Compact Medical Cyclotrons and their Use for Radioisotope Production and Multi-disciplinary Research

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Outline

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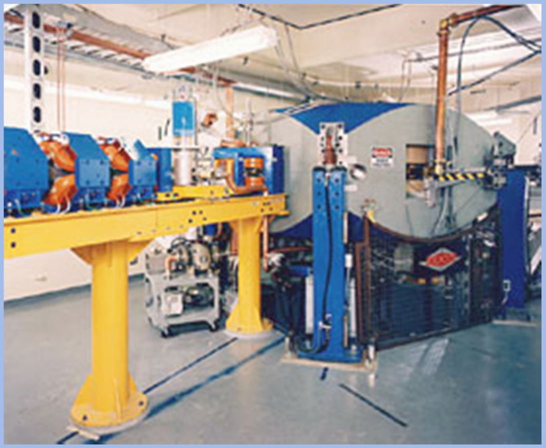
- Compact medical cyclotrons: *tools for medicine and science*
- Design characteristics and operational implications
- Production of standard and novel PET radioisotopes
- Multi-disciplinary research: *tools, methods and some examples*
- Conclusions and outlook

Medical cyclotrons

	Main Use	Typical User	Max. Proton Energy (MeV)	Max. Beam Current (μA)
A	Proton therapy	Hospital	200-250	10^{-3}
B	Radioisotope production / research	Research laboratory	70	500-700
C	SPECT radioisotope production	Research lab. / industry	30	500-1000
D	**PET radioisotope production**	**Hospital / industry**	**15-25**	**100-400**
E	PET radioisotope production	Hospital	10-12	50

A) Varian Comet (250 MeV)

B) Best 70p (70 MeV)



C) ACSI TR30 (30 MeV)

Compact medical cyclotrons

Manufacturer	Model	Particles	Energy (MeV)	Max. Beam Current (μA)	Source	Extracted Beams
ACSI	TR19	H^- (D^-)	14-19 (9)	>300 (100)	Ext. Cusp	2
ACSI	TR24	H^-	15-24	>300	Ext. Cusp	2
Best	15p	H^-	15	400	Ext. Cusp	2
Best	25p	H^-	25	400	Ext. Cusp	2
GE	PETtrace	H^- / D^-	16.5 / 8.4	>80 / 60	Int. PIG	6
IBA	Cyclone 18/9	H^- (D^-)	18 (9)	>100 (65)	Int. PIG	8
IBA	KIUBE	H^-	18	200	Int. PIG adjustable	8
Sumitomo	HM-18	H^- / D^-	18 (10)	>90 / 50	Int. PIG	2

- Commercial accelerators
- Hospital based facilities for PET radioisotope production
- Radiopharmaceutical industry
- > 300 in operation (number continuously growing)

Design constraints
Physics must answer to medicine

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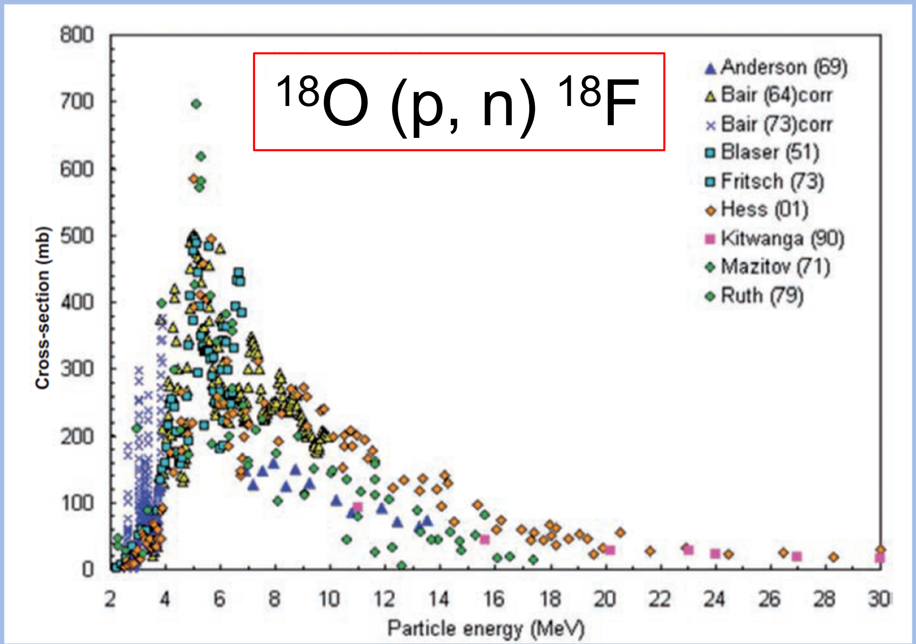
> FDG most common PET radiotracer ➔ ^{18}F (1 dose ~400 MBq)



> Beam energy: 15-25 MeV

> 150 µA in 120 min. ➔ 500 GBq of ^{18}F ➔ 250 GBq of FDG

> $T_{1/2}$ = 110 min. ➔ Production(s) every night … and during the day ?

Design constraints
Radiation protection is an issue!

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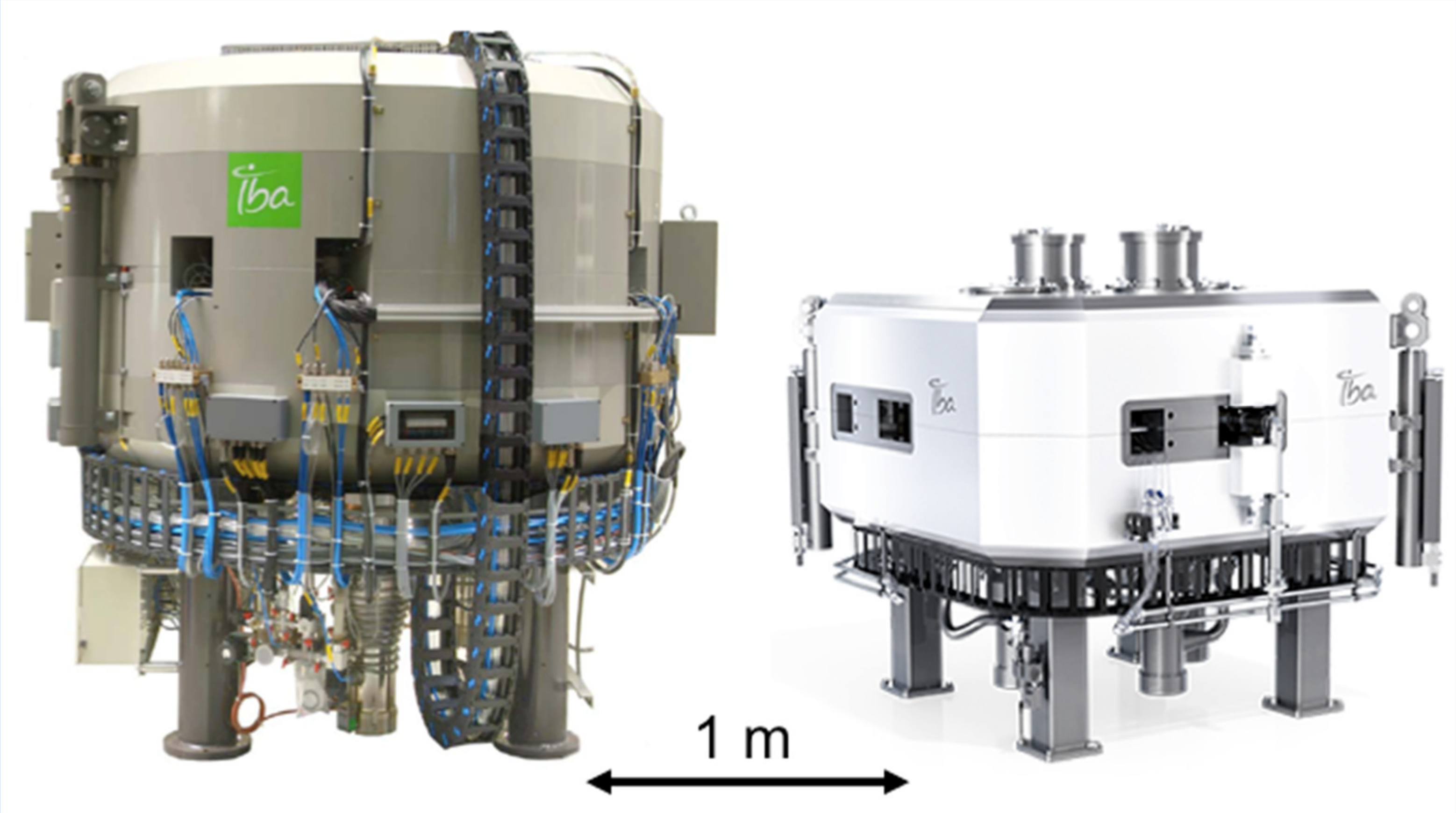
Design constraints
Towards compact solutions



IBA Cyclone 18/9 (first design 1986) vs IBA KIUBE (2016)

Ion source: external or internal?

ACSI TR19/TR24

GE PETtrace

External Cusp

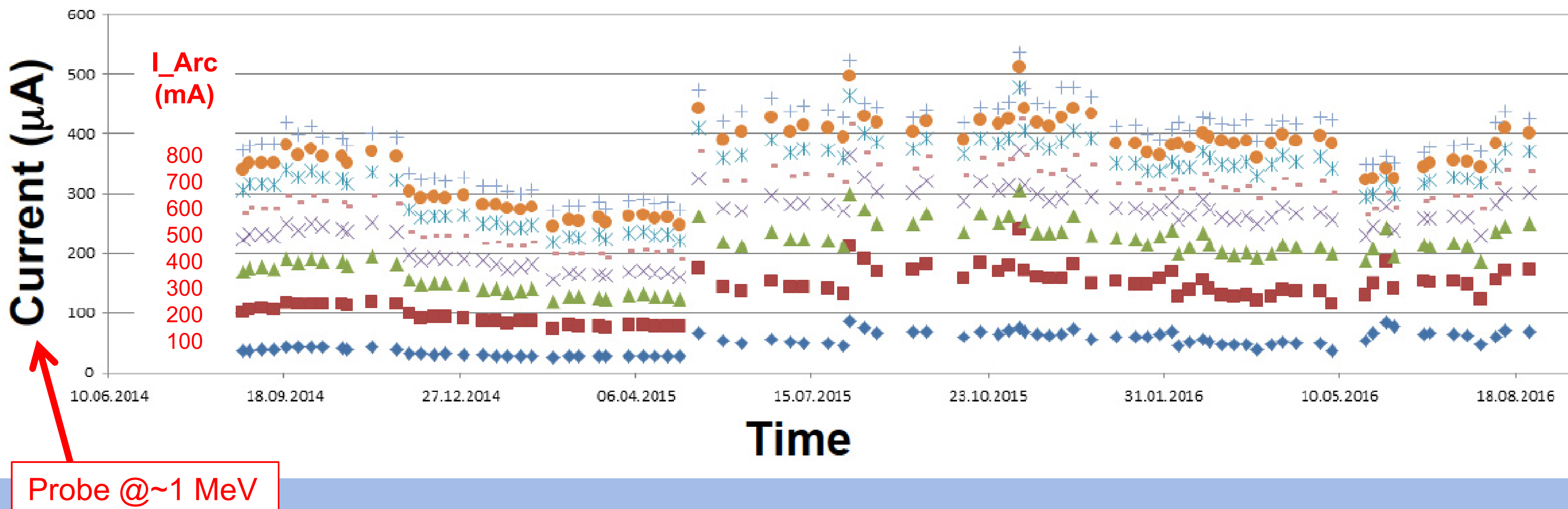
- \+ Vacuum, access, beam current
- − Complex central region, expensive

Internal PIG

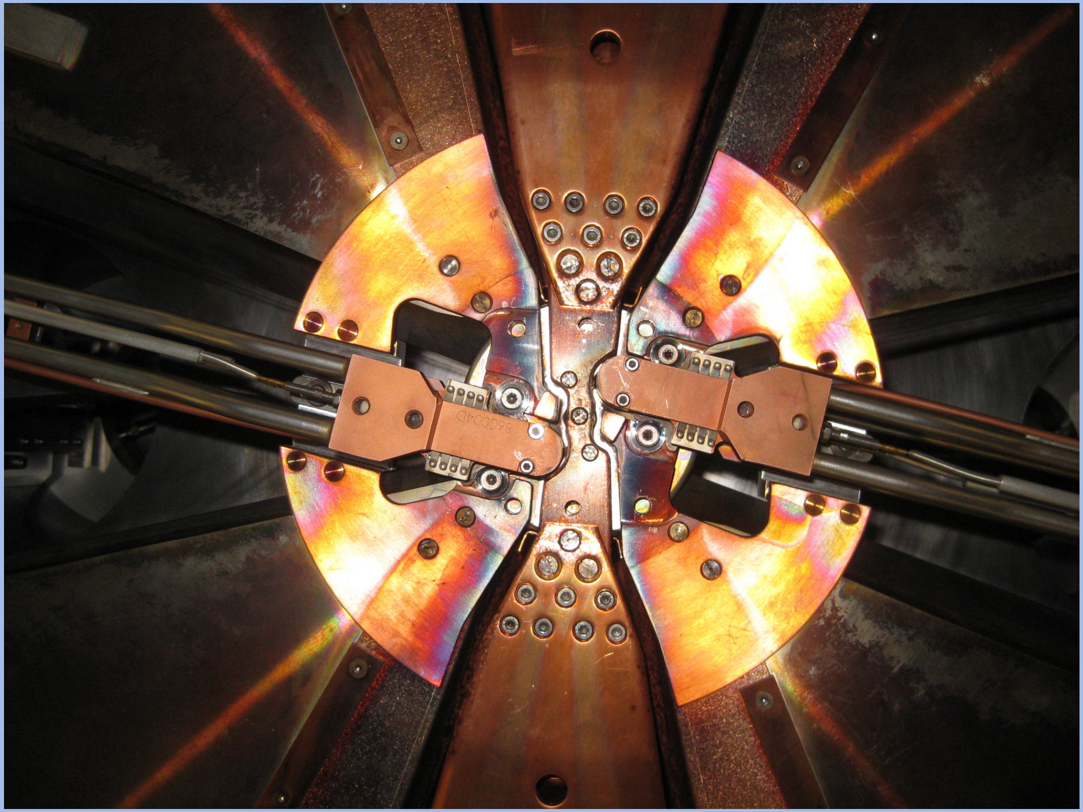
- \+ Easier, cost effective
- − Vacuum (neutral beam!), open cyclotron for maintenance

Ion source

- > Internal PIG : two H^- or H^-/D^- ?
  - D^- almost unused; 2 H^- higher production efficiency
- > Gas purity and regular maintenance are crucial!



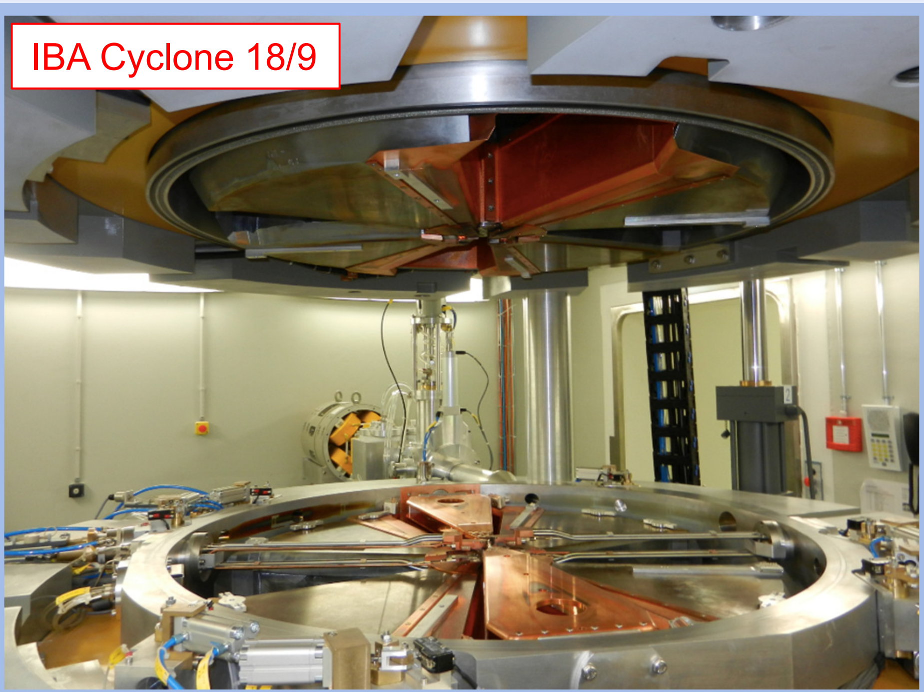
Central region

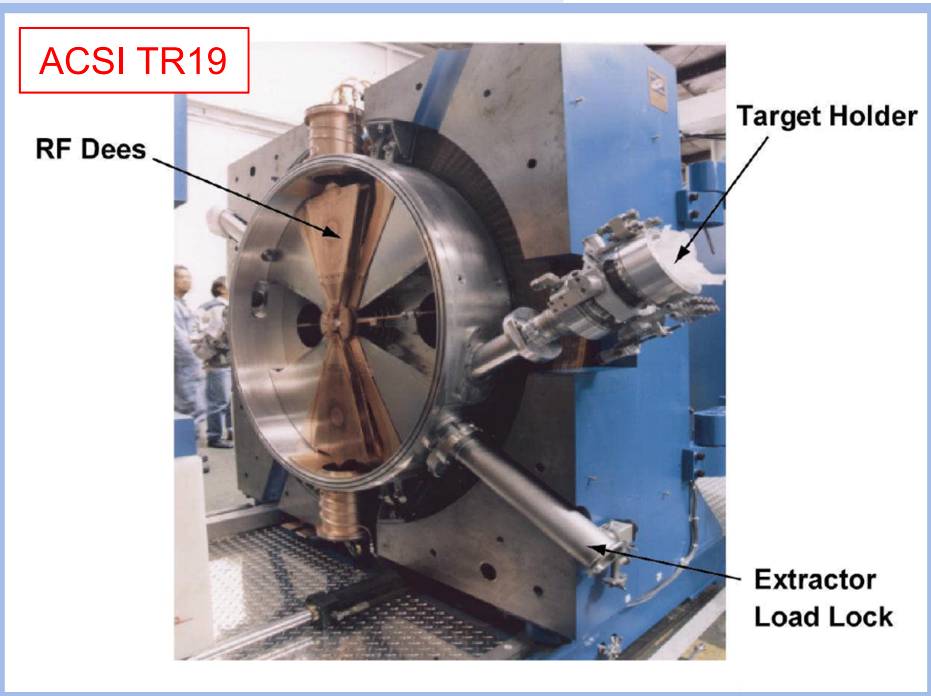


IBA Cyclone 18/18

- Low energy: < 1 MeV (r < 10 cm)
- Optimization during commissioning (shimming)

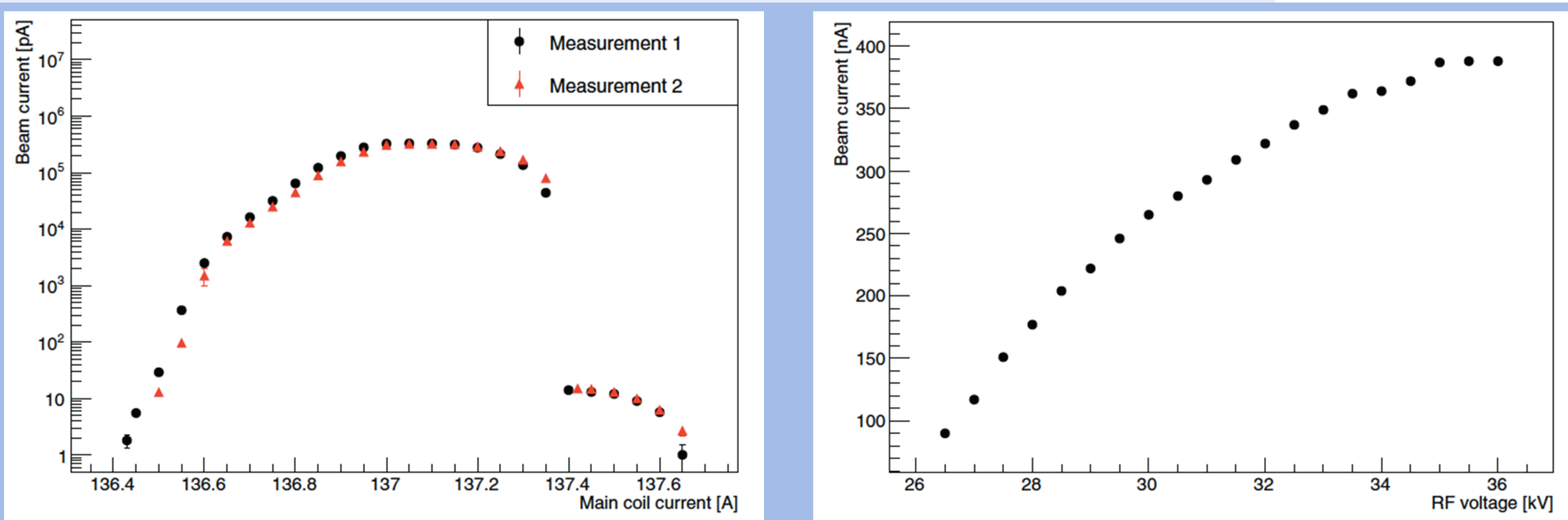
Magnet and RF





- Hill (1.9 T - 60º for IBA, 45º for ACSI) – valley (0.55 T, 0.35 T) structure
- RF: fixed frequency (42 MHz for IBA, 73 MHz for ACSI)
- Different harmonics for H^- (h=2, 4) and D^- (h=4, 8 + flaps)
- Peak voltage variable (up to 25 kV, 50 kV)
- Dee angle (30º, 45º) ➔ different energy gain per turn

Beam current vs B and RF peak voltage

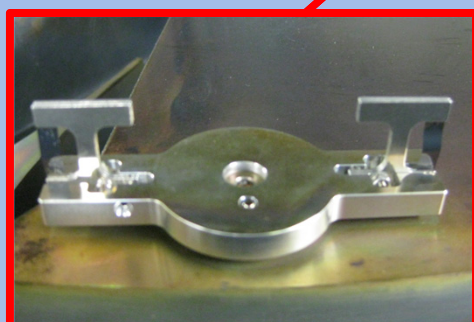


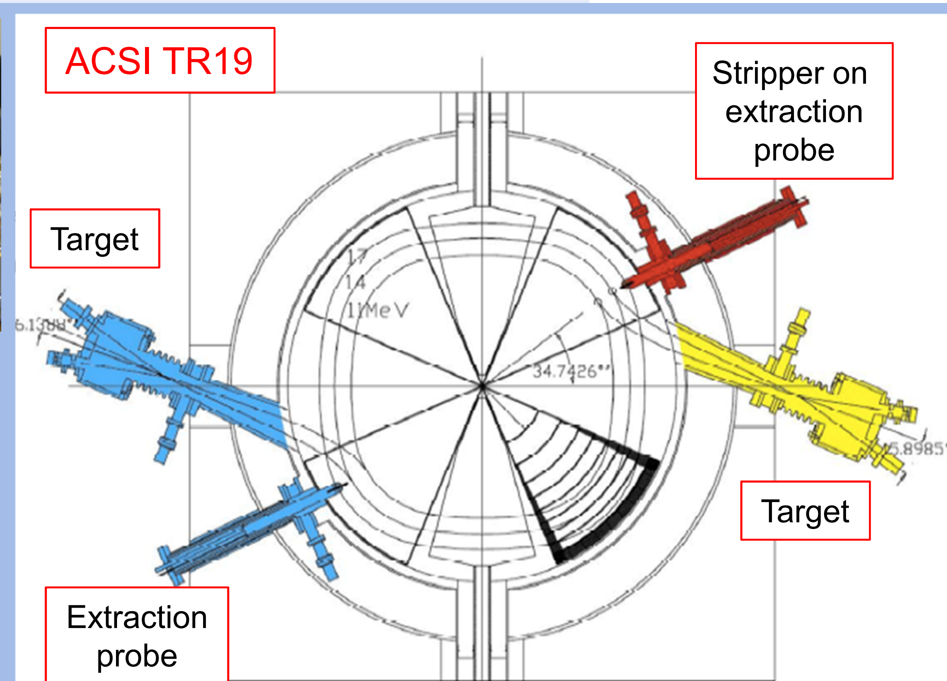
M. Auger et al., Meas. Sci. Technol. 26 (2015) 094006

- Internal PIG source (IBA 18/18)
- Current measurement: high sensitivity Faraday cup (pA)
- Ion source arc current at minimum (1 mA)
- Stable beams down to 1.5 ± 0.1 pA

Extraction

Strippers mounted on rotating carrousel

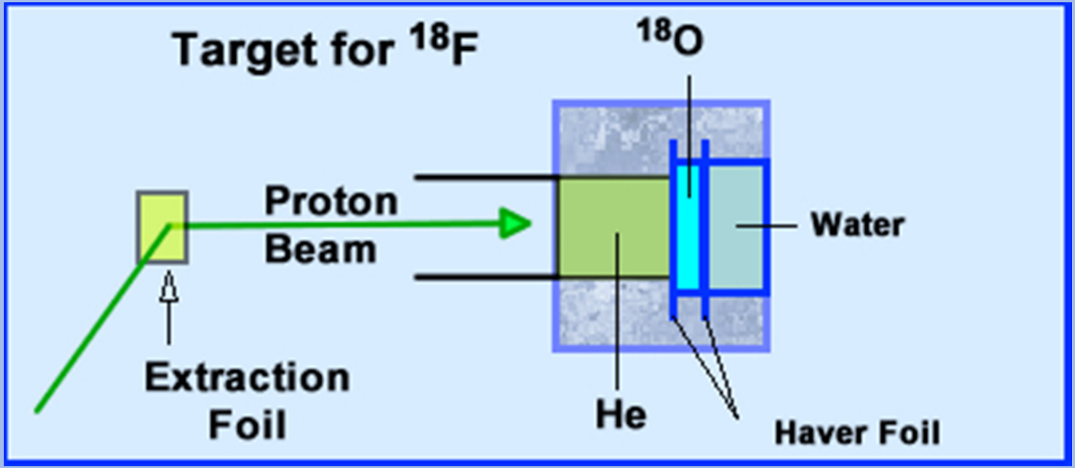




- Strippers must stand high temperatures (~1500 ^{o}C at ~150 µA)
- ~5 µm thick pyrolitic carbon ➔ Efficiency ~100%
- 8 extraction ports (IBA), 6 (GE), 2 (ACSI, Best) ➔ Beam optimization
- Extraction probe ➔ variable energy
- Single or dual beam

Radioisotope production

- Main PET radioisotope: ^{18}F (120 min.)
- Other relevant PET isotopes: ^{11}C (20 min.), ^{13}N (10 min.) and ^{15}O (122 s)



  - Targets: liquid (common), gas and solid (rare)
  - Mounted directly after extraction
  - Main issues: yield, purity, minimize enriched material
  - Modern targets: > 600 GBq in 2 hours (~150 µA)
  - Beam centring and uniformity crucial!

Novel radioisotopes for Therapy + Diagnostics = Theragnostics

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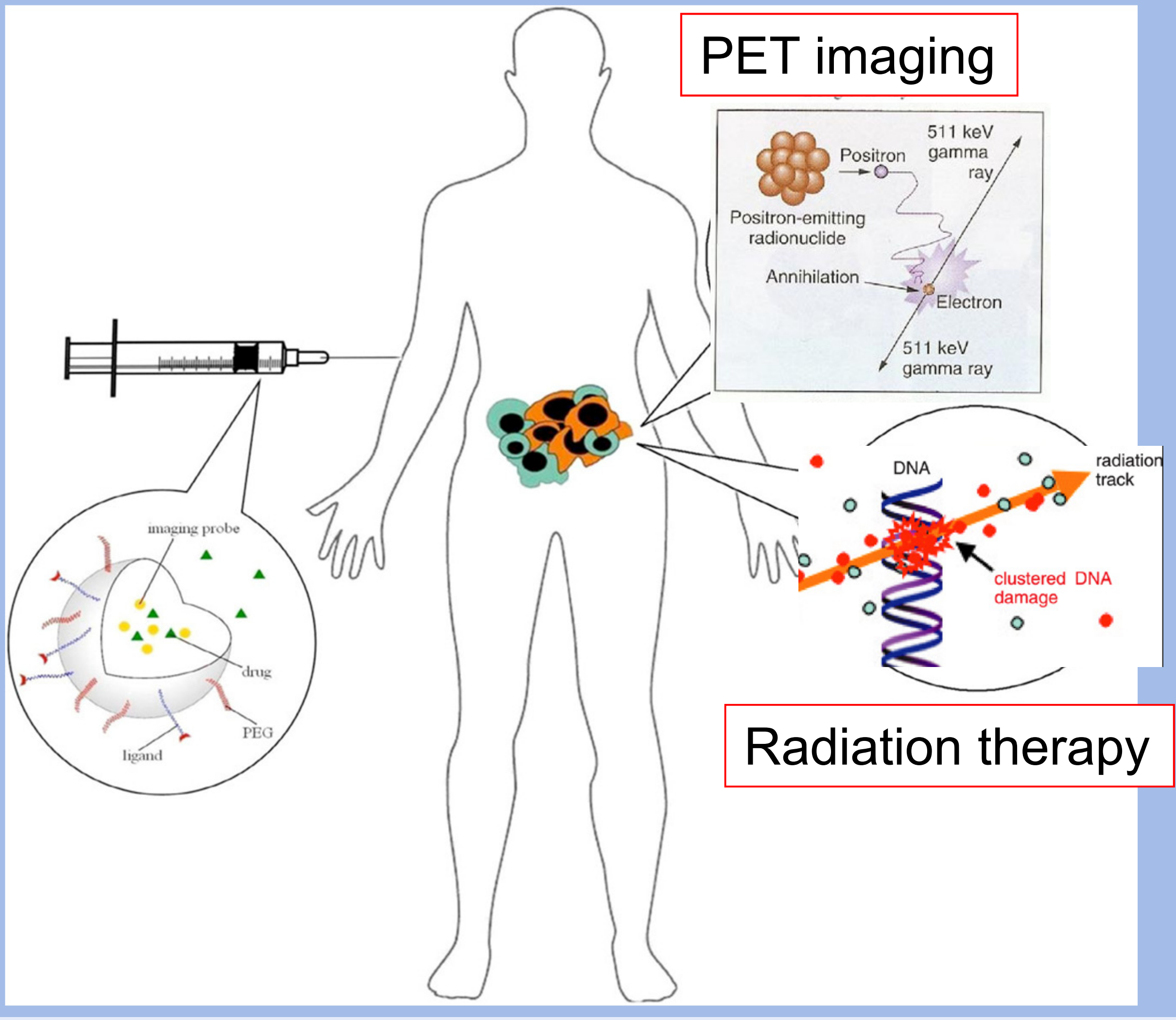

- One biomolecule (vector)
- Two isotopes of the same element
  - Positron emitting (PET)
  - Electron emitting (RT)

Theragnostic isotopes

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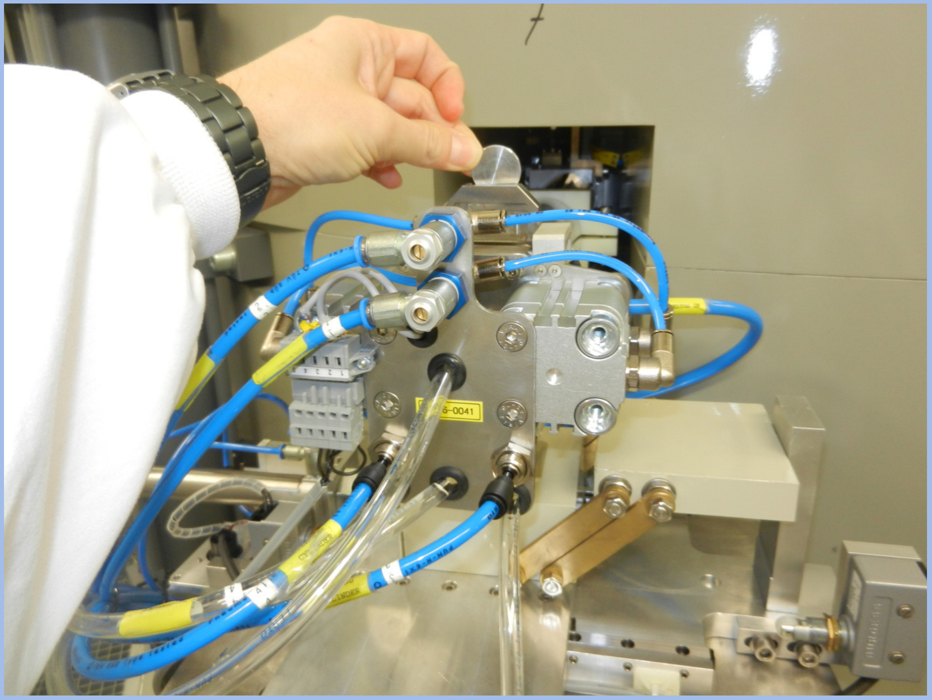
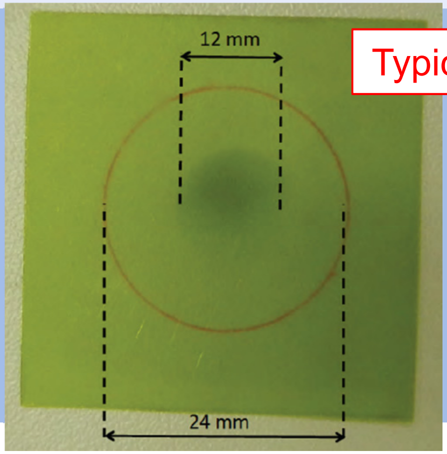
- Promising pairs:
  - ^{64}Cu/^{67}Cu, ^{44}Sc/^{47}Sc and ^{43}Sc/^{47}Sc
- ^{68}Ga promising for PET
  - Generators small quantities for research (~2 patients/day)
- Sc and Ga similar chemistry
- Cyclotron production ?
  - $^{44}Ca(p,n)^{44}Sc$, $^{43}Ca(p,n)^{43}Sc$, $^{46}Ti(p,\alpha)^{43}Sc$
- Solid target station

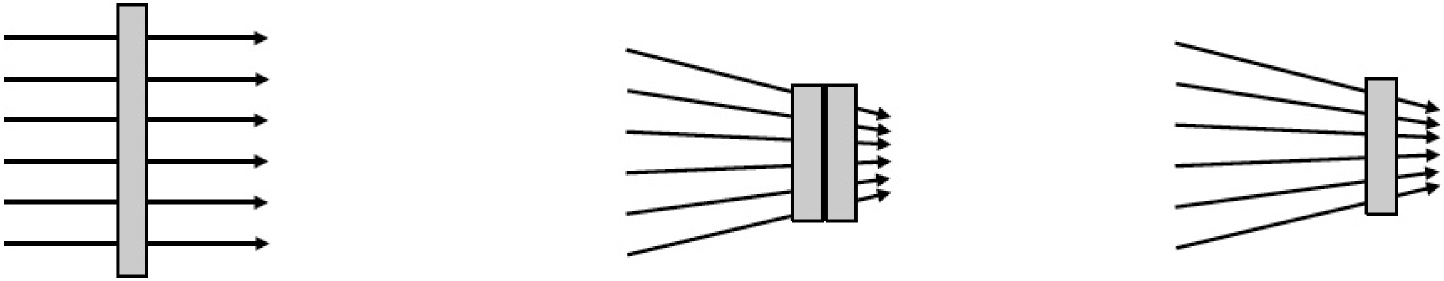


^{43}Sc production with a solid target



- High enriched material is expensive!
- A few mg per irradiation

25 μA proton beam

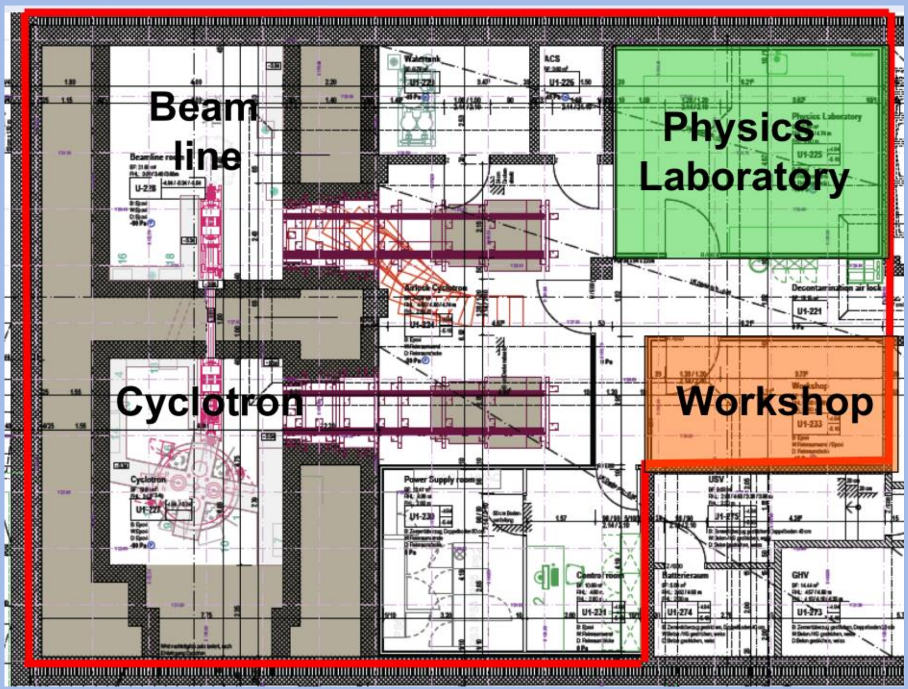


a) m = 10 mg, S = 1 cm²
A = 450 MBq

b) m = 10 mg, <u>S = 0.1 cm²</u>
<u>A = 4500 MBq</u>

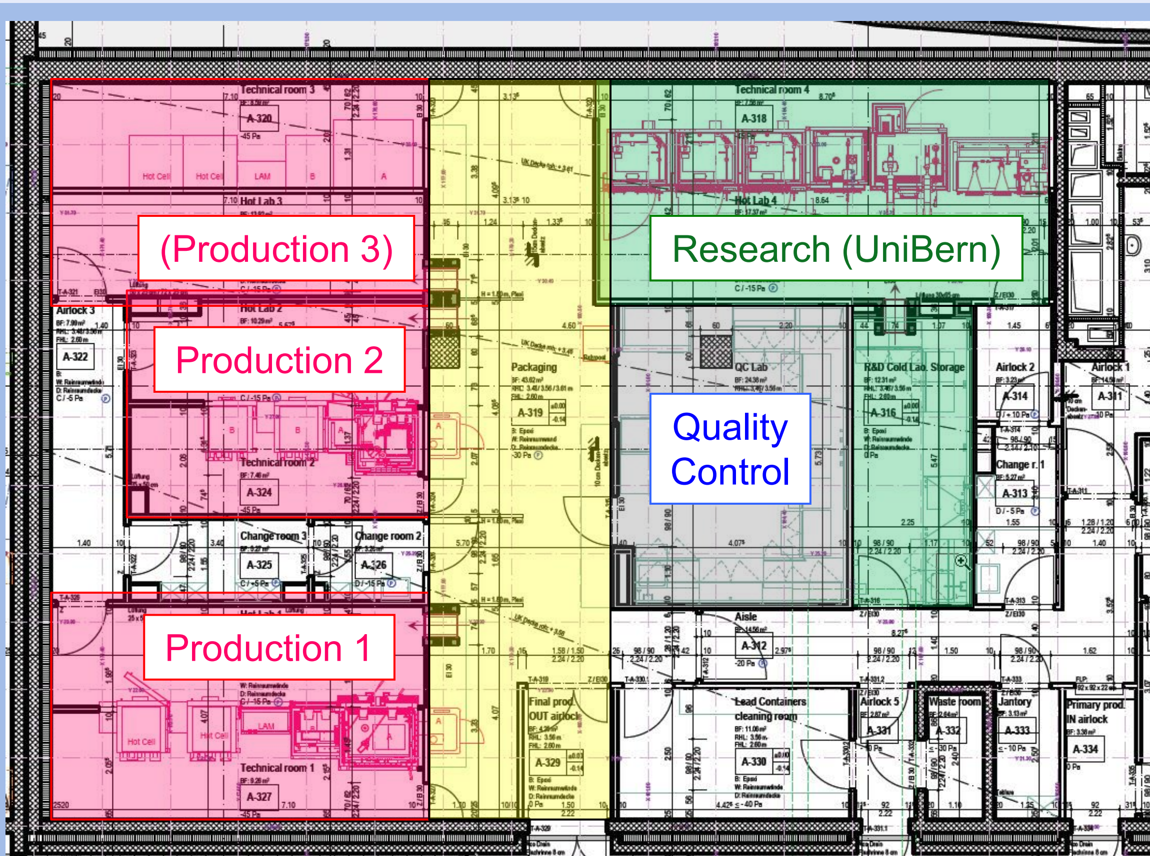
c) <u>m = 1 mg, S = 0.1 cm²</u>
A = 450 MBq

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



- IBA 18 MeV high current cyclotron (up to 150 μA)
- Daily production of ^{18}F for FDG
- **External beam line in a separate bunker: production + research**
- Specific method to produce currents down to 1 pA

The hot labs



> 2 GMP production labs (FDG, ^{18}F compounds, future developments)

> 1 multi-function research lab (A. Türler – UniBern and PSI)

Research activities with the BTL

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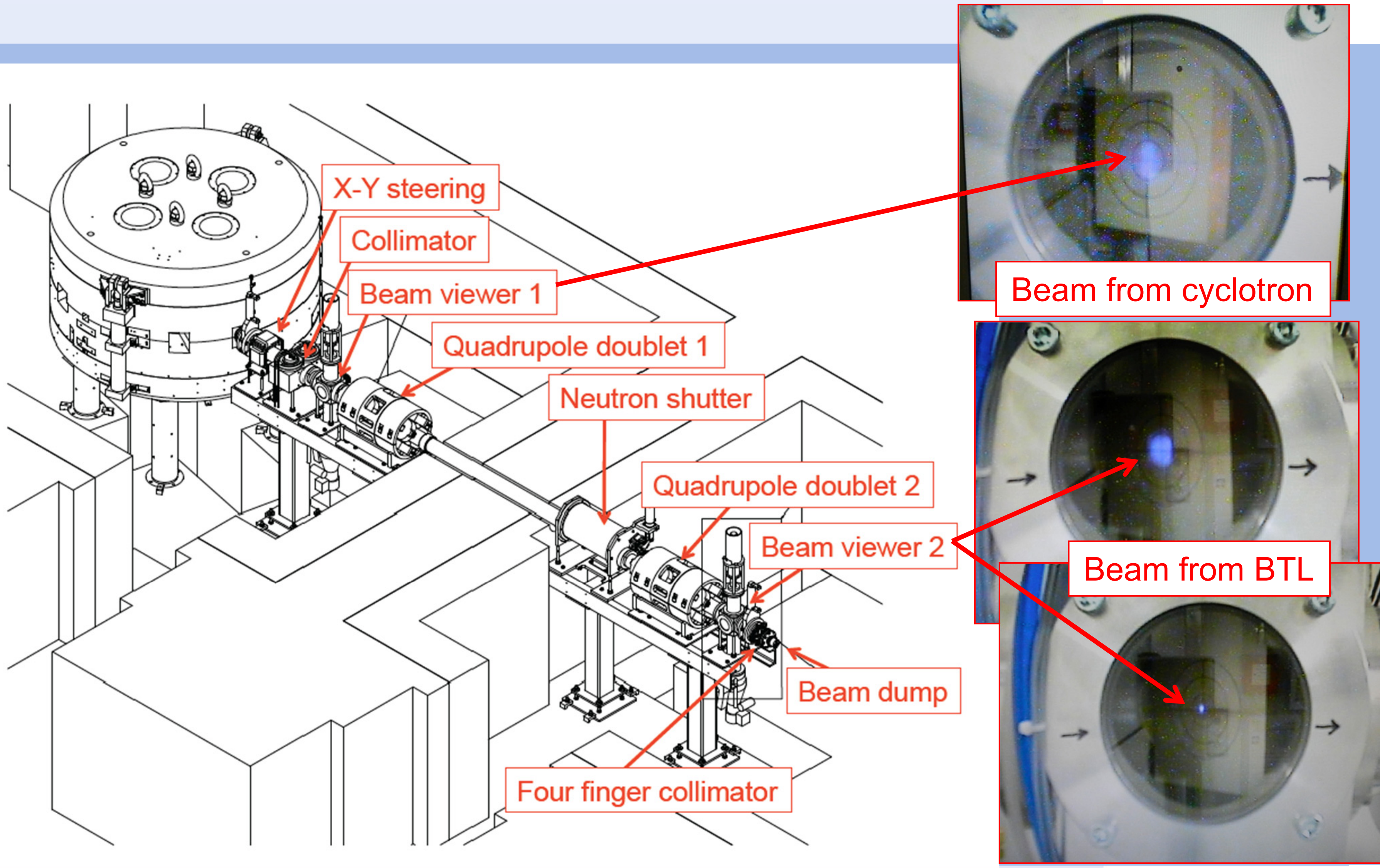
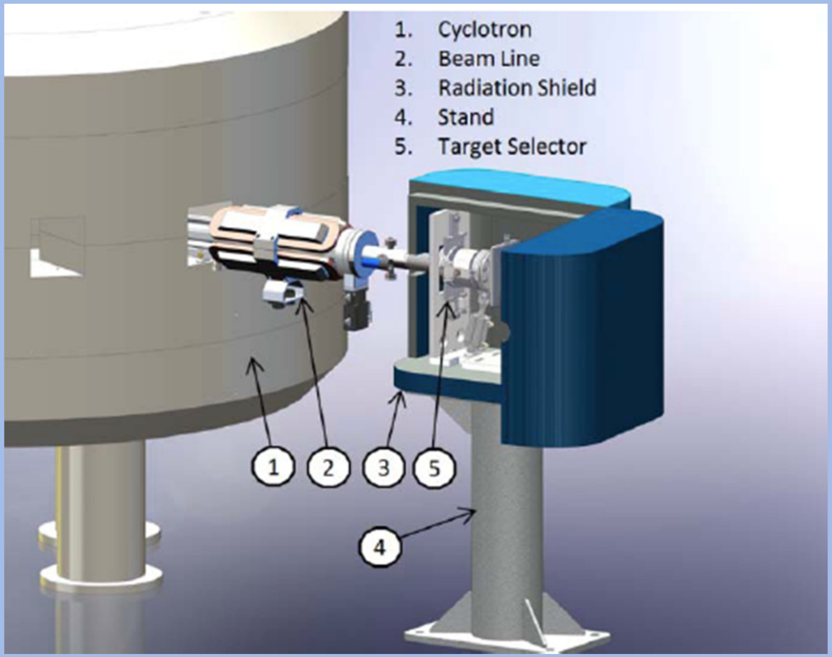


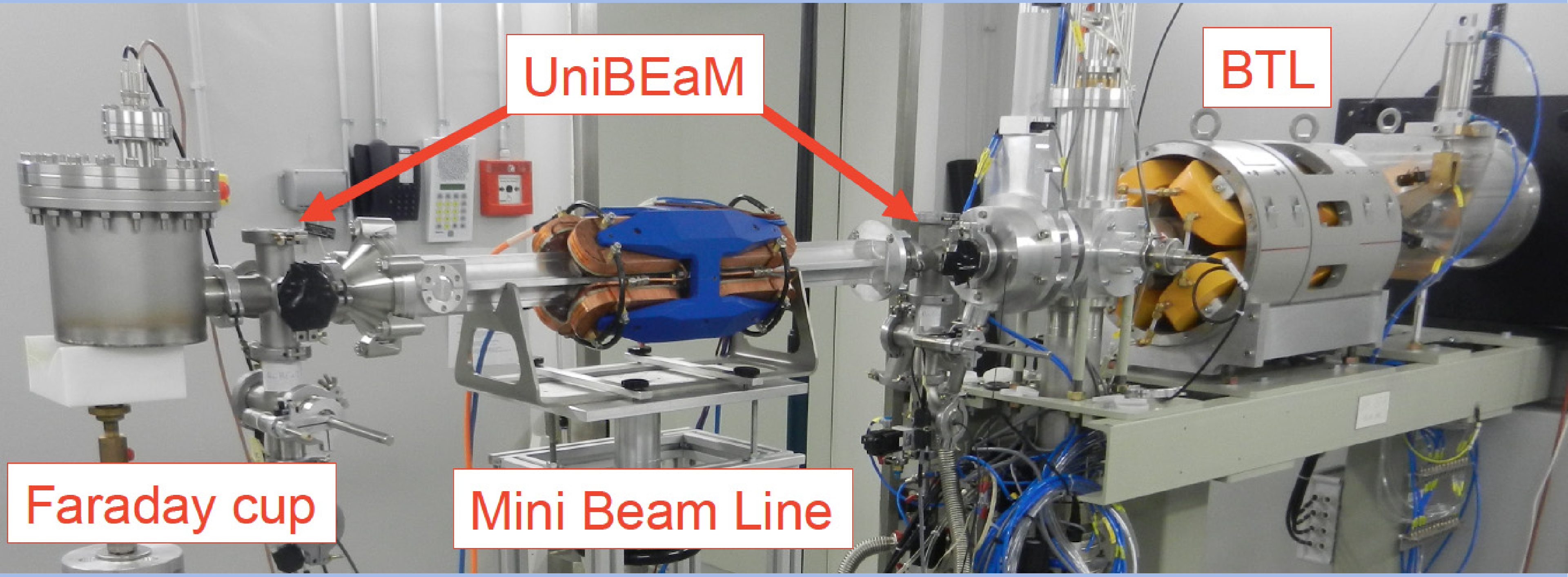
S. Braccini, *AIP Conf. Proc.* vol. 1525, p. 144, 2013

The MiniBeamLine



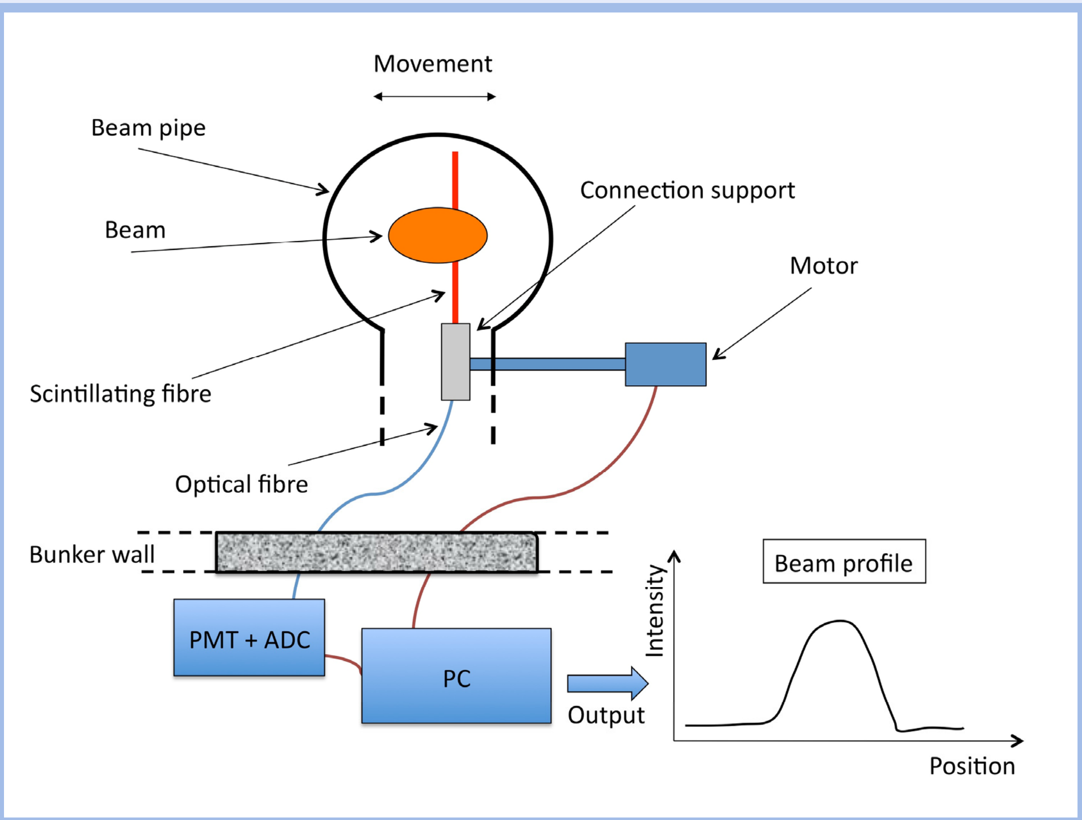
- Quad doublet + XY steering within a single magnet ➔ complex beam optics
- Compact: 40 cm long, 54 kg
- Does not need a second bunker!
- D-Pace, Canada

Characterization of the MiniBeamLine



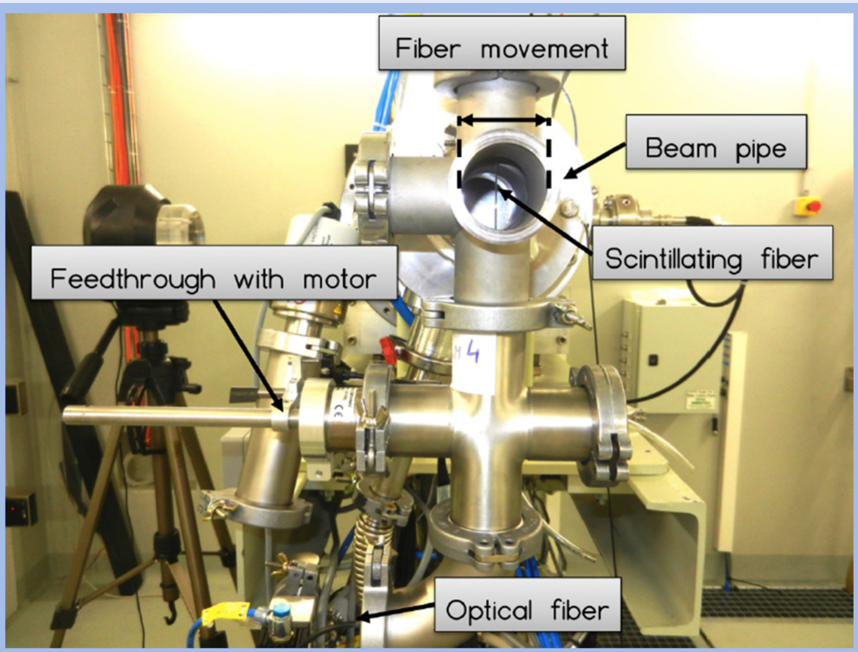
- Beam monitoring detectors are essential
  - High (~10 μA) and low currents (nA, pA)
- Compact medical cyclotrons ➔ “poor” beam diagnostics equipment …

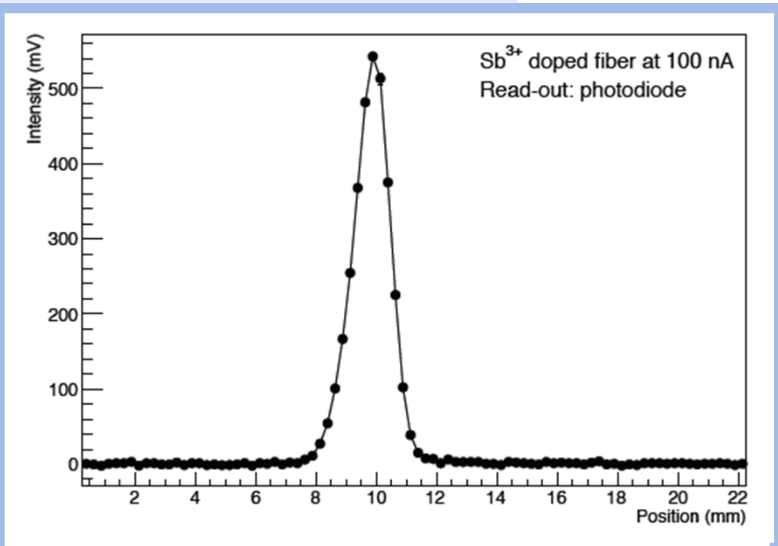
Universal Beam Monitor (UniBEaM)

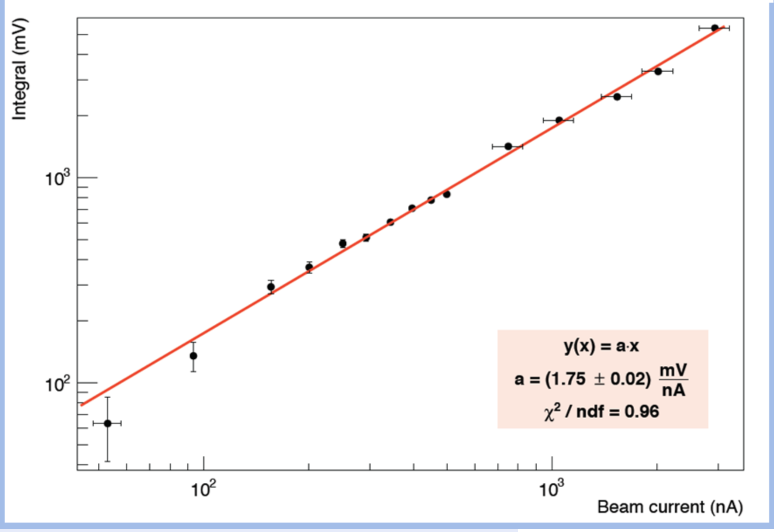


- Beam profiler based on doped optical fibres passed through the beam
- Light signal transported by an optical fibre
- Minimal interference with the beam and occupancy along the beam path

Universal Beam Monitor (UniBEaM)







- Tested range: 1 pA – 20 μA
- Licensed to D-Pace, Canada

M. Auger et al., 2016 JINST 11 P03027

On-line beam monitoring with UniBEaM

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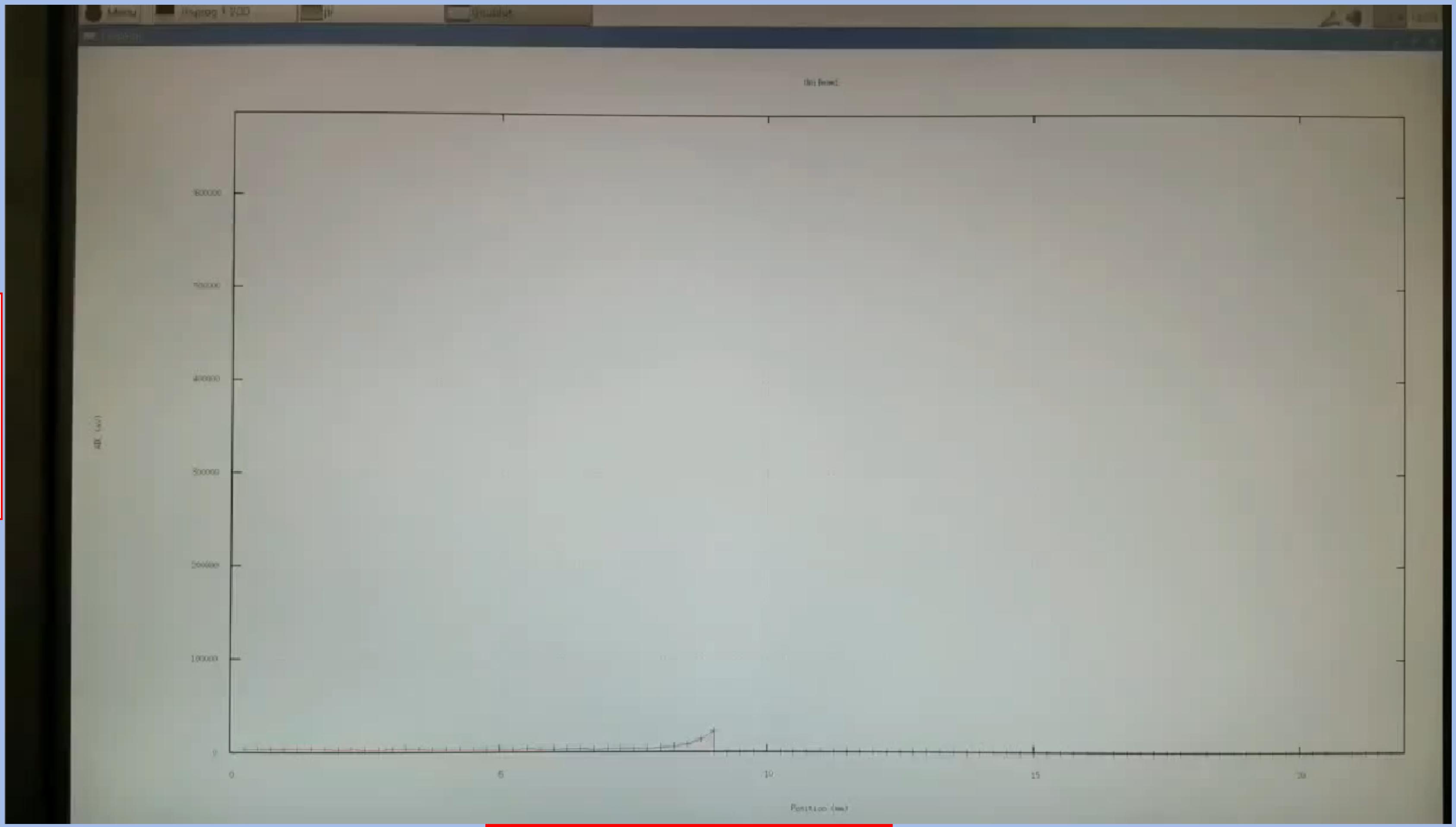
Counts

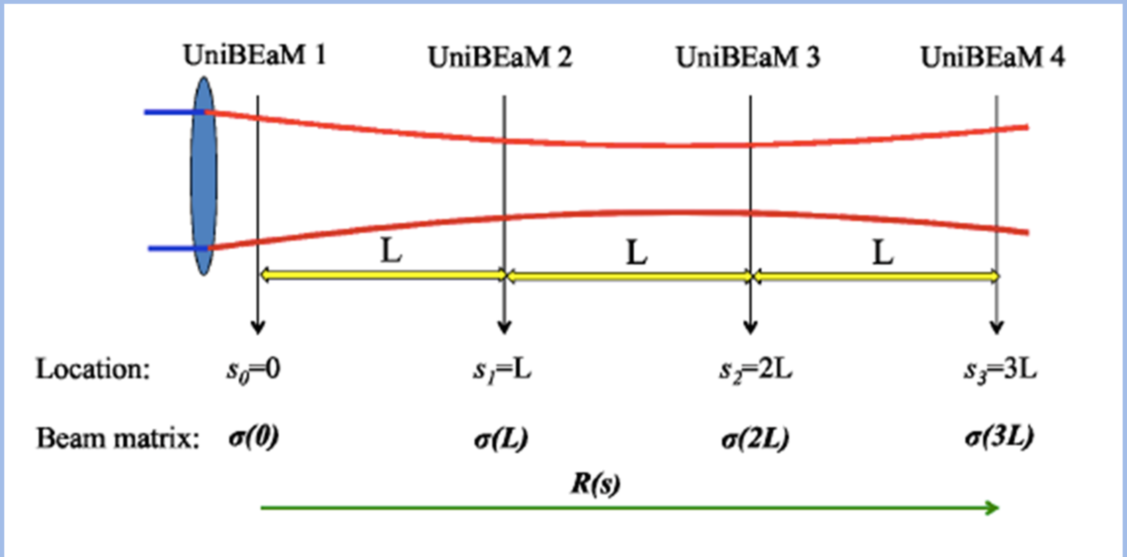


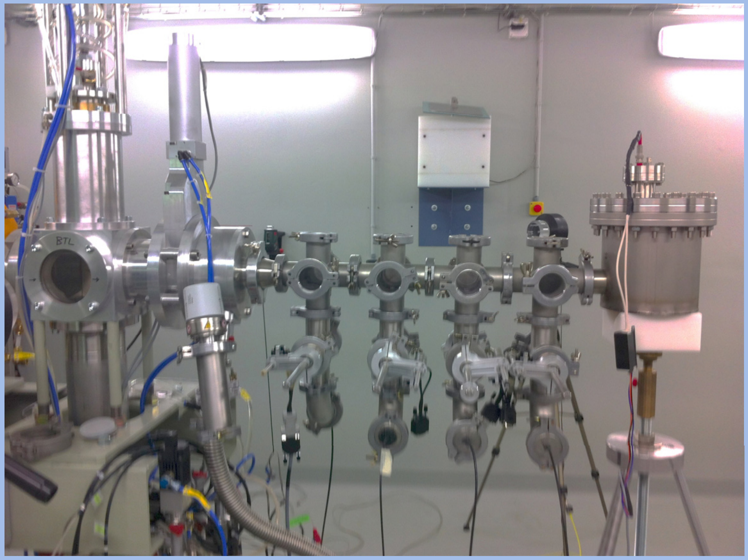
Position [mm]

Transverse beam emittance

- Poorly known (or unknown!) for compact medical cyclotrons
- Crucial for a reliable simulation of the BTL for research activities
- Standard quad variation method

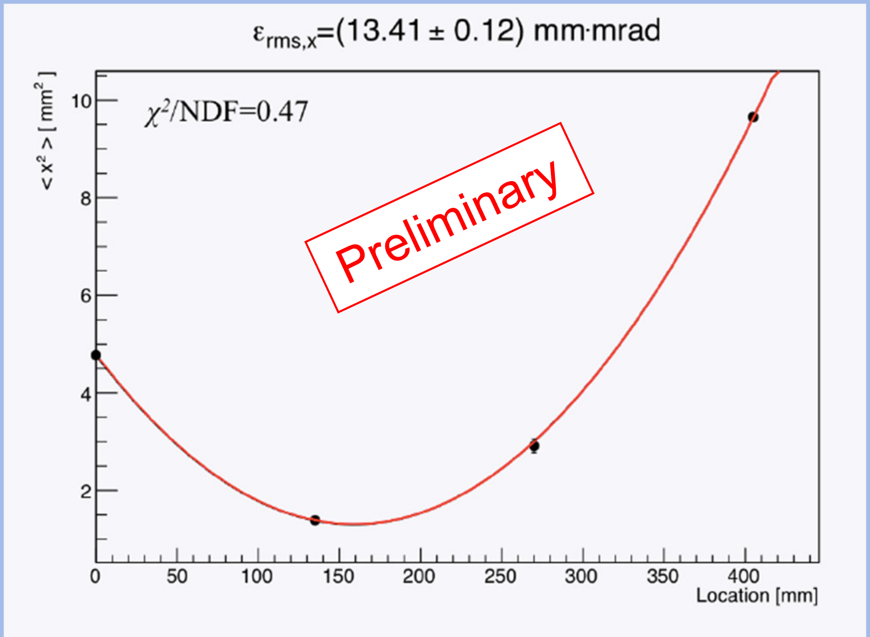
- New on-line method based on 4 UniBEaM detectors





K. Nesteruk et al., Proc. IBIC'15, Sep. 2015, Melbourne, Australia, p. 134.

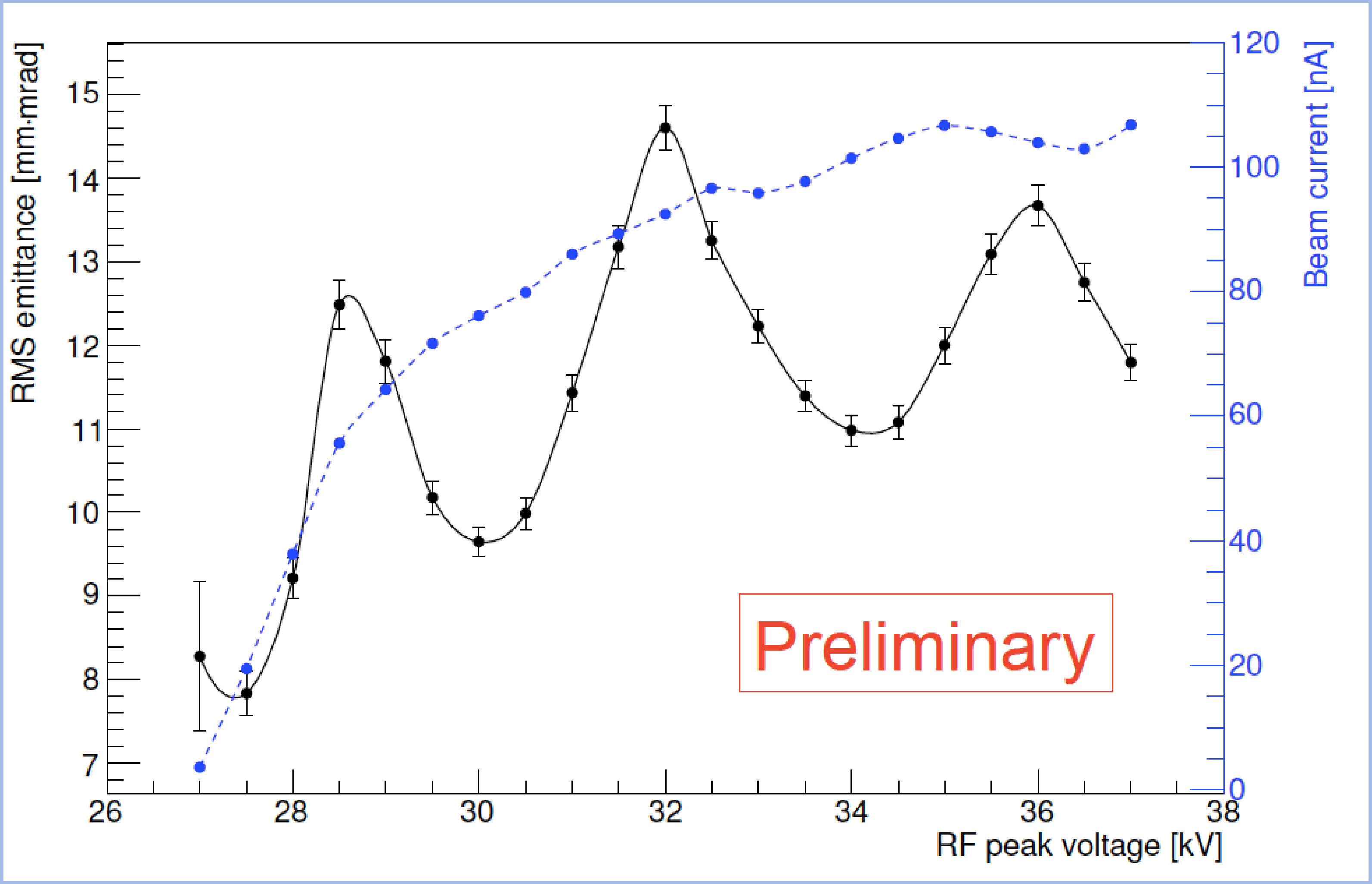
Transverse beam emittance of the Bern Cyclone 18/18



Fit parameter	Horizontal plane	Vertical plane
σ_{11} [mm^2]	4.79 ± 0.09	0.75 ± 0.04
σ_{12} [mm·mrad]	-21.90 ± 0.48	-1.06 ± 0.19
σ_{22} [mrad^2]	137.72 ± 2.06	17.99 ± 1.15
$\tilde{\chi}^2$	0.47	0.76
ε_{rms} [mm·mrad]	13.41 ± 0.12	3.53 ± 0.13

- As expected, the emittance is larger in the horizontal plane
- On-line ➔ study of the emittance as a function of the main coil, RF, stripper angle, etc. (paper in preparation)

Transverse beam emittance vs RF peak voltage



Radiation hardness studies for ATLAS (CERN) and JUICE (ESA)

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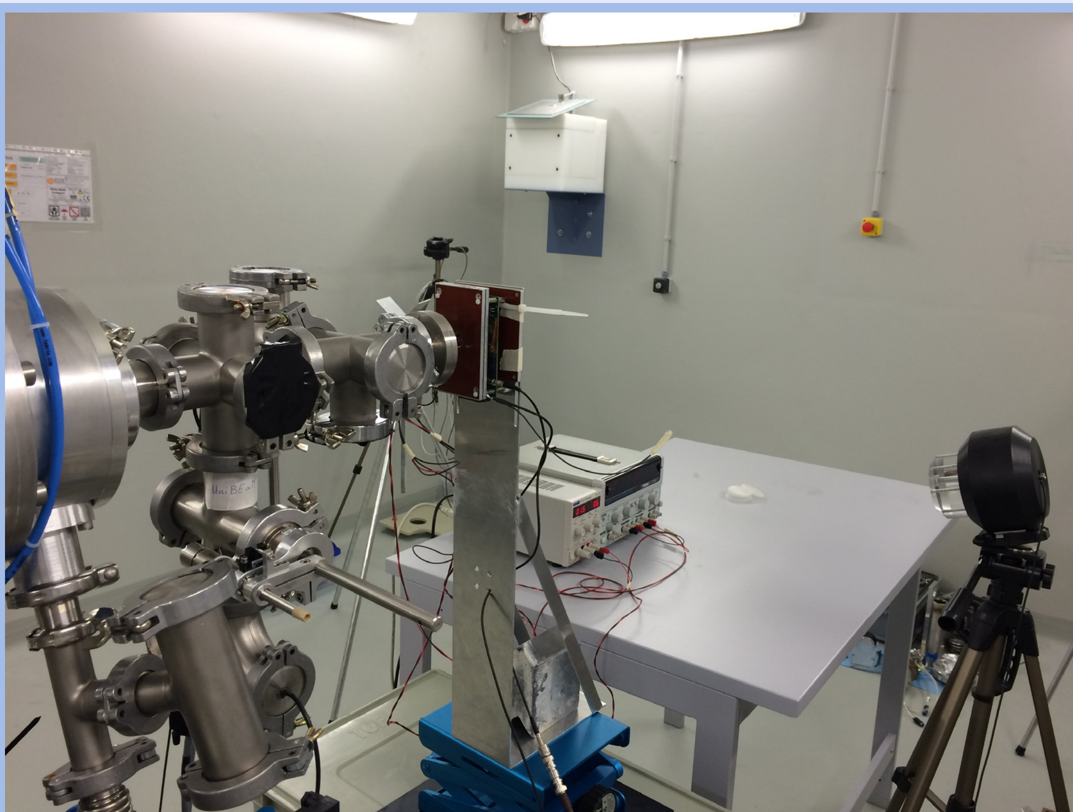

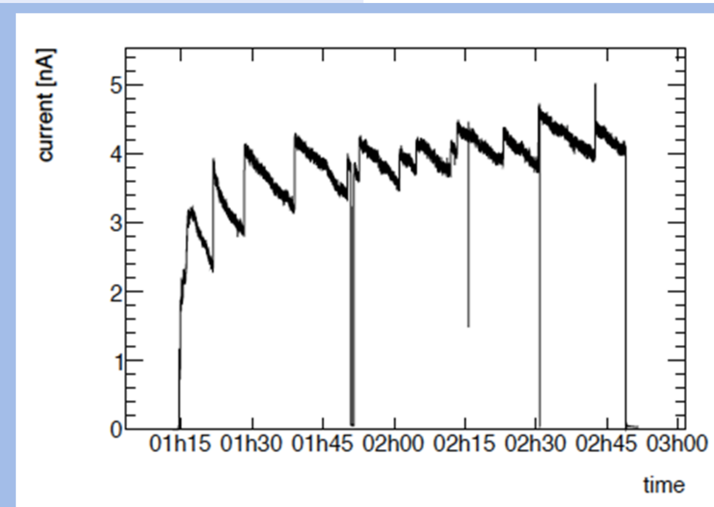

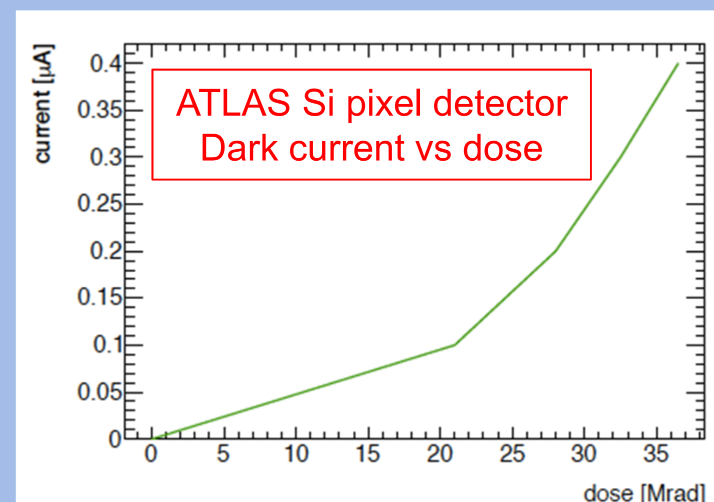

- Beam current in the nA range
- Extraction in air
- Doses in the 1-100 Mrad range (10^3-10^5 Gy)

Neutrons for free …

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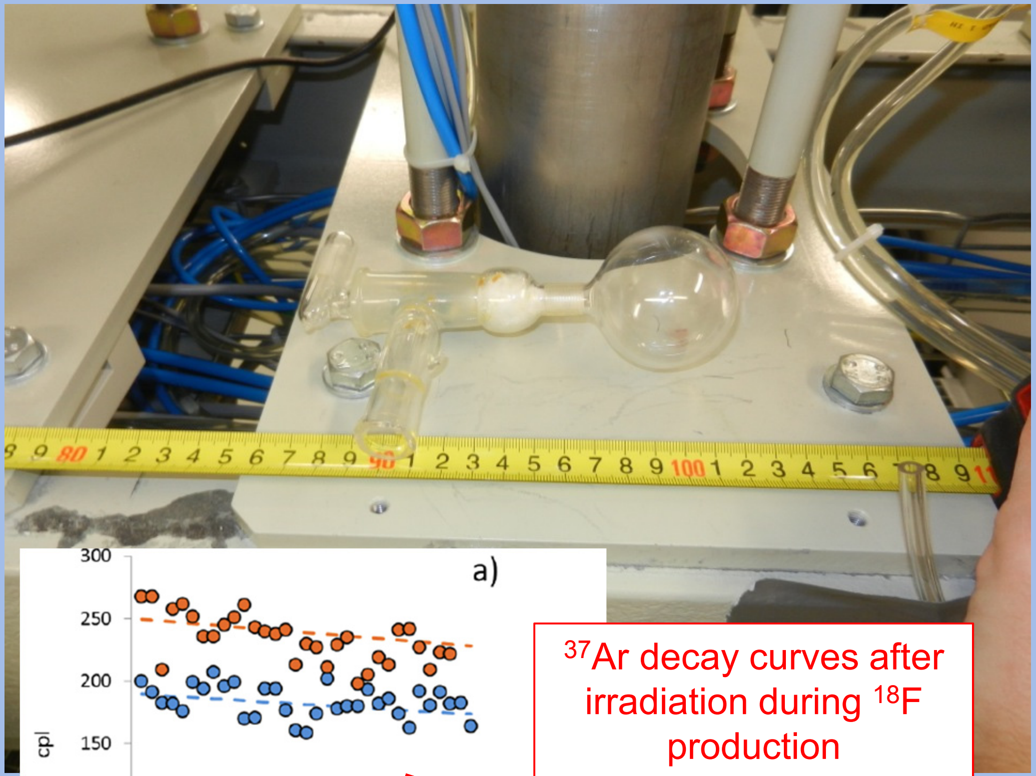

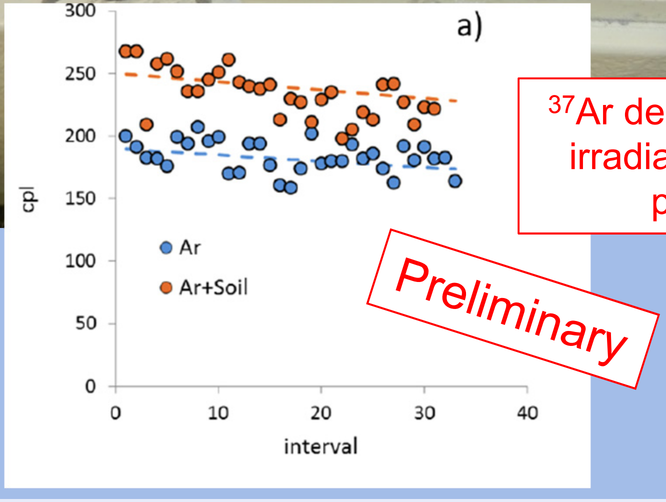

^{37}Ar decay curves after irradiation during ^{18}F production

> Neutrons are produced by (p,n) reactions

> Fast (~1 MeV) and thermal neutrons

> $\Phi \sim 10^5\ (s \cdot cm^2 \cdot \mu A)^{-1}$ thermal neutrons

> They can be used for
  — Radiation protection
  — Environmental studies
  — ^{37}Ar : detection of nuclear explosions
  — …

Conclusions and Outlook

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- Compact medical cyclotrons: tools of choice for PET radioisotope production in a hospital-based environment
- Optimization and maintenance are crucial for high performances
- High science potential beyond radioisotopes for medicine
  - Production and research can run in parallel
- Multi-disciplinary research requires:
  - Access to the beam area (beam transfer line)
  - Low currents down to 1 pA
- This science potential just started to be exploited …

Thank you very much for your attention!