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Cross-section Measurements towards an optimized Production of theraniostic Radionuclides at the Bern medical Cyclotron

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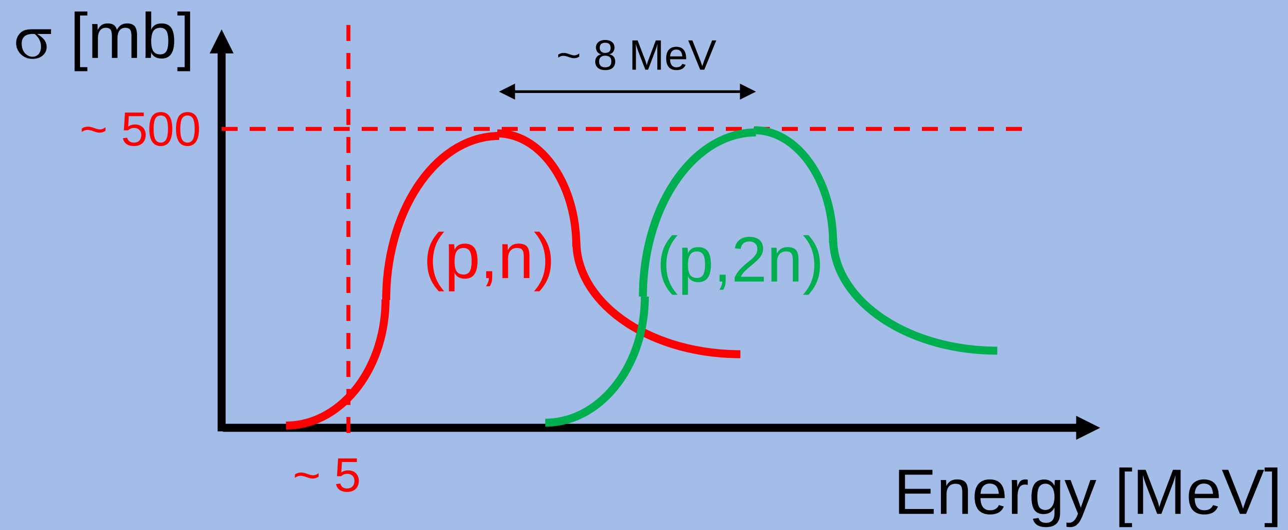
Outline

- Cross sections for the production of medical radionuclides
  - *What do we expect to measure?*
  - *Why cross-sections are important?*
- The Bern medical cyclotron laboratory
  - *GMP production and multi-disciplinary research under the same roof*
- A novel experimental method to measure cross-sections with a medical cyclotron
  - Nuclear and production cross-sections
- Achievements in the last years (cross-sections + production):
  - *^{43}Sc, ^{44}Sc, ^{47}Sc, ^{61}Cu, ^{64}Cu, ^{67}Cu, ^{68}Ga, ^{155}Tb, ^{161}Ho (**), ^{165}Tm, ^{165}Er*

(**) See poster by Edoardo Renaldin

Cross-sections



- Coulomb barrier: $B = \frac{1}{4\pi\epsilon_0}\frac{zZ_N e^2}{r_N}$ + tunnel effect (Z=21, Sc)
- Order of magnitude: geometrical cross-sections (A=50, Sc)
- Several nuclear reactions: (p,n), (p, 2n), (p, 3n), … , (p, α), …

Why cross-section measurements are important ?

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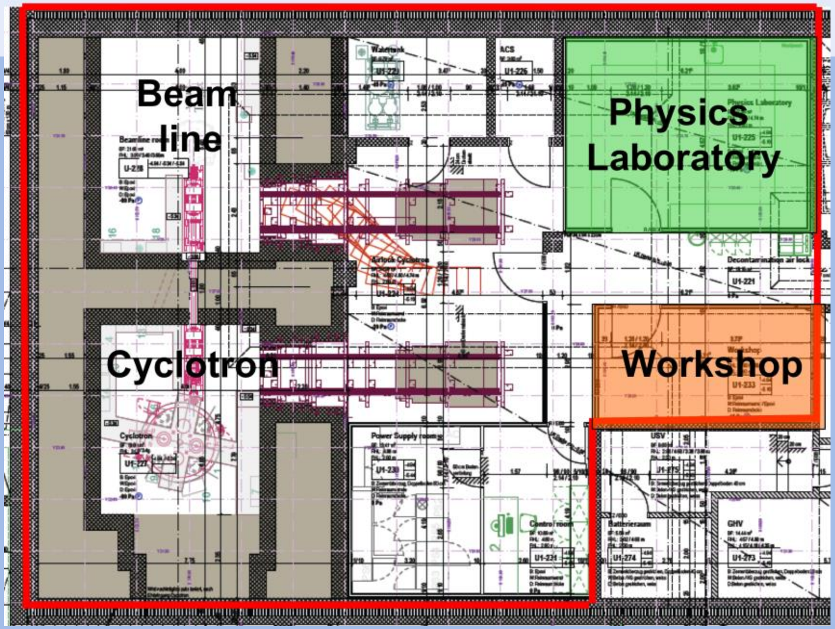
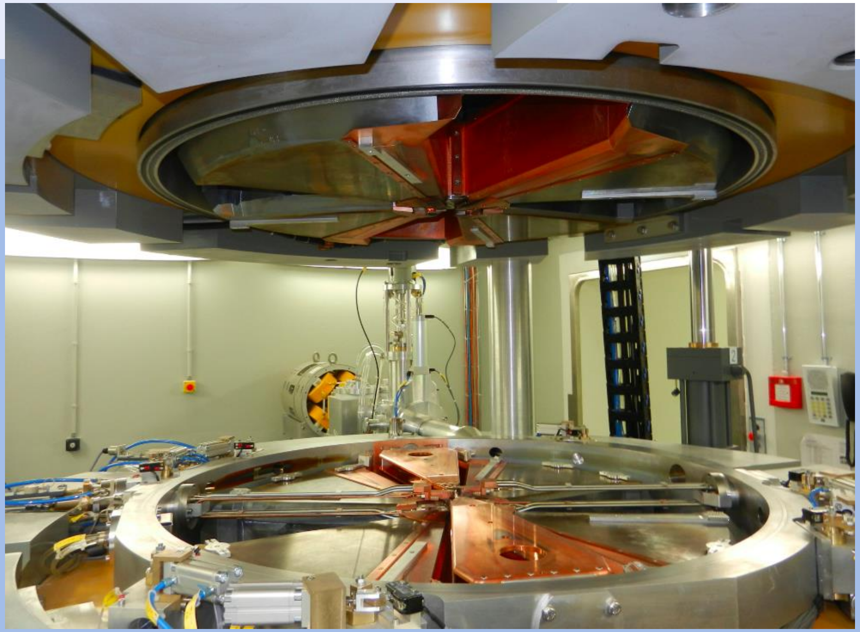
- Target material:
  - Several isotopes of the same element
  - Several elements

- **It is crucial to accurately control not only the production of the desired radionuclide but also the impurities!**

The Bern medical cyclotron and its Beam Transport Line (BTL)





- IBA 18 MeV high current cyclotron (up to 150 μA) – 2 H^- ion sources
- 2 High Current ^{18}F liquid targets: daily production
- 1 hybrid target for ^{68}Ga under test

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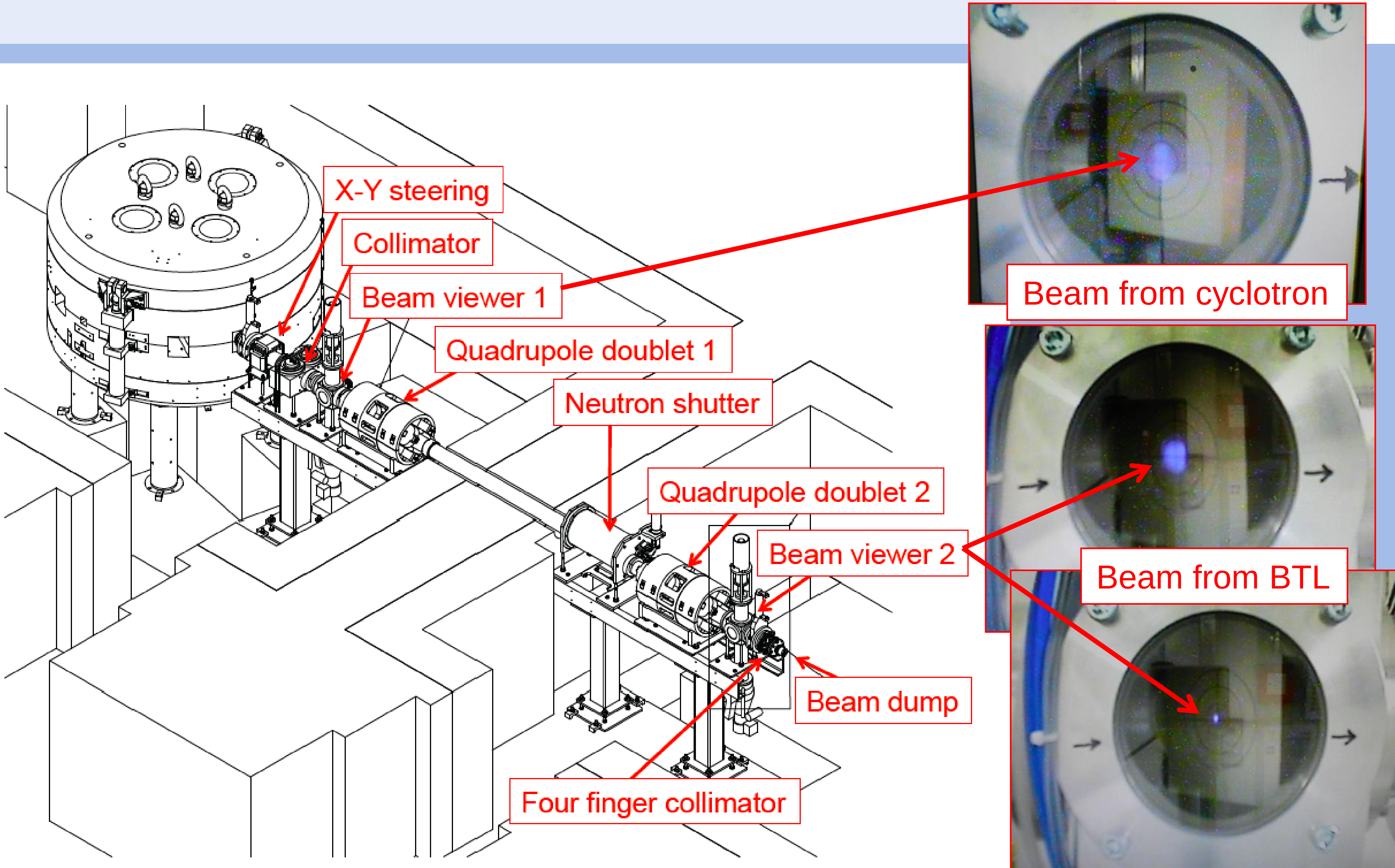
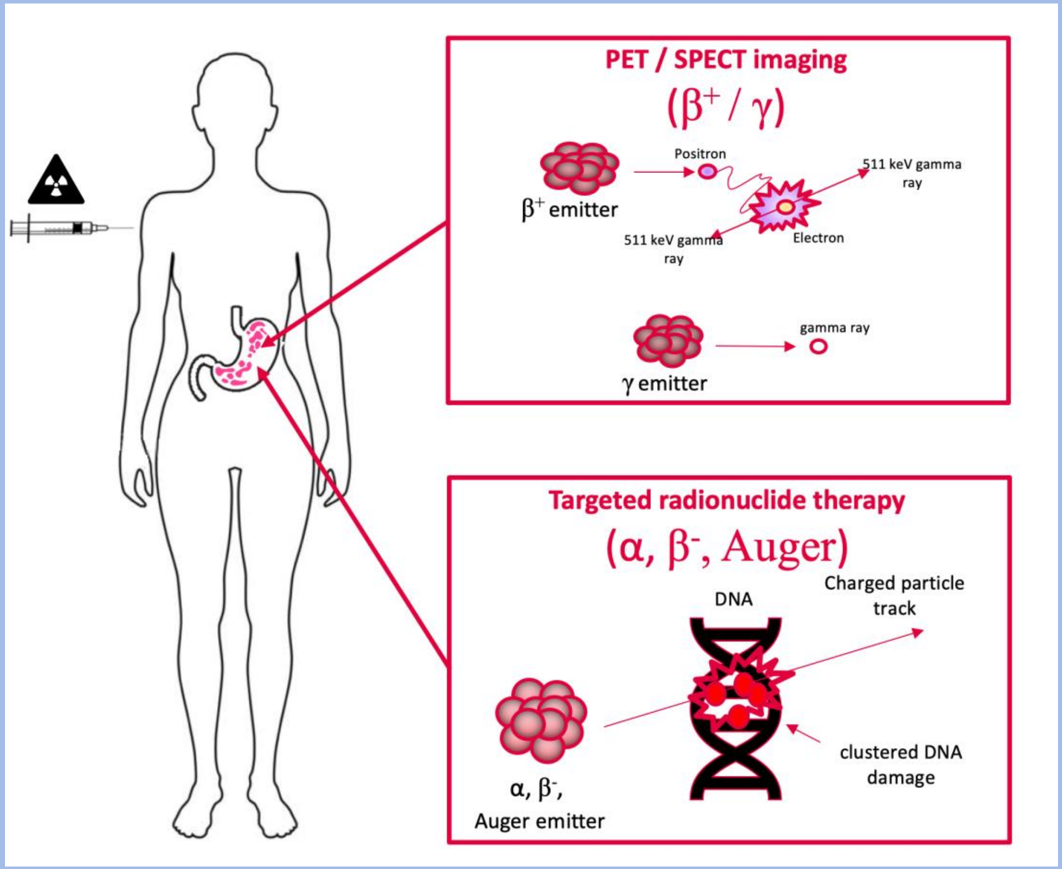
- **External Beam Transfer Line (BTL) in a separate bunker**
- **Solid Target Station (STS)**

Multi-disciplinary research activities with the BTL



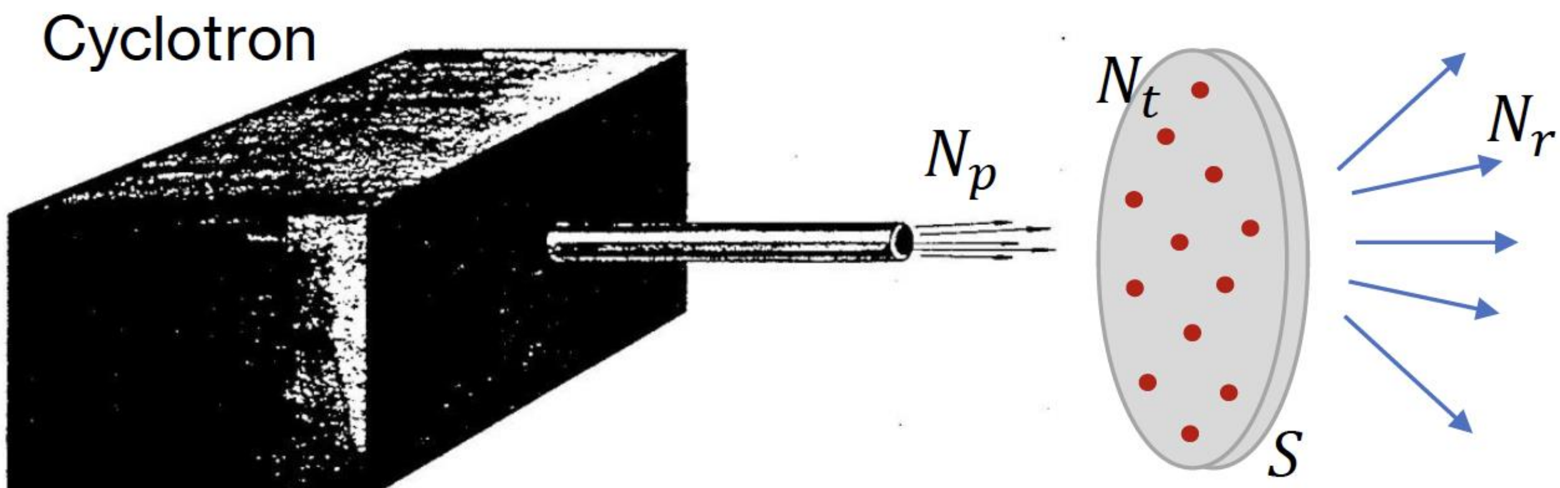
S. Braccini, *AIP Conf. Proc.* vol. 1525, p. 144, 2013

Radionuclides for theranostics in nuclear medicine



- Promising pairs:
  - **^{68}Ga/**^{177}Lu and **^{68}Ga/^{225}Ac**
  - **^{43}Sc/^{47}Sc** and **^{44}Sc/^{47}Sc**
  - **^{61}Cu/^{67}Cu** and **^{64}Cu/^{67}Cu**
  - **^{155}Tb/**^{149}Tb and **^{155}Tb/**^{161}Tb
- Radiometals
- **Target material: powder!**

Cross-section measurement: the standard case



$$\frac{dN_r}{dt} = \sigma_r \cdot \frac{dN_p}{dt} \cdot \frac{N_t}{S}$$

N_t/S or m/S constant and known

$$\sigma_r(E) = \frac{A(t_0)}{(1-e^{-\lambda t_i})} \cdot \frac{q}{I} \cdot \frac{S}{m \cdot \frac{N_A}{m_{mol}} \cdot \eta\epsilon}$$

Cross section measurements with a novel method

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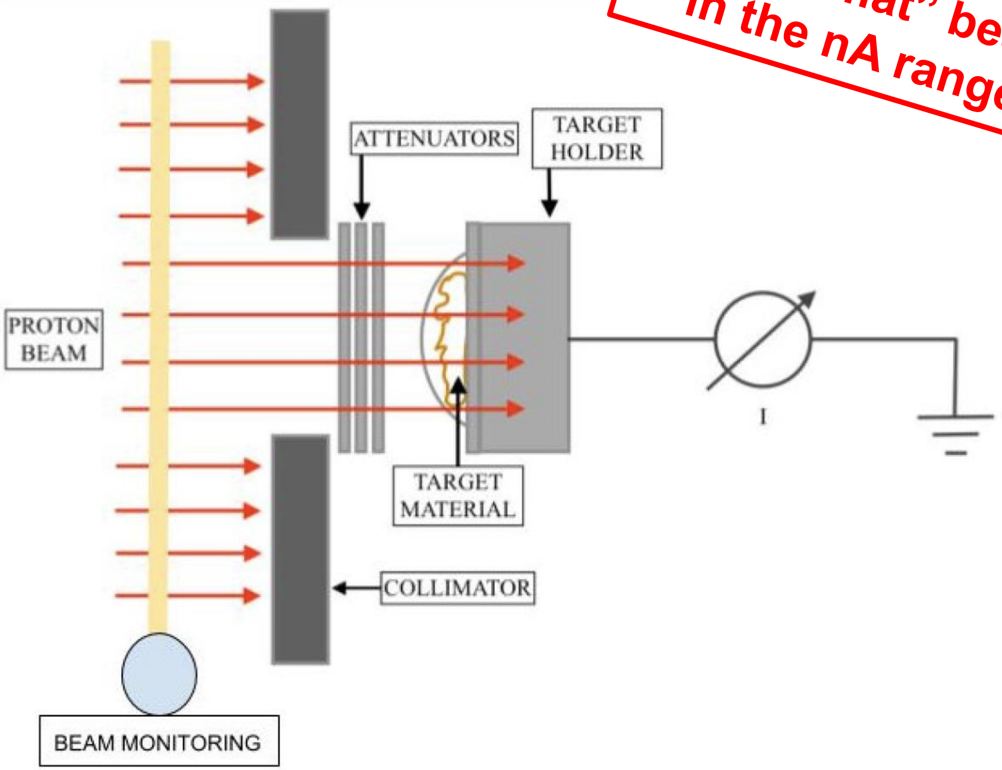
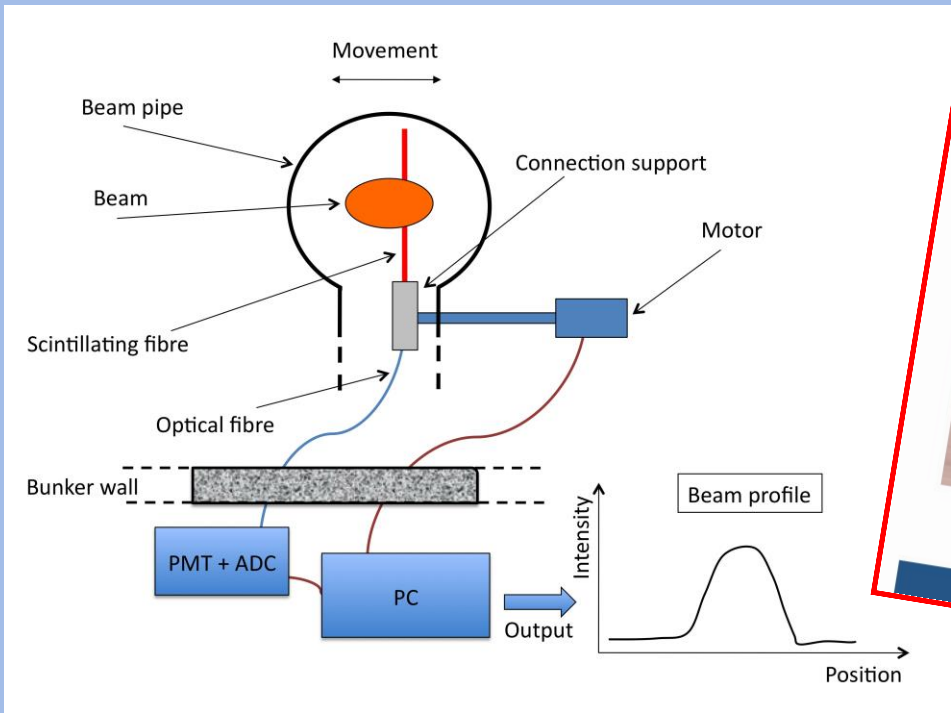
Stable "flat" beam in the nA range



T. S. Carzaniga, M. Auger, S. Braccini, M. Bunka, A. Ereditato, K. P. Nesteruk, P. Scampoli, A. Türler, N. P. van der Meulen, *Measurement of Sc-43 and Sc-44 production cross-section with an 18 MeV medical PET cyclotron*, Appl Radiat Isot. 2017 Nov; 129:96-102.

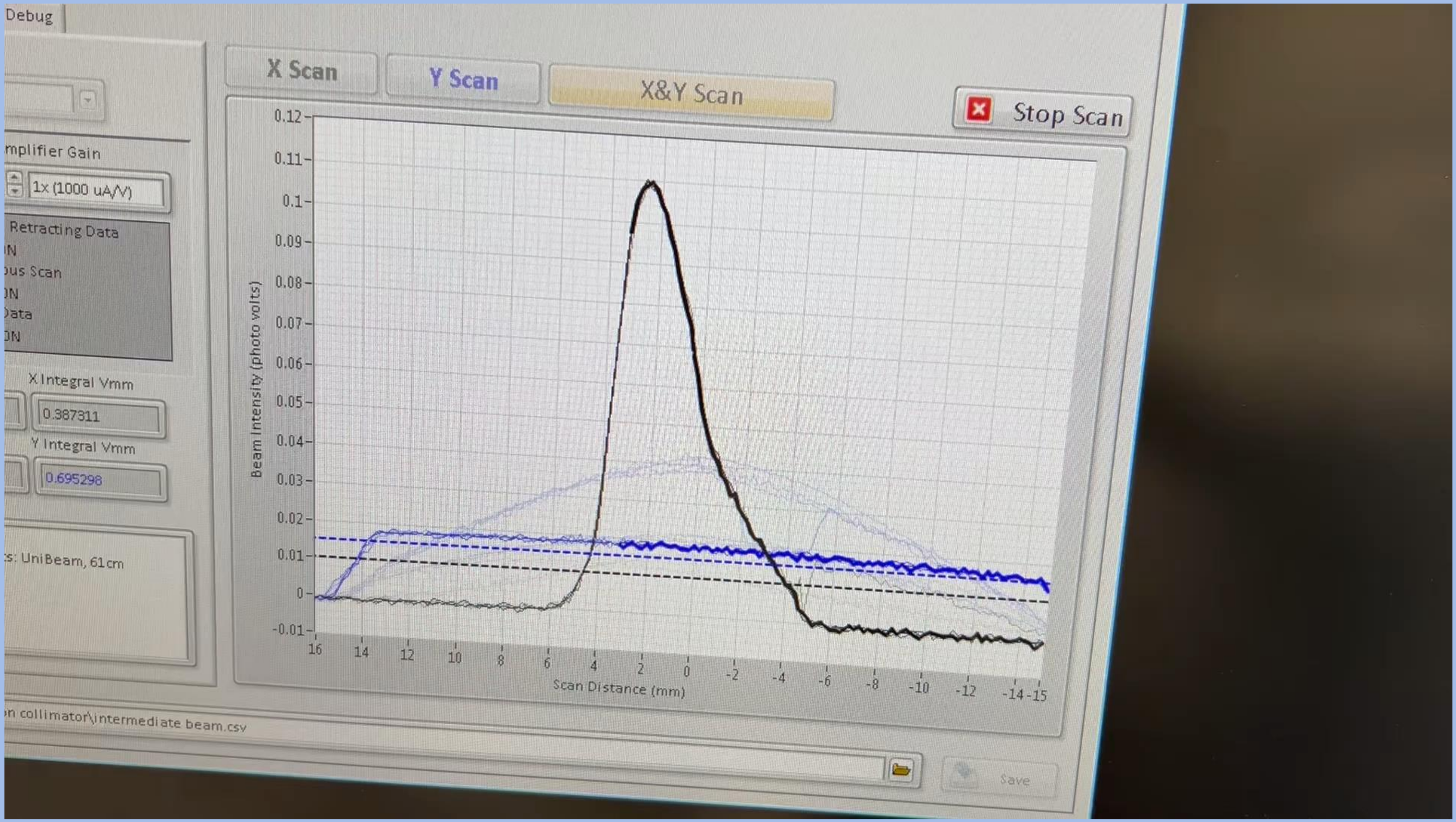
The UniBEaM detector



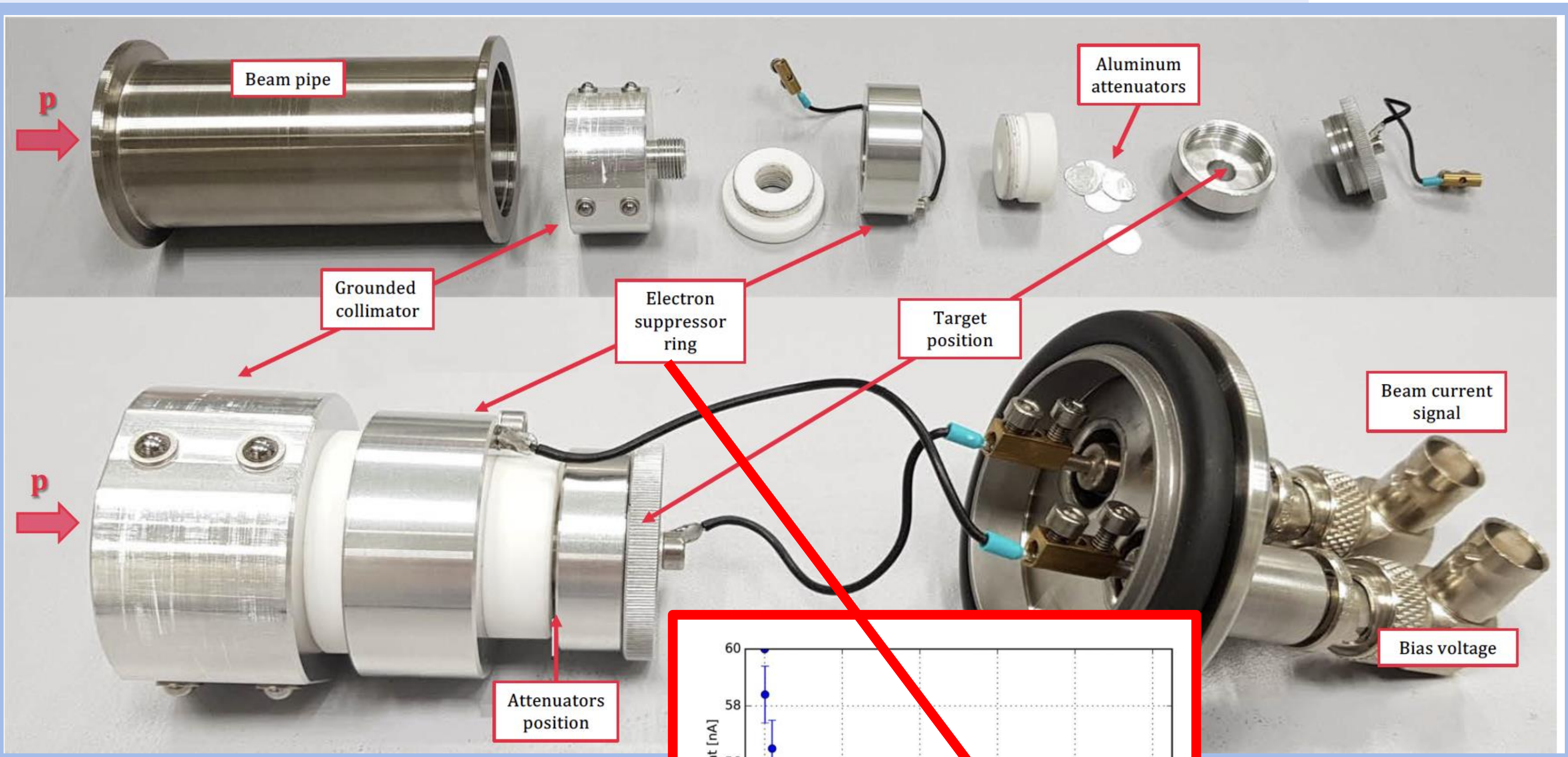
> 2D beam profiler based on (doped) optical fibres passed through the beam
> On-line, minimal interference with the beam
> Developed by LHEP and commercialized by D-Pace (Canada)

S. Braccini et al., 2012 JINST 7 T02001

On-line monitoring with UniBEaM



The target station for cross section measurements



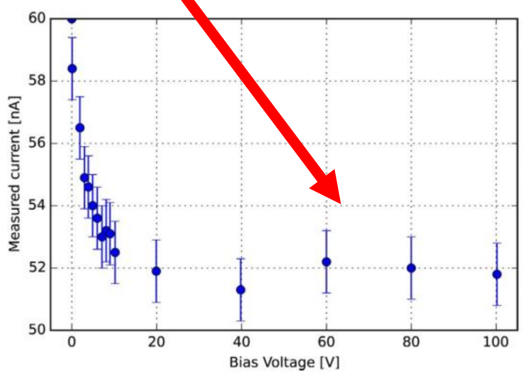


Fig. 4. Effect of the electron suppressor ring on the measured current.

Target preparation

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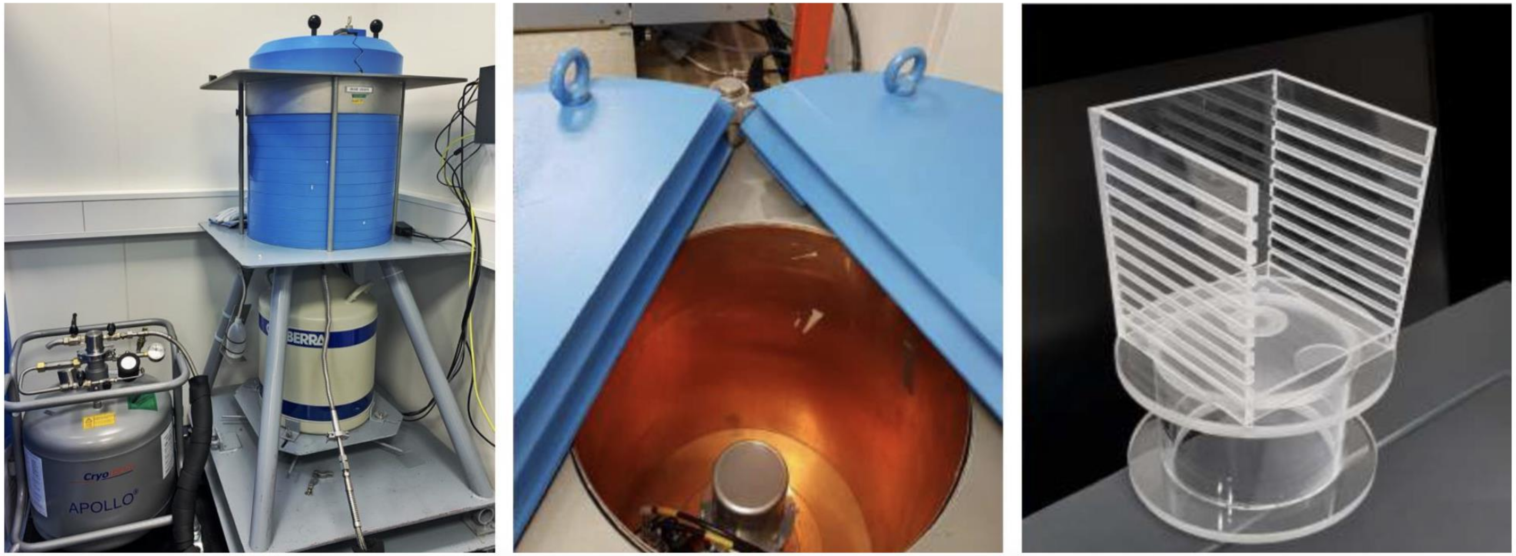
Target for cross section measurements

HPGe detector



Measurements and uncertainties

$$\sigma_r(E) = \frac{A(t_0)}{(1 - e^{-\lambda t_i})} \cdot \frac{q}{\frac{I}{S}} \cdot \frac{1}{m \cdot \frac{N_A}{m_{mol}} \cdot \eta\epsilon}$$

- Beam energy – accurate knowledge of the pristine beam energy is crucial!
- Activity by gamma spectroscopy
  - *Uncertainties on the specific gamma line + HPGe calibration (<3%)*
- Current surface density (current measurement + flatness)
  - *On-line monitored with UniBEaM (~4%)*
- Mass of the target
  - *Measured during target construction (~4%)*
- Isotopic ratio of the target + stoichiometric number
  - *Known from the manufacturer of the target material*

Beam energy measurement (1): magnetic deflection in the BTL

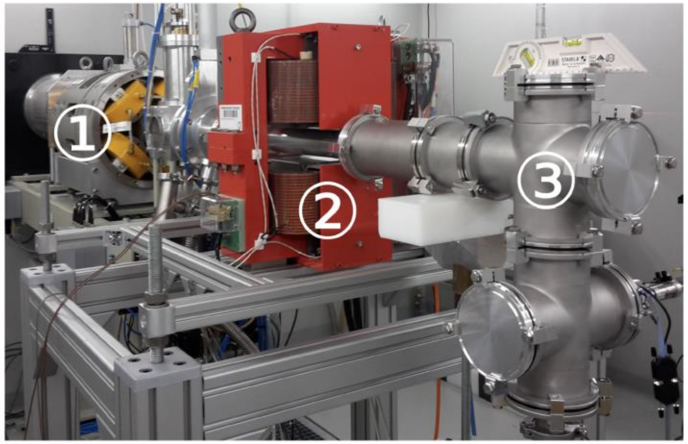
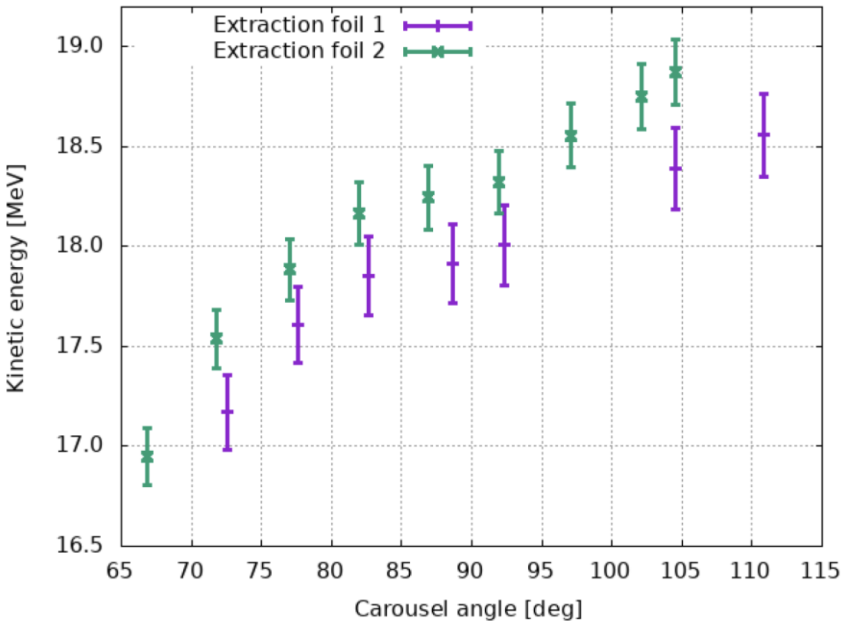


Figure 2. Experimental set-up: the Beam Transfer Line (BTL) quadrupole doublet (**1**), the dipole bending magnet (**2**), and the UniBEaM detector (**3**).



<u>WARNING</u>

The beam energy changes with the cyclotron operational parameters!

P. Häffner et al., Instruments 2019, 3(4), 63

Cross sections and radio-nuclidic purity: the case of ^{68}Ga

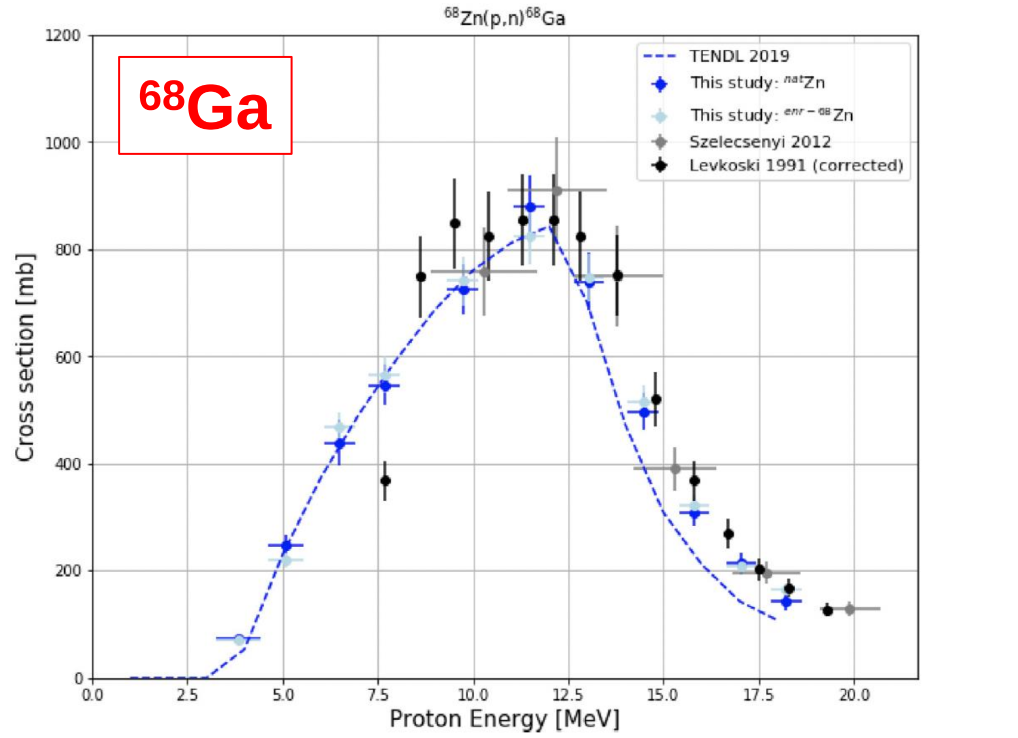


Fig. 4. ^{68}Zn(p,n)^{68}Ga cross section measured from natural and enriched ^{68}Zn targets with the isotopic composition marked as (A) in Table 1.

S. Braccini at al., *Optimization of ^{68}Ga production at an 18 MeV medical cyclotron with solid targets by means of cross-section measurement of ^{66}Ga, ^{67}Ga and ^{68}Ga,* Appl. Radiation and Isotopes, Volume 186, August 2022

Cross sections and radio-nuclidic purity: the case of ^{68}Ga

- ^{67}Ga is the main impurity
- Two nuclear reactions: $^{67}Zn(p,n)^{67}Ga$ and $^{68}Zn(p,2n)^{67}Ga$
- Only production cross-sections can be directly measured
- The production cross-sections depend on the enrichment level …
- … using of two different enriched materials: the (p,n) and (p,2n) nuclear reactions can be disentangled by inverting a linear equation system

$$\begin{cases} \sigma\left({}^{nat}Zn(p,x)^{67}Ga\right) \\ \quad = \epsilon_{67}^{nat}\cdot\sigma\left({}^{67}Zn(p,n)^{67}Ga\right) + \epsilon_{68}^{nat}\cdot\sigma\left({}^{68}Zn(p,2n)^{67}Ga\right) \\ \sigma\left({}^{enr}Zn(p,x)^{67}Ga\right) \\ \quad = \epsilon_{67}^{enr}\cdot\sigma\left({}^{67}Zn(p,n)^{67}Ga\right) + \epsilon_{68}^{enr}\cdot\sigma\left({}^{68}Zn(p,2n)^{67}Ga\right) \end{cases}$$

Cross sections and radio-nuclidic purity: the case of ^{68}Ga

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Production cross-sections

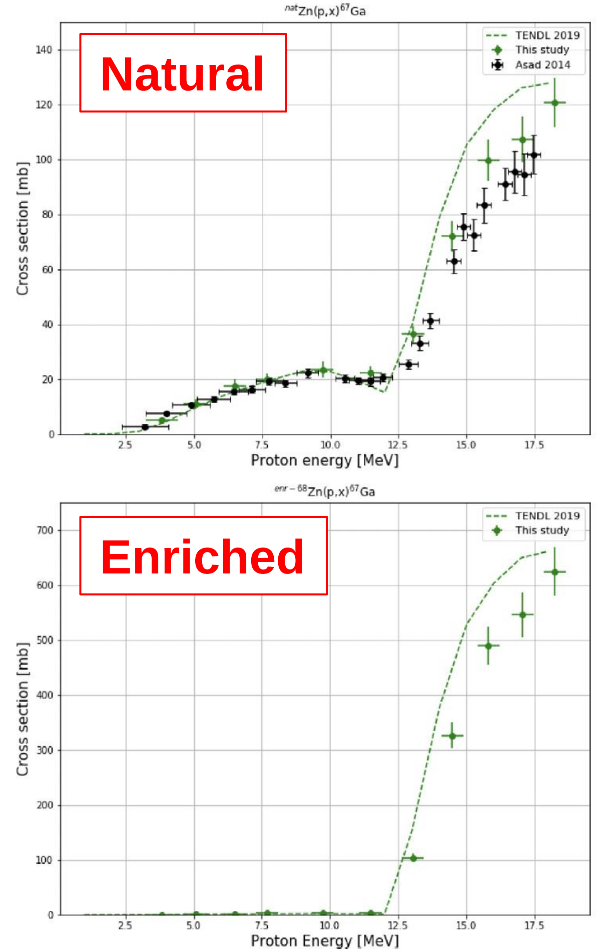


Fig. 5. Production cross section of ^{67}Ga from ^{nat}Zn (a) and $^{enr-68}Zn$ (b) targets with the isotopic composition marked as (A) in Table 1.

Nuclear cross-sections

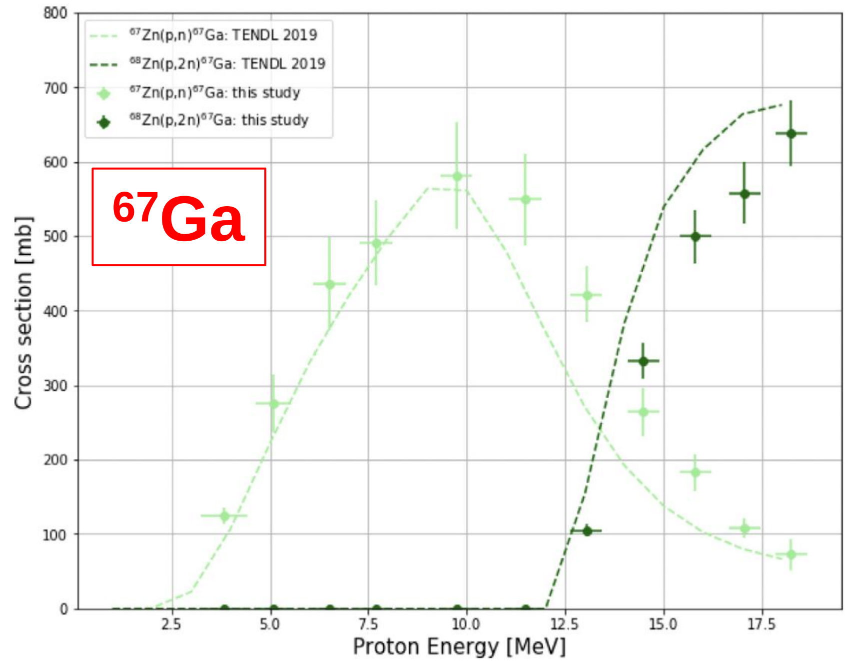
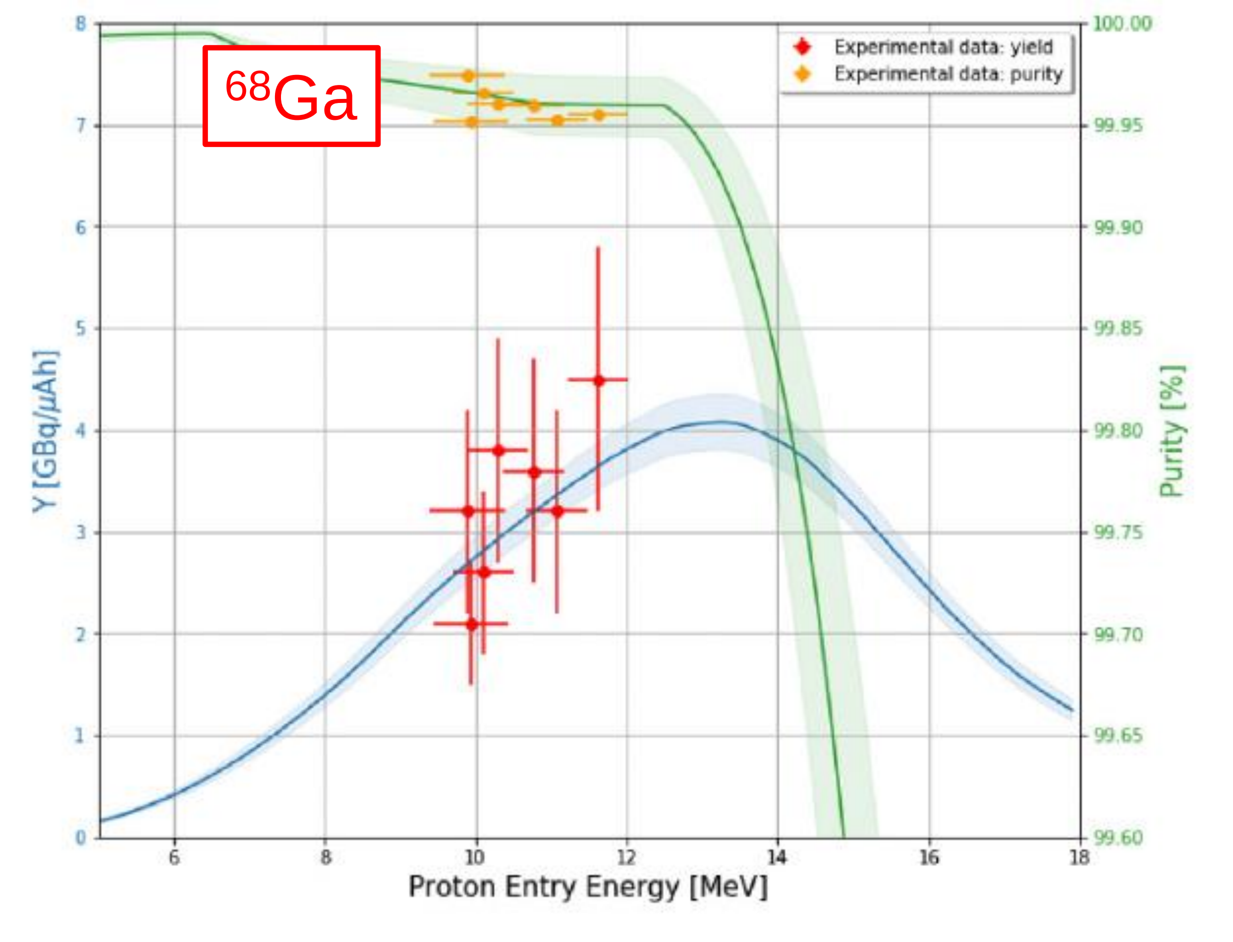


Fig. 6. $^{67}Zn(p,n)^{67}Ga$ and $^{68}Zn(p,2n)^{67}Ga$ reaction cross sections.

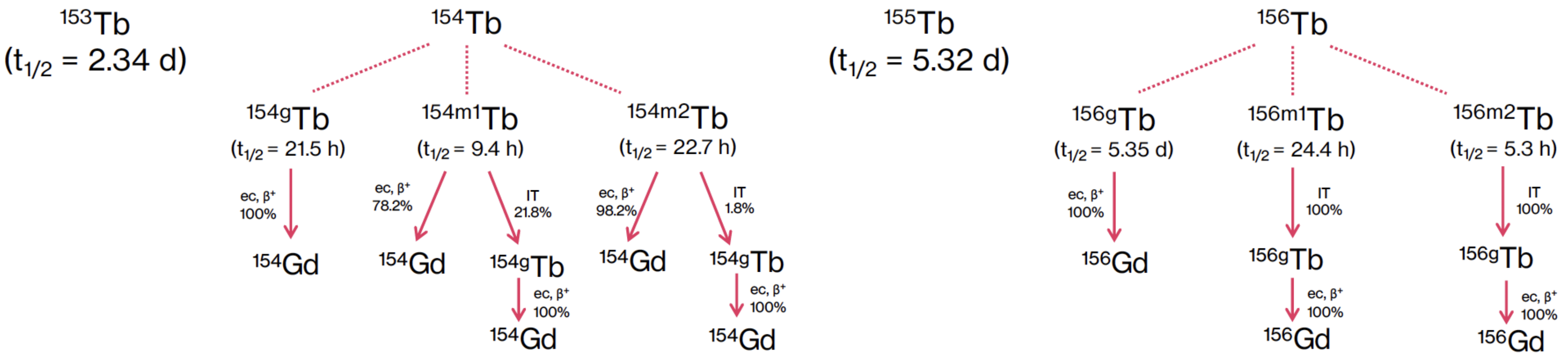
Yield, purity and production tests: example ^{68}Ga



A complex case: terbium

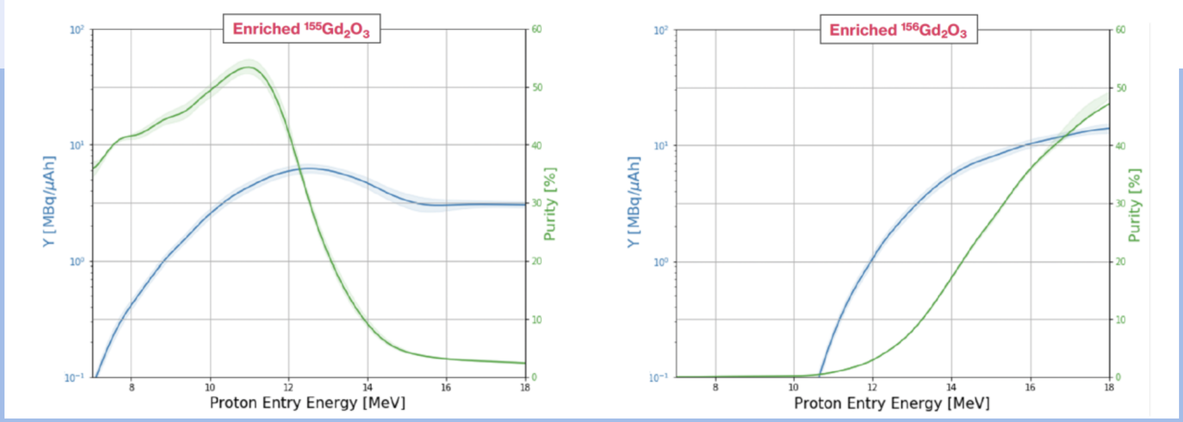
Terbium radioisotopes

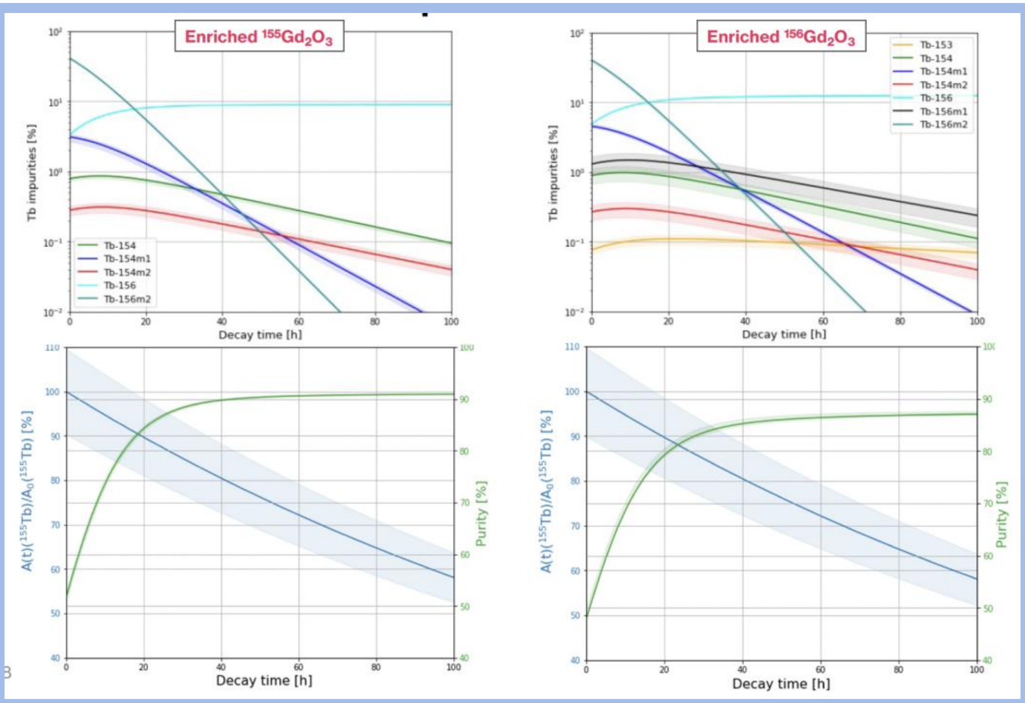
	^{152}Gd	^{154}Gd	^{155}Gd	^{156}Gd	^{157}Gd	^{158}Gd	^{159}Gd
Nat [%]	0.20	2.18	14.80	20.47	15.65	24.84	21.86
Enr-155 [%]	<0.02	0.5	**91.90*(30)***	5.87	0.81	0.65	0.27
Enr-156 [%]	<0.01	0.05	0.87	**93.30*(10)***	4.38	1.08	0.32



G. Dellepiane et al, *Appl. Radiat. Isot.* **2022**, *184*, 110175

A complex case: terbium





Our starting point:
commercial Solid Target Station (STS)

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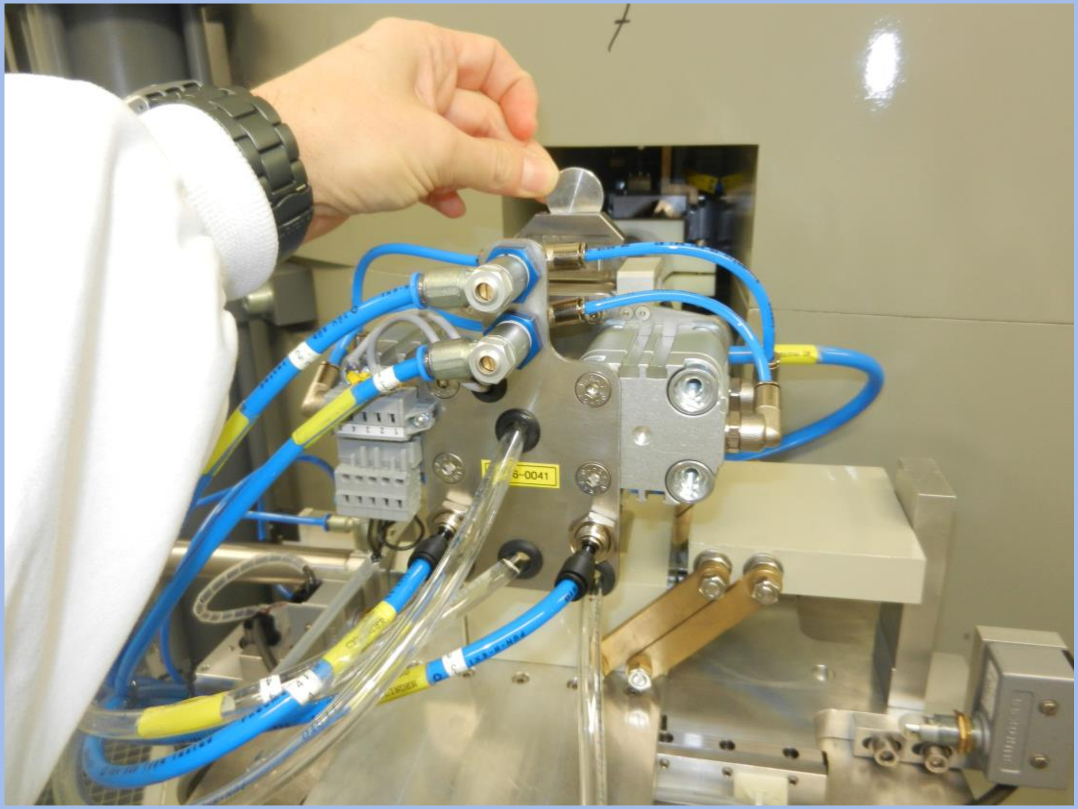
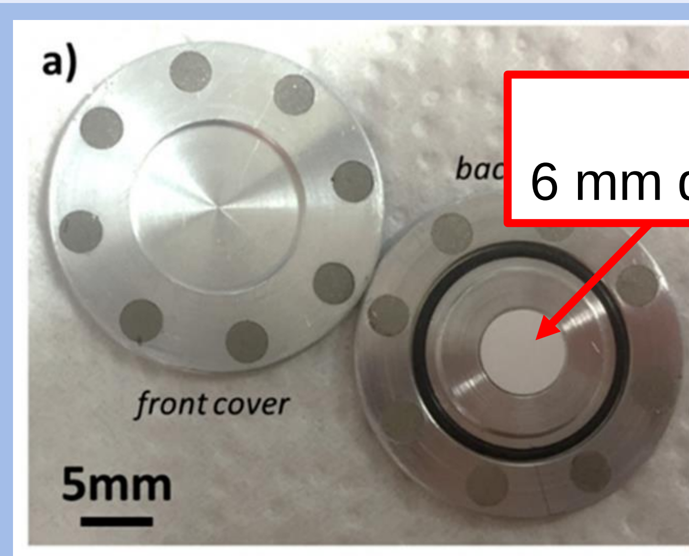


- IBA Nirta “COSTIS”
- Target:
  - 24 mm diameter 2 mm thick disk
  - electro-plated materials
- Manual insertion and recovery of the disk
- Cooling: water in the back, helium in the front

The target “coin”



- High-purity aluminum
- Two halves kept together by permanent magnets
  - SmCo, 350°C Curie temperature
- O-ring (viton) to avoid radioactive degassing
- Variable thickness of the front (entry energy variation)

Beam energy measurement (2): special “coin” for the STS

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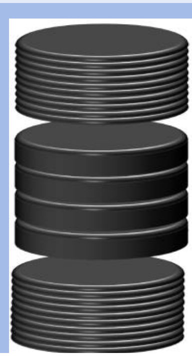
Monitor reaction

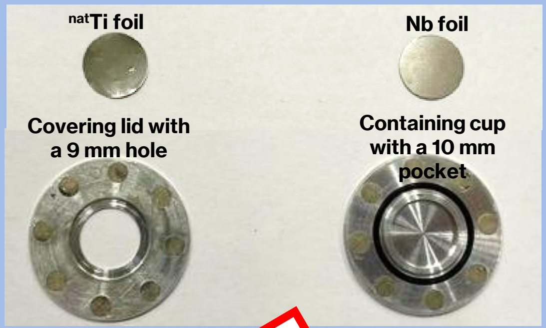
$^{nat}Ti(p,X)^{48}V$



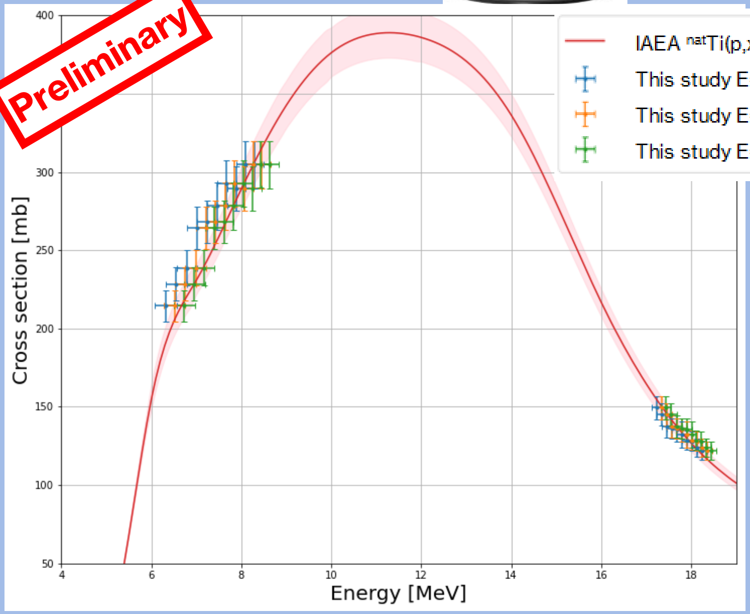
Titanium
10 × 12.5 µm

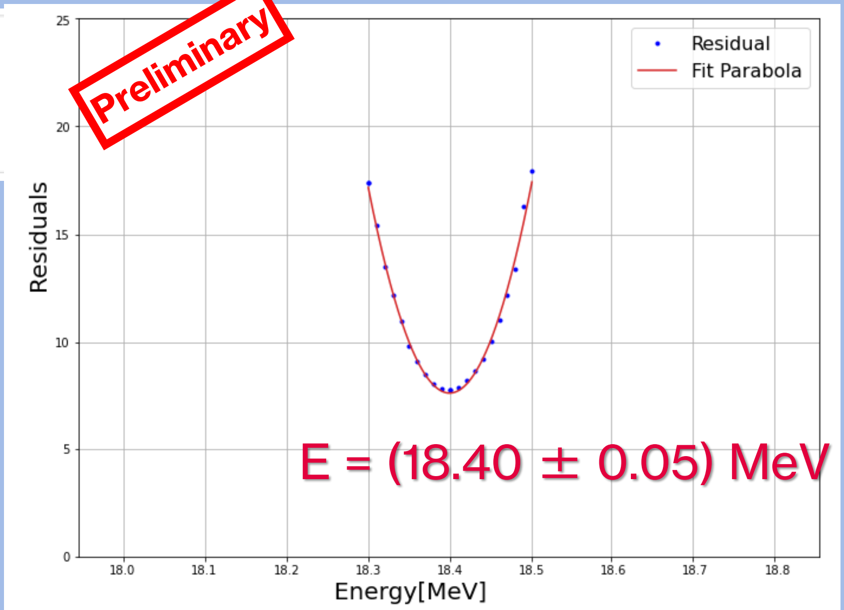
Niobium
4 × 125 µm

Titanium
10 × 12.5 µm



Closed target coin





Elnaz Zyaee, Master Thesis, 2021; A. Gottstein, PhD Thesis; paper in preparation

The receiving station in the BTL and the CZT detector

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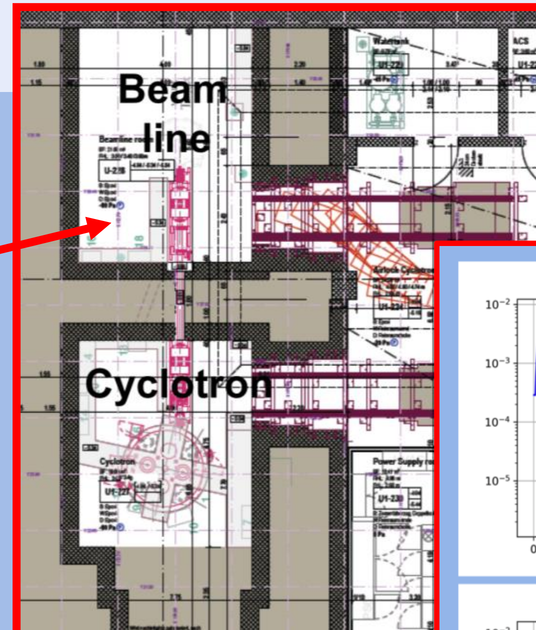

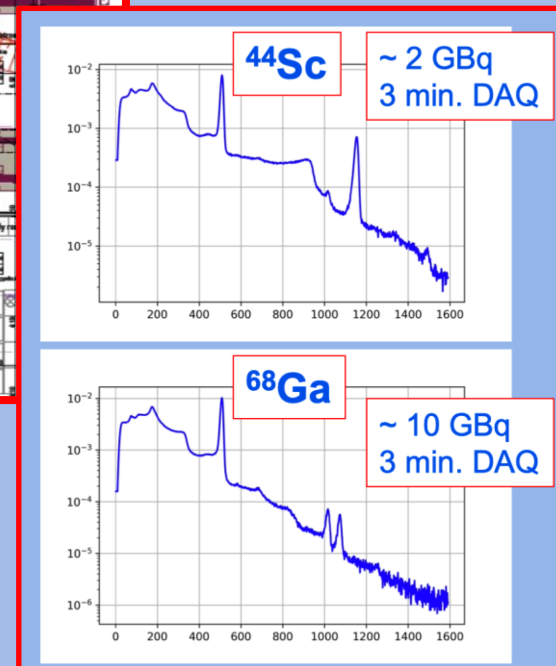

- ~ 1 cm^3 CdZnTe (CZT) crystal
- Up to 40 cm from target (movable)
- Gamma spectroscopy

Conclusions and Outlook

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- We are developing tools and methods to optimize the production of non-conventional radioisotopes (for theragnostics in particular)
  - Beam monitoring detectors
  - Irradiation methods using solid targets
  - Cross-sections using a medical cyclotron

- Work is in progress on several radionuclides:
  - Cross-sections
  - Production yields

- … we are open to collaborations!

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- Master and Bachelor Students
- LHEP mechanics and electronics workshop
- SWAN Team
- Collaborations: PSI, CERN, TRIUMF, U. Wisconsin, U. Bologna, …

https://www.lhep.unibe.ch/research/medical_applications/index_eng.html