A compact medical cyclotron for research into medical and multi-disciplinary applications

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Outline

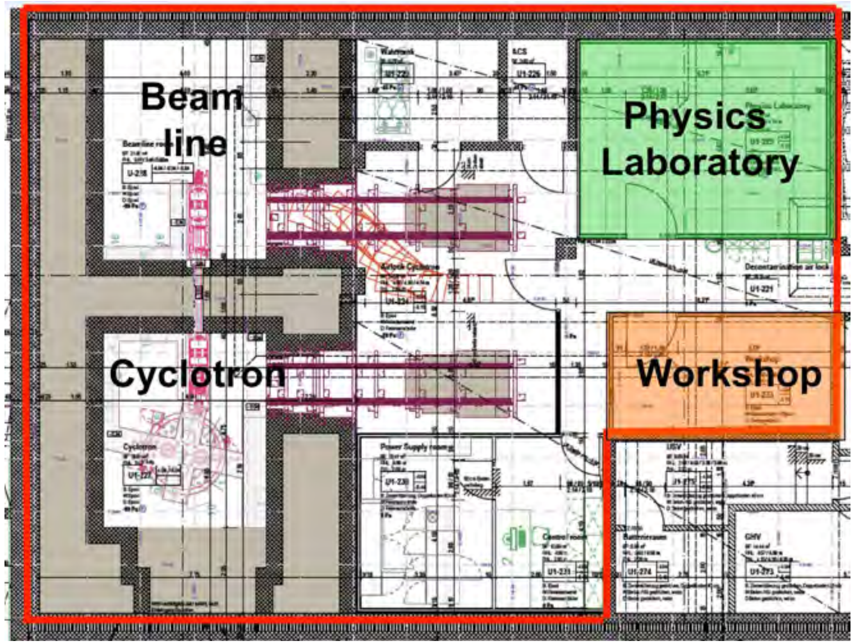
- The Bern medical cyclotron laboratory
  - GMP industrial production of radiopharmaceuticals and academic research under the same roof
- Multi-disciplinary research based on tools and methods from high-energy physics
  - Radioisotopes for theranostics in nuclear medicine
  - Targets, beam monitoring detectors and irradiation systems
  - Radiation hardness
  - Proton induced neutron beams
  - Cell irradiation in both conventional and FLASH regime

The cyclotron at the Bern University Hospital (Inselspital)

In operation since 2013

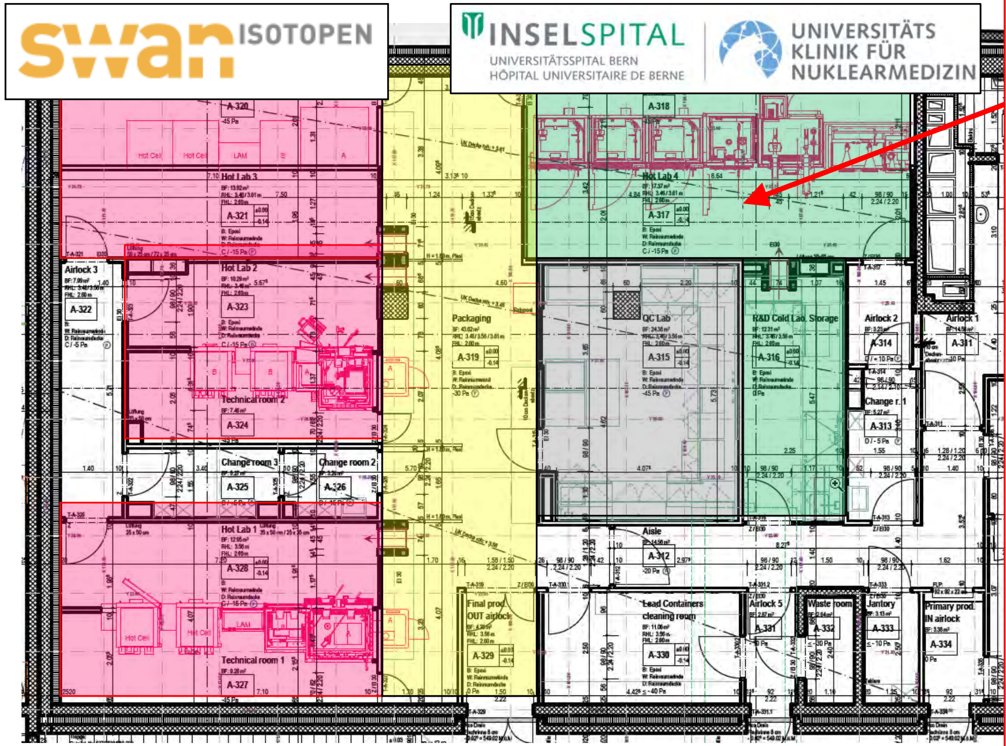
AccelApp'24 Norfolk, Virginia

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



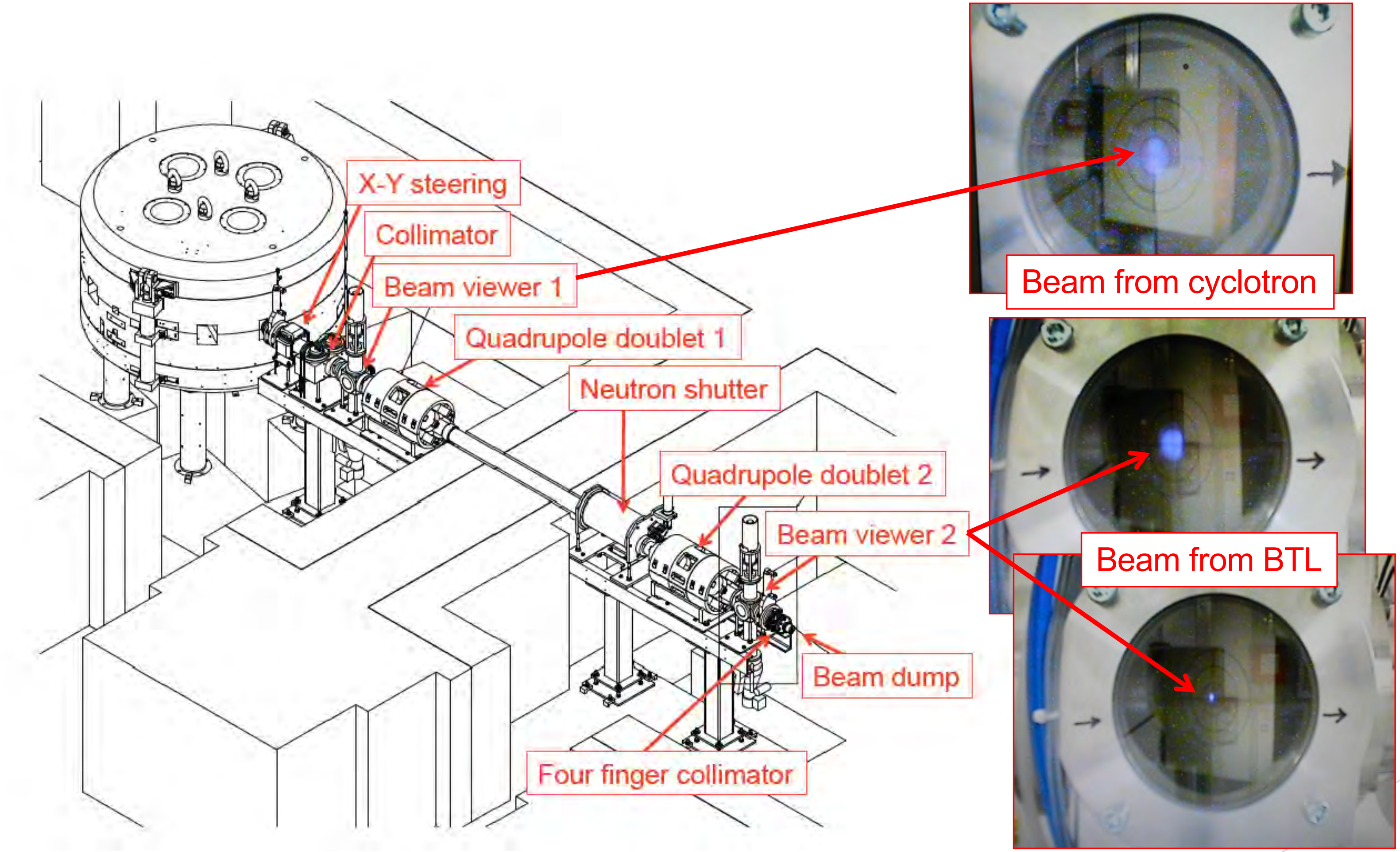
- IBA 18 MeV high current cyclotron (up to 150 μA) – 2 H^- ion sources
- 2 ^{18}F liquid targets: daily GMP industrial production (up to 1 TBq per run)
- **External Beam Transfer Line (BTL) in a separate bunker: research**
- **Solid target Station (STS): research**
- **Specific method to produce currents down to 1 pA**

The hot labs



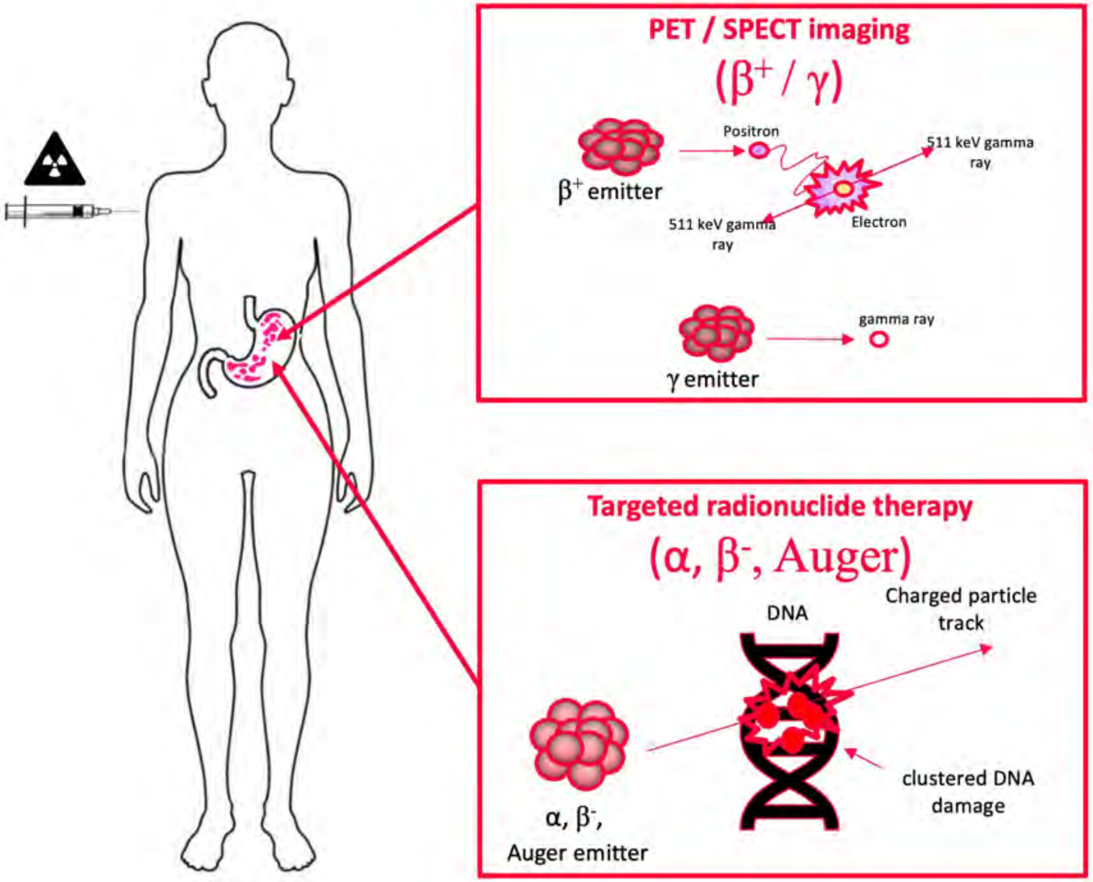
- 3 GMP production labs (SWAN Isotopen AG – ^{18}F, ^{68}Ga, ^{177}Lu radiopharmaceuticals)
- 1 GMP clinical research lab (Nuclear Medicine, Inselspital)

The BTL



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

Theranostics in nuclear medicine

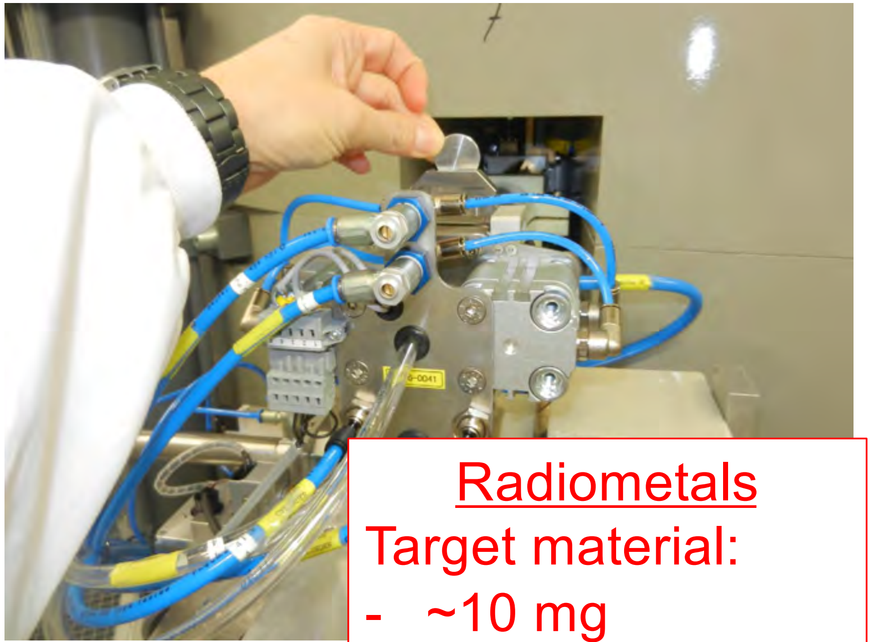


- Promising pairs:
  - ^{68}Ga/^{177}Lu and ^{68}Ga/^{225}Ac
  - ^{43}Sc/^{47}Sc and ^{44}Sc/^{47}Sc
  - ^{61}Cu/^{67}Cu and ^{64}Cu/^{67}Cu
  - ^{155}Tb/^{149}Tb and ^{155}Tb/^{161}Tb
- Radiometals

Our starting point: commercial solid target station

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



<u>Radiometals</u>

Target material:

- ~10 mg
- ~ 5 mm diameter
- Powder

Target: ?

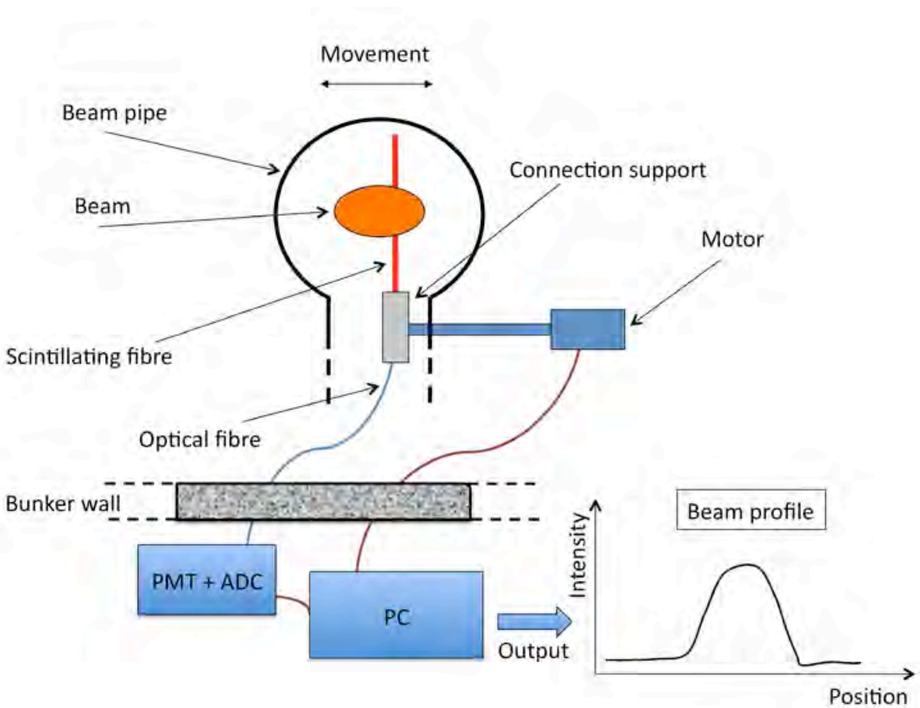
Beam: ?

Radioprotection: ?

Our strategy

- Accurate knowledge of the beam (position, shape, energy)
  - Beam monitoring detectors
- Novel targets + *transfer systems*
- Nuclear data
  - Production cross sections (also for impurities!)
- Novel irradiation systems

The UniBEaM detector



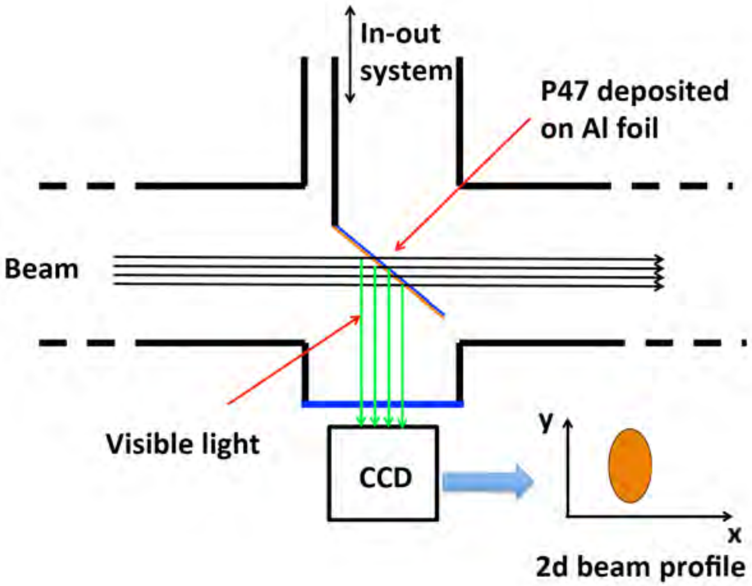
- 2D beam profiler based on (doped) optical fibres passed through the beam
- On-line, minimal interference with the beam
- Developed by LHEP and commercialized by D-Pace (Canada)

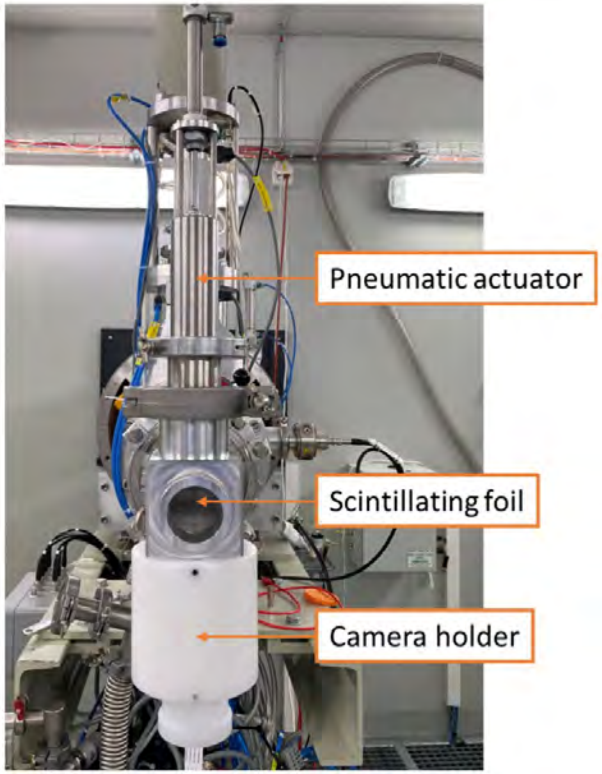
M. Auger et al., J. Instrum. 2016, 11, P03027001
D. Potkins et al., Phys. Procedia 2017, 90, 215–222

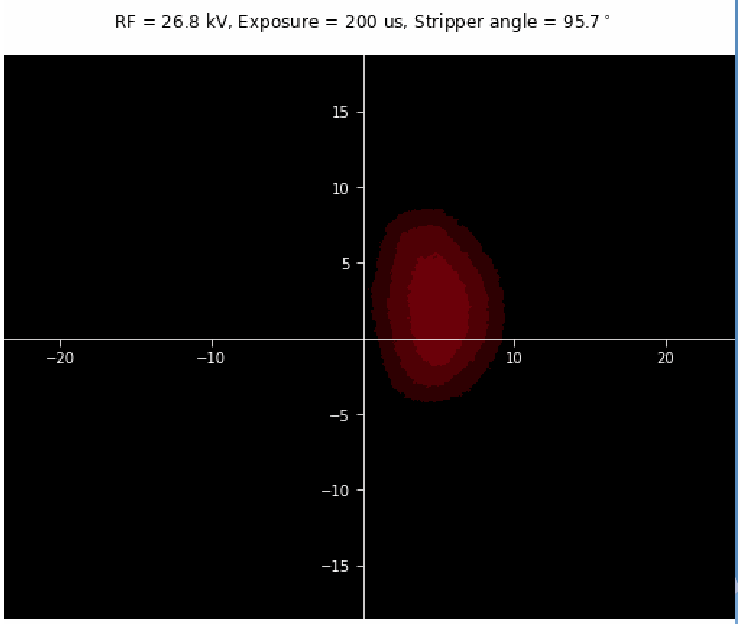
On-line monitoring with UniBEaM

Norfolk, Virginia
AccelApp'24

The Pi2 detecor

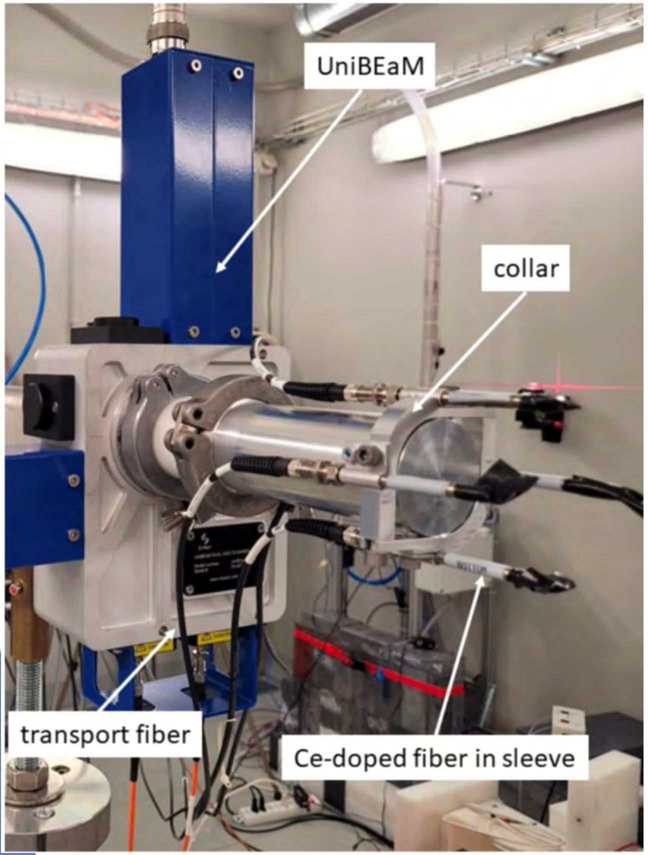


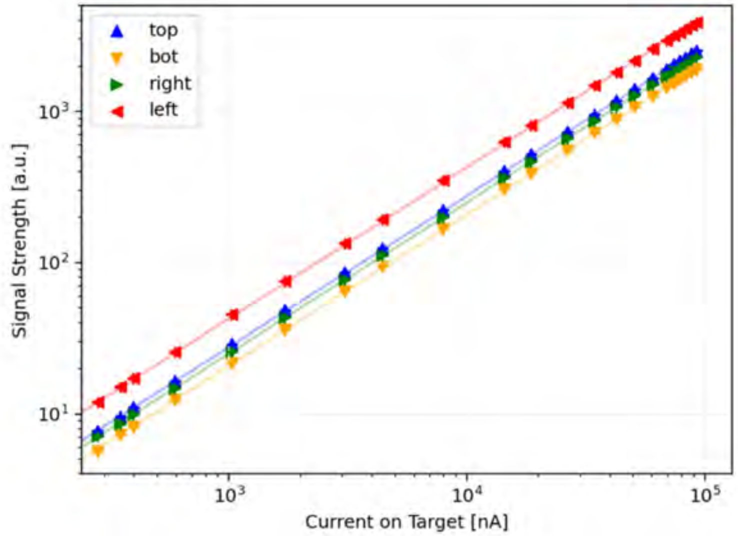


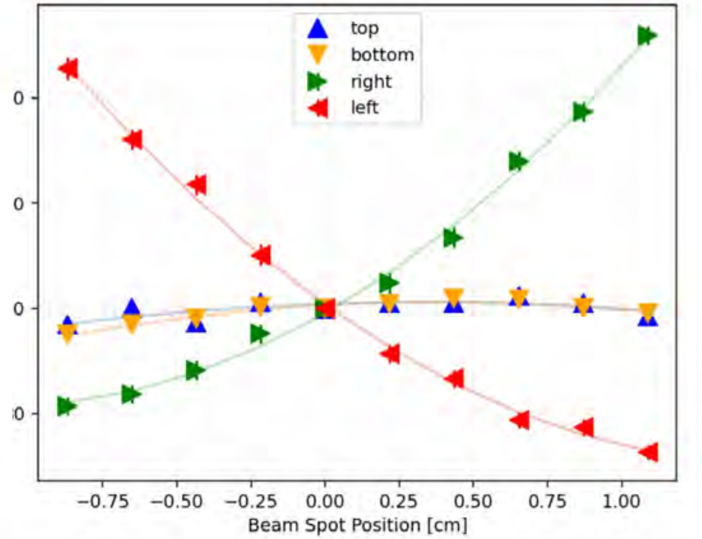


S. Braccini et al., Appl. Sci. 2023, 13, 3657

The Collar detector



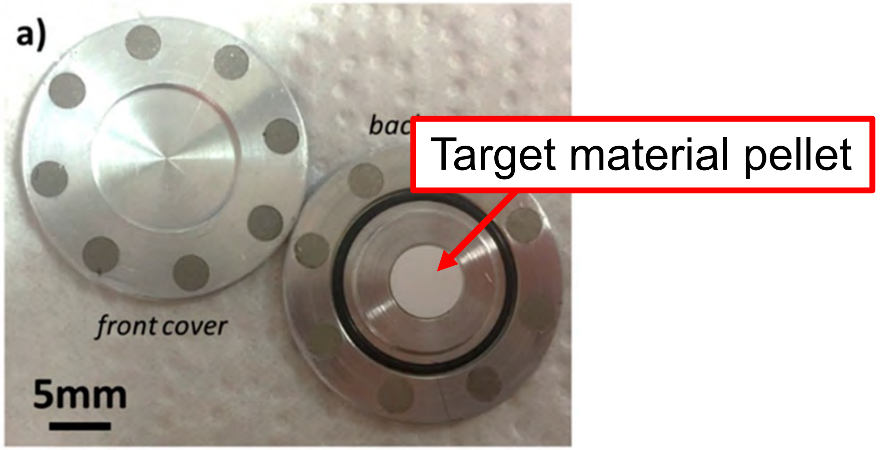




- Scintillating fibres located around the beam pipe in front of the target
- In collaboration with TRIUMF and D-Pace

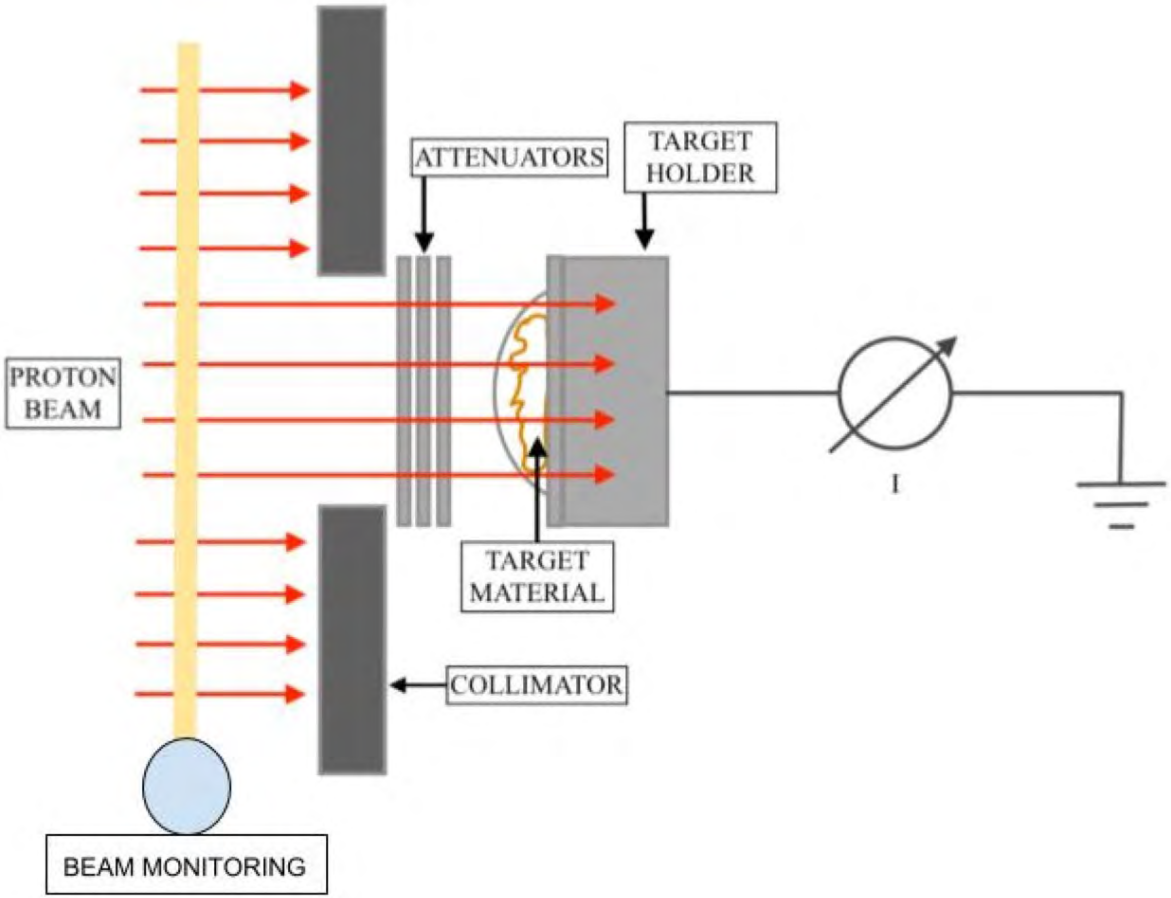
C. Hoehr et al., Proc. IPAC’23, Venice, Italy

The target coin



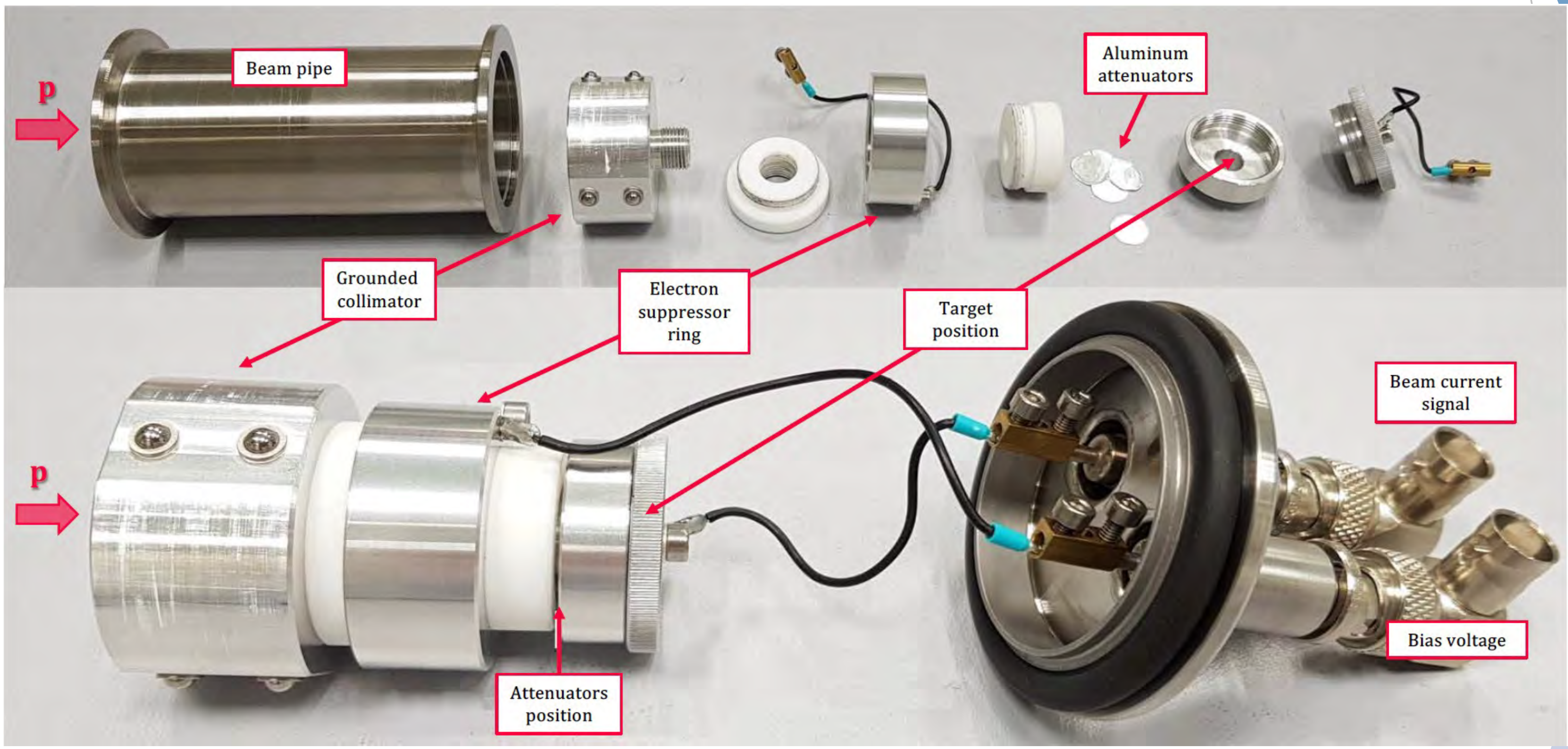
- High-purity aluminum
- Two halves kept together by permanent magnets
  - SmCo, 350°C Curie temperature
- O-ring (viton) to avoid radioactive degassing
- Variable thickness of the front (entry energy variation)

Cross section measurements with a novel method



T. Carzaniga et al., Appl. Radiat. Isot. 129 (2017) 96–102

The target station for cross section measurements



Studied radionuclides of medical interest:

^{43}Sc, ^{44}Sc, ^{47}Sc, ^{48}V, ^{61}Cu, ^{64}Cu, ^{67}Cu, ^{66}Ga, ^{67}Ga, ^{68}Ga, ^{155}Tb, ^{165}Er, ^{165}Tm, ^{167}Tm

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

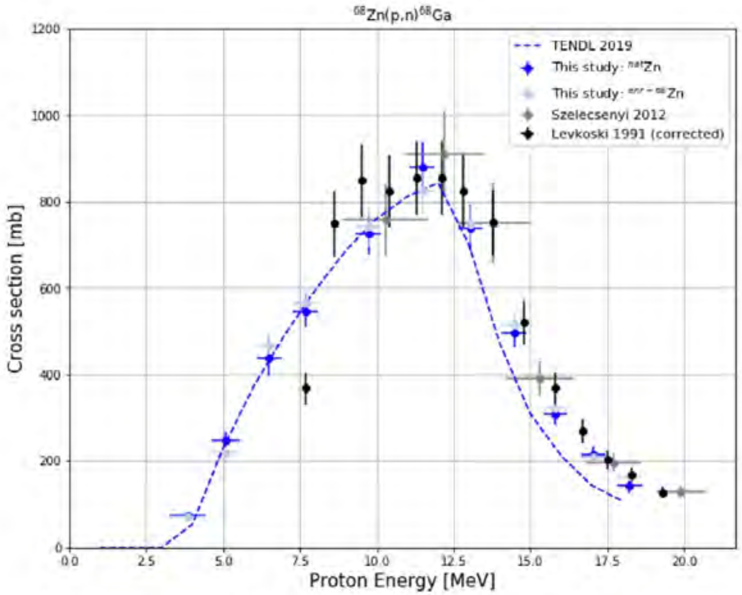


Fig. 4. ^{68}Zn(p,n)^{68}Ga cross section measured from natural and enriched ^{68}Zn targets with the isotopic composition marked as (A) in Table 1.

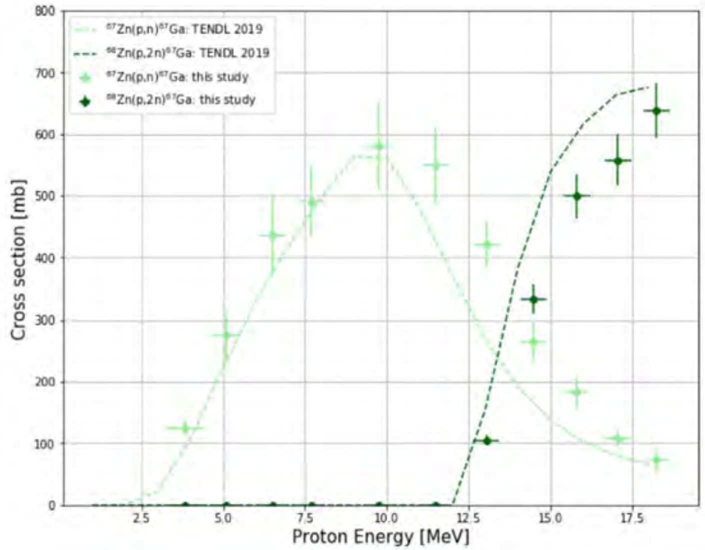
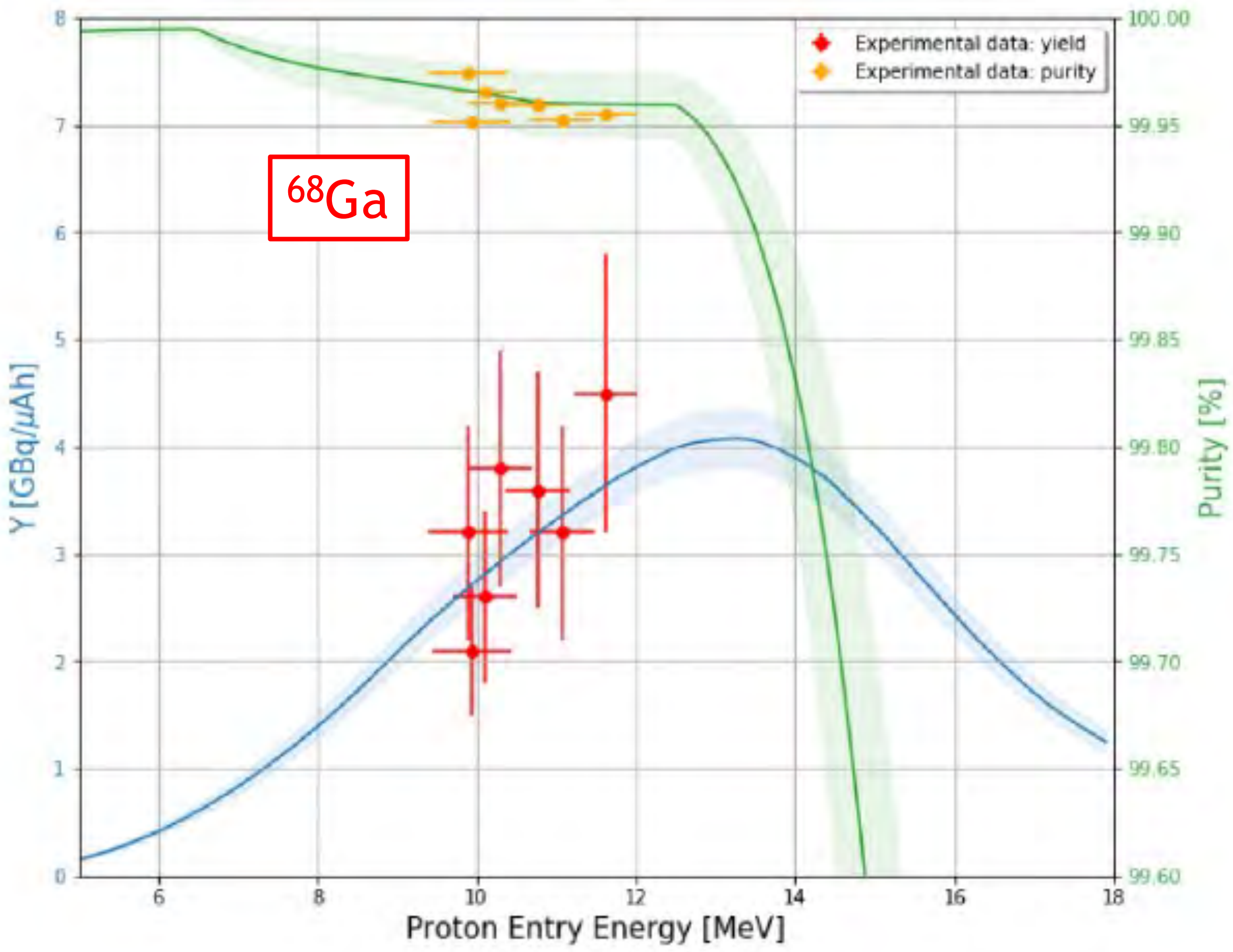


Fig. 6. ^{67}Zn(p,n)^{67}Ga and ^{68}Zn(p,2n)^{67}Ga reaction cross sections.

- Use of two different enriched materials: the (p,n) and (p,2n) ^{67}Ga nuclear reactions can be measured!

S. Braccini at al., Appl. Radiat. Isot., 186 (2022) 110252

Yield, purity and production tests



Some produced radioisotopes

Isotope	Reaction	Target	Mass [mg]	Charge [μAh]	Y [GBq/μAh]
^{44}Sc	(p,n)	$^{enr-44}$CaO pellet	30	27	0.6
^{47}Sc	(p,α)	$^{enr-50}$TiO$_2$ pellet	35	3.9 E-3	0.001
^{61}Cu	(p,α)	$^{enr-64}$Zn pellet	40	2.7 E-4	0.14
^{64}Cu	(p,n)	$^{enr-64}$Ni deposition	63	160	0.13
	(p,α)	$^{enr-67}$ZnO pellet	59	2.7 E-4	0.02
^{67}Cu	(p,α)	$^{enr-70}$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$_2$O$_3$ pellet	40	1.1 E-3	0.004
	(p,2n)	$^{enr-156}$Gd$_2$O$_3$ 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$_2$O$_3$ pellet	59	1.1	0.02
^{167}Tm	(p,n)	$^{enr-167}$Er$_2$O$_3$ pellet	41	0.01	0.003

G. Dellepiane et al, Appl Rad Isot 189 (2022): 110428 (scandium)
G. Dellepiane et al, Appl Rad Isot 191 (2023): 110518 (copper)
S. Braccini et al., Appl Rad Isot 186 (2022): 110252 (gallium)
G. Dellepiane et al, Appl Rad Isot 184 (2022): 110175 (terbium)

Contributions to fundamental physics:
High Efficiency Cyclotron Trap Assisted Positron Moderator, Instruments 2 (2018) 10.
High-resolution laser resonance ionization spectroscopy of $^{143-147}$Pm, Eur. Phys. J. A (2020) 56:69

^{44}Sc is ready for clinical applications

15 GBq in 5 h irradiation!

molecules

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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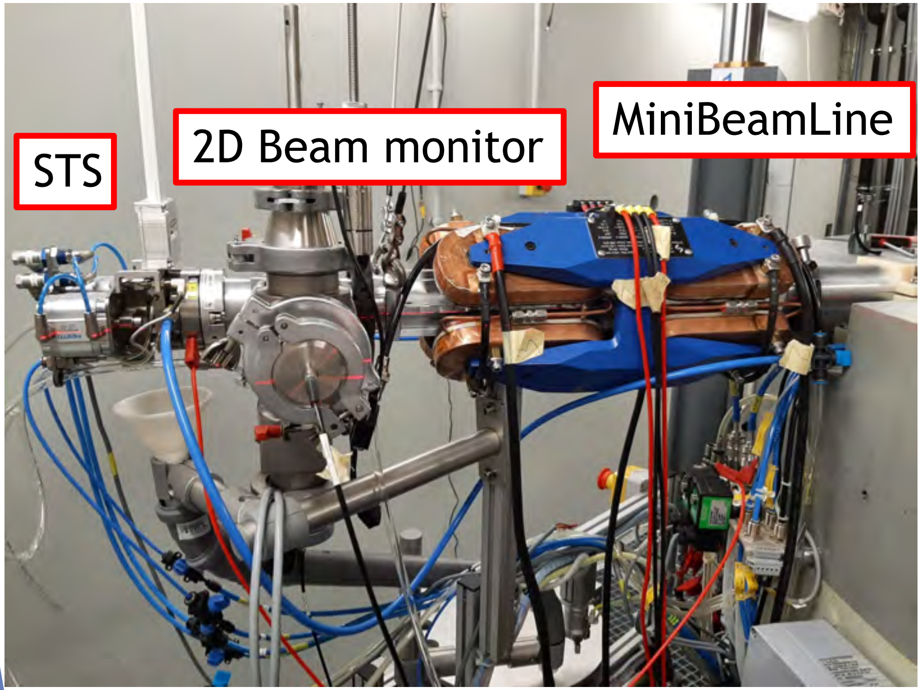
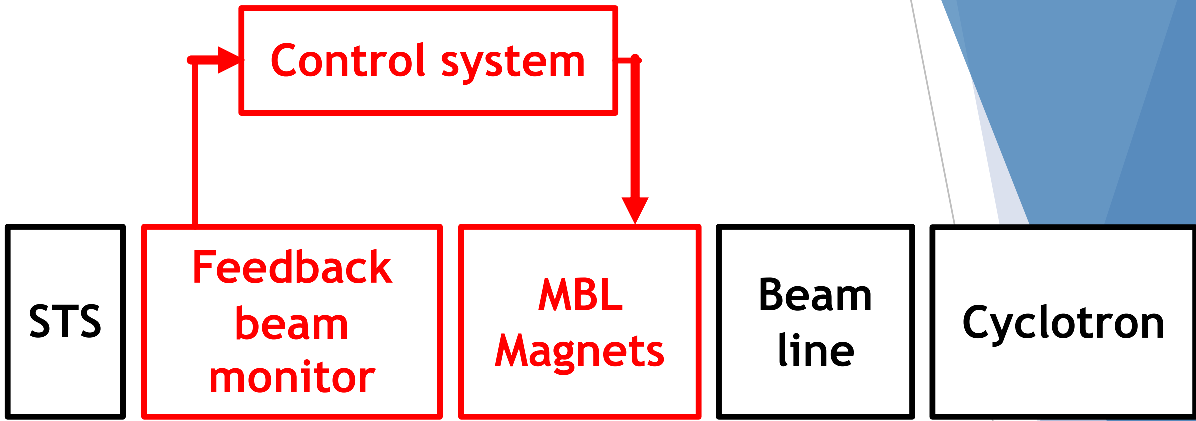
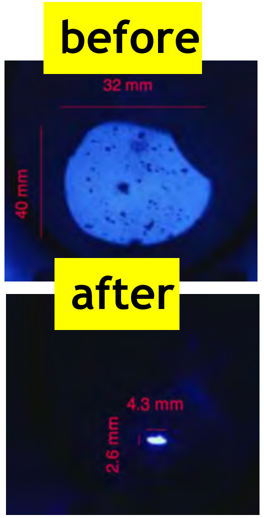
In collaboration with PSI

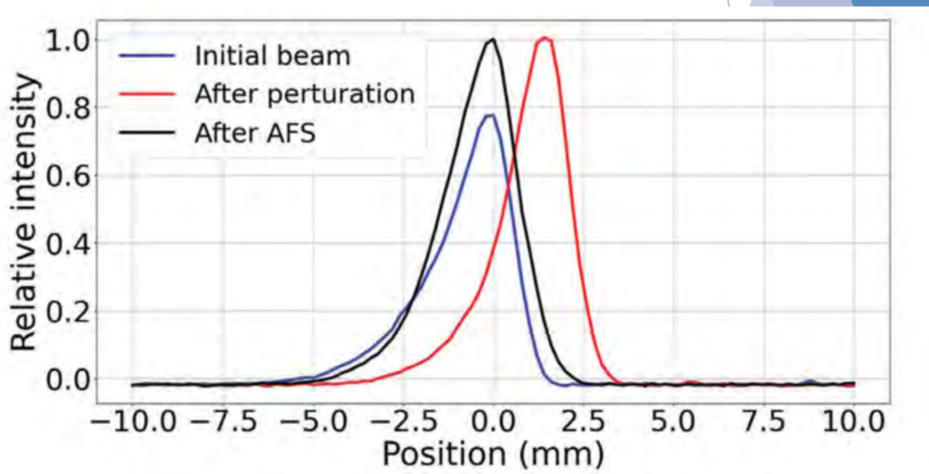
IBA Award 2020

The Automatic Focusing System (AFS)





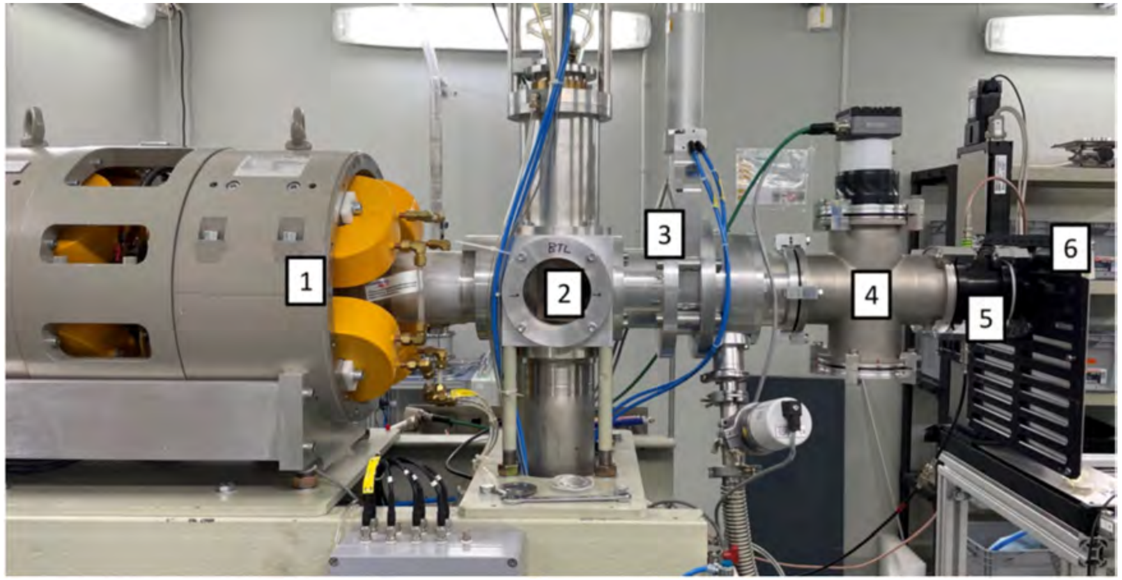




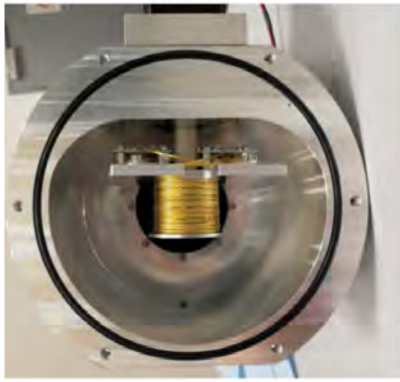
P. Haffner et al., Appl. Sci. 11.6 (2021): 2452

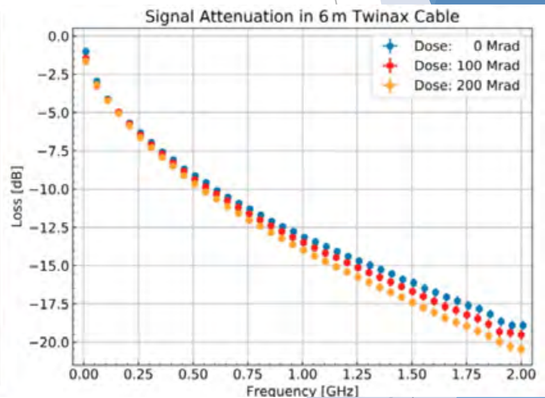
Radiation hardness studies

Applications in space (Juice mission), HEP (ATLAS at CERN), material science



Example: Twinax cable for ATLAS pixel detector

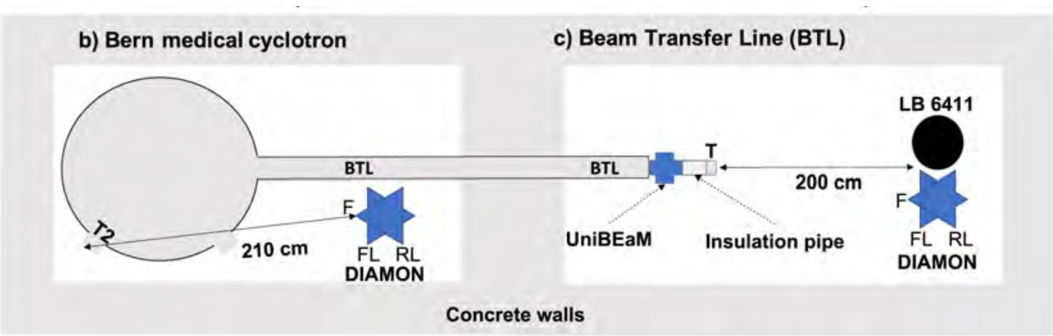


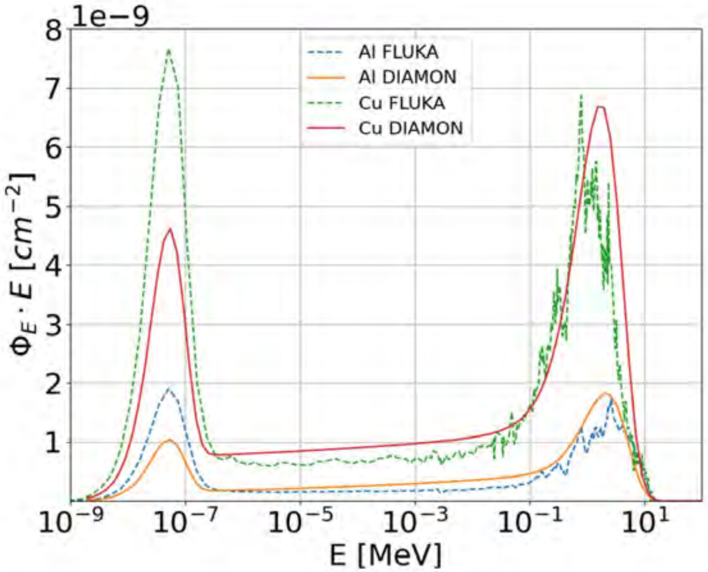


J. Anders at al., 2022 JINST 17 P04021

AccelApp'24 Norfolk, Virginia

Proton induced neutron beams





- Several materials for the target (Al, Cu, Li, ^{18}O-water)
- DIAMON neutron spectrometer
- In collaborator with

POLITECNICO MILANO 1863 RAYLAB

S. Braccini et al., Sci Rep 12, 16886 (2022).

Cell irradiation

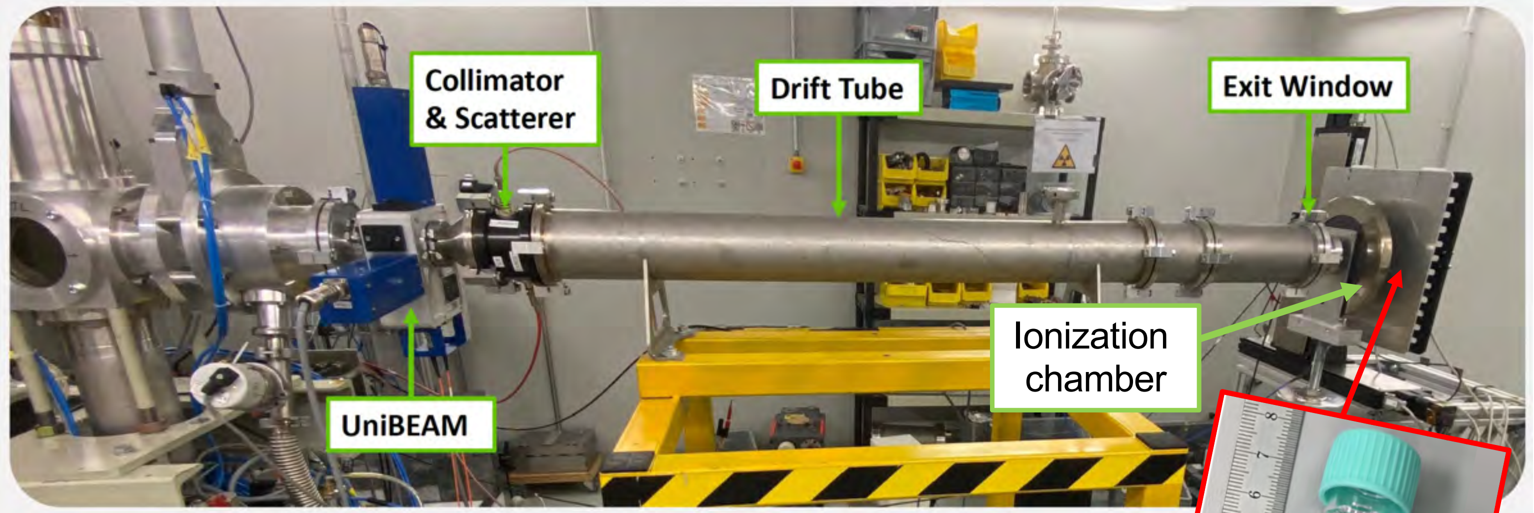
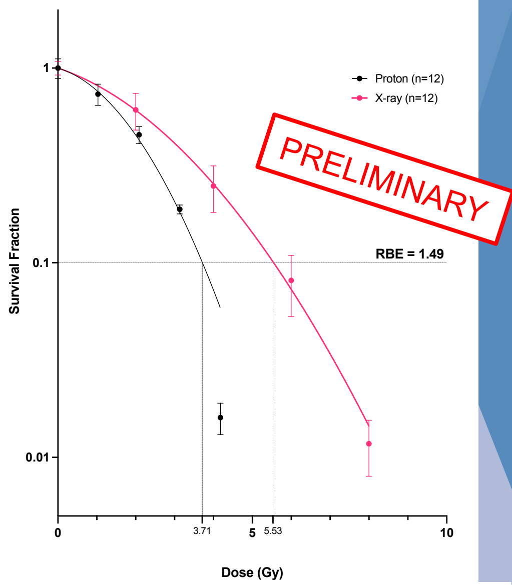


Fig 3. Setup for cell irradiations in BTL Bunker.

The cells are plated on a flask

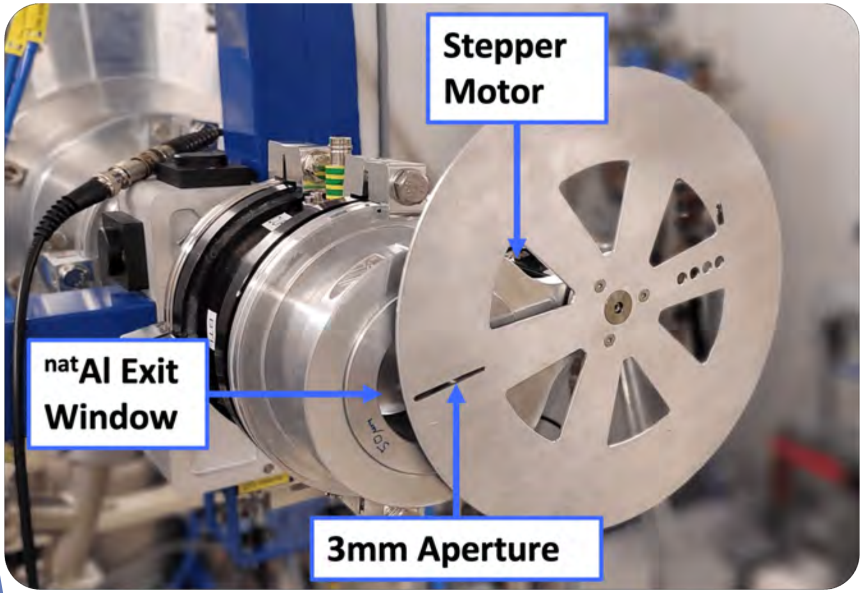
Protons vs photons



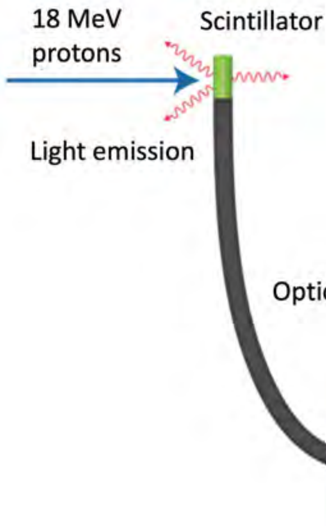
Cell survival of B16-F10 mouse melanoma
https://zenodo.org/records/10478639

In collaboration with the
Institute of Anatomy of the Univesity of Bern

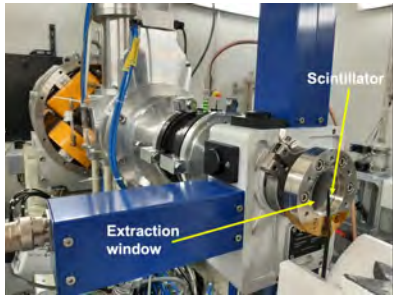
Exploring the FLASH regime

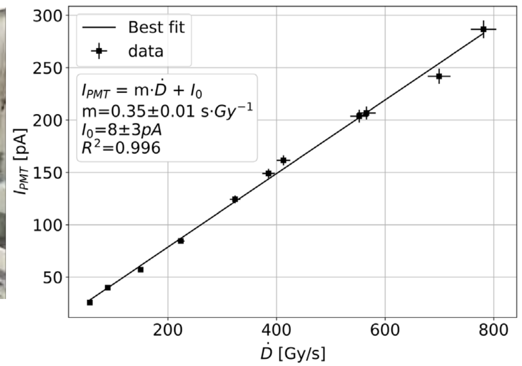


High currents are an advantage!



PRecision dOsimetry in FLASH radiotherapy with Optical Fibers (PROOF)





P. Casolaro et al., 11th Int. Beam Instrum. Conf. (2022)

Norfolk, Virginia
AccelApp'24

Conclusions and Outlook

- Medical cyclotrons:
  - Tools of choice for radioisotope production in a hospital-based environment
  - Have a high scientific potential
  - Excellent for the training of young scientists
  - Production and research can run in parallel

- Several multi-disciplinary research programs at the Bern medical cyclotron in the last 10 years

- … we are open to collaborations!

Acknowledgements

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- LHEP mechanics and electronics workshop; SWAN Team

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