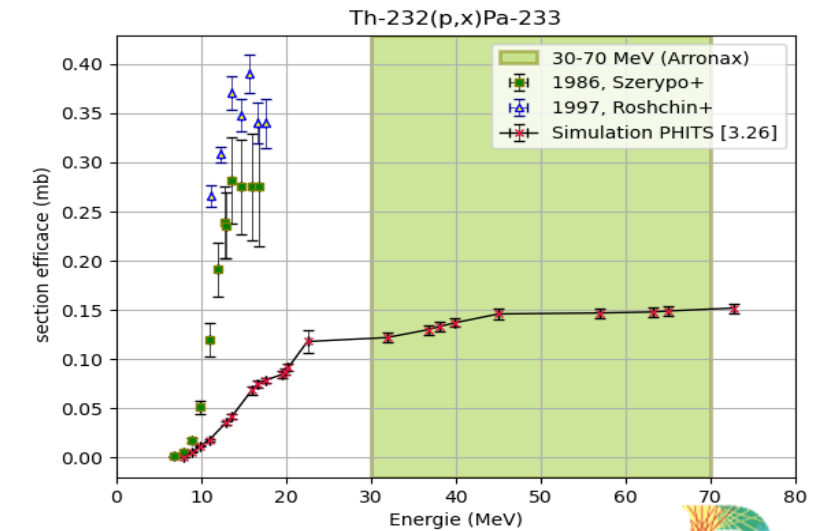
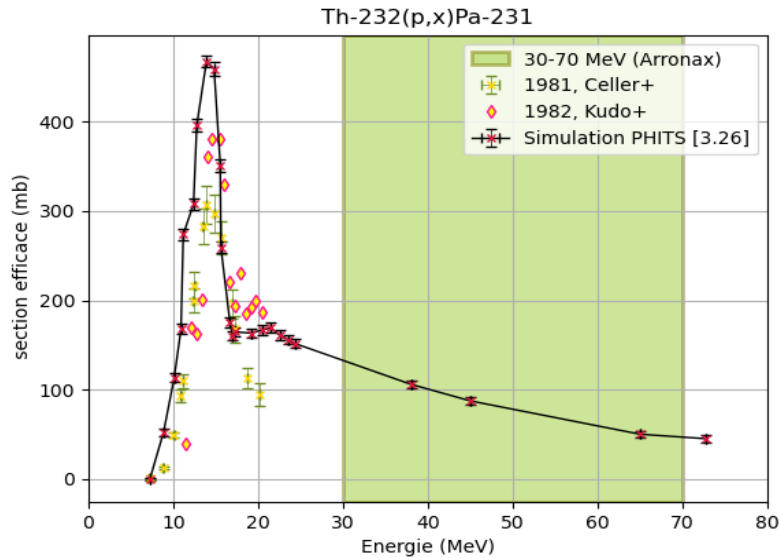
→ BePAT ! ←

Irradiation station and beam line

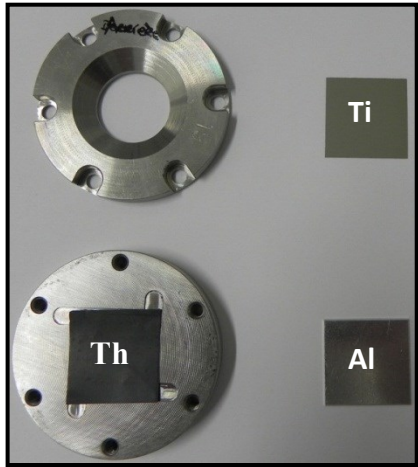
Melissa AZZOUNE (MD)



Contaminants



Some rules for the preparation of the BePAT samples



Capsule and metal foils

- **Samples**

- Metal foil

- Metal foil electrodeposited after digestion and chemical separation (in the future)

- **Sample activity**

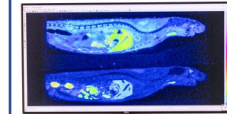
- Insensitive to γ and X

- $A(\alpha) + A(\beta+) + A(\beta-) < 20 \text{ kBq}$

} **Specific calculations required !**

- **Challenge**

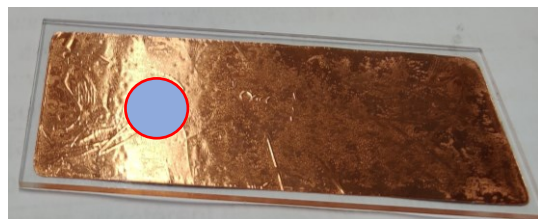
- Short-lived isotope !



BeaQuant



air



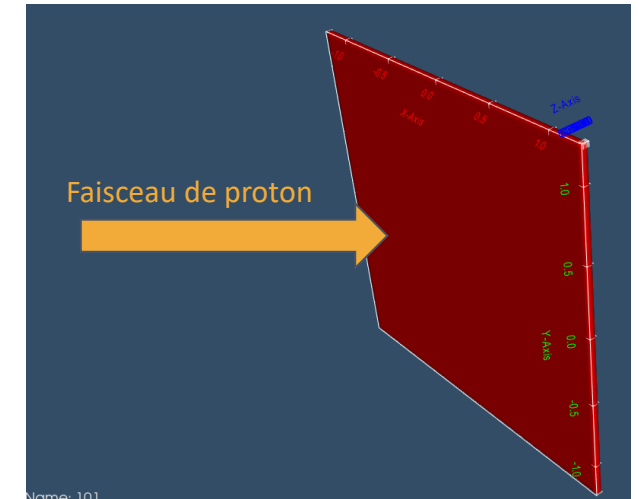
Metal foil can be electrodeposited after digestion and chemical separation

Cible	Source
Th 232 (11,72g/cm ³)	Protons
6,25 cm ² (2,5.2,5 cm ²) epaisseur 43,2 μm	2,5 cm d'extension latérale

$$\sigma(E) = \frac{M \cdot Y(E)}{N a e x \rho}$$

ou

$$\sigma(E) = \frac{M \cdot Act(tirr)}{N a e x \rho \Phi (1 - \exp(-\lambda tirr))}$$



Modèle physique → INCL Cascade Intranucléaire de Liège
tdchain.lst → rendement [atm/sources] si >10⁻⁸ sinon →tdchain.act → activité [Bq]

nuclide	yield	nuclide	yield
H 2	1.000E-08	Kr 84	1.000E-07
He 4	1.000E-08	Kr 85	2.100E-07
Co 70	1.000E-08	Kr 86	1.210E-06
Ni 71	1.000E-08	Kr 87	1.310E-06
Cu 68	1.000E-08	Kr 88	2.450E-06
Cu 70	2.000E-08	Kr 89	2.130E-06
Cu 71	2.000E-08	Kr 90	1.880E-06

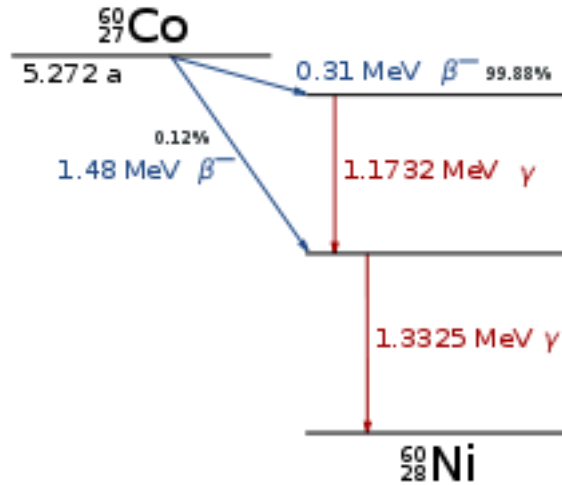
nuclide	atoms	radioactivity	
	[atoms/cc]	[Bq/cc]	[Bq]
H 3	3.2542E+03	5.8015E-06	1.5664E-07
He 6	2.9263E+00	2.5144E+00	6.7890E-02
He 8	8.0768E-03	4.7006E-02	1.2692E-03
Li 8	5.2072E-02	4.2973E-02	1.1603E-03
Li 9	1.0599E-03	4.1203E-03	1.1125E-04
Be 7	1.9679E+01	2.9666E-06	8.0097E-08
Be 8	4.9126E-18	4.1621E-02	1.1238E-03
Be 10	1.3998E+01	2.0341E-13	5.4922E-15
Be 11	2.6077E-19	1.3089E-20	3.5339E-22

Simulation PHITS-DCHAIN → Act(total)

Constraint → $A(\alpha)+A(\beta)\leq 20\text{kBq}$

Act < 1% tot-Act except Pa/U

branching ratio **NNDC**



branching ratio

Fichier batch

PHITS-DCHAIN
OMP=X

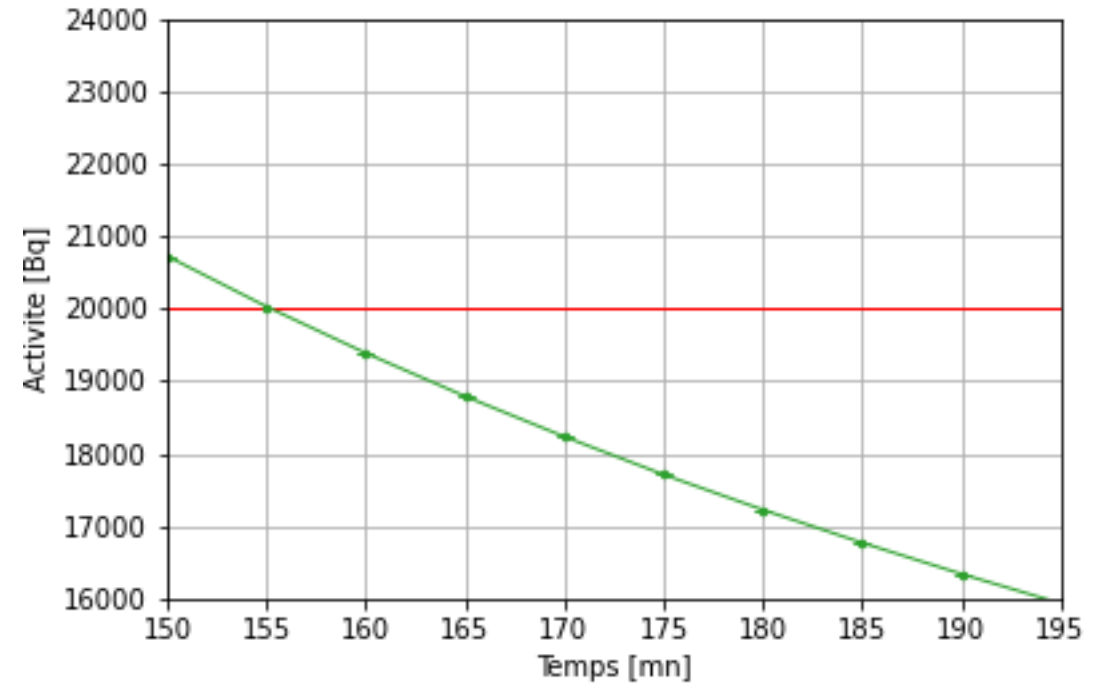
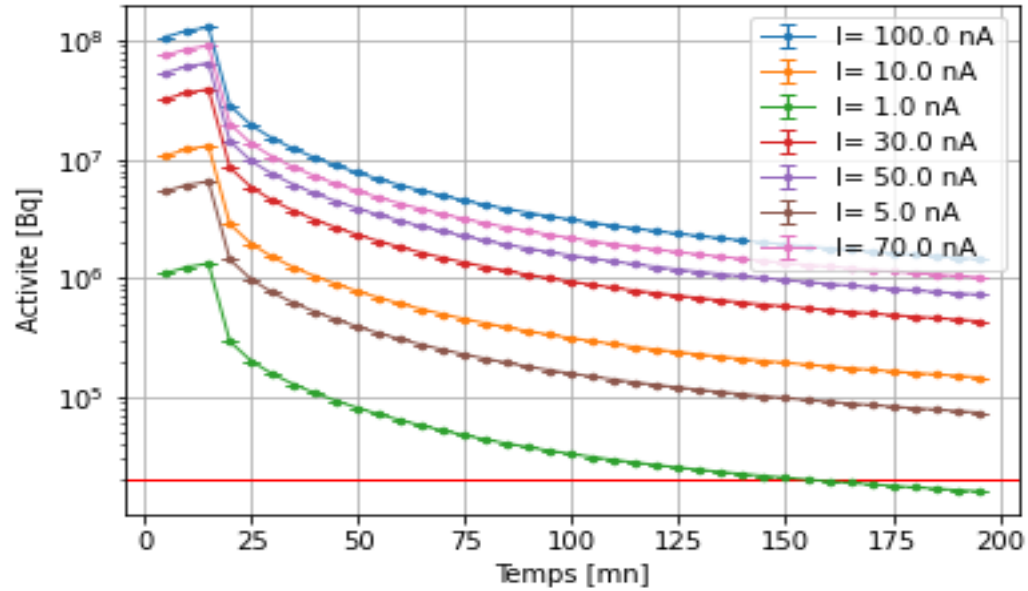
Analyse
Python

Activites

Spectres

(E,tirr,l)

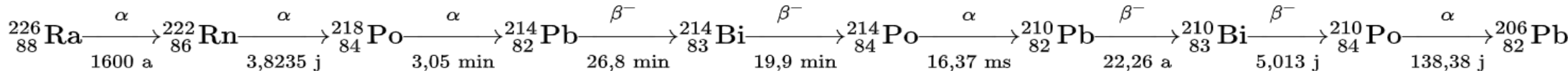
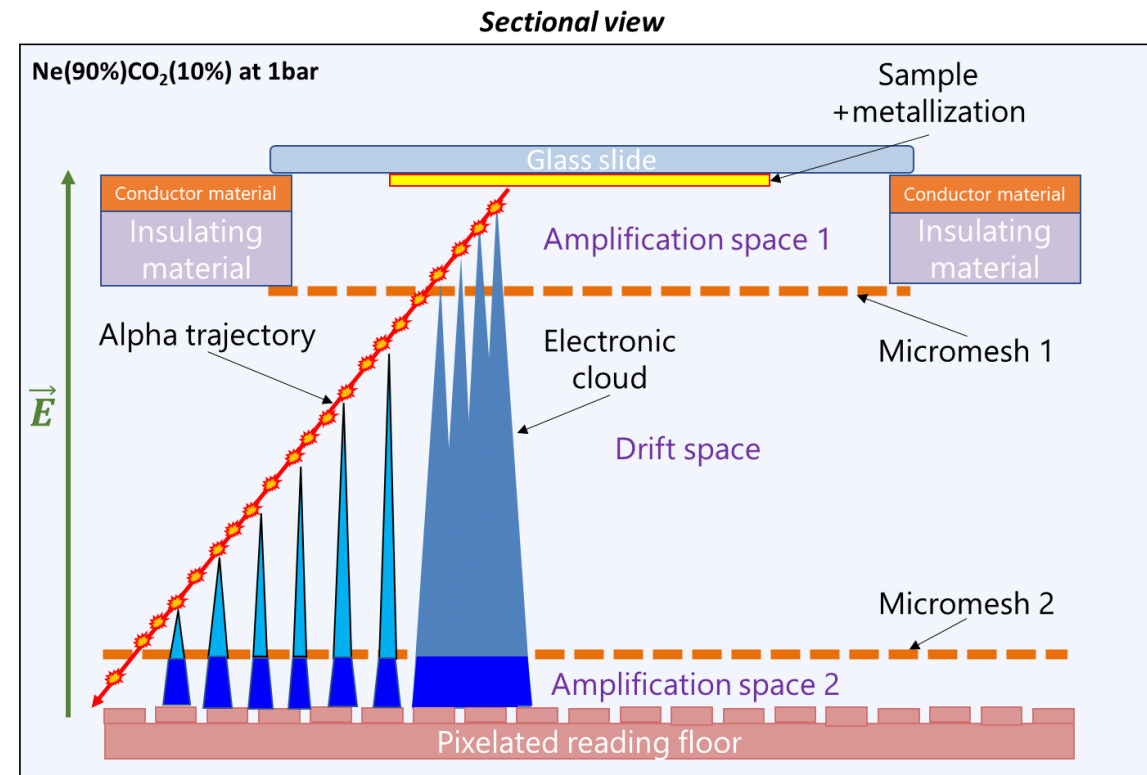
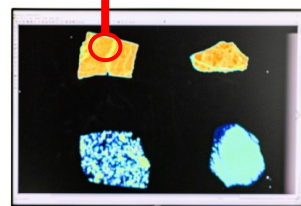
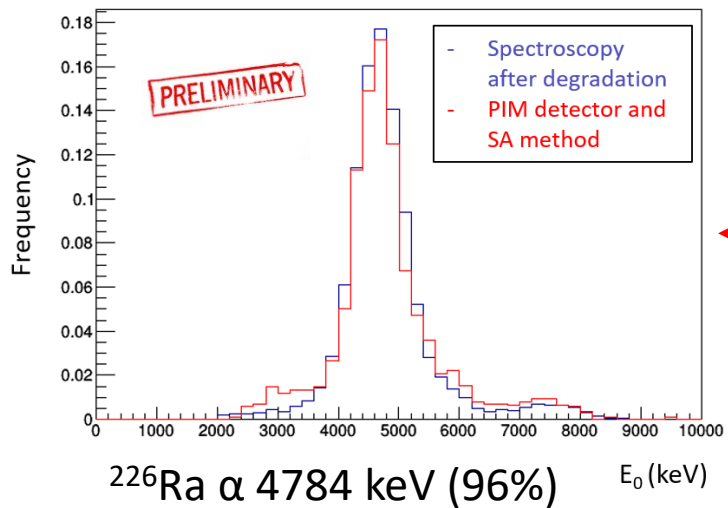
nuclide		radioactivity		
		atoms [atoms/cc]	[Bq/cc]	[Bq]
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Be	10	1.3998E+01	2.0341E-13	5.4922E-15
Be	11	2.6077E-19	1.3089E-20	3.5339E-22



Contraintes $\rightarrow A(\alpha)+A(\beta)\leq 20\text{kBq}$
 $\rightarrow I = 1 \text{ nA}$
 $\rightarrow t_{\text{irr}} = 15 \text{ min}$

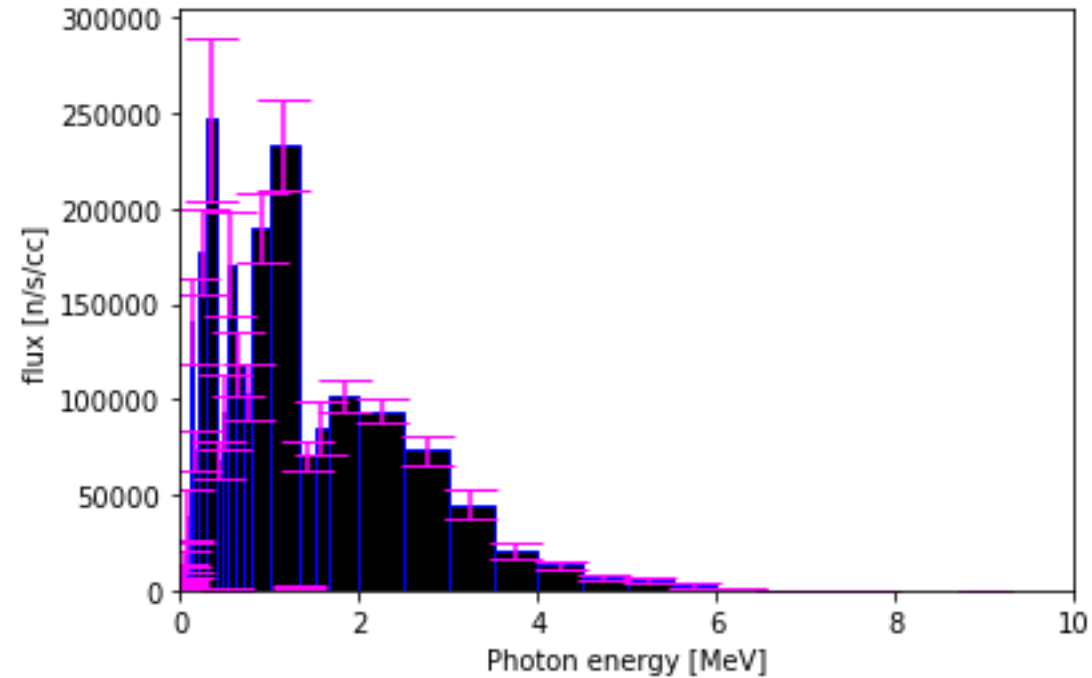
AZZOUNE 2022

Lefeuvre *et al.*, 2022



gamma-ray spectrum weighted by energy (42-groups)

grp.	energy [MeV]		flux [n/s/cc]	energy flux [MeV/s/cc]	relative error
	upper	lower			
1	50.000	30.000	0.0000E+00	0.0000E+00	0.0000E+00
2	30.000	20.000	0.0000E+00	0.0000E+00	0.0000E+00
3	20.000	14.000	0.0000E+00	0.0000E+00	0.0000E+00
4	14.000	12.000	0.0000E+00	0.0000E+00	0.0000E+00
5	12.000	10.000	3.4274E-08	3.7702E-07	3.9448E-02
6	10.000	8.000	2.5845E-08	2.3260E-07	3.9432E-02
7	8.000	7.500	2.6211E-08	2.0313E-07	3.9404E-02
8	7.500	7.000	2.4590E-08	1.7828E-07	3.9308E-02
9	7.000	6.500	9.7197E+04	6.5608E+05	6.6655E-02
10	6.500	6.000	1.0106E+06	6.3162E+06	4.0591E-02
11	6.000	5.500	3.3388E+06	1.9198E+07	3.4109E-02
12	5.500	5.000	6.5112E+06	3.4184E+07	2.5902E-02
13	5.000	4.500	7.2631E+06	3.4500E+07	1.9996E-02
14	4.500	4.000	1.3590E+07	5.7756E+07	2.0798E-02
15	4.000	3.500	2.2669E+07	8.5009E+07	1.8877E-02
16	3.500	3.000	3.6049E+07	1.1716E+08	2.1157E-02
17	3.000	2.500	6.8483E+07	1.8833E+08	1.4998E-02
18	2.500	2.000	8.6090E+07	1.9370E+08	1.2366E-02
19	2.000	1.660	8.0379E+07	1.4709E+08	1.0404E-02
20	1.660	1.500	7.6818E+07	1.2137E+08	2.7601E-02
21	1.500	1.340	8.0274E+07	1.1399E+08	1.9271E-02
22	1.340	1.330	7.7190E+06	1.0305E+07	1.0502E-01
23	1.330	1.000	2.1836E+08	2.5439E+08	1.4559E-02
24	1.000	0.800	1.8044E+08	1.6239E+08	1.4900E-02
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- Monte Carlo simulation software PHITS
- **Irradiation scenarios + Energy spectrum**
- Tally: [T-DCHAIN] + DCHAIN <3



Perspectives

1. Comparison with experimental measurements
2. Study of the isotopic purity
3. Influence of other parameters : Target thickness, incident particles, other production channels (Ac-226/Th-226)
4. Spectrometry

Backup

