# Optimizing solid-target production of non-conventional theranostic radionuclides at the Bern medical cyclotron


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# The Bern medical cyclotron and its Beam Transfer Line (BTL)

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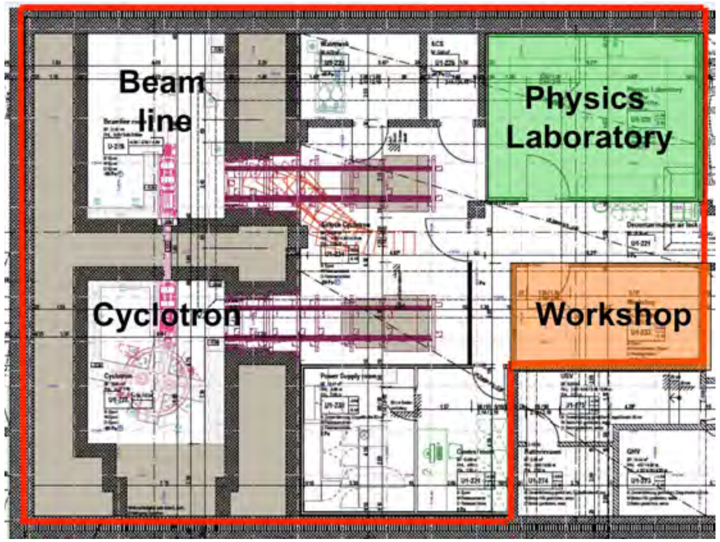


**In operation since 2013 at the Bern University Hospital (Inselspital)**

- IBA 18 MeV high current cyclotron (up to 150 $\mu$A) – 2 $H^-$ ion sources

- 4 High Current $^{18}$F liquid targets: daily production
- 2 hybrid targets for $^{68}$Ga (under test)

swan ISOTOPEN

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

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# Multi-disciplinary research activities with the BTL

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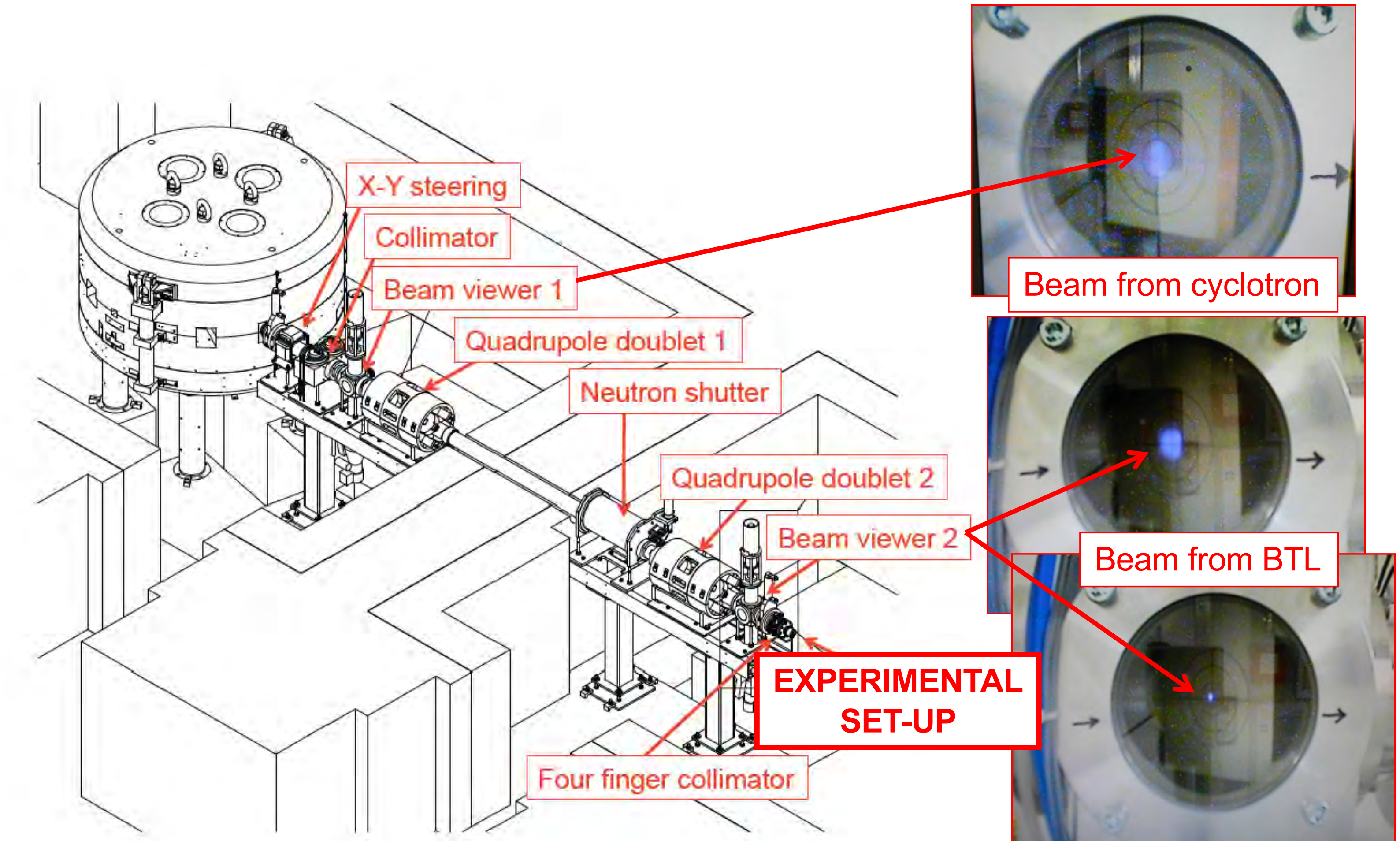
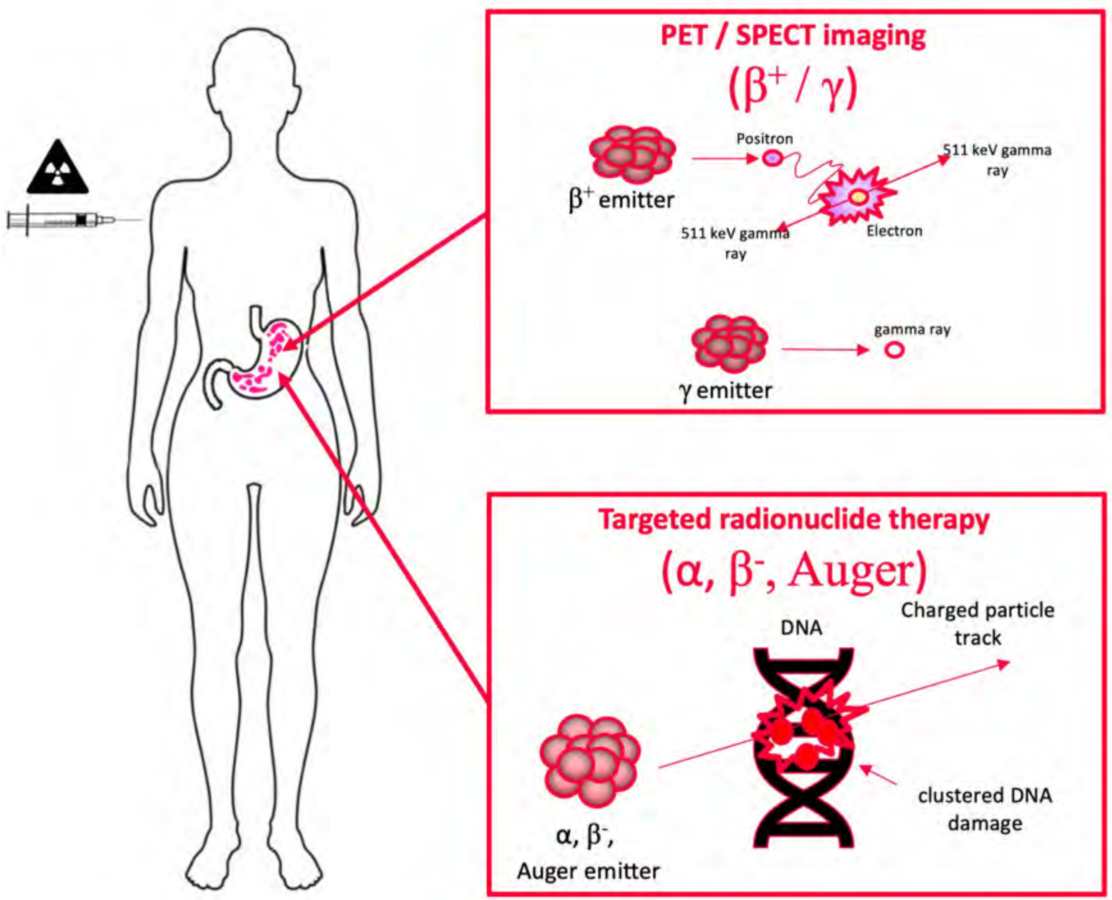



S. Braccini, *AIP Conf. Proc.* vol. 1525, p. 144, 2013

# Theranostics = Therapy + Diagnostics




- 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
- Promising Auger emitters: $^{103}$**Pd**, $^{135}$**La (*)**
- Radiometals

**Solid targets:**
- **~ 10 mg**
- **~ 5 mm diameter**
- **Material: powder**
- **Beam: ?**

(*) See talks by: G. Dellepiane (U. Bern and TeraCare); P. Grundler, A. Moiseeva, N. van der Meulen (PSI); J. Engle (U. Wisconsin Madison)

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# Our starting point:
# commercial Solid Target Station (STS)

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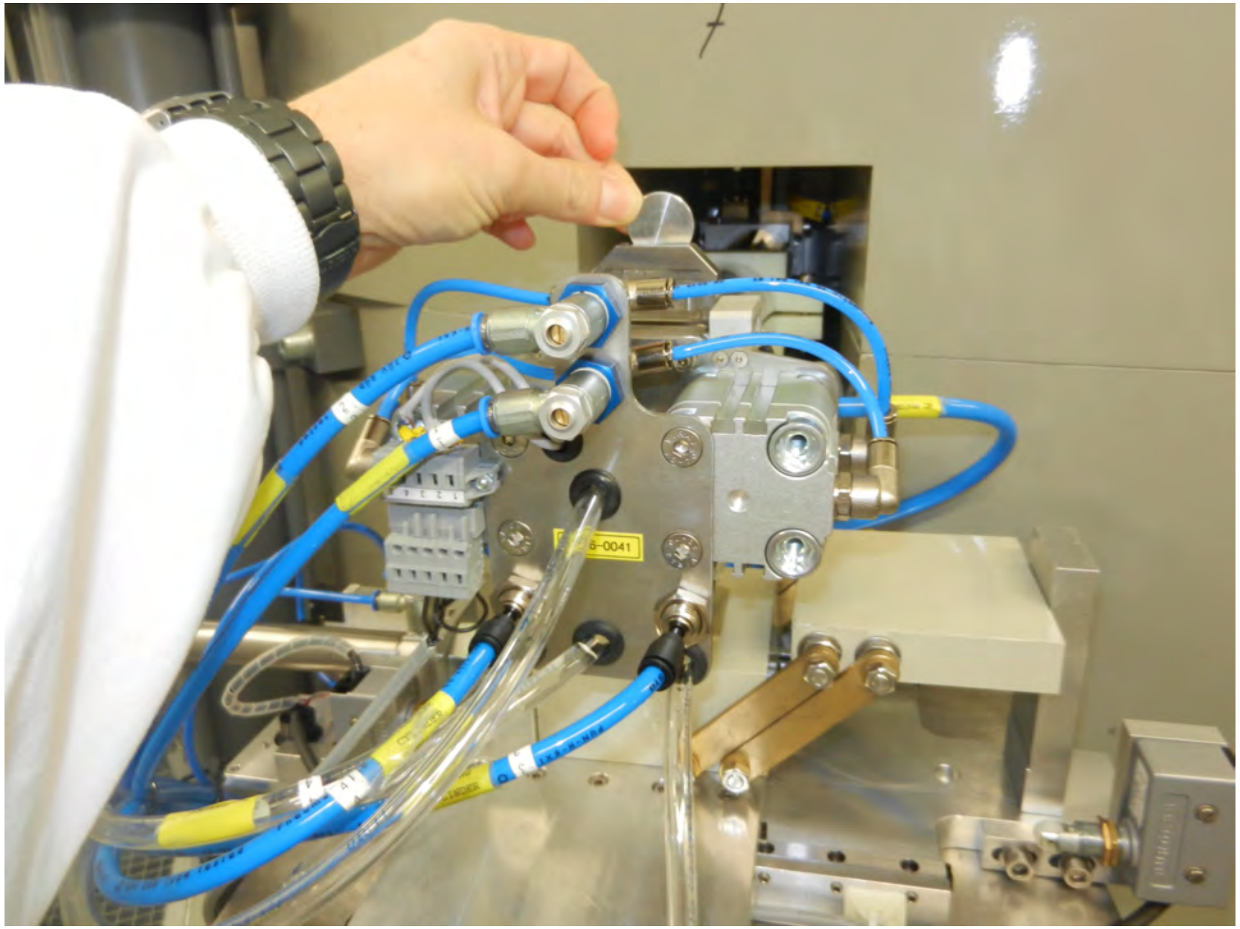
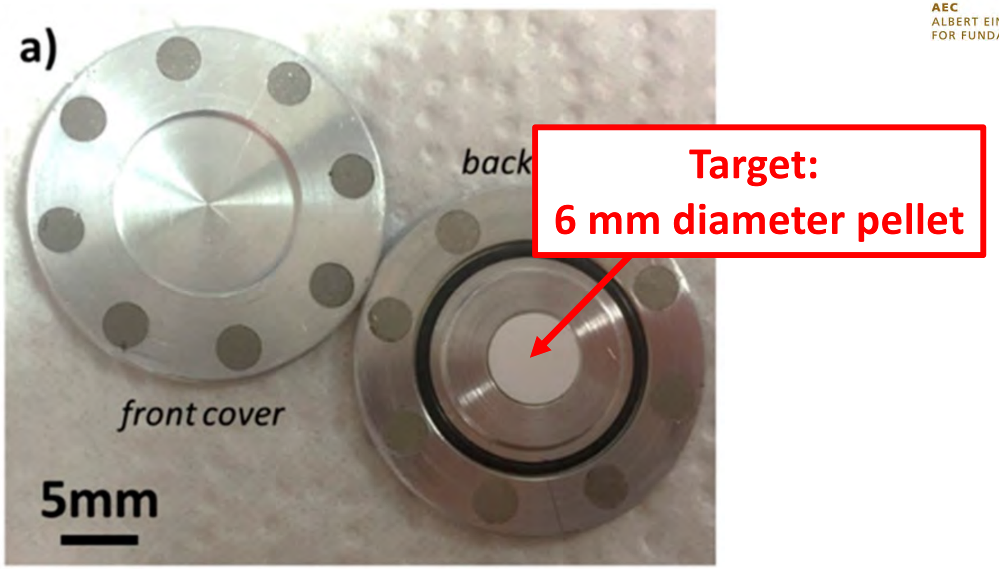


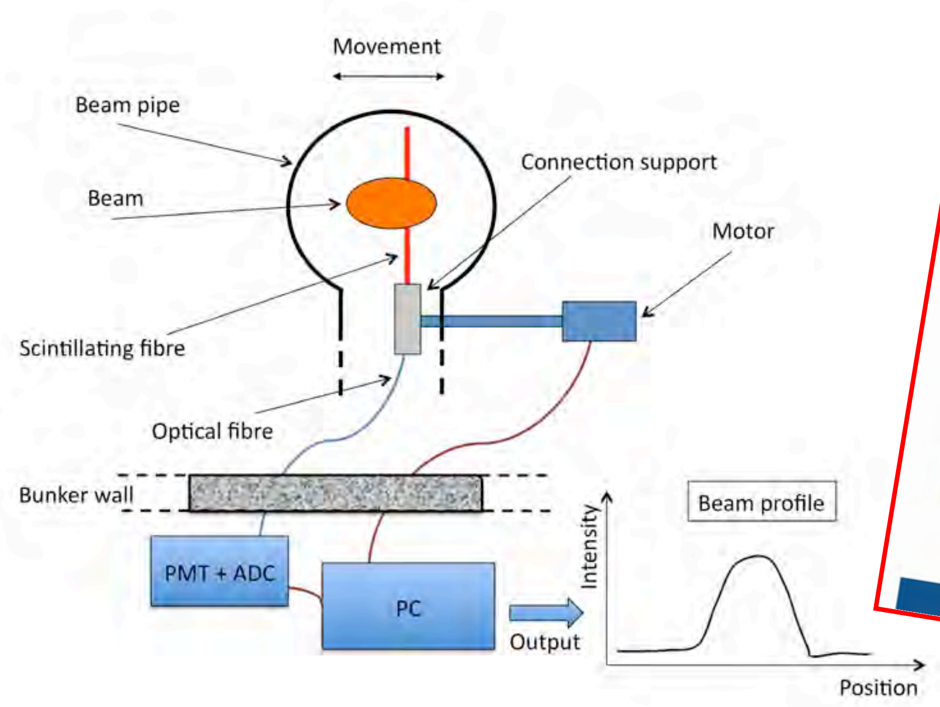
- IBA Nirta “COSTIS”
- Target:
  - 24 mm diameter 2 mm thick disk
  - electro-plated materials
- Manual insertion and recovery of the disk
- Cooling: water in the back, helium in the front

# The magnetic 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)
- Can be easily opened inside a hot cell

# The UniBEaM detector





- 1D 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

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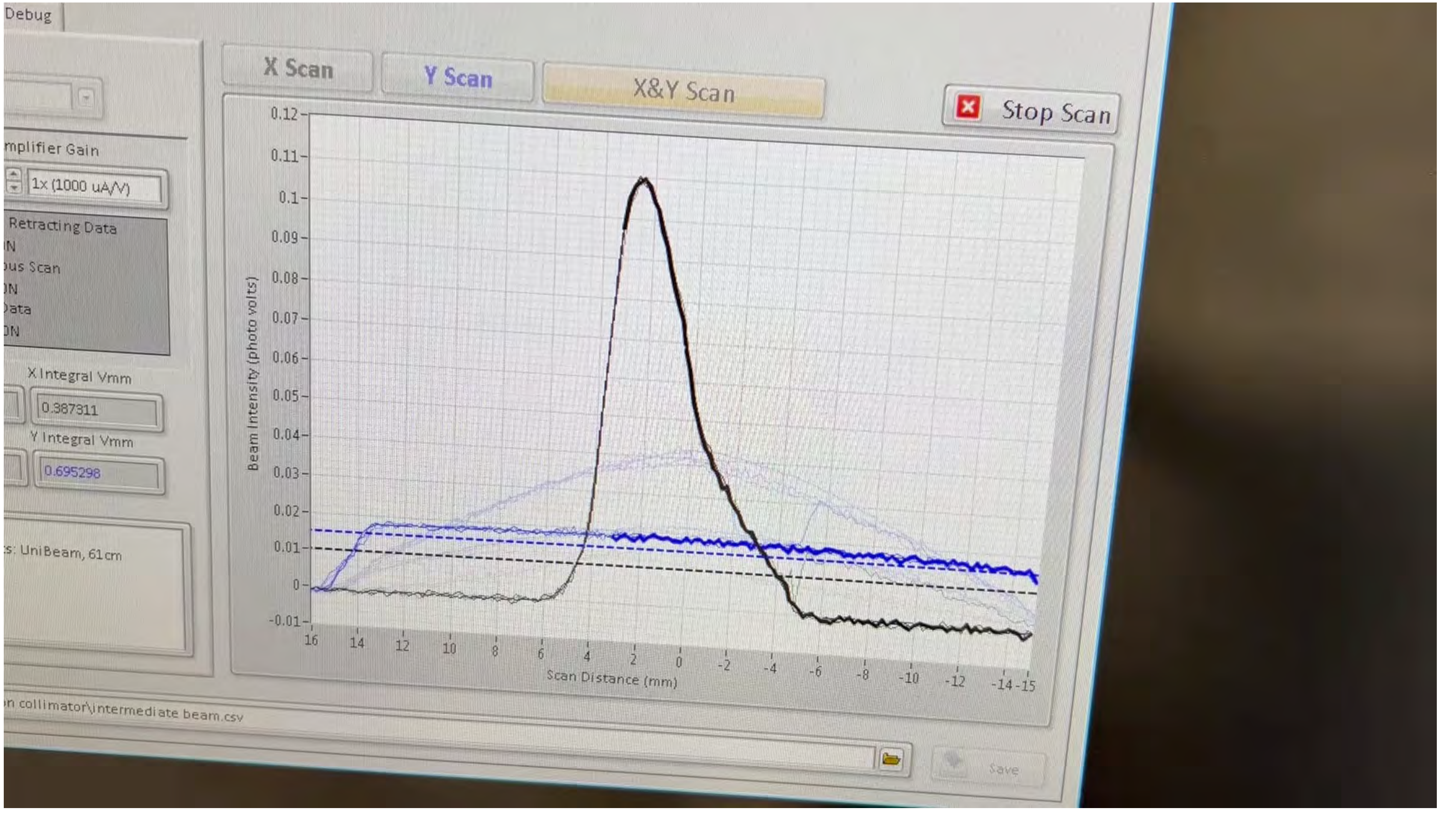

# The $\pi^2$ detector

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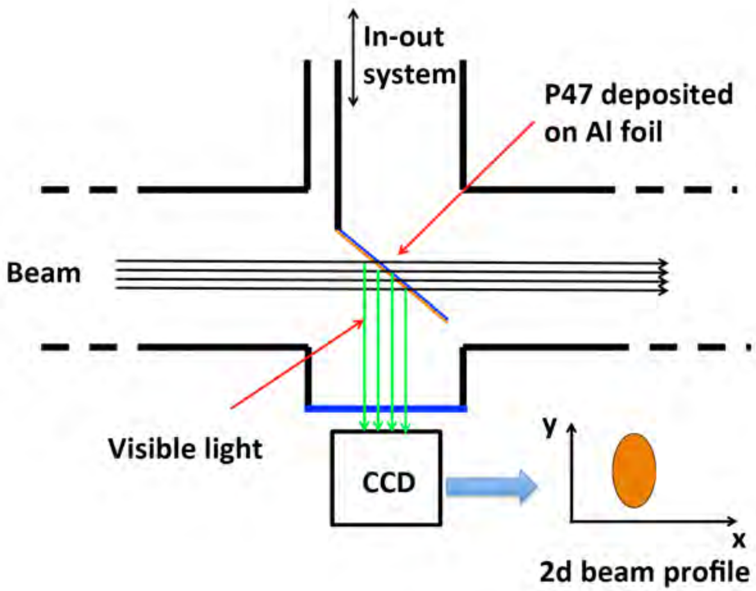


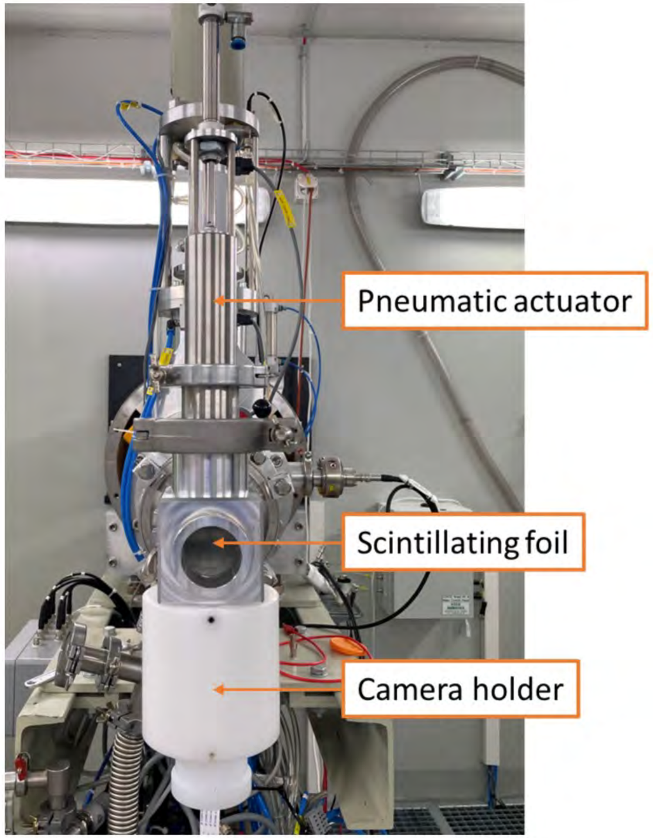


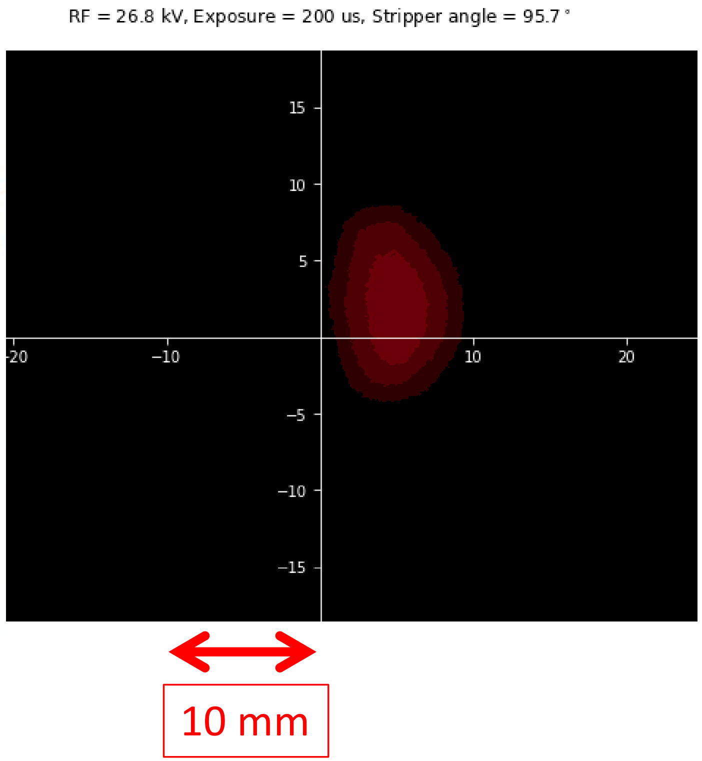


S. Braccini et al., Appl. Sci. 2023, 13, 3657

# Beam-first collimator alignment is critical!

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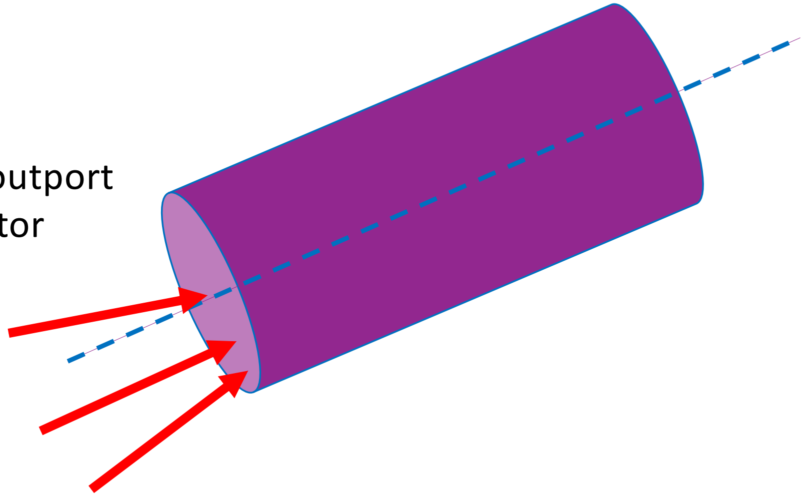
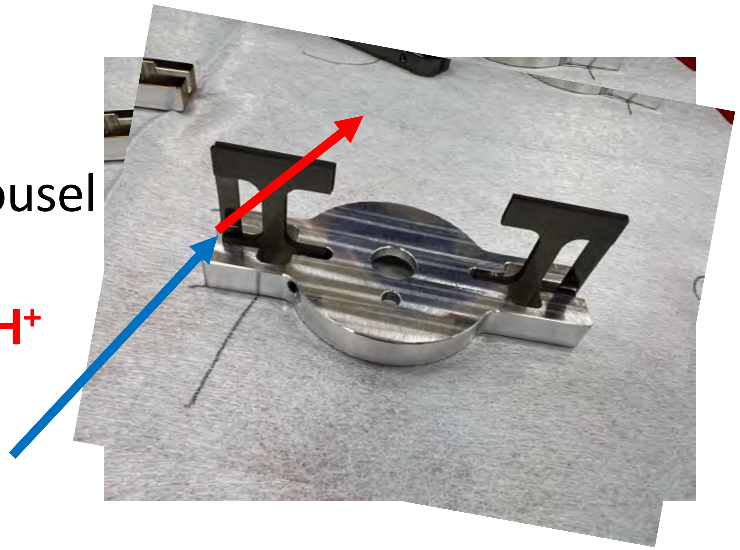
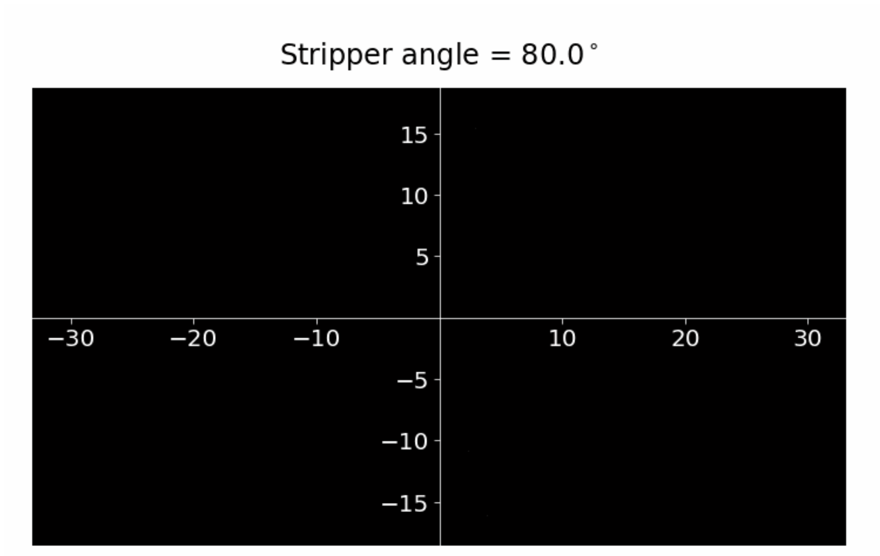
Cyclotron outport collimator



Stripper carrousel

Beam H$^-$ ➔ H$^+$






2D image taken with the $\pi^2$ detector

# Solution: modify the stripper carrousel

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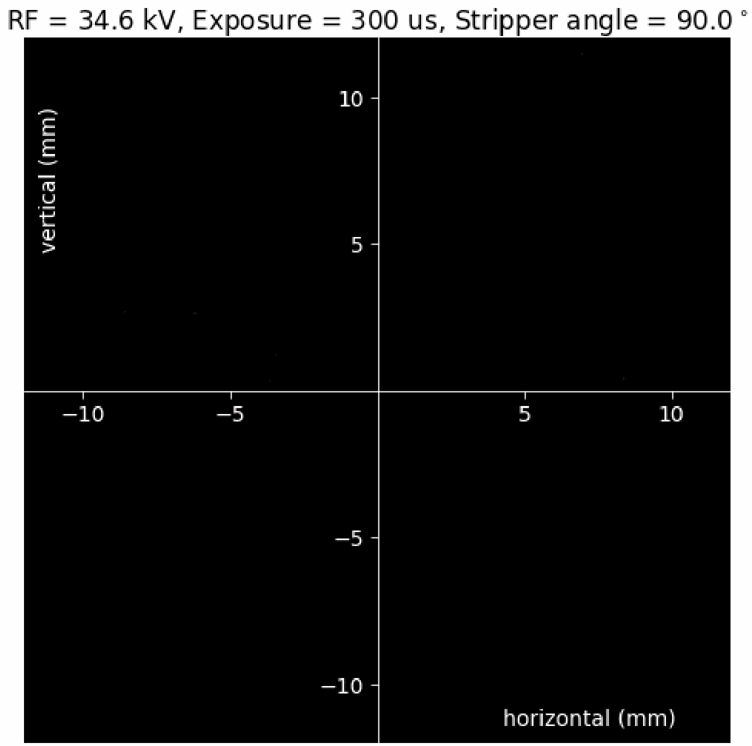


> Arms of different lengthw

  > 38 mm, 35 mm, …

**The position of the stripper has implications on the beam energy!**

# Beam energy measurement (1): magnetic deflection

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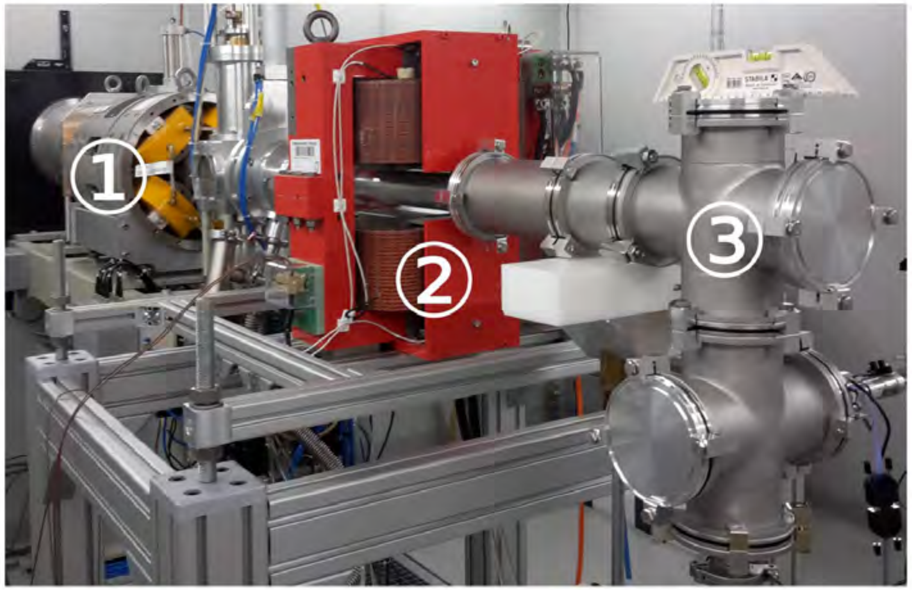
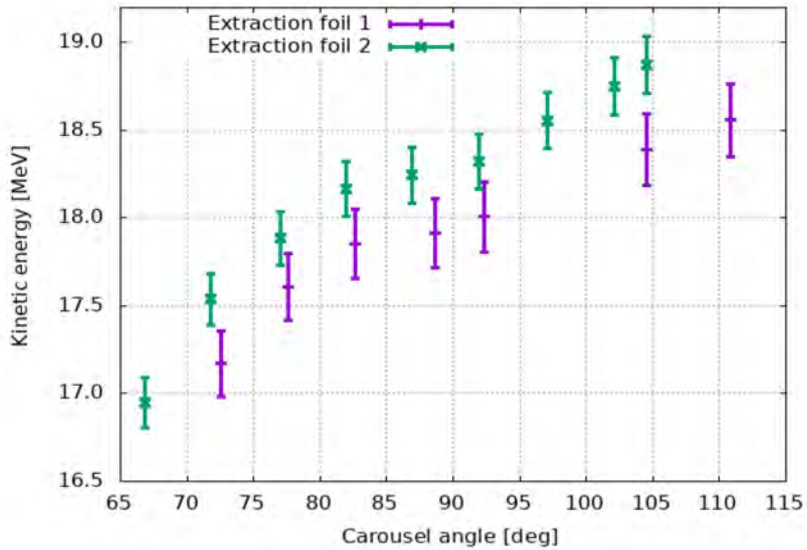
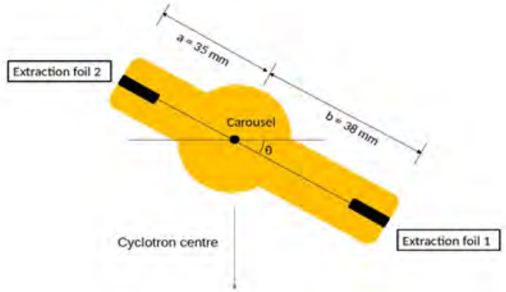



**Figure 2.** Experimental set-up: the Beam Transfer Line (BTL) quadrupole doublet (**1**), the dipole bending magnet (**2**), and the UniBEaM detector (**3**).




In collaboration with CERN

P. Haffner et al., Instruments 2019, 3, 63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# Beam energy measurement (2): monitoring reaction + stacked foils + special "coin"

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**(1)**

**Monitor reaction**

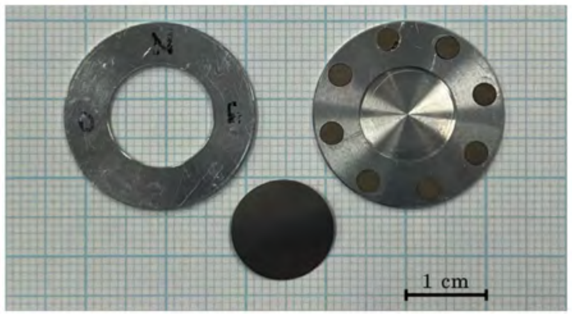
**$^{nat}Ti(p,X)^{48}V$**

**(2)**


$10 \times$ Ti (25µm)
$3 \times$ Cu (25µm)
$1 \times$ Nb (125µm)
$20 \times$ Ti (25µm)

**Stacked folis**

**(3)**

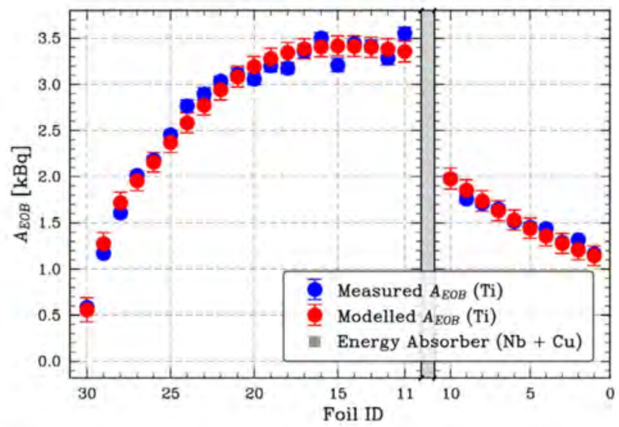



**Special «coin»**

**Irradiation**

**Gamma spectroscopy of each foil**

**(4)**

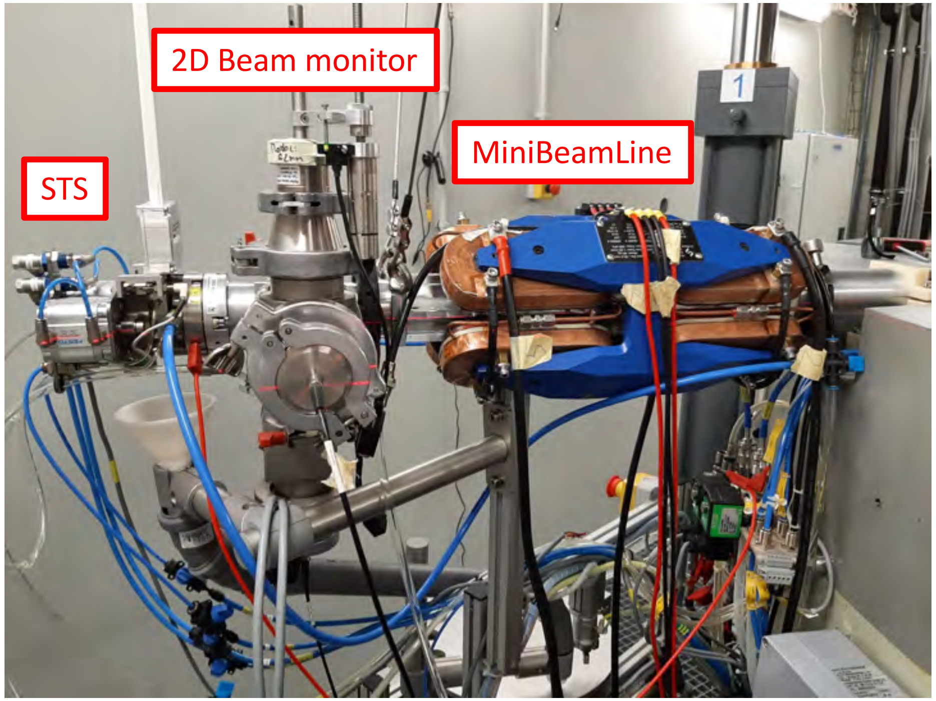


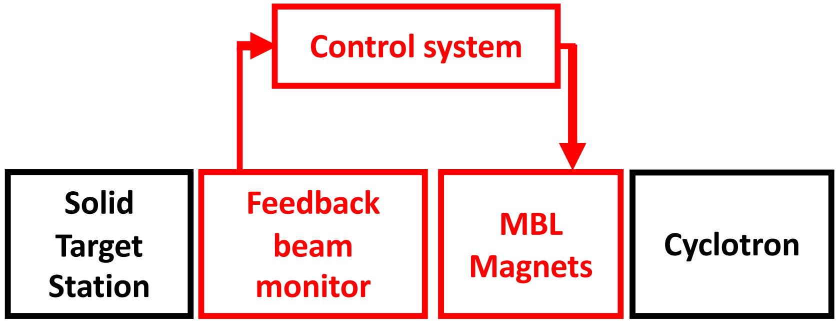

(a) 'Pristine BTL energy'①: Measured activities versus model predictions using the best fit energy of $E_0$ = 18.03 MeV. The grey bar schematically indicates the energy absorbing Cu/Nb layers.

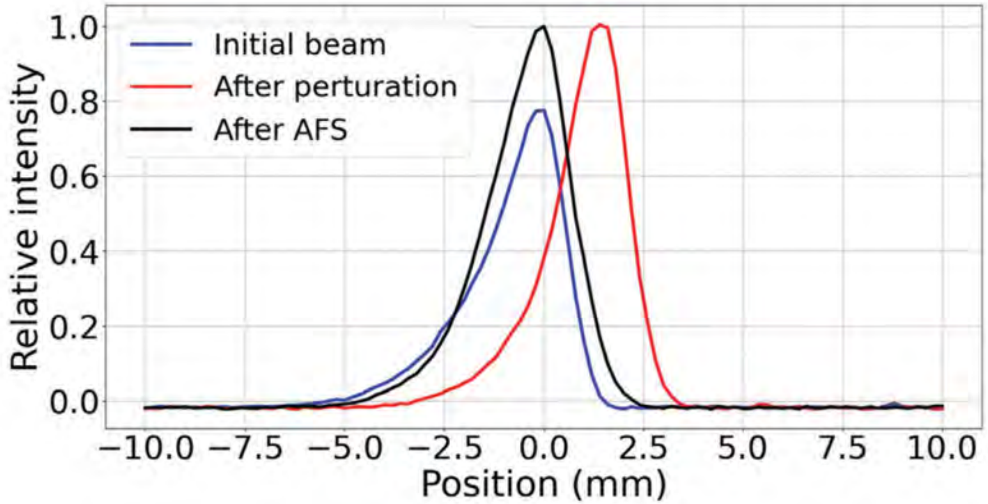
**Bayesian fit of the measured activity profile**

A. Gottstein et al., Nuclear Instruments and Methods in Physics Research A 1084 (2026) 171241

# Automatic Focusing System (AFS)




P. Haffner et al., Appl. Sci. 11.6 (2021): 2452

# The Solid Target Station in the BTL bunker (Nov. 2025)

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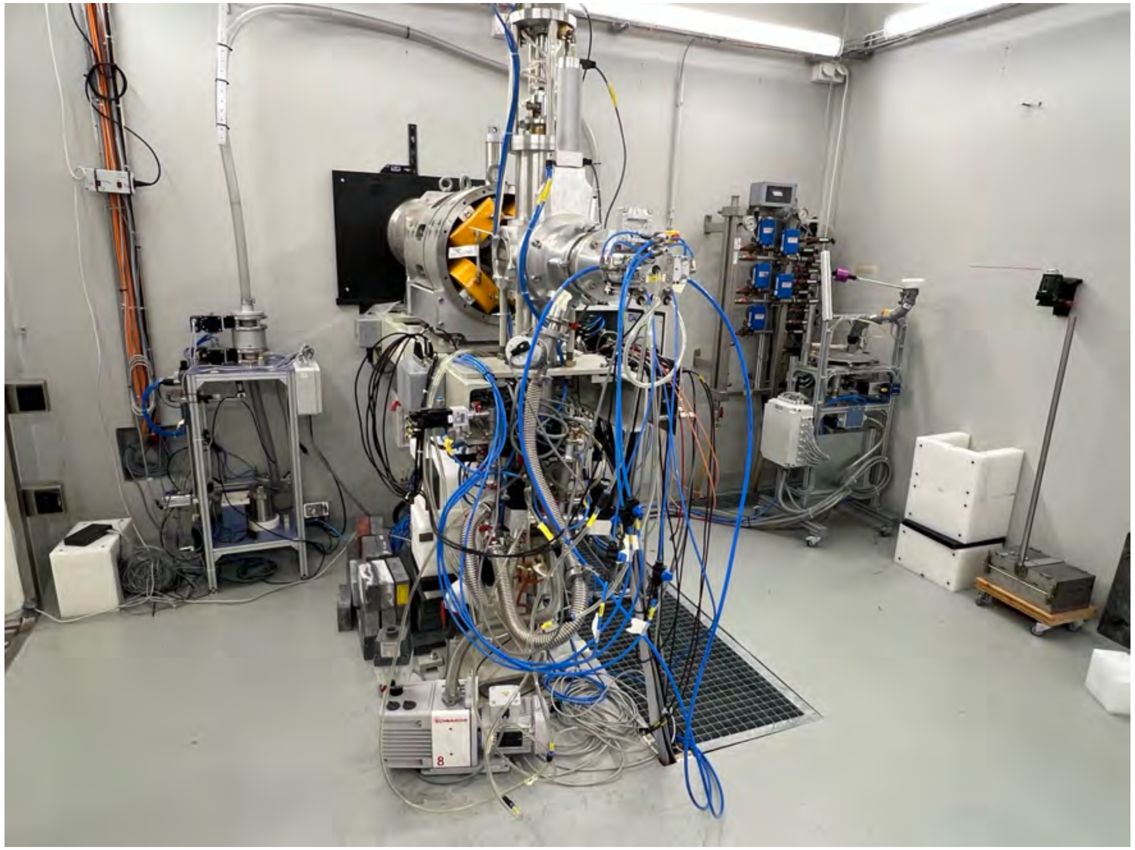
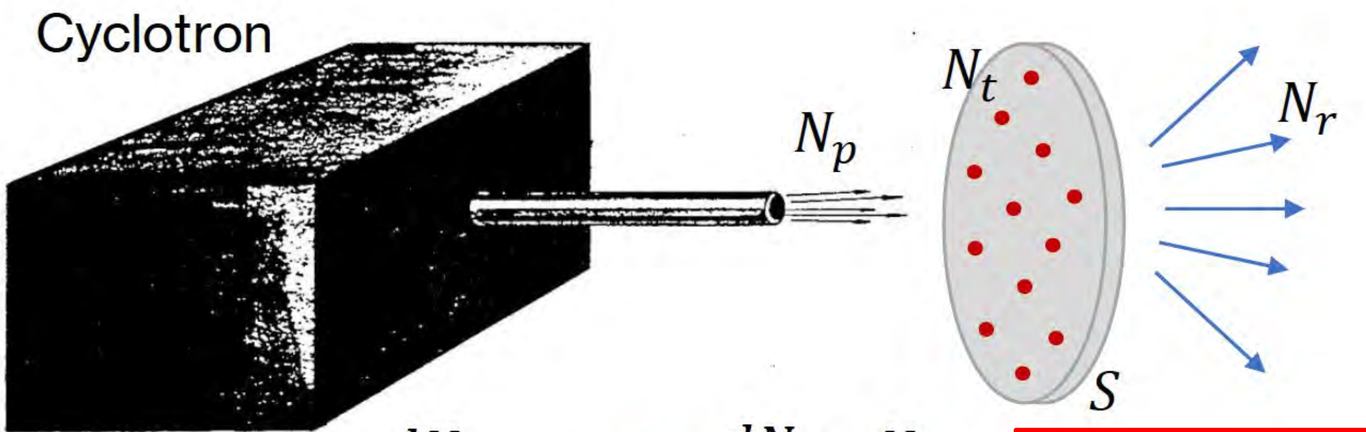
Irradiation configuration
during “STS weeks”



“Garage” configuration
for all other multi-disciplinary activities

# Cross-section measurement: the standard case






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

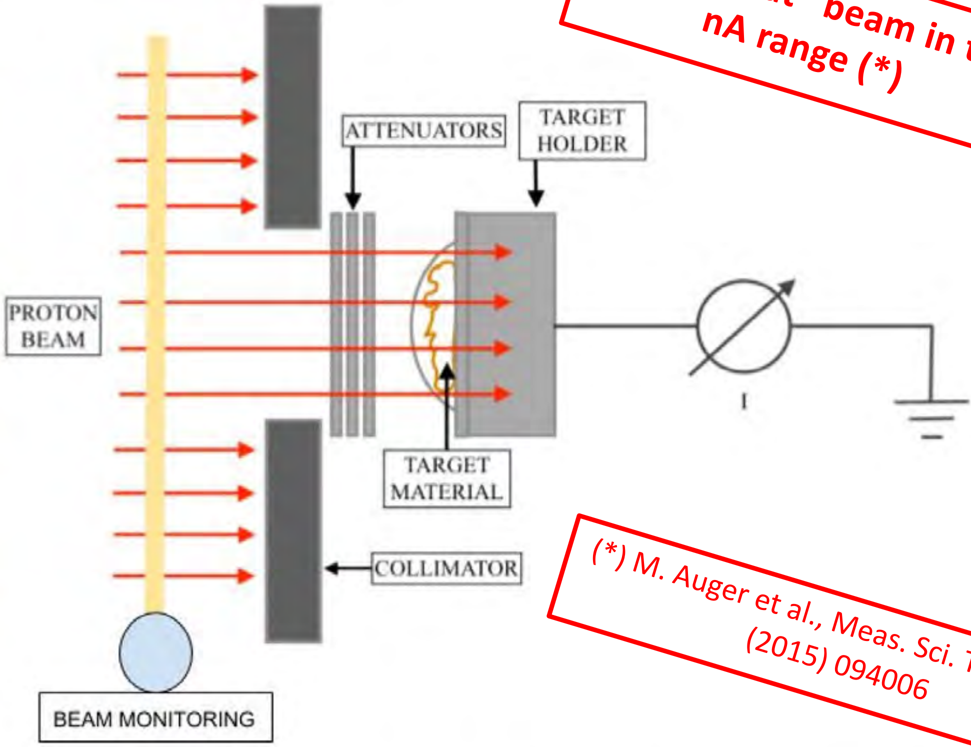
**$N_t/S$ or m/S constant and known**

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

# Cross section measurements with a novel method



Stable "flat" beam in the nA range (*)




(*) M. Auger et al., Meas. Sci. Technol. 26 (2015) 094006

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 target station for cross section measurements

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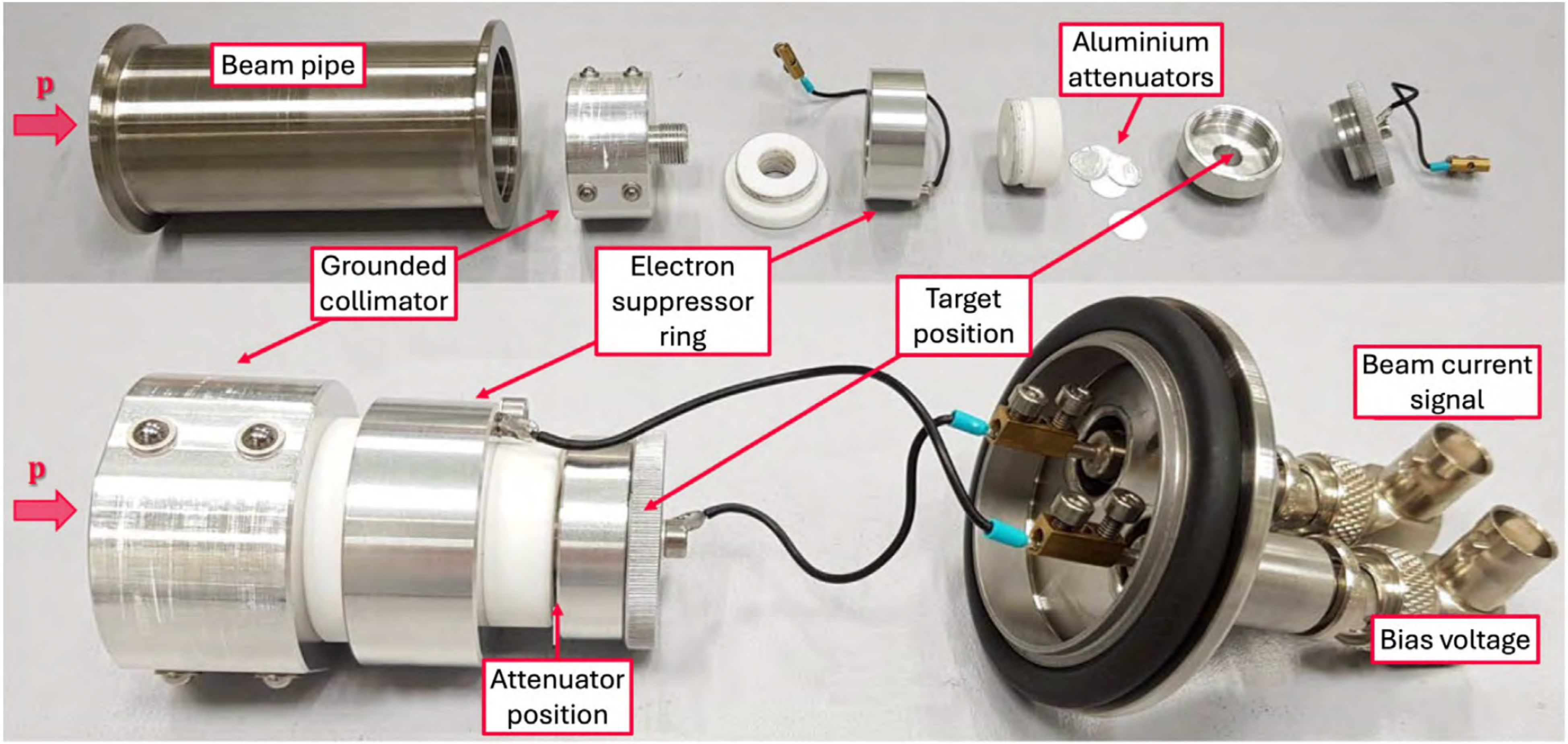

# Radio nuclidic purity and cross sections

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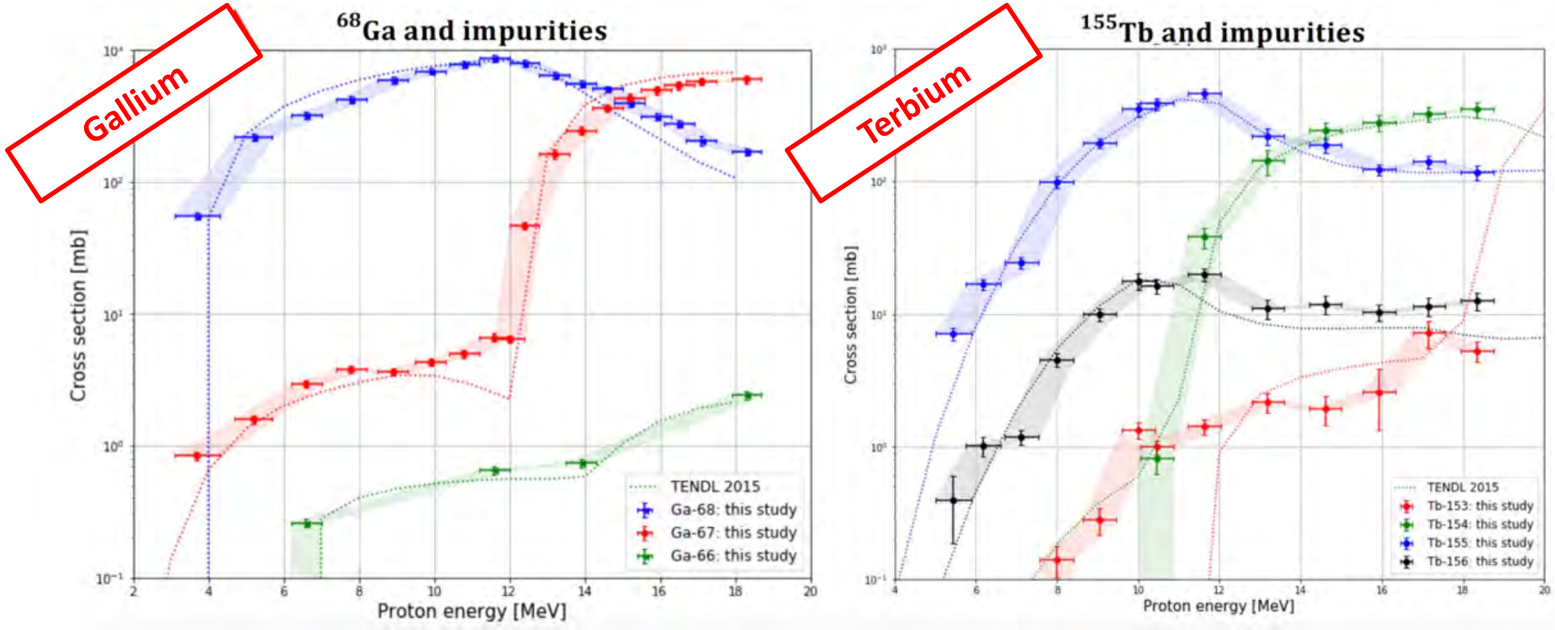
**Cross sections measured:**

$^{43}Sc$, $^{44}Sc$, $^{47}Sc$, $^{61}Cu$, $^{64}Cu$, $^{67}Cu$, $^{68}Ga$, $^{99m}Tc$, $^{155}Tb$, $^{165}Er$, $^{167}Tm$, $^{161}Ho$, $^{103}Pd$, $^{135}La$



# Some produced medical radioisotopes

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| Isotope | Reaction | Target | Mass [mg] | Charge [$\mu$Ah] | Y [GBq/$\mu$Ah] |
|---|---|---|---|---|---|
| $^{44}$Sc | (p,n) | $^{enr-44}$CaO pellet | 30 | 27 | 0.6 |
| $^{47}$Sc | (p,$\alpha$) | $^{enr-50}TiO_2$ pellet | 35 | 3.9 E-3 | 0.001 |
| $^{61}$Cu | (p,$\alpha$) | $^{enr-64}$Zn pellet | 40 | 2.7 E-4 | 0.14 |
| $^{64}$Cu | (p,n) | $^{enr-64}$Ni deposition | 63 | 160 | 0.13 |
| | (p,$\alpha$) | $^{enr-67}$ZnO pellet | 59 | 2.7 E-4 | 0.02 |
| $^{67}$Cu | (p,$\alpha$) | $^{enr-70}$ZnO pellet | 34 | 1.7 E-3 | 0.001 |
| $^{68}$Ga | (p,n) | $^{enr-68}$Zn pellet | 40 | 0.24 | 4.5 |
| $^{155}$Tb | (p,n) | $^{enr-155}Gd_2O_3$ pellet | 40 | 1.1 E-3 | 0.004 |
| | (p,2n) | $^{enr-156}Gd_2O_3$ pellet | 40 | 1.1 E-3 | 0.01 |
| $^{165}$Er | (p,n) | $^{nat}$Ho metal disk | 160 | 1.7 | 0.07 |
| $^{165}$Tm | (p,2n) | $^{enr-166}Er_2O_3$ pellet | 59 | 1.1 | 0.02 |
| $^{167}$Tm | (p,n) | $^{enr-167}Er_2O_3$ pellet | 41 | 0.01 | 0.003 |

Review : G. Dellepiane et al., Research on theranostic radioisotope production at the Bern medical Cyclotron, Il Nuovo Cimento, 2021.

# $^{44}$Sc is ready for clinical applications

molecules

Molecules 2020, 25(20), 4706

MDPI

*Article*

## Developments toward the Implementation of $^{44}$Sc Production at a Medical Cyclotron


Nicholas P. van der Meulen [1,2,*], Roger Hasler [2], Zeynep Talip [2], Pascal V. Grundler [2], Chiara Favaretto [2], Christoph A. Umbricht [2], Cristina Müller [2], Gaia Dellepiane [3], Tommaso S. Carzaniga [3] and Saverio Braccini [3]

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In collaboration with the Paul Scherrer Institute (PSI)

IBA Award 2020

# $^{68}$Ga production from $^{68}$Zn

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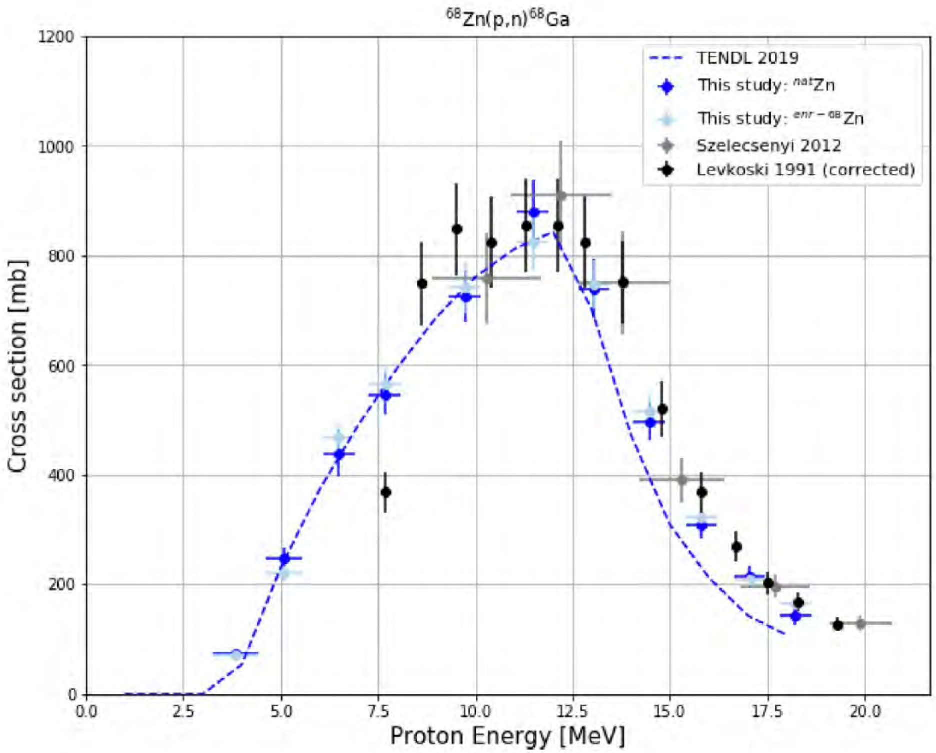


S. Braccini at al., *Optimization of $^{68}$Ga production at an 18 MeV medical cyclotron with solid targets by means of cross-section measurement of $^{66}$Ga, $^{67}$Ga and $^{68}$Ga,* Appl. Radiation and Isotopes, Volume 186, August 2022.

# Cross sections and radio-nuclidic purity: the case of $^{68}Ga$ and its impurity $^{67}Ga$

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**Production cross-sections**

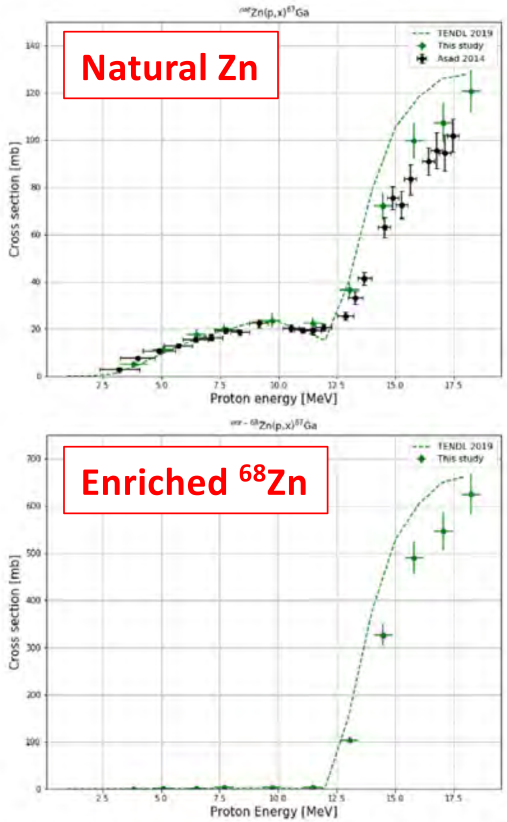


Fig. 5. Production cross section of $^{67}Ga$ from $^{nat}Zn$ (a) and $^{enr-68}Zn$ (b) targets with the isotopic composition marked as (A) in Table 1.

**Nuclear cross-sections**

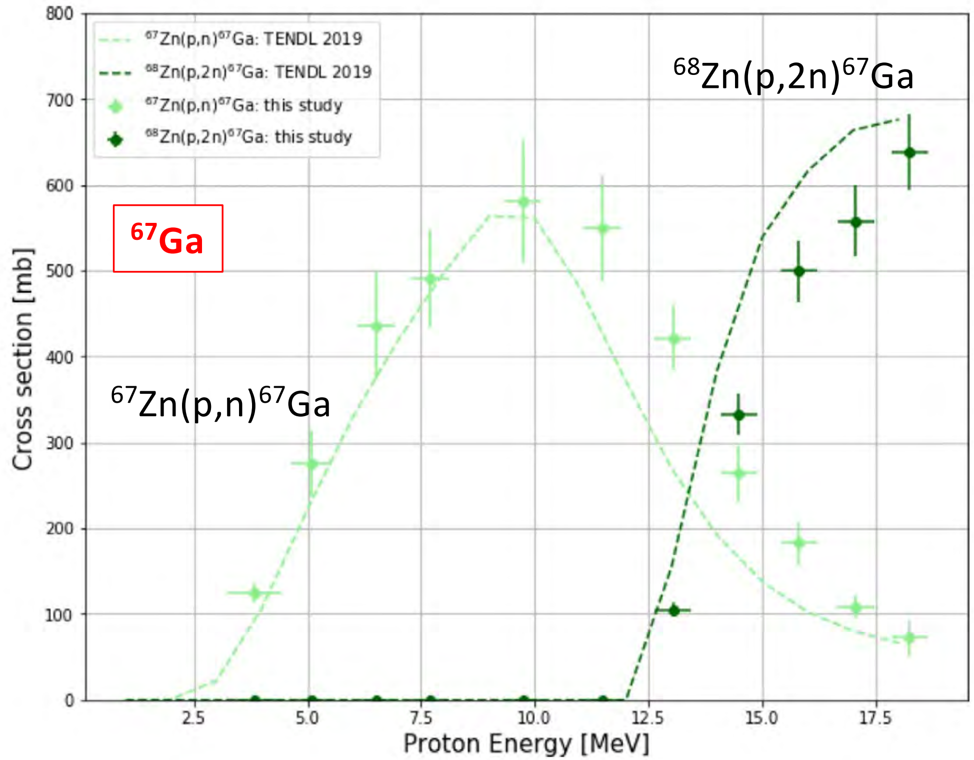


Fig. 6. $^{67}Zn(p,n)^{67}Ga$ and $^{68}Zn(p,2n)^{67}Ga$ reaction cross sections.

# Yield, purity and production tests
# Example: $^{68}$Ga

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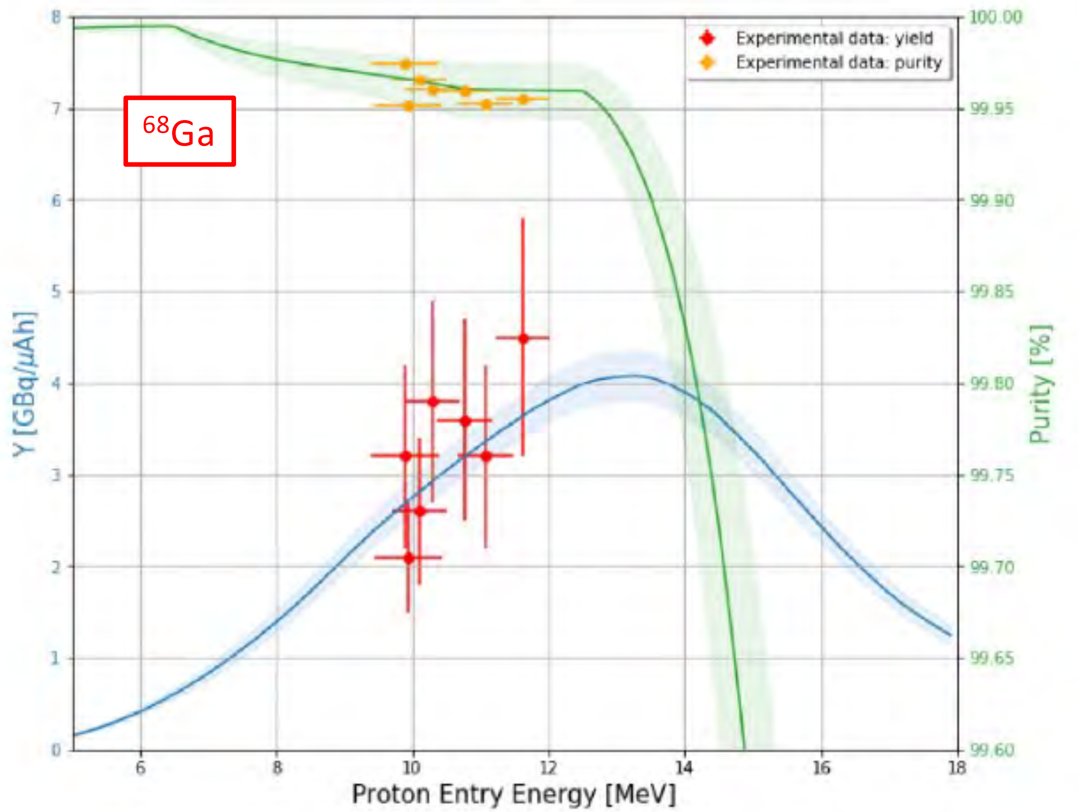

# A fundamental physics question: Does a bound dineutron exist?

Swiss National Science Foundation

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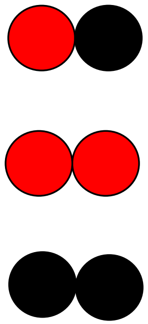
Two nucleon bound states:



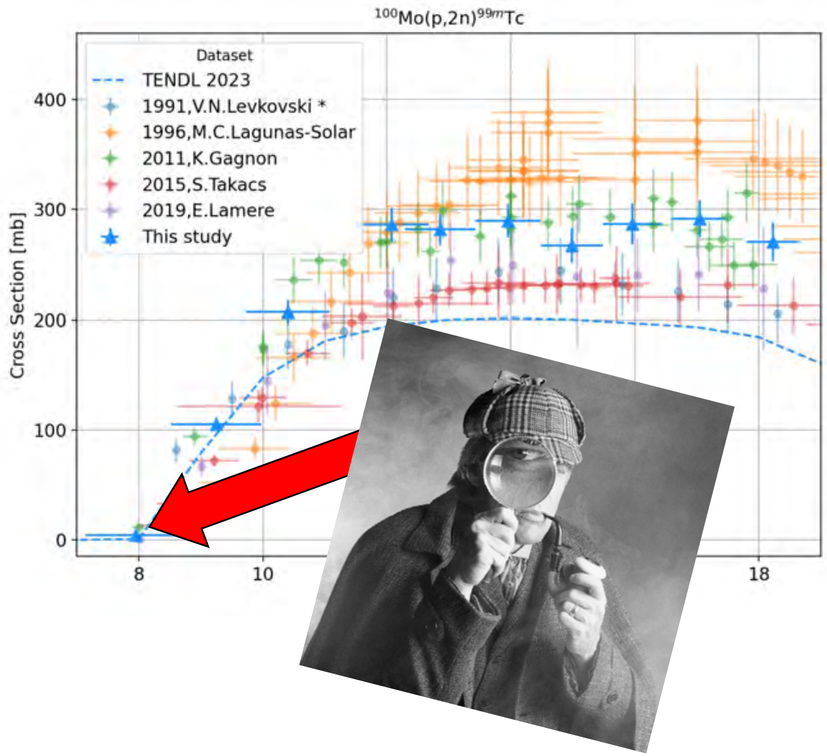
pn: deuteron ✅

pp ❌

nn: diNeutroN ($^2n$) ?

**Implications for Big Bang Nucleosynthesis (BBN) !**

- The reaction $^{100}Mo$ (p, $^2n$) $^{99m}Tc$ has a lower threshold!



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# *Physics is beautiful and useful!*

Ugo Amaldi

# Acknowledgements

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> PhD students: L. Eggimann, A. Gottstein, A. Oliveira (2024), G. Dellepiane (2023), P. Häffner (2021), T. Carzaniga (2019), K. Nesteruk (2017)

> Master (20) and Bachelor (27) Students (since 2013)

> LHEP mechanics and electronics workshop

> SWAN Team

> Collaborations: PSI, Inselspital, CERN, TRIUMF, INFN-LNL, U. Wisconsin, U. Bologna, …


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