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ETH zürich

Isabella Colizzi :: PhD candidate :: Paul Scherrer Institute

Upgrade of a clinical facility to achieve a high transmission and gantry angle-independent FLASH tune

CYC22 :: 07.12.2022

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What is FLASH-RT?

A differential **protective** effect on helathy tissue when irradiated at **ultra-high dose rate** (>40 Gy/s) compared to a similar irradiation at «conventional» dose rate (0.01–0.05 Gy/s) [1]

July, 2014

RADIATION TOXICITY

Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

Vincent Favaudon,[1,2*] Laura Caplier,[3†] Virginie Monceau,[4,5‡] Frédéric Pouzoulet,[1,2§] Mano Sayarath,[1,2¶] Charles Fouillade,[1,2] Marie-France Poupon,[1,2||] Isabel Brito,[6,7] Philippe Hupé,[6,7,8,9] Jean Bourhis,[4,5,10] Janet Hall,[1,2] Jean-Jacques Fontaine,[3] Marie-Catherine Vozenin[4,5,10,11]

[1] [2]

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

ELSEVIER

2019

First in Human

Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis [a,b,*], Wendy Jeanneret Sozzi [a], Patrik Gonçalves Jorge [a,b,c], Olivier Gaide [d], Claude Bailat [c], Fréderic Duclos [a], David Patin [a], Mahmut Ozsahin [a], François Bochud [c], Jean-François Germond [c], Raphaël Moeckli [c,1], Marie-Catherine Vozenin [a,b,1]

[a] Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne; [b] Radiation Oncology Laboratory, Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne; [c] Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne; and [d] Department of Dermatology, Lausanne University Hospital and University of Lausanne, Switzerland

[1] FLASH-RT, Alejandro Mazal

FLASH-Proton therapy (PT)

- Numerous proton centers around the world have begun to look at whether it's possible to use current treatment equipment to achieve FLASH dose rates

JAMA Oncology | Original Investigation

Proton FLASH Radiotherapy for the Treatment of Symptomatic Bone Metastases
The FAST-01 Nonrandomized Trial

Experimental Set-up for FLASH Proton Irradiation of Small Animals Using a Clinical System

Annalisa Patriarca, PhD,* Charles Fouillade, PhD,*,† Michel Auger, MSc,* Frédéric Martin, MSc,* Frédéric Pouzoulet, PhD,‡ Catherine Nauraye, PhD,* Sophie Heinrich, PhD,‡

Commissioning of a clinical pencil beam scanning proton therapy unit for ultra-high dose rates (FLASH)

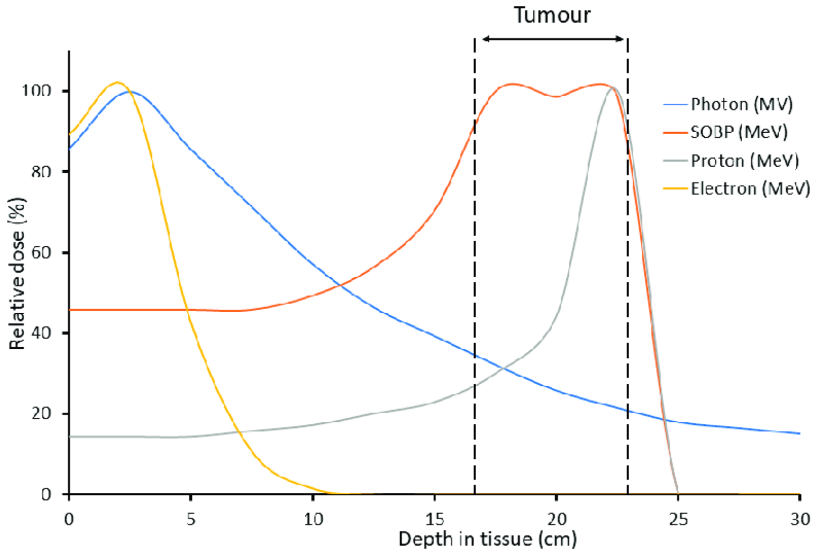
Konrad P. Nesteruk[a)] Michele Togno and Martin Grossmann
Center for Proton Therapy, Paul Scherrer Institute, Villigen, Switzerland

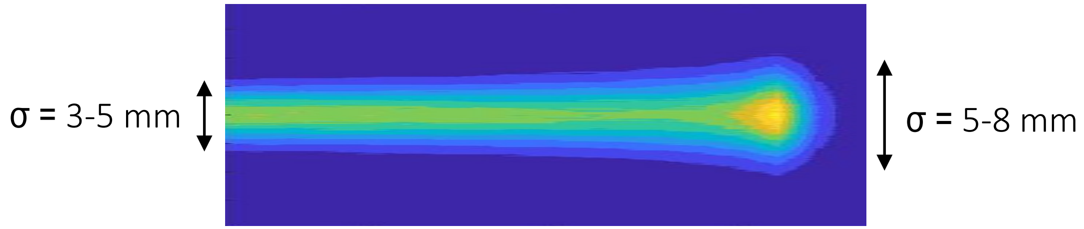
[3] [4] [5]

- The maximum extracted beam intensities from a proton therapy **cyclotron** are in the range 100–800 nA, **800 nA** for PSI, thereby meeting the continuous current requirement for FLASH

Why Proton Therapy?

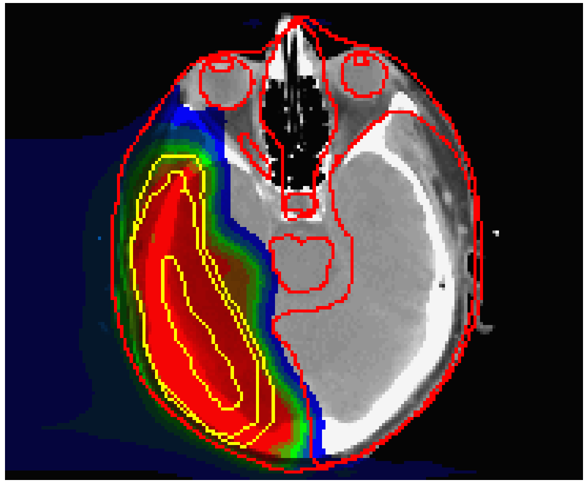
Depth dose curve in water

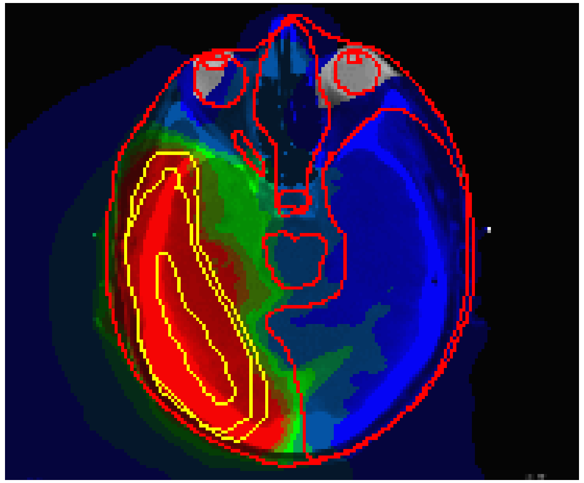




protons

photons

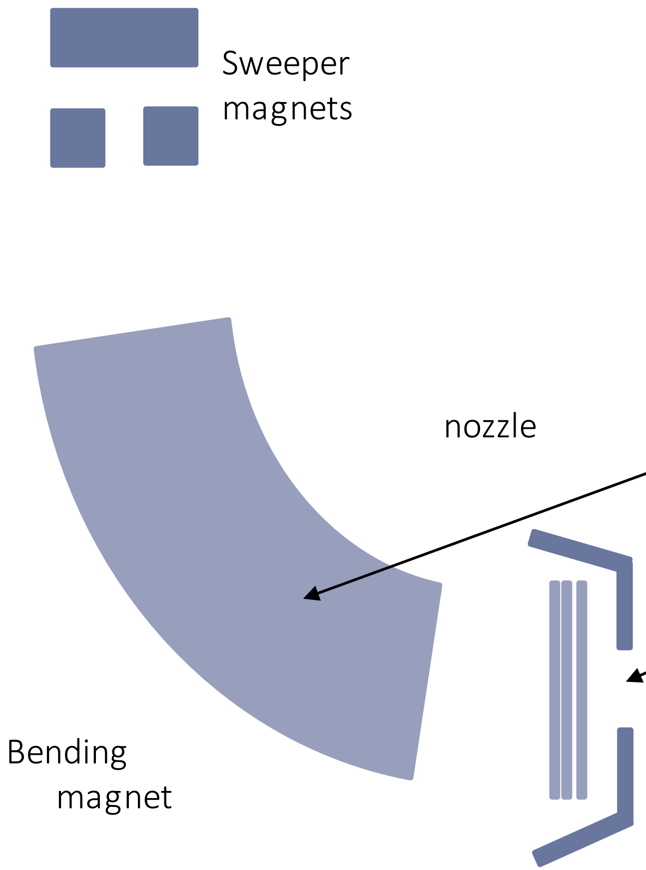




Reduce dose to healthy organs

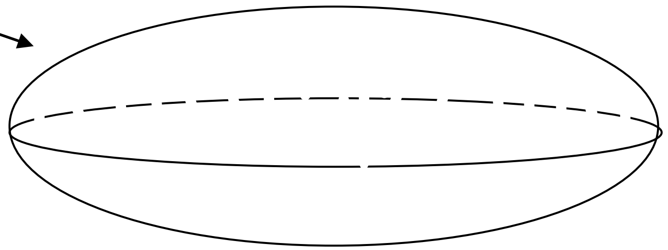
Increase conformity

How is conformal dose distribution achieved in PT?

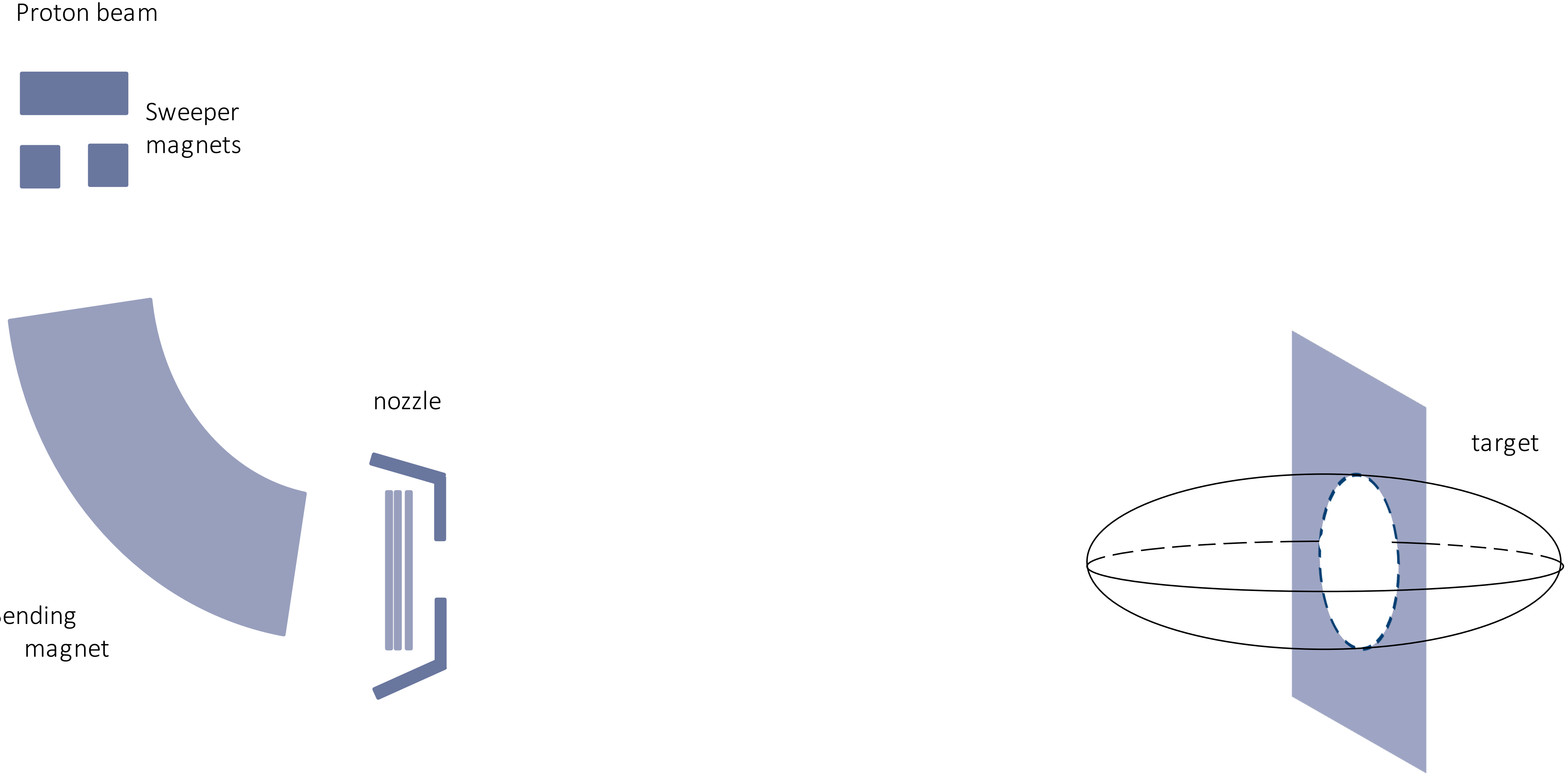


Gantry 2 PSI

Pedroni Eros, et al. 2004



Pencil Beam Scanning (PBS)



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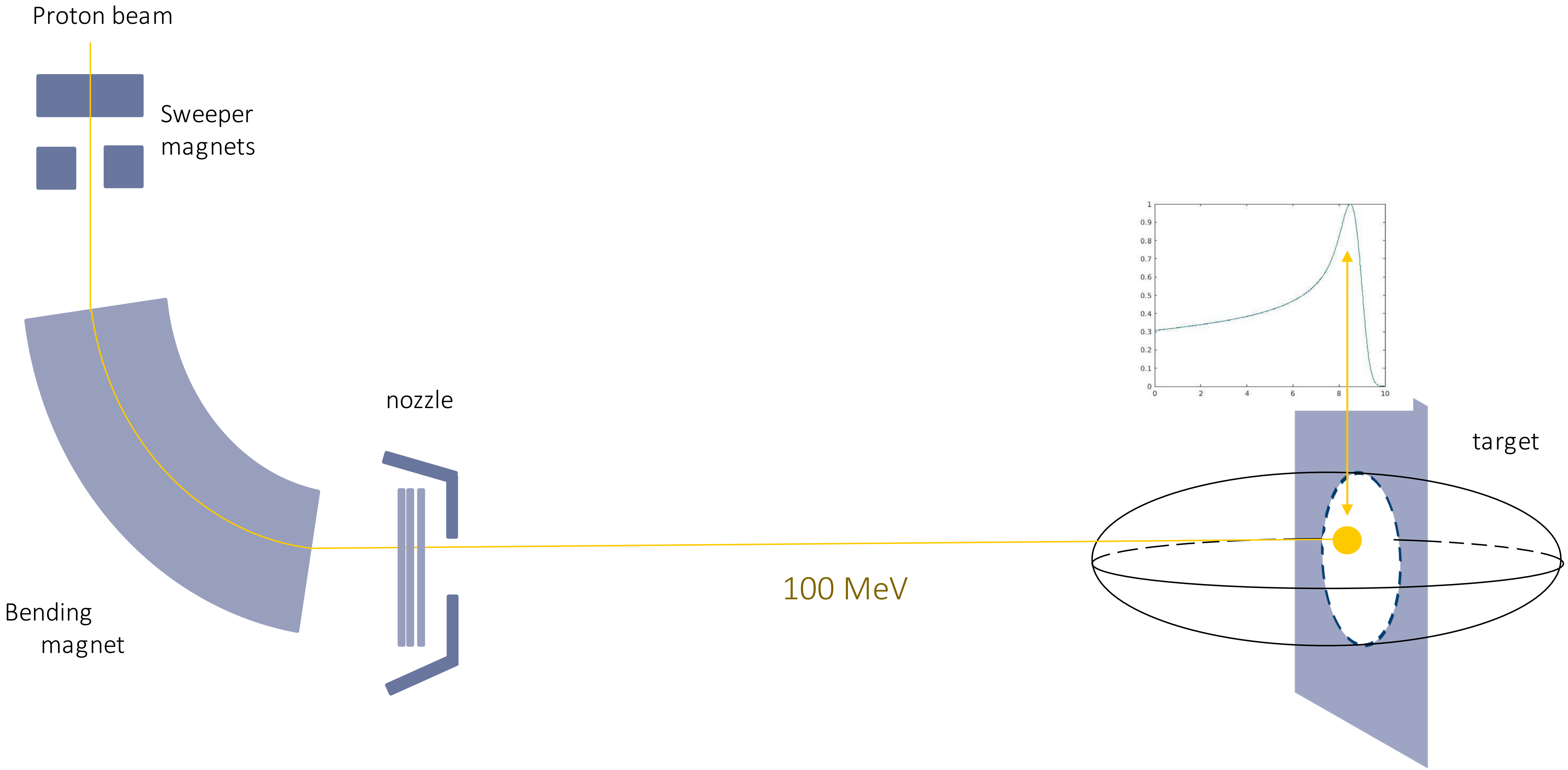

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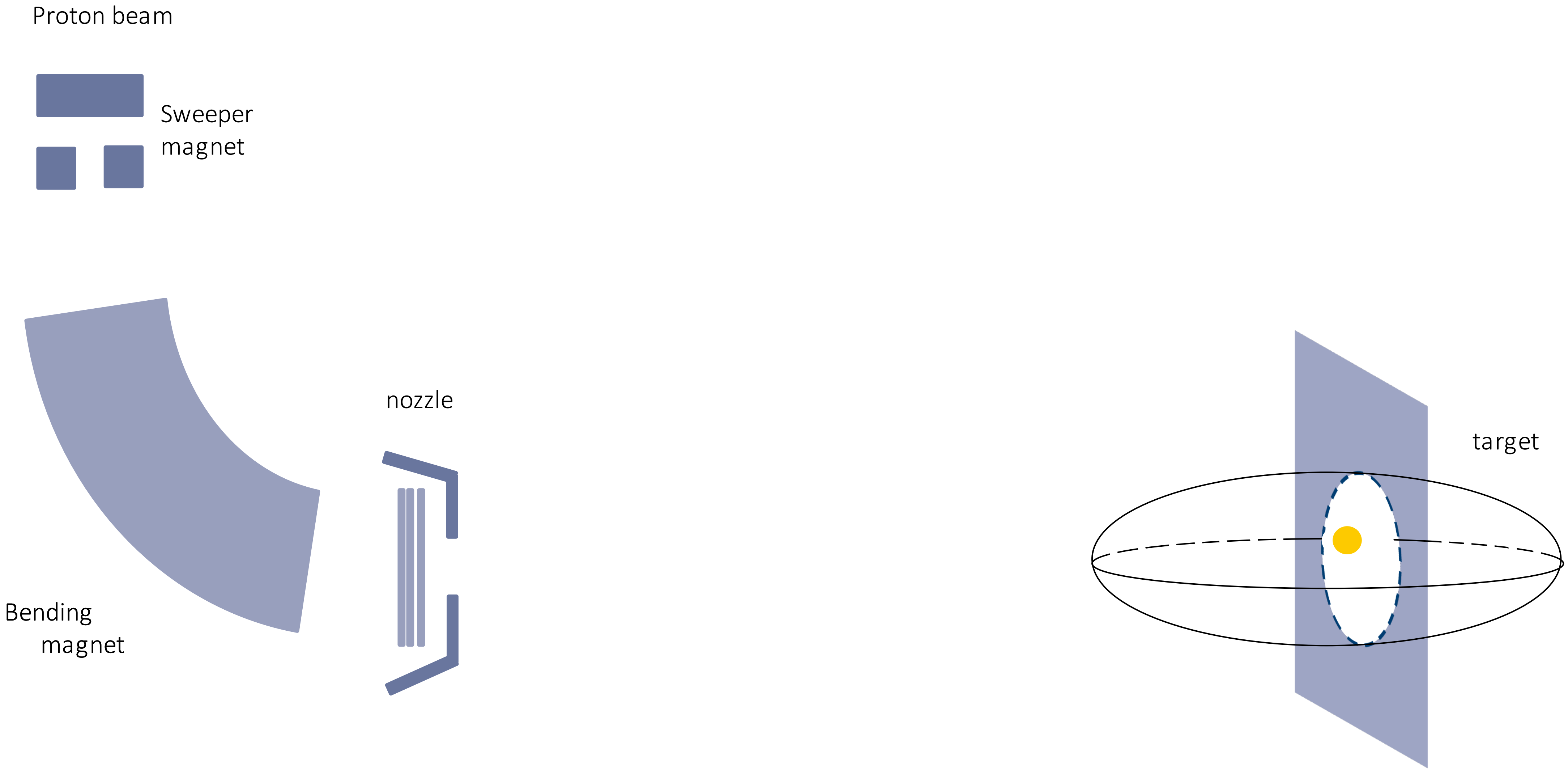

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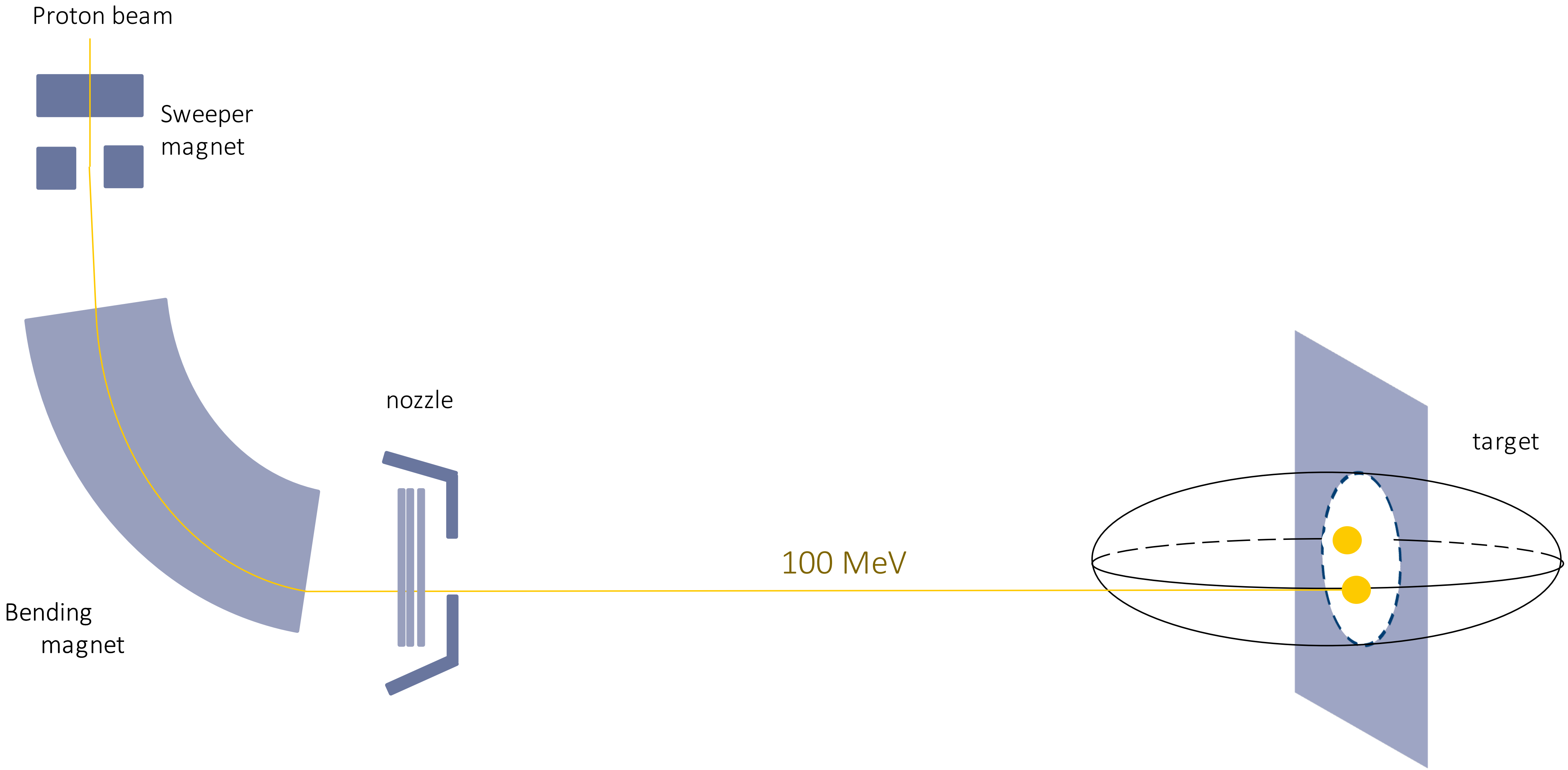

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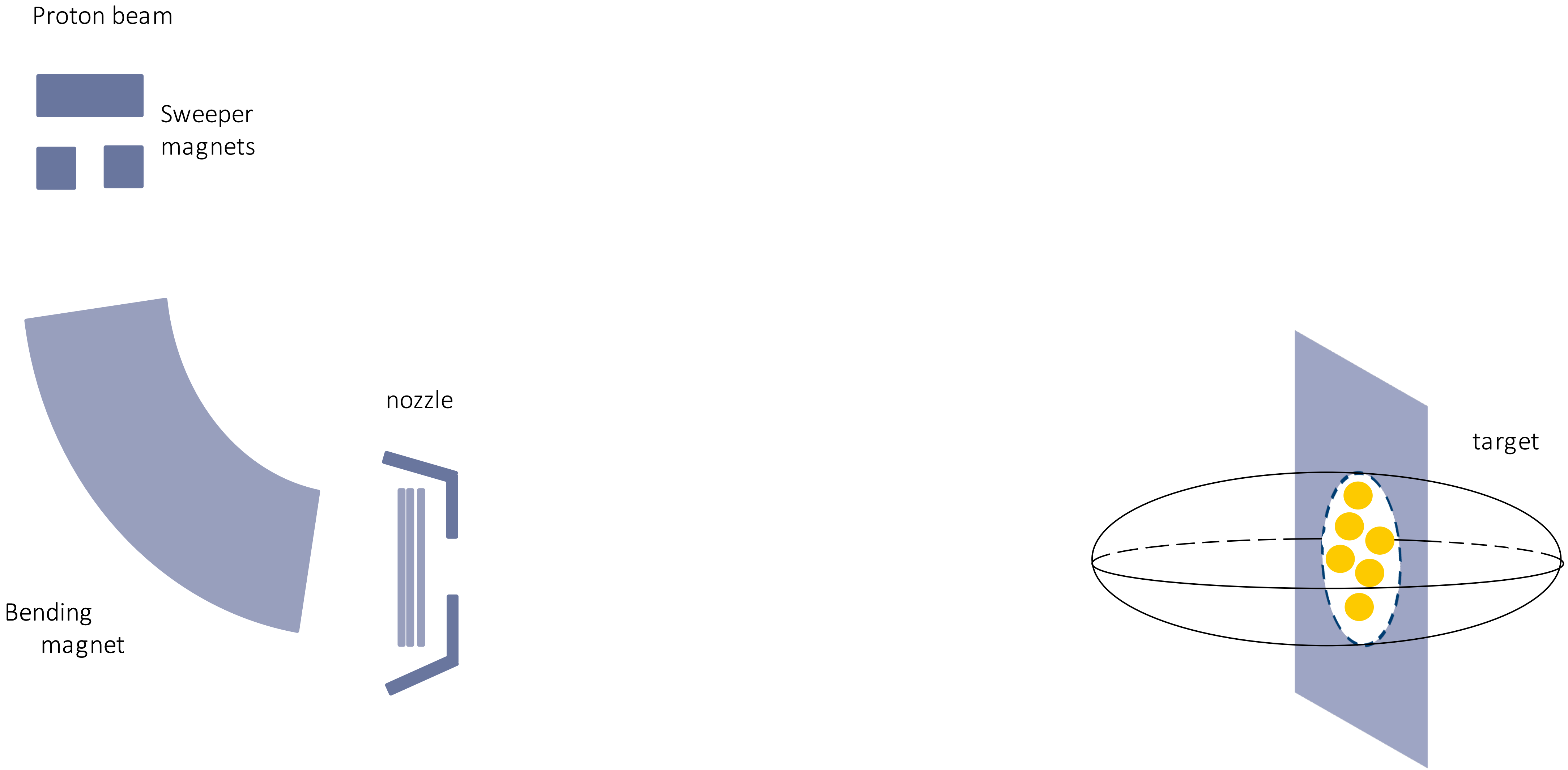

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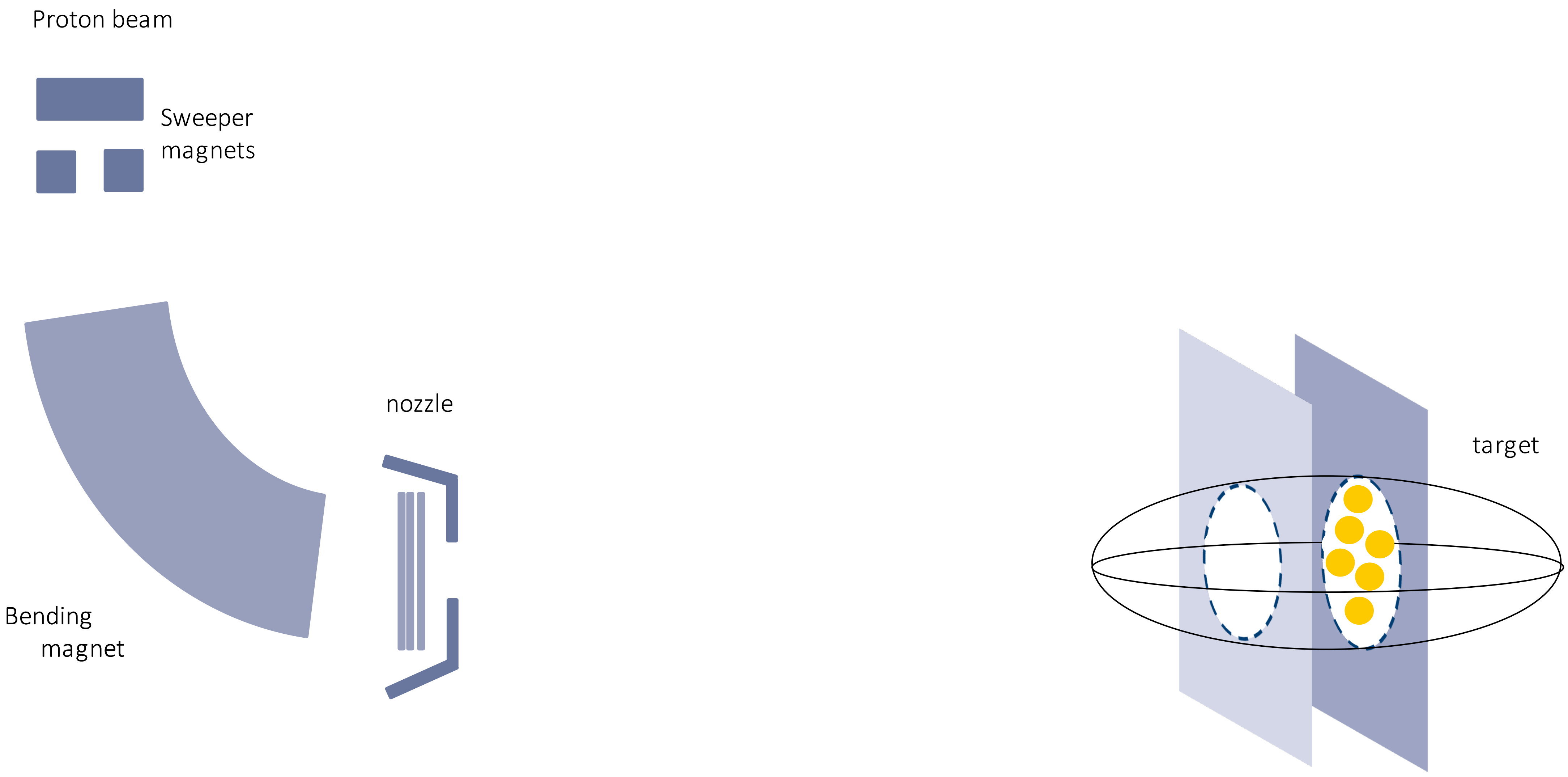
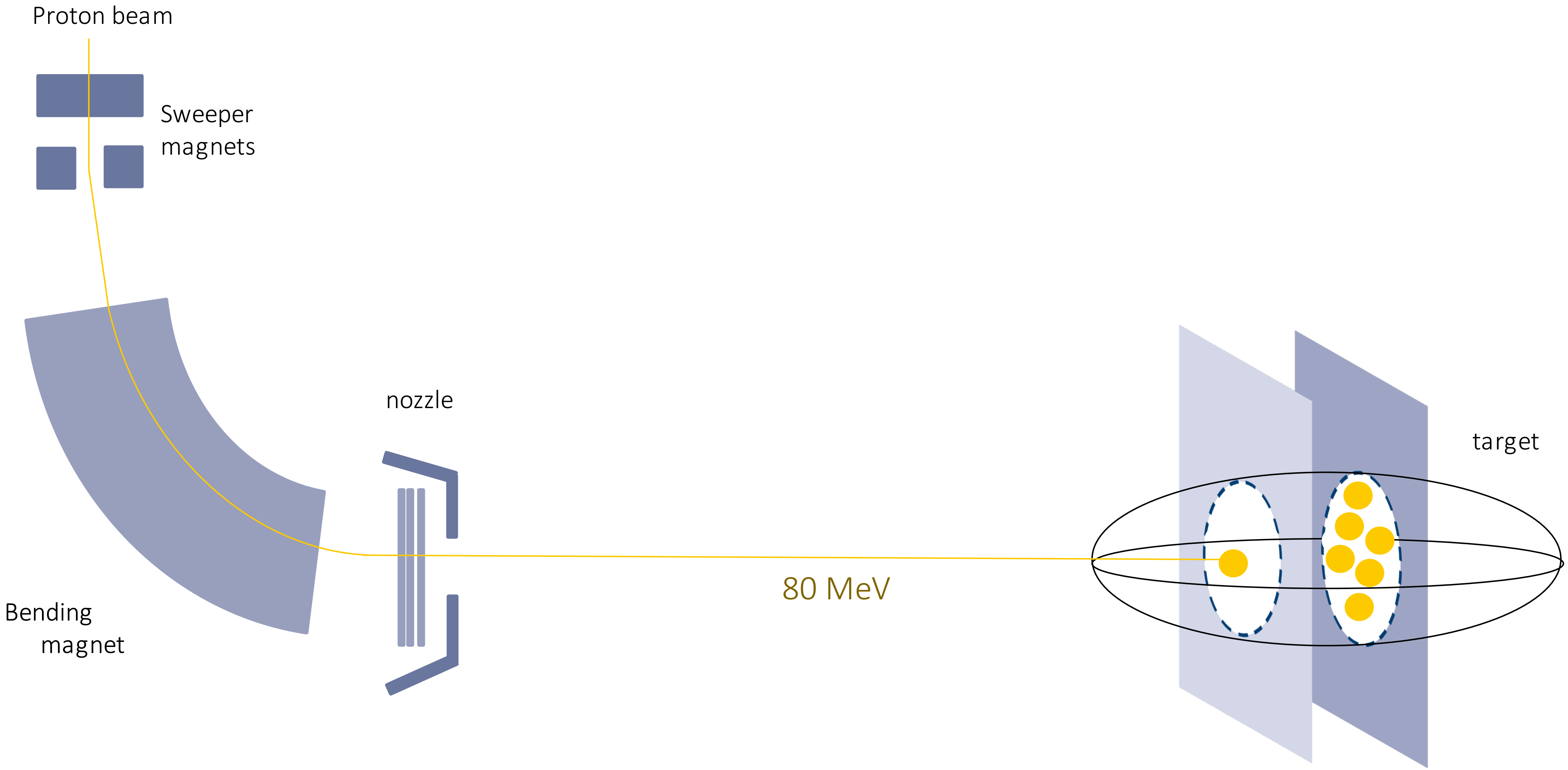
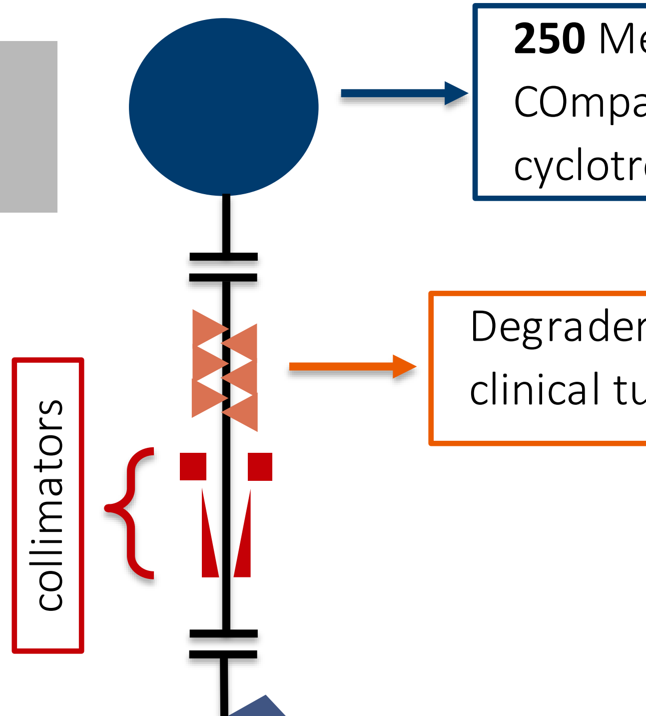
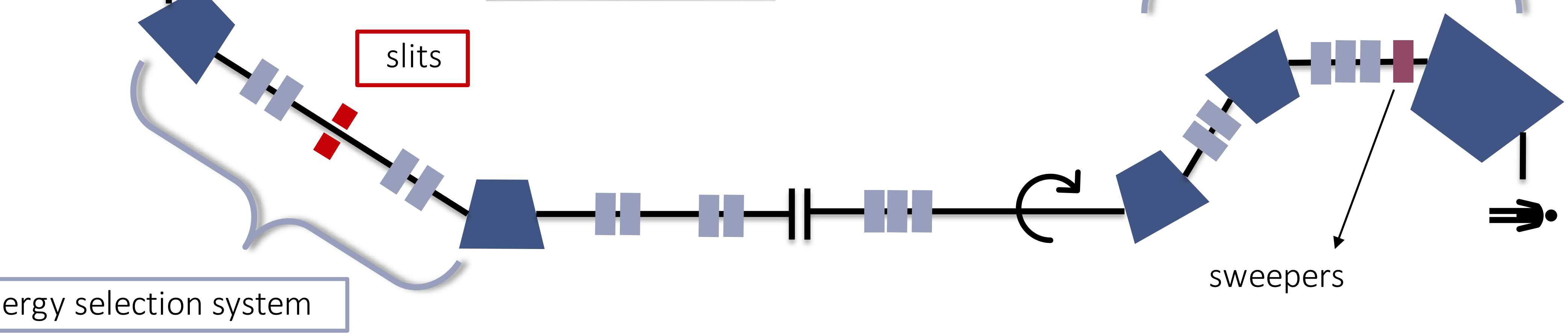


Pencil Beam Scanning (PBS)



PSI beamline





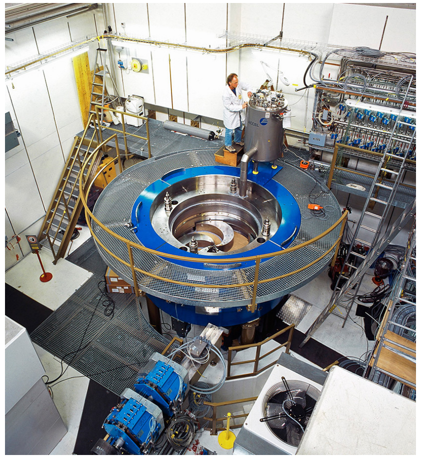
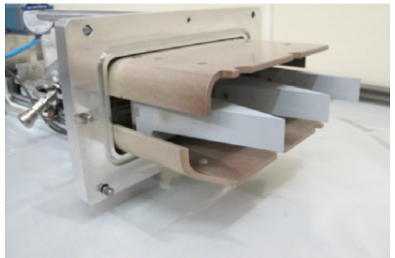


Photo: Paul Scherrer Institute

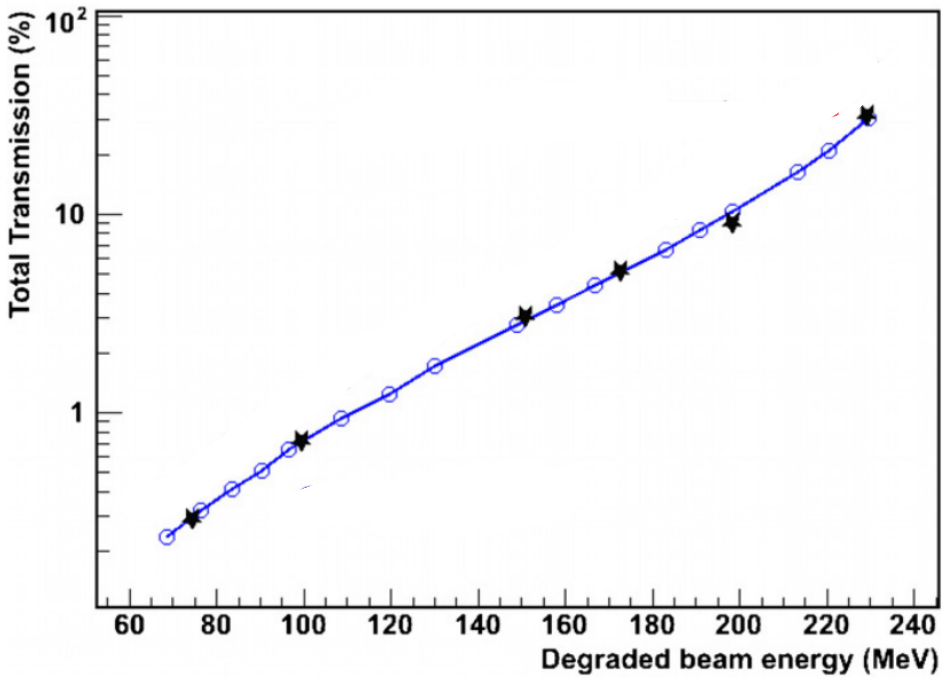
From [8]



From [6]

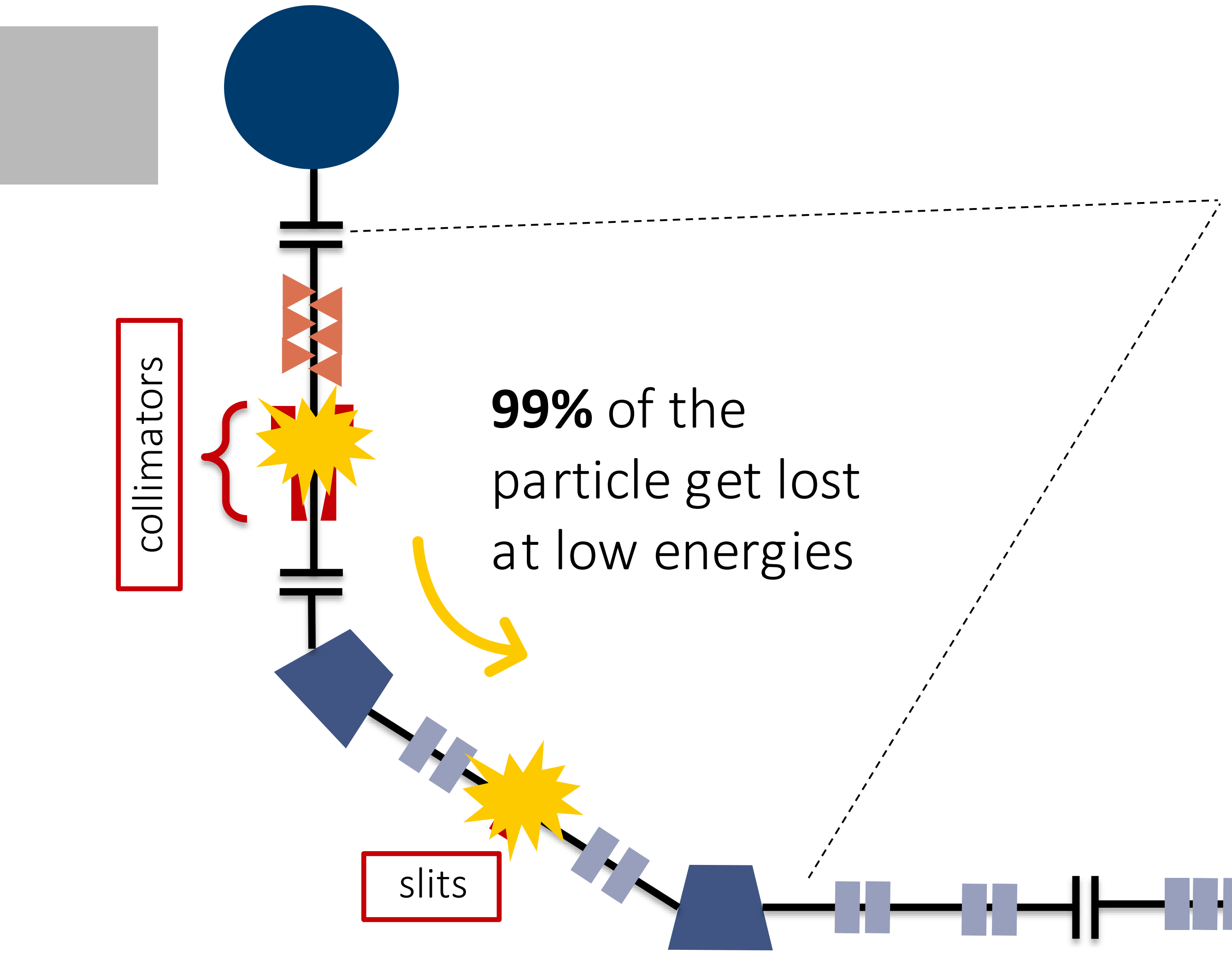
From [7]

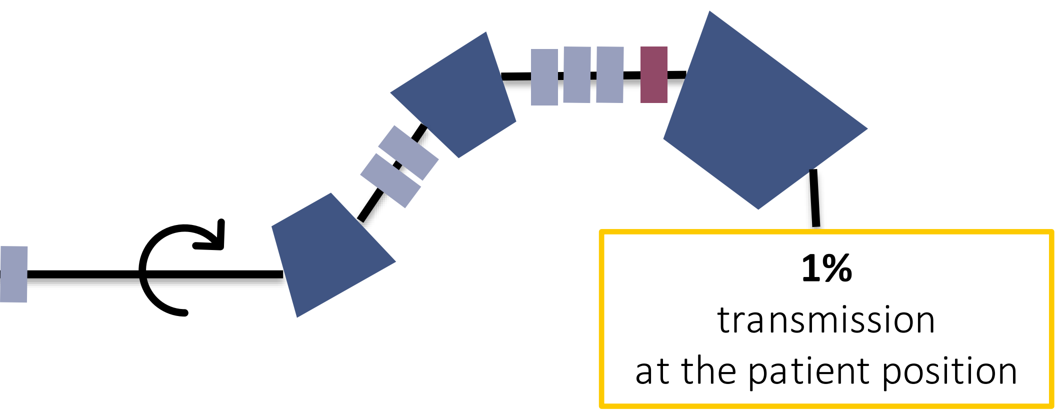
Transmission



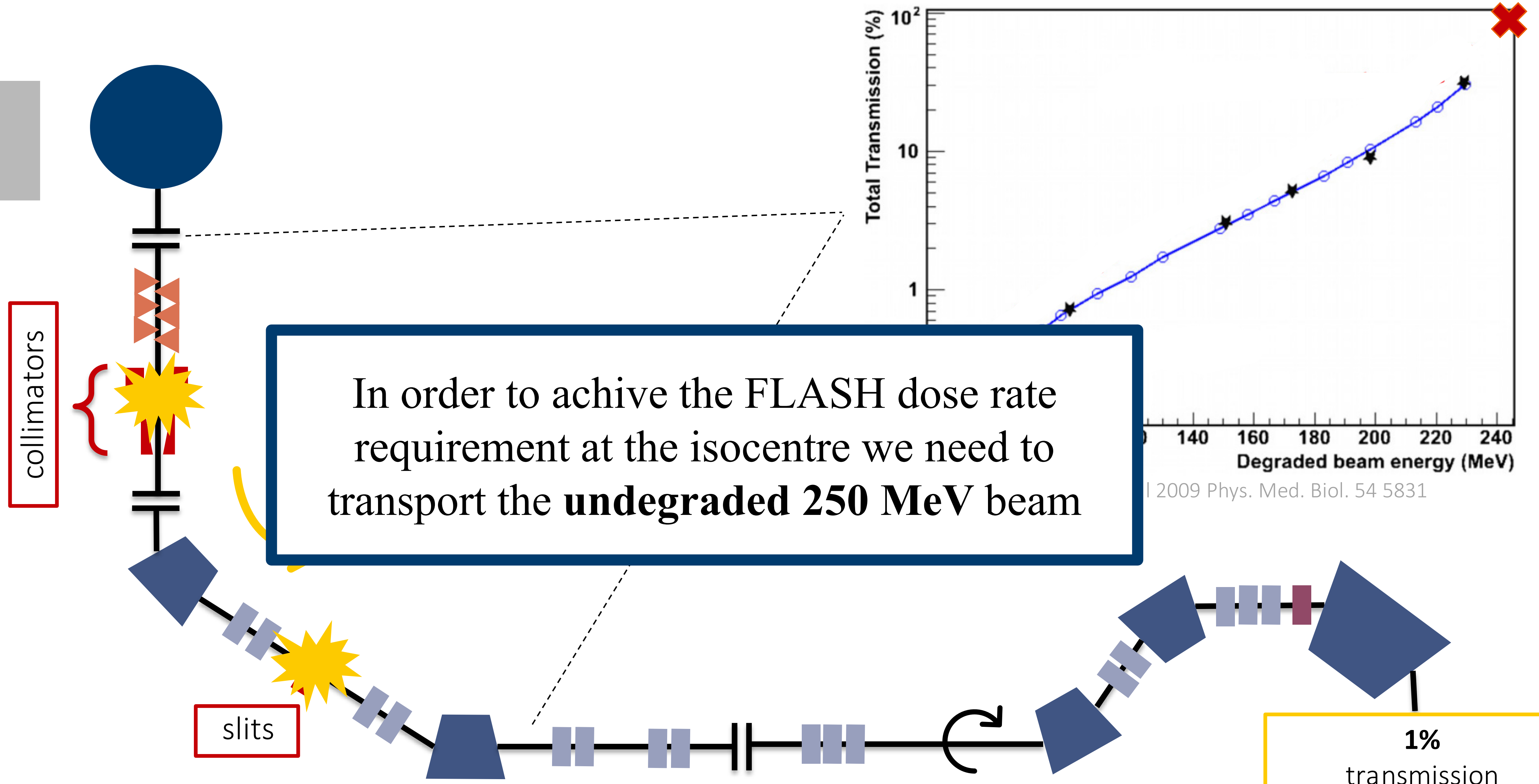
M J van Goethem et al 2009 Phys. Med. Biol. 54 5831

99% of the particle get lost at low energies





Transmission



In order to achive the FLASH dose rate requirement at the isocentre we need to transport the **undegraded 250 MeV** beam

1%
transmission
at the patient position

Problem: asymmetric emittance

The undegraded beam from the cyclotron has a slightly **asymmetric** emittance in the transverse planes that generates gantry **angle-dependent** tunes

→ For pencil beam scanning FLASH-PT we want a gantry **angle-independent** tune

↓ Reduce complexity

↑ Facilitate planning

→ For pencil beam scanning FLASH-PT we want a **small and symmetric beam size**

From [7]

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Objectives

Adapt PSI Gantry 2 to transport ultra-high dose rate **without affecting clinical operation**

Achieving the **beam characteristics** of small and symmetric beam size, gantry angle independent tune and regular spot grid at the patient position required for **Pencil Beam Scanning FLASH-PT**

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Adaptation of Gantry 2

Beam optics for 250 MeV

Beam characteristics at the patient position

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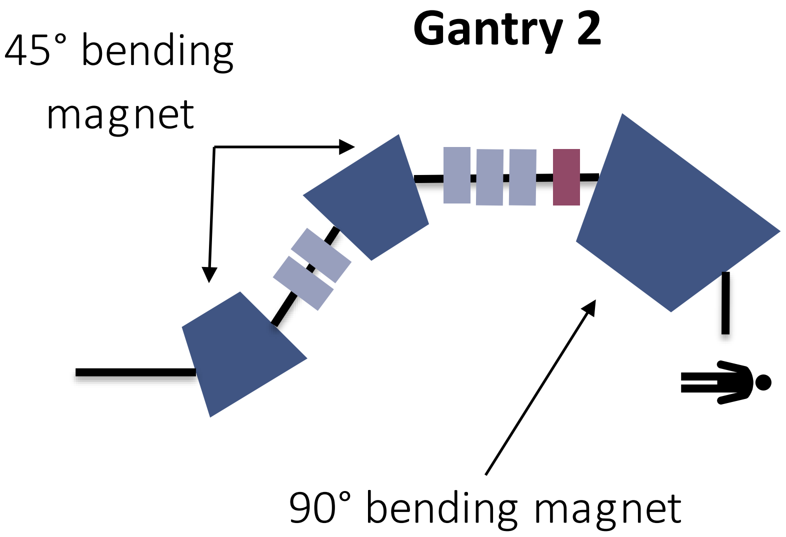
Adaptation of Gantry 2

Beam optics for 250 MeV

Beam charachteristics at the patient position

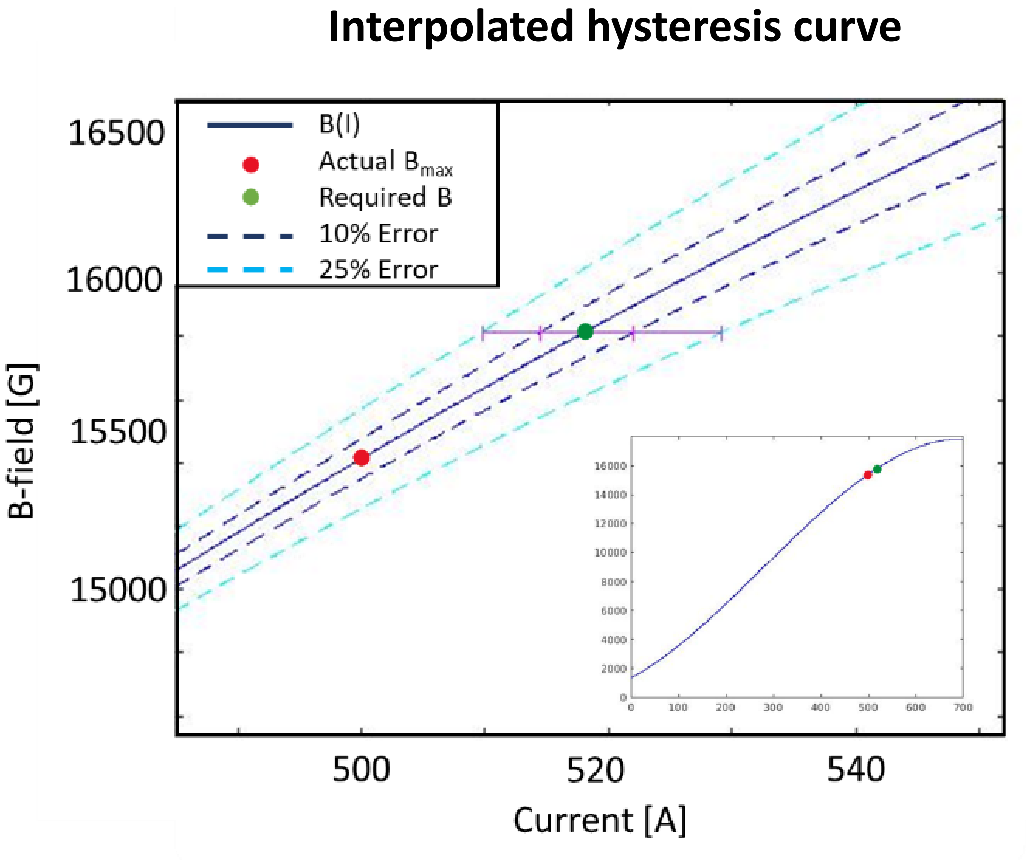
Gantry 2



From [7]

- PSI Gantry 2 dipole magnets were designed to transport energy up to 230 MeV
- The dipoles are already partially saturating at 230 MeV

G2 adaptation to 250 MeV



- We derived the maximum currents specifications of the power supply for transporting 250 MeV
- The new configuration was tested and implemented ***without affecting clinical operation***
- We investigated thermal protection aspects: no adaptation to magnets parameters (such as cooling water flow etc.) were needed.
- No big power consumption: FLASH treatment < 500 ms

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Adaptation of Gantry 2

Beam optics for 250 MeV

Beam characteristics at the patient position

Simulations and beam tuning

Optimisation criteria:

- Beam size smaller than magnets and collimators aperture
- Three imaging point (after the energy selection system, at the coupling point between the beamline and the gantry and at the isocentre)
- Beam waist at the isocentre
- Symmetric beam size at the isocentre
- Angle-independent beam size at the isocentre

Simulations in TRANSPORT [I] and MINT [II] (PSI developed tool)

[I] Rohrer U, Transport G. Framework. 2007

[II] Baumgarten, Christian. "MinT: A Fast Lightweight Envelope/Monte-Carlo Beam Optics Code for the Proton Beam-lines of the Paul Scherrer Institute." arXiv preprint arXiv:2202.07245 (2022).

PSI Beamline: diagnostic elements

Strip chamber monitors

- Along the beamline
- Profile measurement

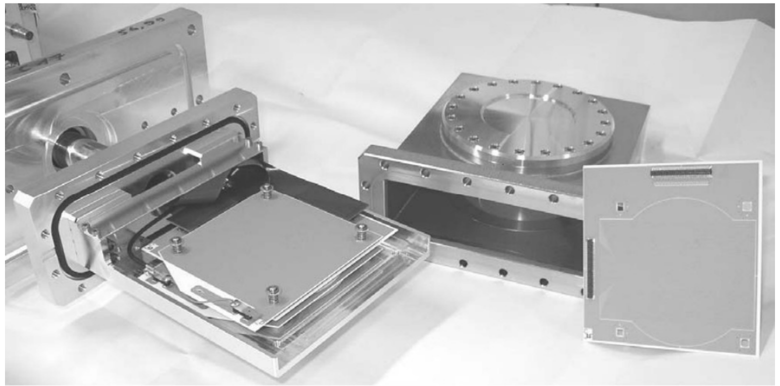


FIGURE 1. Thick profile monitor with pressurized air actuator. To the right: centre plate with vertical strips (the horizontal strips are on the reverse side).

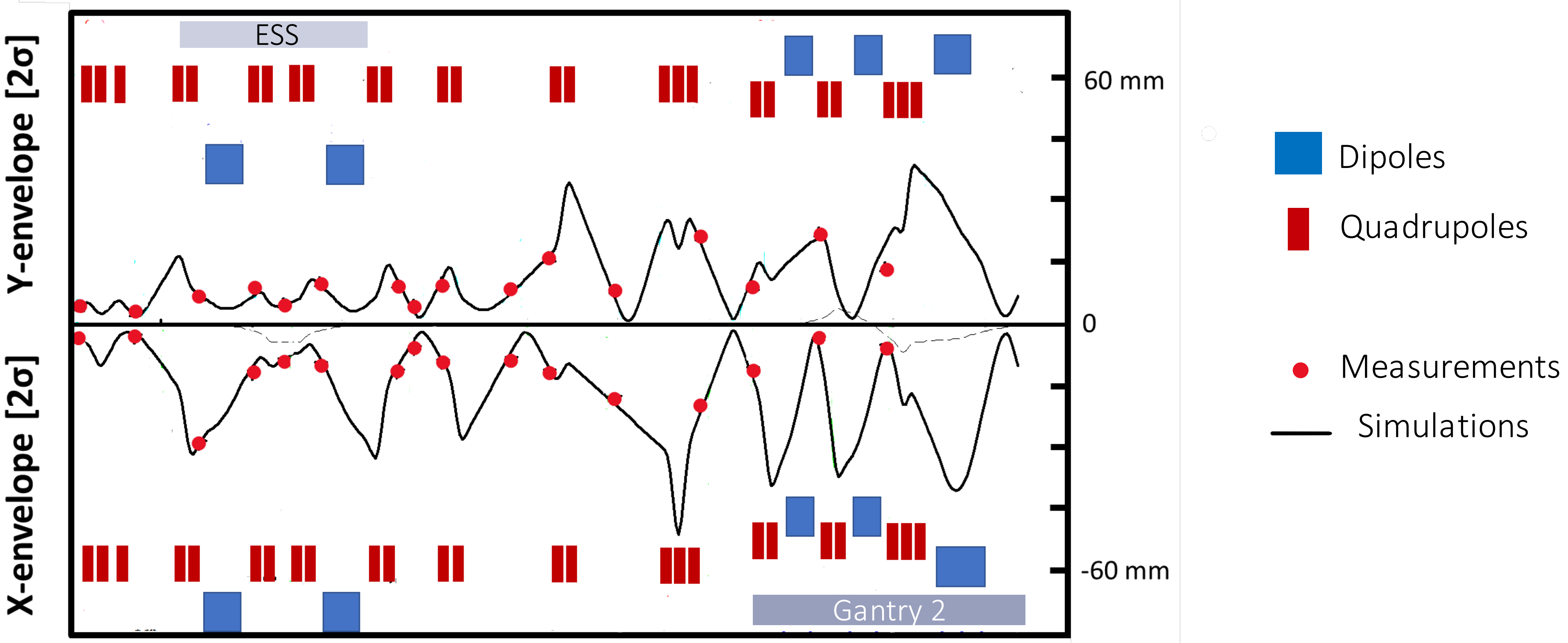
Dölling, Rudolf. et al 2006, Dölling, Rudolf. et al 2004.

Plane parallel ionisation chambers

- In the nozzle
- Current measurement
- From the ratio between the current at from the cyclotron and the current measured in the nozzle, we could calculate the transmission

Lin, Shixiong, et al. Medical physics 36.11 (2009)

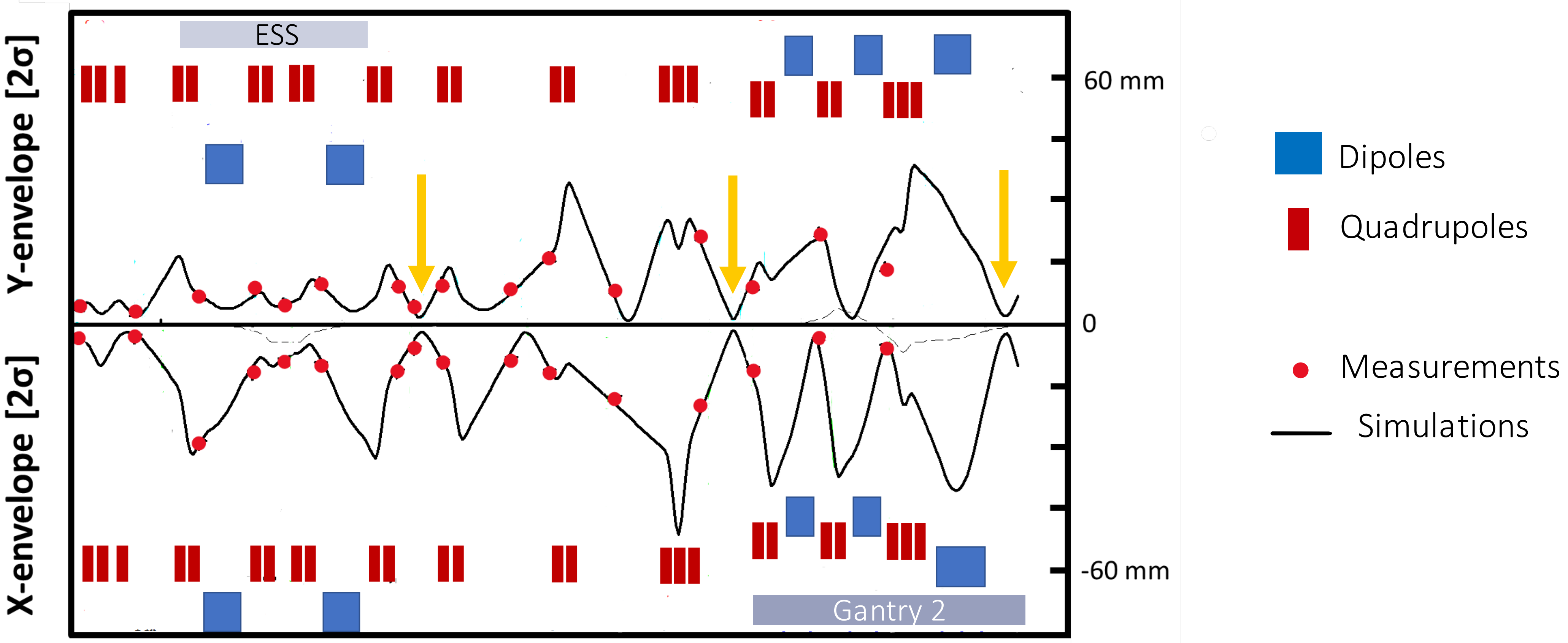
Beam tune - Transport



Distance to the treatment room

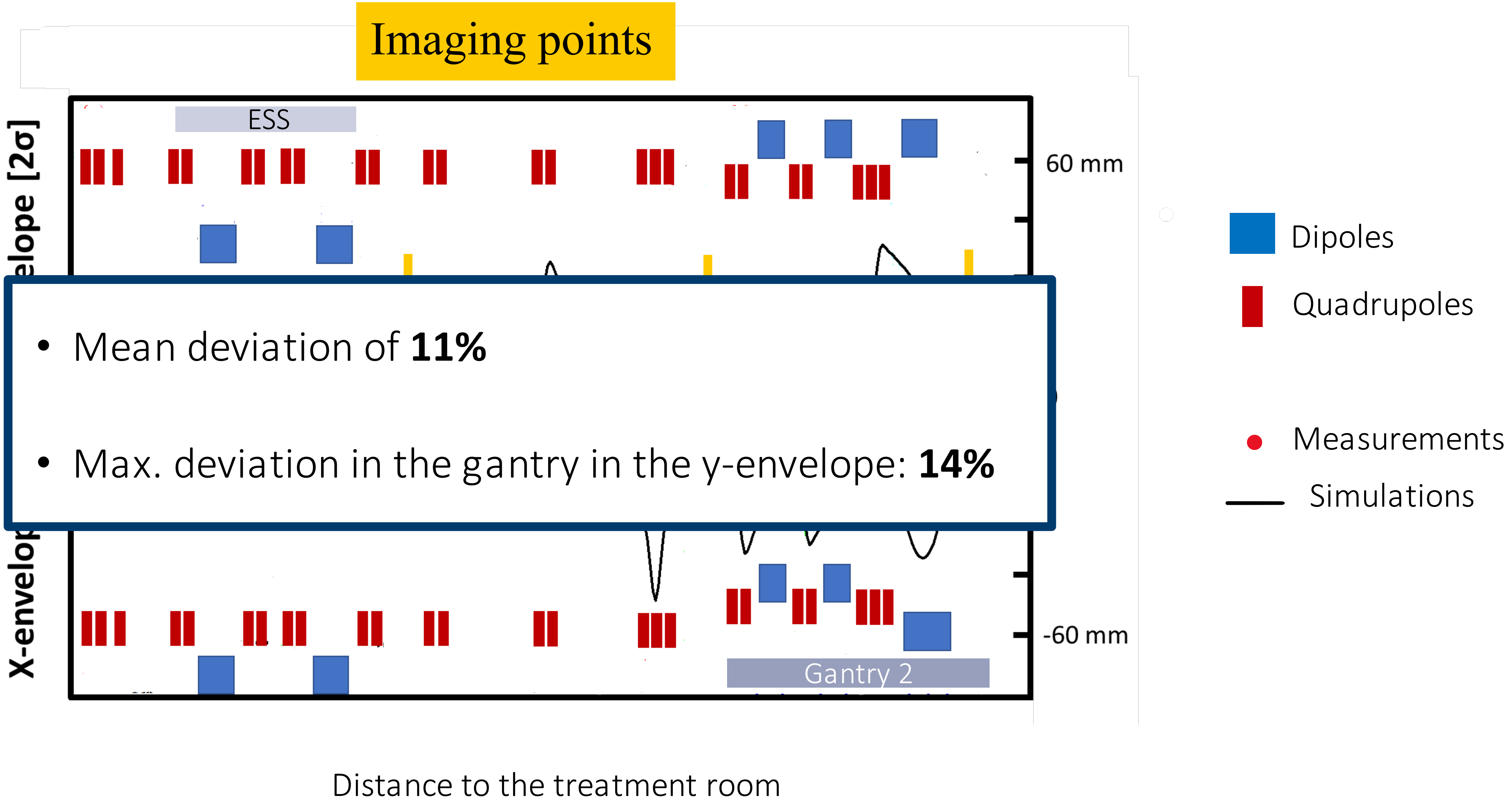
Beam tune - Transport

Imaging points



Distance to the treatment room

Beam tune - Transport



- Mean deviation of **11%**
- Max. deviation in the gantry in the y-envelope: **14%**

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Discussion

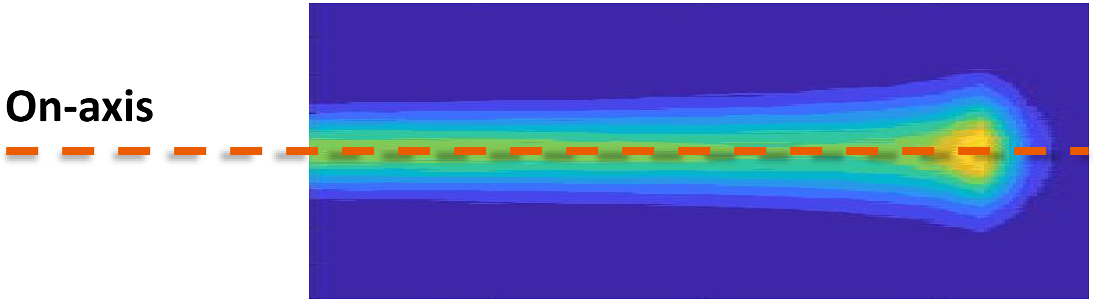
Possible reasons for discrepancy:

- the initial beam size definition may not be accurate
- deformation of the beam in y due to the vertical deflector used to reduce the beam current (0.2 nA)
- the profile monitors along the beamline do not work optimally at low current and for very narrow beams with a width comparable to or smaller than the strip pitch, the width is usually overestimated

Simulations provided us a beneficial guide for beam line tuning, offering an important qualitative description of our beam transport

Transmission

- Almost **90%** transmission measured at the patient position
- We can achieve a current of 720 nA **(>9000 Gy/s on axis),** thus enabling investigations of FLASH radiotherapy (>40 Gy/s) with protons



PSI Gantry 2 is now a versatile irradiation facility able to work under different dose rate conditions

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Adaptation of Gantry 2

Beam optics for 250 MeV

Beam charachteristics at the patient position

Matrix matching optimisation criteria

- **Problem**: gantry-angle dependent beam size at the isocentre
- **Solution**: Matrix Matching* criteria to achieve angle-independent tune

Optimisation criteria:

- Symmetric beam size at the gantry entrance
- Beam waist at the gantry entrance
- Diagonal transfer matrix from the gantry entrance to the isocentre.

*Benedikt, Michael, and Christian Carli. "Matching to gantries for medical synchrotrons." Proceedings of the 1997 Particle Accelerator Conference (Cat. No. 97CH36167). Vol. 2. IEEE, 1997.

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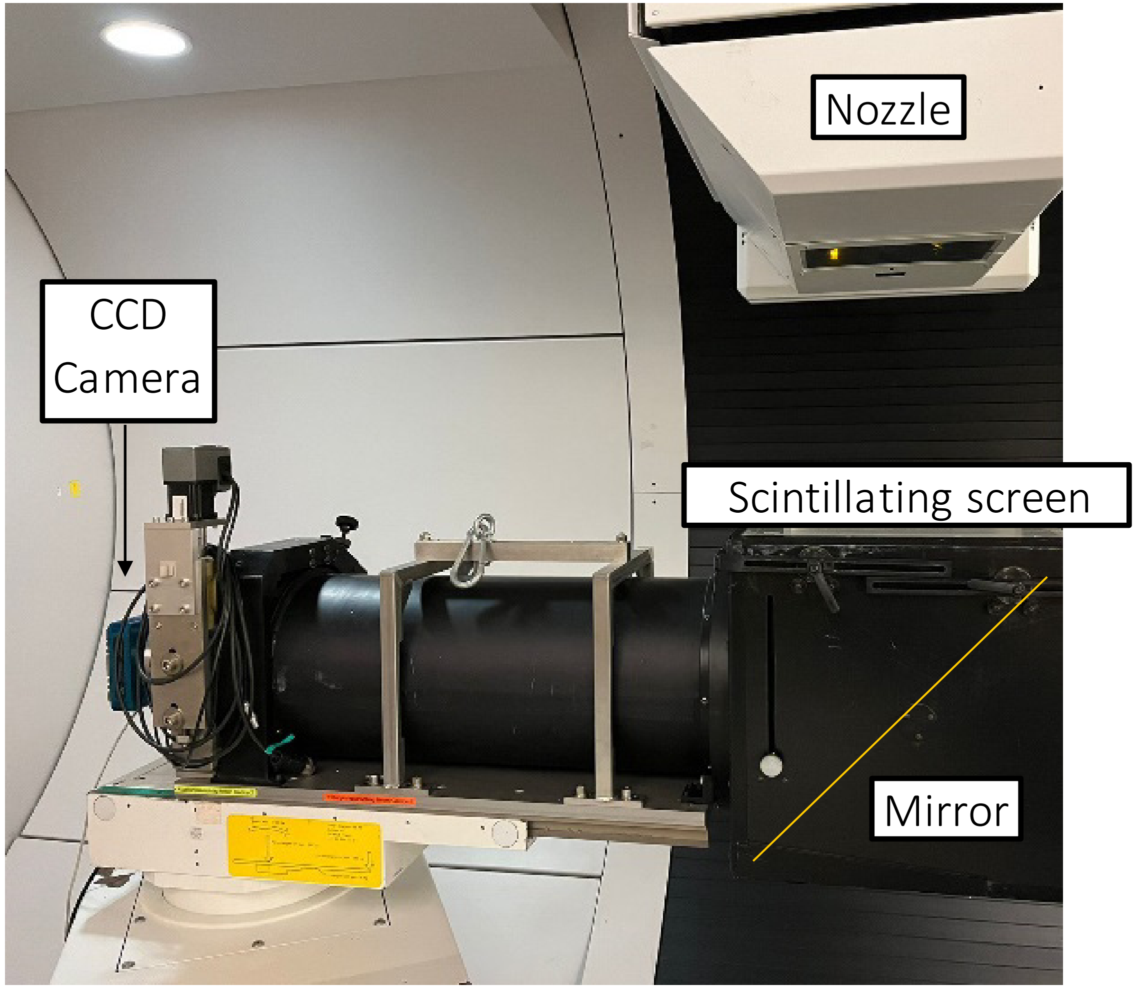
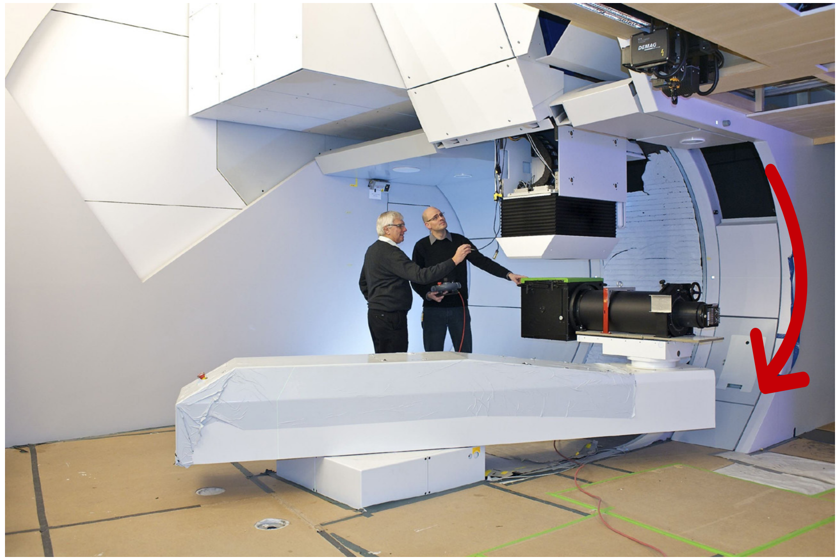
Measurement

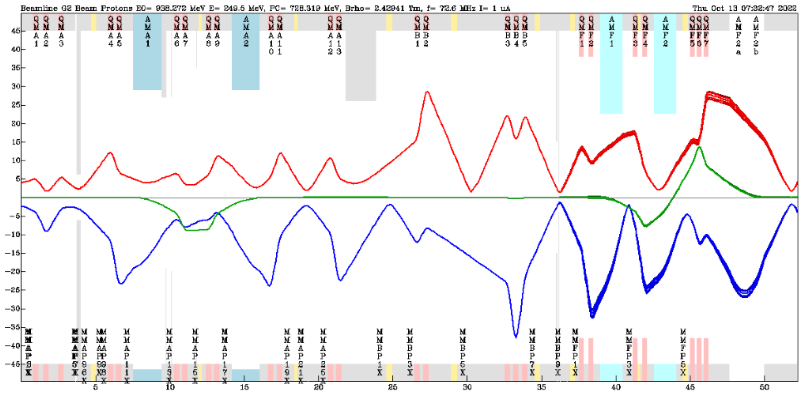


- Beam size at the isocentre measured with a (charge coupled device) CCD camera
- Resolution of 0.3 mm
- The nozzle can be rotated from 0° to 190°



AZ, Markus Fischer

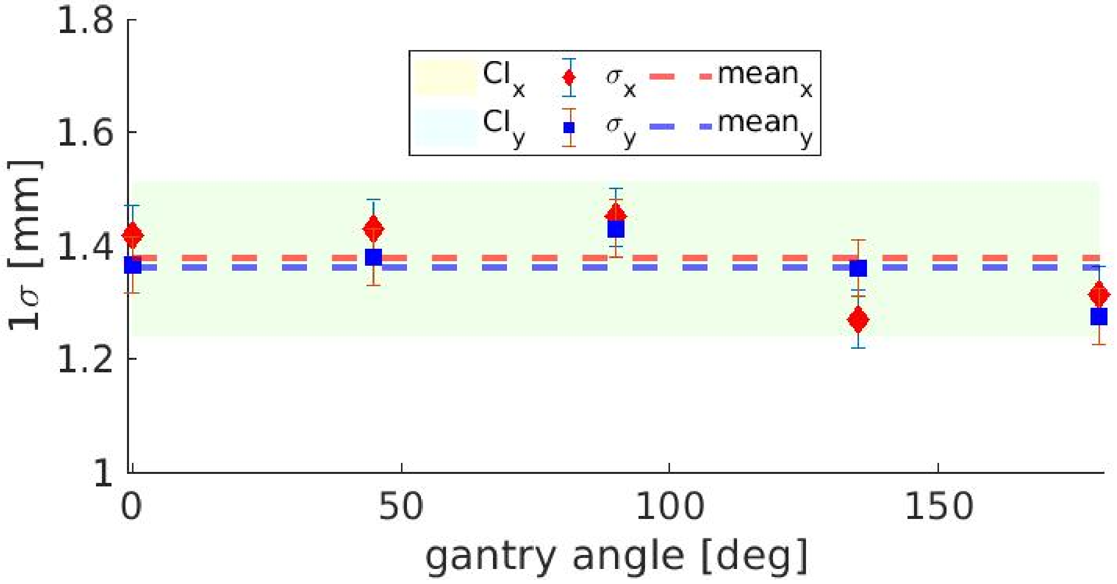
Beam size at the patient position



- Mean value:
  - σ_x = 1.37 mm
  - σ_y = 1.36 mm

Deviation below 10%

Scattering effects in the patient will cancel this deviation



- Multi Coulomb Scattering in the nozzle and in air contribute to almost **30%** of the measured beam size at isocentre. Therefore, scattering contributes to achieving a symmetric beam at the isocentre

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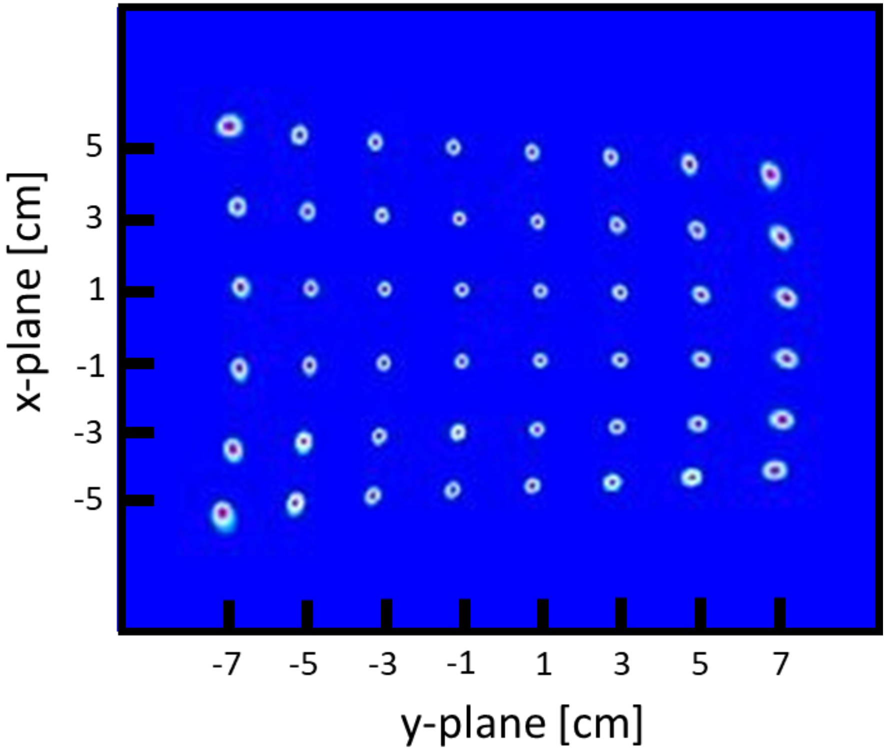
Scanning map

Scanning map: **12 x 16** cm^2 (limited scanning range due to higher momentum)



- Non parallelism due to the effective field edge curvature (> 0.4 m^{-1}) at the exit of the poles and the large gap of the last dipole.

From [11]

- Treatment area always at the isocentre, so only slightly affected by the distortion
- Treatment size for FLASH irradiation usually small (< 3 x 3 cm)

Is Gantry 2 ready for clinical trials?

- Monitors (recombination effects, dose rate dependency, ...)
- Regulations to use high dose in Gantry 2
- The biggest challenges in delivering FLASH with a cyclotron are related to beam energy changes.

UPSTREAM with a degrader	DOWNSTREAM with range shifters or energy modulators (ridge filter)
• Reduce significantly the transmission • Small beam size	• Less losses • Increases the beam beam size (advantage of small spots) • Already used for FLASH in Gantry 1 [9]

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UPSTREAM with a degrader

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DOWNSTREAM with range shifters or energy modulators (ridge filter)

- Less losses
- Increases the beam beam size (advantage of small spots)
- used for FLASH in Gantry 1 [9]

Combination of the two

Conclusion

We adapted a cyclotron-based proton gantry to achieve **ultra-high dose rates** at 250 MeV fully transparently to clinical activity

We have achieved the **desired beam quality** (symmetric and small beam size at the isocenter, angle independent beam size, regular grid) for FLASH PBS

Since most of the modifications are performed on the beam optics, the **method transferable** to other facilities, too.

As a result, PSI Gantry 2, an operating clinical gantry, will provide a unique setting for researching FLASH-PT and demonstrating FLASH's adaptability in the clinic.

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Many thanks go to:

- Vivek Maradia
- Renè Kunzi
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- Damien C. Weber
- Antony J. Lomax
- David Meer
- Serena Psoroulas

And the PSI magnetic and power supply group

Foundation:

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Thank you for your attention!

Appendix:

- References
- PSI beamline – Gantry 2
- Accurate comparison measurement-simulation (beam tune)

Contact:

Isabella Colizzi

isabella.colizzi@psi.ch

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References

[1] Favaudon, Vincent, et al. "Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice." Science translational medicine 6.245 (2014): 245ra93-245ra93

[2] Bourhis, Jean, et al. "Treatment of a first patient with FLASH-radiotherapy." Radiotherapy and oncology 139 (2019): 18-22.

[3] Mascia, Anthony E., et al. "Proton FLASH Radiotherapy for the Treatment of Symptomatic Bone Metastases: The FAST-01 Nonrandomized Trial." JAMA oncology (2022).

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[5] Patriarca, Annalisa, et al. "Experimental set-up for FLASH proton irradiation of small animals using a clinical system." International Journal of Radiation Oncology* Biology* Physics 102.3 (2018): 619-626.

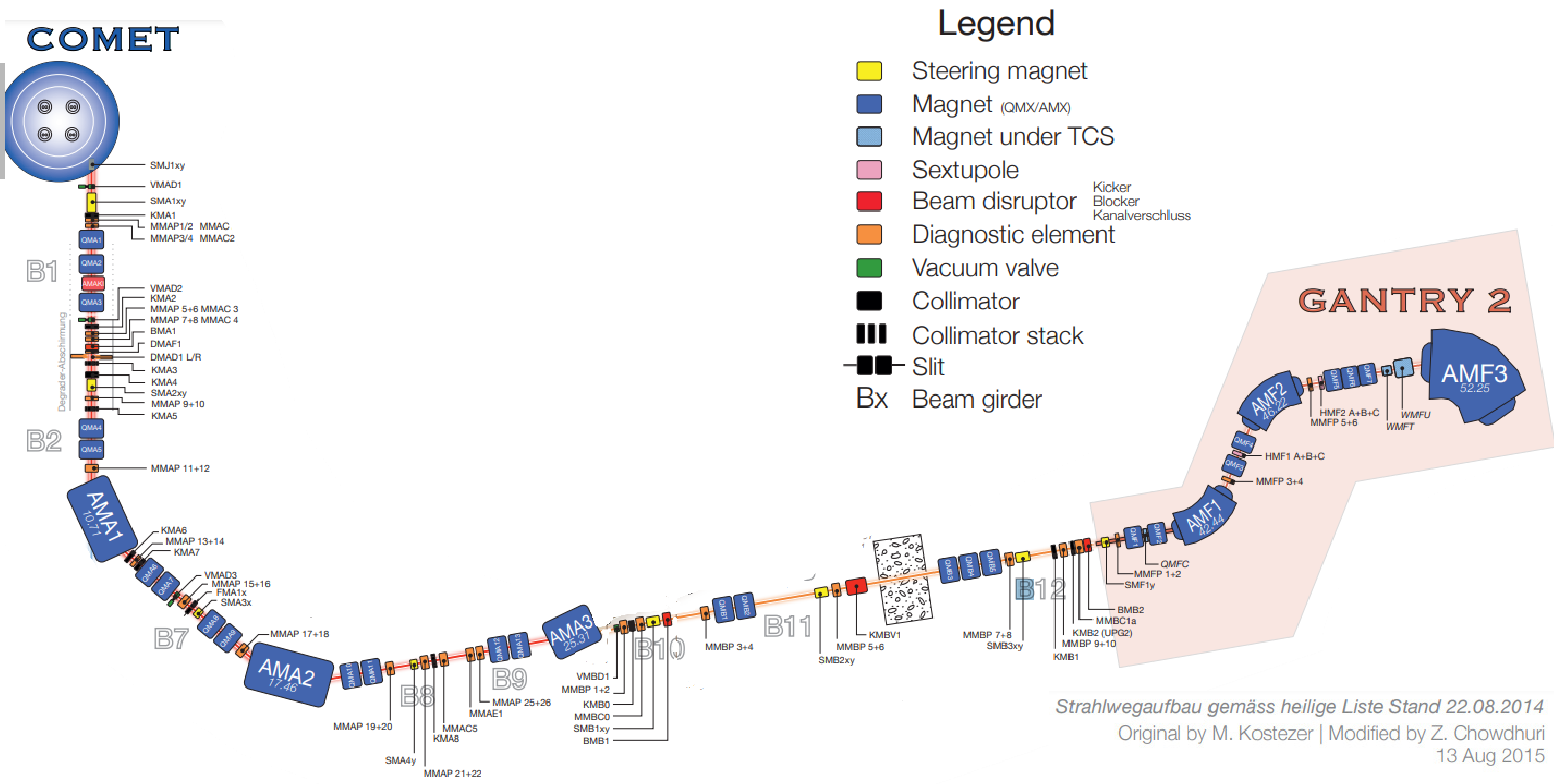
[6] Gerbershagen, Alexander, et al. "Measurements and simulations of boron carbide as degrader material for proton therapy." Physics in Medicine & Biology 61.14 (2016): N337.

[7] Pedroni, Eros, et al. "The PSI Gantry 2: a second gen-eration proton scanning gantry." Zeitschrift für medizinische Physik 14.1 (2004): 25-34.

[8] Owen, Hywel, et al. "Technologies for delivery of proton and ion beams for radiotherapy." International Journal of Modern Physics A 29.14 (2014): 1441002

[9] Nesteruk, Konrad P., et al. "Commissioning of a clinical pencil beam scanning proton therapy unit for ultra-high dose rates (FLASH)." Medical physics 48.7 (2021): 4017-4026.

PSI beamline



Comparison Measurement-Simulation