IMT Atlantique
Bretagne-Pays de la Loire
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Subatech

PRISMA
Physics of Radiation InteractionS with Matter and Applications

ARRONAX

PHD HOURS

Production cross section measurements for isotopes of medical interest

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Nuclear medicine: use of radioisotopes as open sources to diagnose or treat patients.

↳ injection of the radionuclide only (^{82}Rb, ^{131}I, ^{223}Rn) or vectorized.

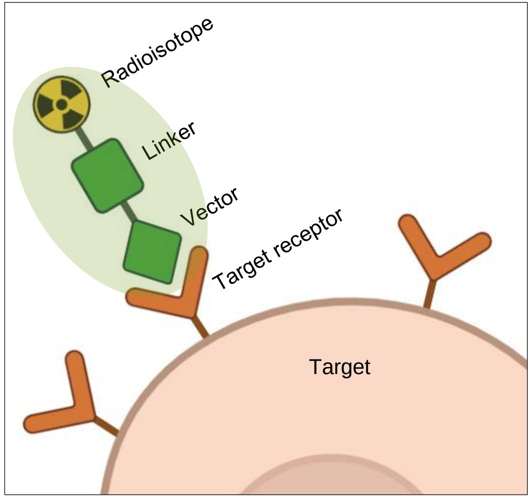
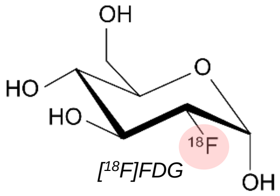
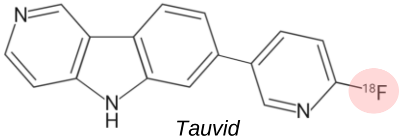


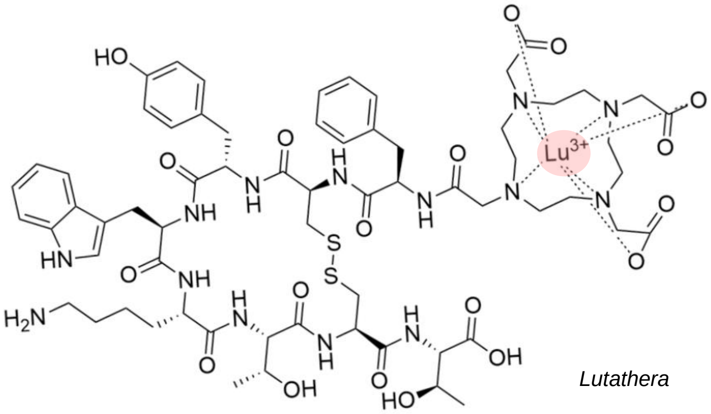
Figure 1 : Radiolabeling of the radioisotope



[^{18}F]FDG



Tauvid



Lutathera

Context – Production cross section measurements – ^{nat}Ni(d,x)^{61}Cu – Conclusion

Not all radioisotopes are of interest : their **chemical** and **physical properties** (half-life, decay modes etc.) are of importance.

The **LET** (Linear Energy Transfer) of a charged particle is the amount of energy that it transfers to the material traversed per unit distance.

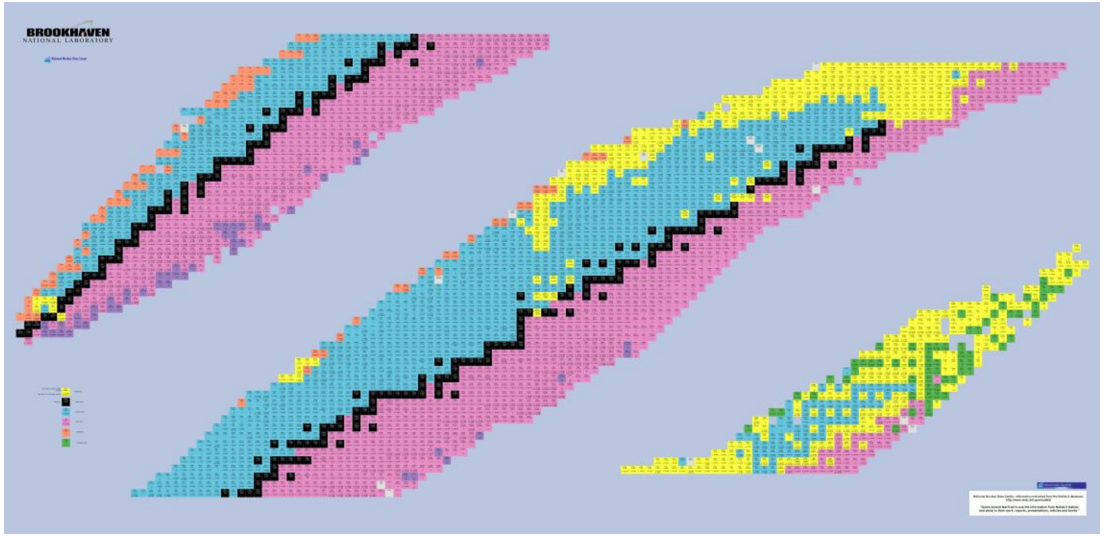


Figure 2 : *Chart of the nuclide*

Low LET particles ⇒ Highly penetrating radiation used for **diagnosis**

High LET particles ⇒ low penetrating radiation used for **therapy**

For **diagnostic** : X-rays, γ-rays and β+ emitters

- **SPECT** (Single Photon Emission Computed Tomography) : Detection of low energy gamma emissions (70 – 300 keV)
- **PET** (Positron emission tomography) : Detection in coincidence of the two 511 keV γ emitted by the annihilation of the β^+ particle with an electron

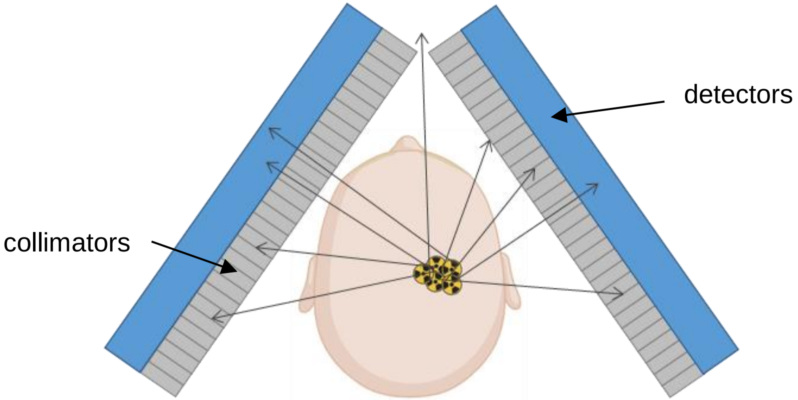


Figure 3 : Principle of a SPECT machine.

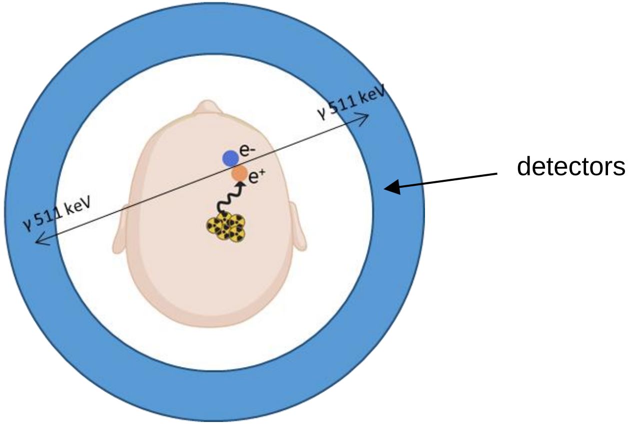


Figure 4: Principle of a PET machine.

For **therapy**

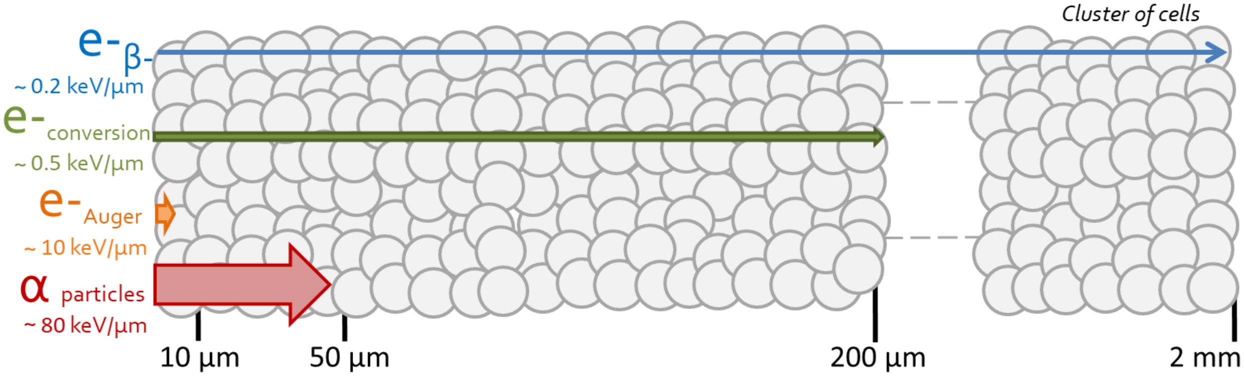


Figure 5 : LET and range of different particles in tissues [1]

- **Vectorized internal radiotherapy** : vectorized radioisotope injected to the patient.
- **Brachytherapy**: sealed radioisotope placed near the tumour.

Personalised medecine

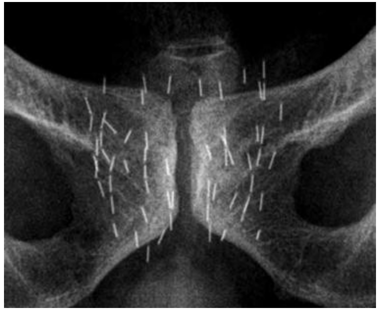


Figure 6: ^{125}I seeds used to treat prostate cancer [2]

[1] Duchemin, C. (2015), "Étude de voies alternatives pour la production de radionucléides innovants pour les applications médicales" [Doctoral thesis, Nantes Université]

[2] J.L. Guinot *et al., "*Comparison of permanent 125I seeds implants with two different techniques in 500 cases of prostate cancer", *J Contemp Brachytherapy,* vol. 7, no. 4, p 258-264, Aug. 2015

- ☐ **Production** of medical isotopes
    - Few of them comes from the radioactive chain of heavy nuclei (^{223}Ra, ^{212}Pb…)
    - Generally produced in research reactors, cyclotrons, linacs etc.

↳ Several production routes are possible for an isotope of interest ⇒ the **production cross sections** is needed to optimize its production while limiting the contaminants.

Measured experimentally

Predicted with theoretical models

Example of ^{nat}Ni(d,x)^{61}Cu

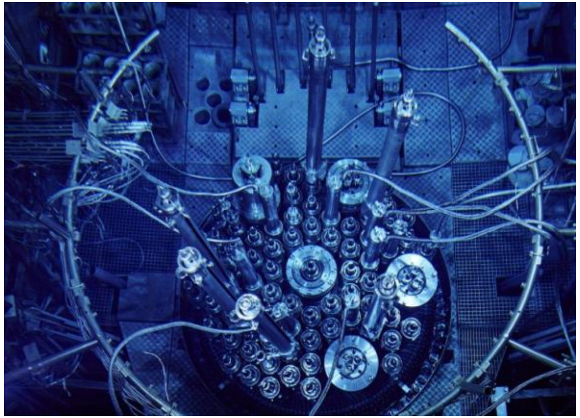


Figure 7: BR2 reactor at SCK CEN

Figure 8: ARRONAX cyclotron C70XP

$$\mathbf{Act} = \varphi\,\chi\,\frac{N_a\,\rho}{A}\left(1 - e^{-\lambda\, t_{irr}}\right)\int_{E_f}^{E_i}\frac{\boldsymbol{\sigma}(\mathbf{E})}{\frac{dE}{dx}}\,dE$$

Activation formula

☐ Parameters of the **target** :

- A : atomic mass (g.mol^{-1})
- ρ : density (g.cm^{-3})
- $\frac{dE}{dx}$: LET of the incident particle in the target (MeV.cm^{-1})
- χ : isotopic purity

☐ Parameters of the **beam** :

- φ : incident particles flux (particles.s^{-1})
- t_{irr} : irradiation time (s)
- E_i et E_f, Incident energy of the particle and the final energy (MeV)

☐ Parameters of the **radionuclide produced** :

- λ : decay constant (s^{-1})
- Act : Activity of the radionuclide produced (Bq)
- $\sigma(E)$: production cross section at the energy E varying between E_i and E_f (cm^2)
- N_a : Avogadro constant (mol^{-1})

$$\mathbf{Act} = \varphi\,\chi\,\frac{N_a\,\rho}{A}\left(1 - e^{-\lambda\,t_{irr}}\right)\int_{E_f}^{E_i}\frac{\boldsymbol{\sigma}(\mathbf{E})}{\frac{dE}{dx}}\,dE$$

For thin targets (≈ 10 µm)

$$\mathbf{Act} = \varphi\,\chi\,\frac{N_a\,\rho}{A}\left(1 - e^{-\lambda\,t_{irr}}\right)e\,\boldsymbol{\sigma}(\boldsymbol{E})$$

e : target thickness (cm)

$$\boxed{\sigma(E) = \frac{A\ \boldsymbol{Act}}{N_a\,\rho\,e\,\boldsymbol{\varphi}\,\chi\,\left(1 - e^{-\lambda\,t_{irr}}\right)}}$$

❑ **Stacked-foils technique**: several measurements of the production cross section **in one irradiation**.

❑ Composition of one pattern of a stack:

- **Degrader**: decreases the energy of the beam ⇒ select the energy desired.
- **Target**: where the reaction of interest takes place.
- **Catcher**: stops the recoiled nucleus coming from the target.

❑ **Activity** measurements: use of **HPGe** detectors.

↳ Several measurements of a single foil to have data for short and long-lived radioisotopes.

$$\boxed{\sigma(E) = \frac{A\ \ Act}{N_a\ \rho\ e\ \varphi\ \chi\ \left(1 - e^{-\lambda\, t_{irr}}\right)}}$$

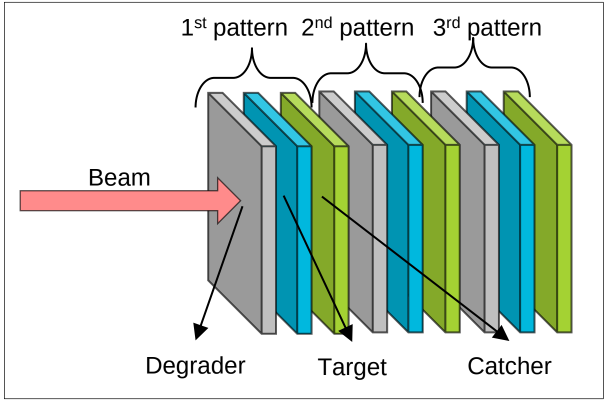
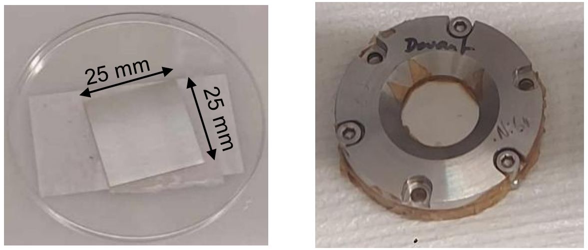


Figure 9: Principle of the stacked-foils technique



Context – Production cross section measurements – ^{nat}Ni(d,x)^{61}Cu – Conclusion

- ❑ **Relative method**: use of monitor reactions for which the IAEA has recommended values for their production cross sections.
  ↳ ≈ 10 % of uncertainties.

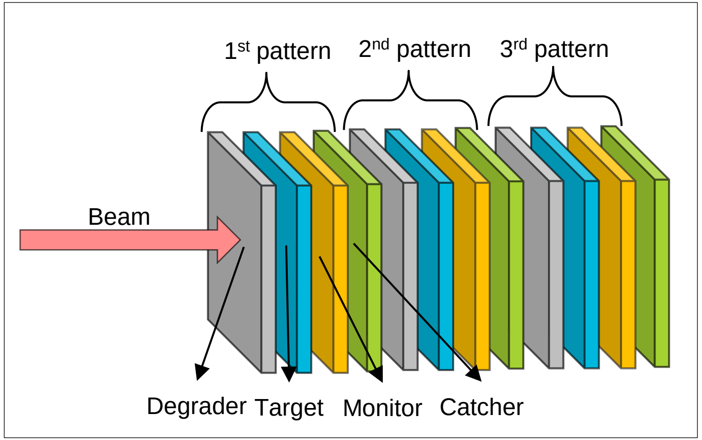


Figure 11: Scheme of the stack when using a monitor foil to measure the beam flux

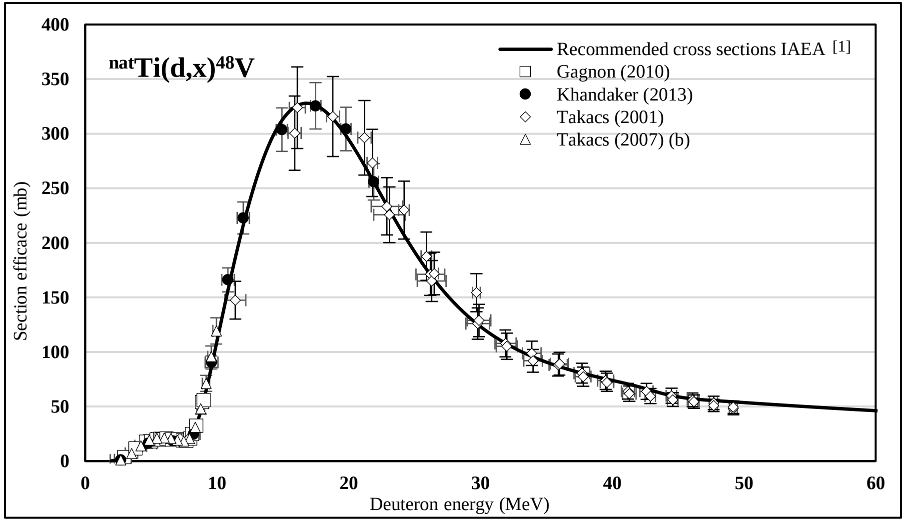


Figure 10: Experimental production cross sections of the ^{nat}Ti(d,x)^{48}V reaction

$$\boxed{\varphi = \frac{A\ \ Act}{N_a\ \rho\ e\ \sigma(E)\ \chi\ \left(1 - e^{-\lambda\ t_{irr}}\ \right)}}$$

[1] A. Hermanne *et al.*, ‘Reference Cross Sections for Charged-particle Monitor Reactions’, *Nuclear Data Sheets*, vol. 148, p. 338–382, Feb. 2018

- **Absolute method**: use of a Faraday cup coupled with an electron repeller to measure the number of charges crossing the stack during the irradiation.
  ↳ < 3 % of uncertainties

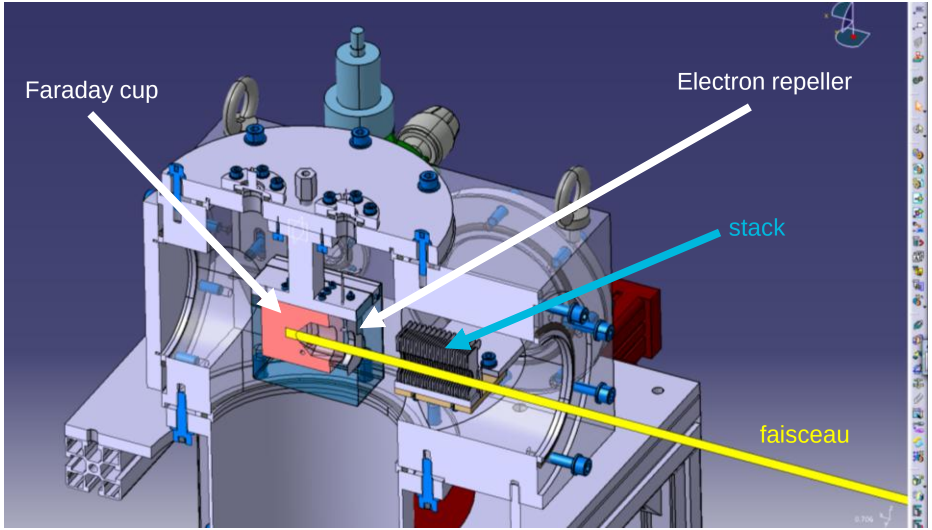


Figure 12: Scheme of the Faraday cup setup

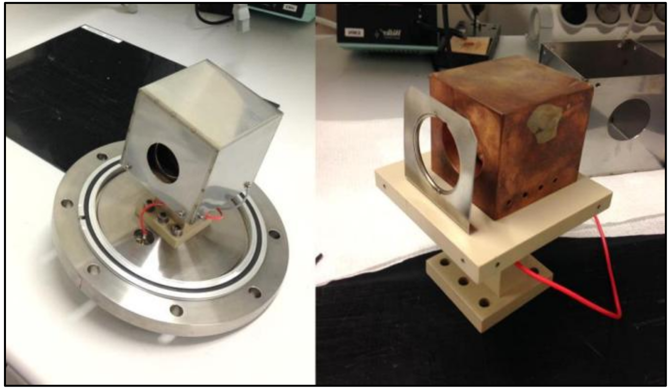


Figure 13: Faraday cup and electron repeller used in the experiments

Copper isotopes	Half-life	Decay mode
^{61}Cu	**3.339 h**	**β^+ (61 %) EC (39 %)**
^{64}Cu	12.70 h	EC (44.01 %), β^- (38.5 %), β^+(17.49 %)
^{67}Cu	61.81 h	β^- (100 %)

<u>Table 1:</u> Copper isotopes of interest for medicine

PET imaging (^{61}Cu, ^{64}Cu)

Therapy (^{67}Cu)

→ ^{61}Cu can be used for **PET applications**:

↳ Adequate half-life

↳ β^+ decay : $E_{moy} = 524$ keV, $E_{max} = 1216$ keV

↳ Suitable to be linked with small molecules / peptides that have fast biokinetics [1].

- ➢ Possibility of having “true” **theranostic pairs** ⇒ combination of a therapy isotope (^{67}Cu) with an imaging isotope (^{61}Cu or ^{64}Cu).

  ↳ assess the tumour localization, development and the targeting capabilities of the radionuclide before and during treatment.

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[1] M. Fani *et al*., “61Cu-Labeled Radiotracers: Alternative or Choice?”, *J Nucl Med*, vol. 64, no. 12, pp. 1855–1857, Dec. 2023.

Context – Production cross section measurements – ^{nat}Ni(d,x)^{61}Cu – Conclusion

- ☐ Reassessment of the **relative intensity** of one of the most intense γ-ray of ^{61}Cu:

γ-ray (keV)	NDS (2015) [1]	ENSDF (2020) [2]	Bleuel et al. [3]
282.956	100 %	100 %	100 %
656.008	**88.3 ± 1.5 %**	**82 ± 14 %**	**79.4 ± 1.0 %**
1185.234	30.7 ± 0.6 %	28.6 ± 0.6 %	28.8 ± 0.4 %
373.050	17.6 ± 0.4 %	16.8 ± 0.4 %	16.87 ± 0.22 %

Table 2: Relative intensities to the γ-ray at 282.956 keV of the main γ-rays of ^{61}Cu.

- ☐ **^{nat}Ni(d,x)^{61}Cu** can be used as a monitor reaction [4] for **production cross section measurements** ⇒ impacts the determination of the production cross sections of other radioisotopes.

[1] K. Zuber *et al.*, 'Nuclear Data Sheets for A = 61', *Nuclear Data Sheets*, vol. 125, p. 1–200, Mar. 2015
[2] ENSDF document available from the National Nuclear Data Centre 61Cu EC Decay dataset
[3] D. L. Bleuel *et al.*, 'Precision measurement of relative γ -ray intensities from the decay of 61Cu', *Applied Radiation and Isotopes*, vol. 170, 109625, Apr. 2021
[4] A. Hermanne *et al.*, 'Reference Cross Sections for Charged-particle Monitor Reactions', *Nuclear Data Sheets*, vol. 148, p. 338–382, Feb. 2018

Context – Production cross section measurements – ^{nat}Ni(d,x)^{61}Cu – Conclusion

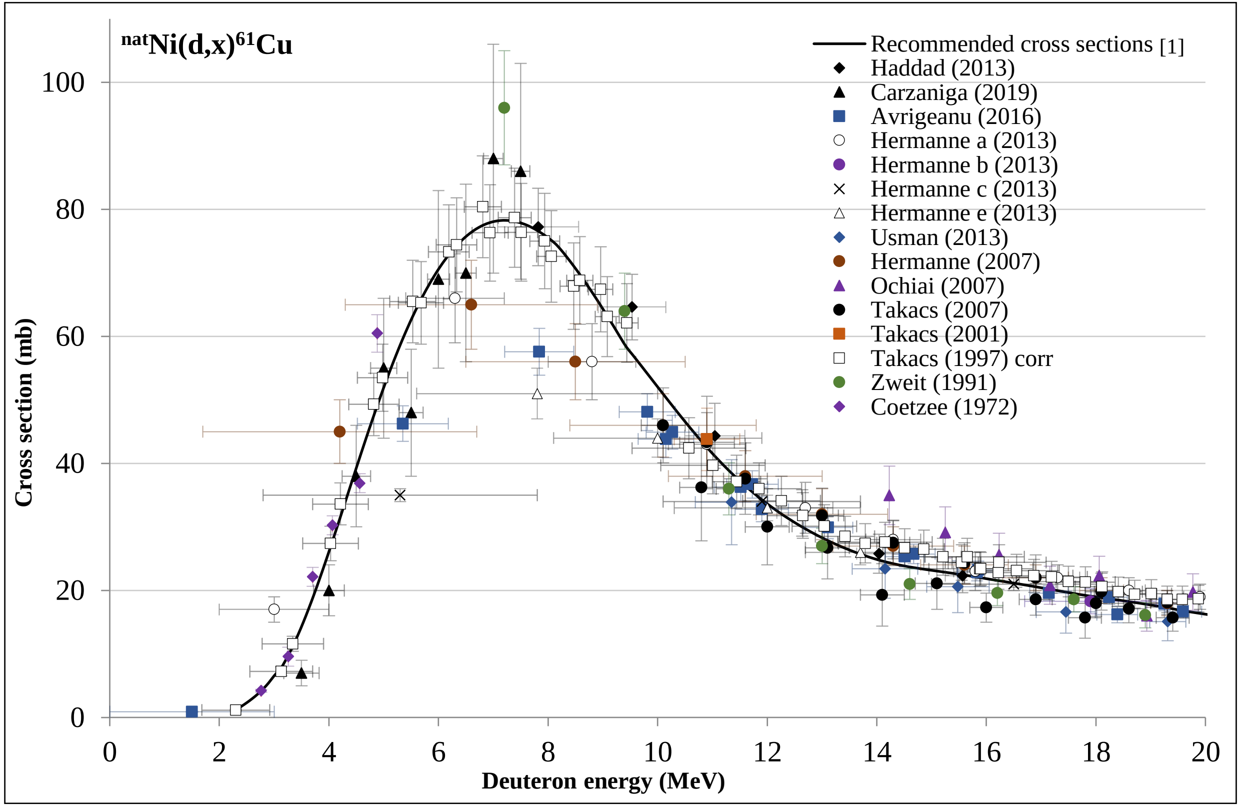

Figure 14: *Experimental production cross sections of the ^{nat}Ni(d,x)^{61}Cu reaction.*

15 different data sets ⇒ significant disparities between the data.

↳ for example : the peak value varies between **51 mb** and **96 mb.**

Motivations :

1. New measurements at low energy of the ^{nat}Ni(d,x)^{61}Cu cross sections.
2. Comparison of the experimental data with the literature and the recommended cross sections.
3. Assess the impact of the re-evaluation of the relative intensities of the γ-rays of ^{61}Cu on the measurements and the literature.

[1] A. Hermanne *et al.*, ‘Reference Cross Sections for Charged-particle Monitor Reactions’, *Nuclear Data Sheets*, vol. 148, p. 338–382, Feb. 2018

- ❑ 4 campaigns of measurement accomplished at the **GIP Arronax**:
  - Deuteron beam of 16 MeV
  - 1 hour irradiation at 100 nA of intensity
  - Measurement of the flux:
    - ✓ 3 with monitor reactions : **^{nat}Ti(d,x)^{48}V**, **^{nat}Ti(d,x)^{46}Sc**
    - ✓ 1 with a Faraday cup

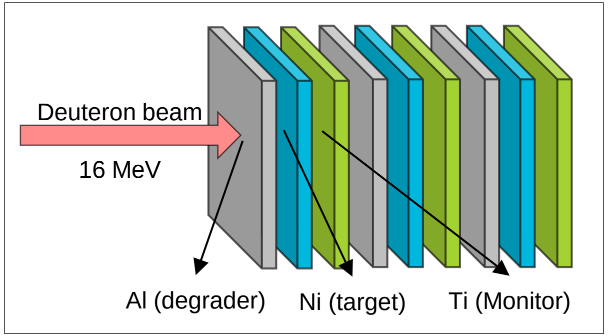

Figure 15: Schematical representation of the stack used in the experiments

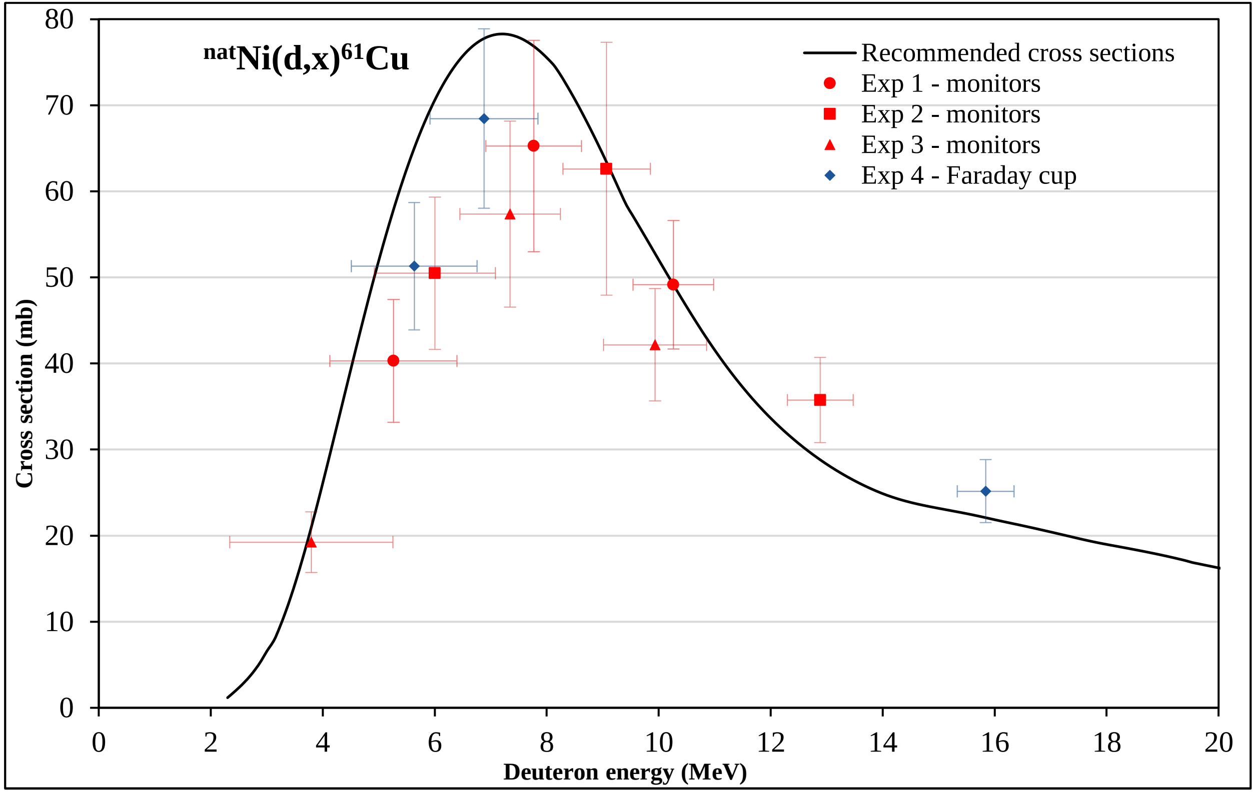

Figure 17: Experimental production cross sections of the $^{nat}Ni(d,x)^{61}Cu$ reaction.

Observations:

- ❑ 12 measurements done in 4 different experiments ⇒ overall consistency.
- ❑ The peak of the recommended cross sections is **20 % greater** than the one measured.
- ❑ the maximum we measure is slightly **shifted** to **higher energy** compared to the recommended curve.

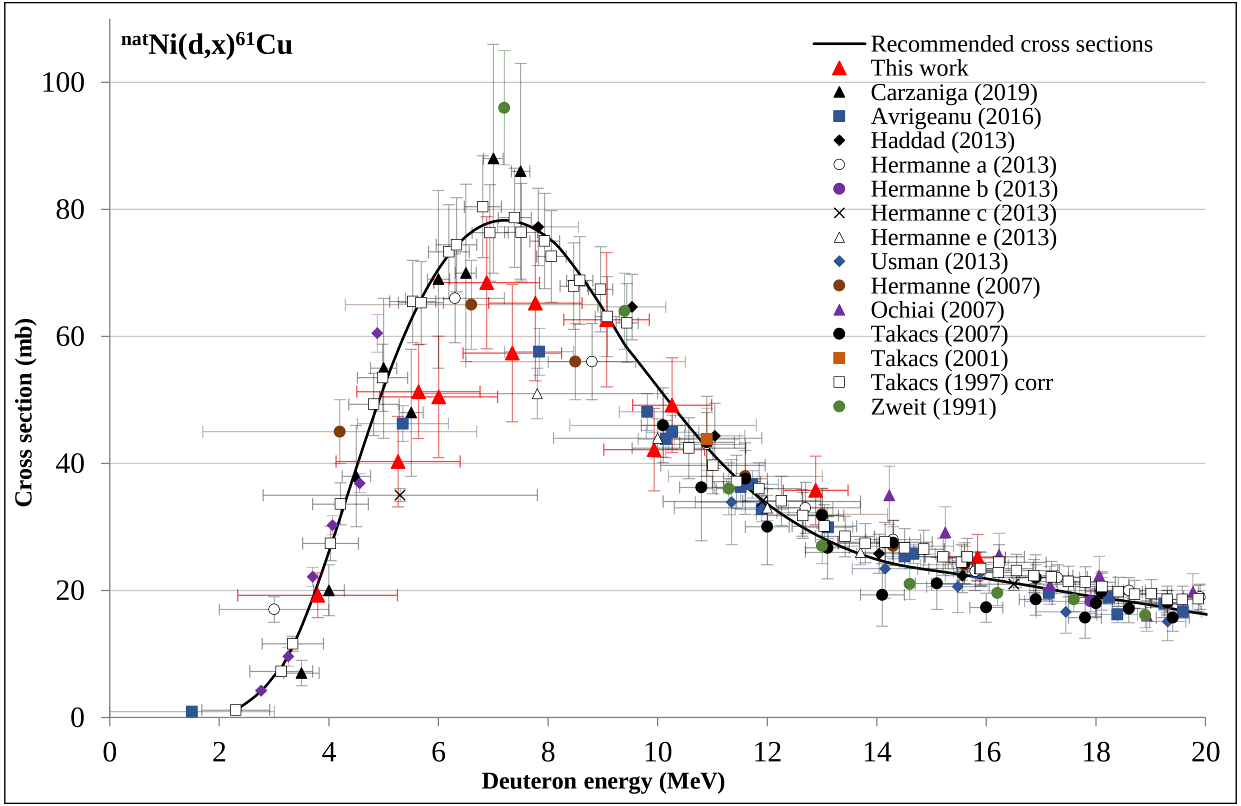

Figure 18: Experimental production cross sections of the ^{nat}Ni(d,x)^{61}Cu reaction.

Observations:

- ☐ Our data are consistent with the experimental data of Avrigeanu *et al.*
- ☐ With Carzaniga *et al.* ⇒ same observations as with the recommended cross sections
- ☐ The **low** and **high energy** parts are in agreement with existing data and with the recommended cross sections.
- ☐ Large discrepancy around the maximum from the 15 different data sets available.

↳ Investigation will be pursued to figure out what is going on.

Context – Production cross section measurements – ^{nat}Ni(d,x)^{61}Cu – **Conclusion**

- ❑ New production cross section measurements of the reaction ^{nat}Ni(d,x)^{61}Cu have been performed at the GIP Arronax at low energy :
  - → Good agreement with the data of Avrigeanu *et al.* and at low and high energy with the literature and the recommended cross sections.
  - → There's a **slight shift** in **energy** at the peak and its value is **20 % lower** than the recommended value.
  - → Investigation to be pursued to figure out what is going on at the maximum.

↳ **Outlook** : New measurements with the Faraday cup setup will be performed. An evaluation of the impact of the γ-rays of ^{61}Cu will also be conducted.

- ❑ What's next ?
  - → Study of other isotopes of medical interest : ^{nat}Pd(α,x)^{111}Ag, ^{nat}Ce(α,x)^{140}Nd, ^{68}Zn(α,x)^{71}Ge.
  - → Study the Faraday cup setup with an α beam.
  - → Prediction of production cross sections : Study of some of the nuclear reaction models used in the Monte-Carlo code PHITS, comparison with the evaluated nuclear library TENDL-2023.

THANK YOU FOR YOUR ATTENTION

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