Generation of clinical proton minibeams using magnetic focussing

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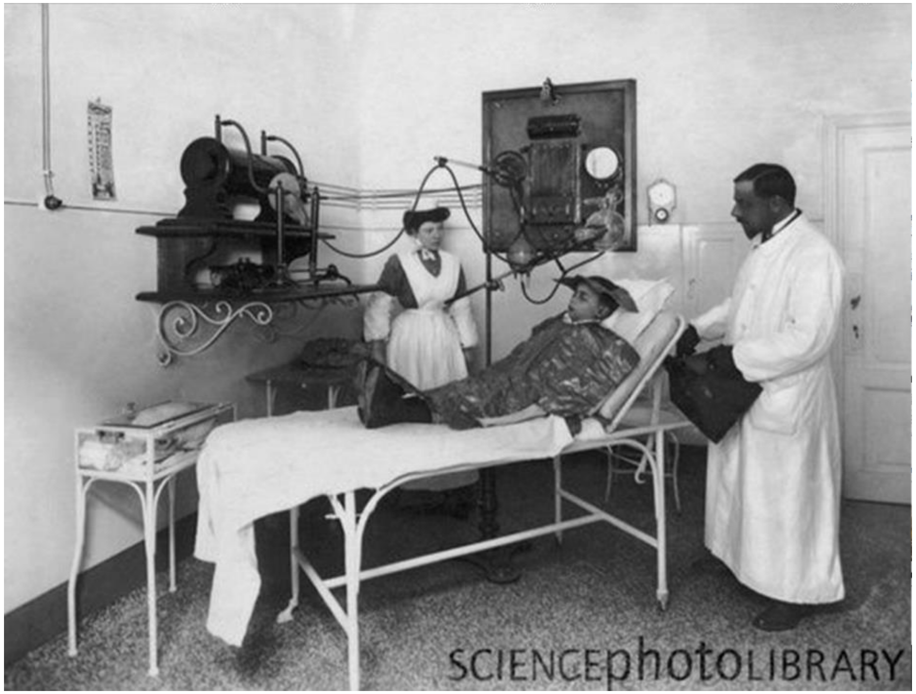
Clinical proton minibeams

are used for

proton minibeam radiation therapy.

Radiation therapy (RT)

- radiation therapy: eliminate cancer using ionising radiation
- most treatments using x-rays
- x-rays discovered Nov 1895 (Röntgen)
- first treatment with x-rays Jan 1896 (Grubbé)
- proton therapy suggested 1946 (Wilson)
- first treatment with protons 1954

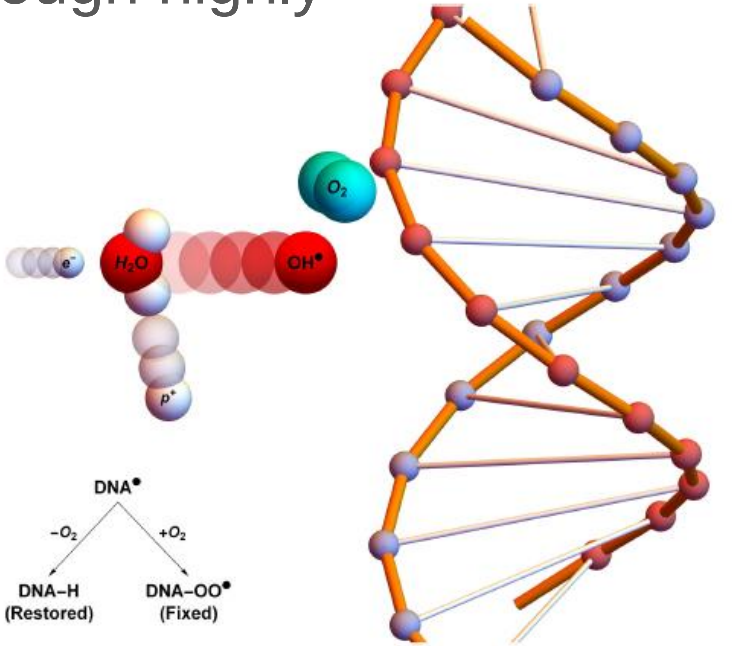


Source: Giap and Giap, *Historical perspective and evolution of charged particle beam therapy*, Transl Cancer Res 2012;1(3):127-136

Radiation therapy (RT)

Basic principle

1) radiation ionises molecules throughout the cell
2) direct DNA damage or indirect through highly reactive (free) radicals
3) DNA damage accumulates (SSB, DSB, base damage…)
4) cell death



Source: http://www.ox.ac.uk/news/science-blog/breath-fresh-air-—-shedding-light-oxygen-radiation-and-cancer-treatment, 03.05.19

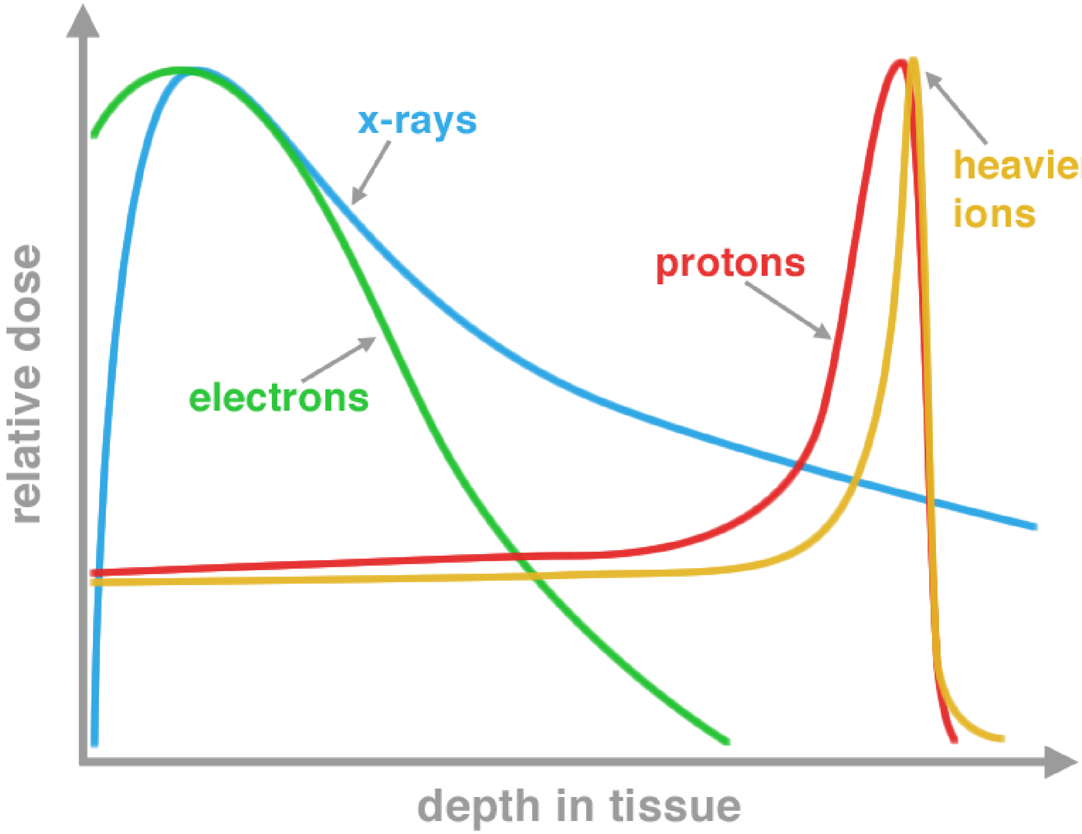
Clinical proton minibeams

are used for

<u>proton</u> minibeam radiation therapy.

Radiation therapy (RT)

Particles used for RT

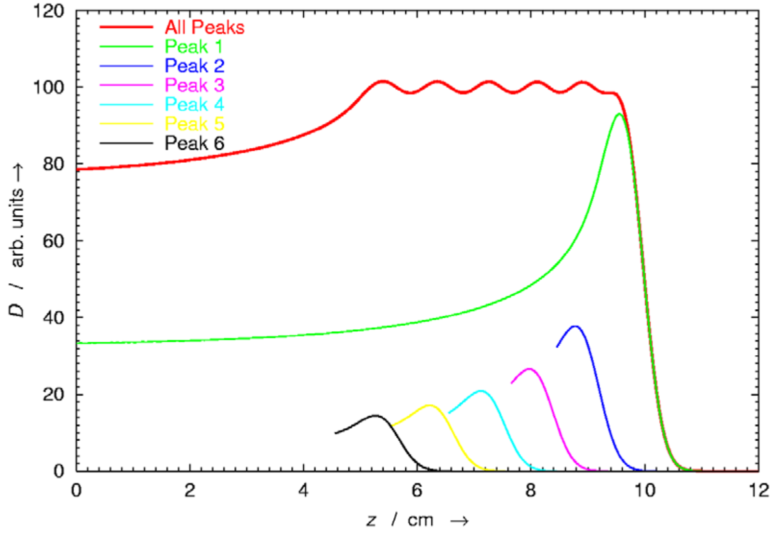


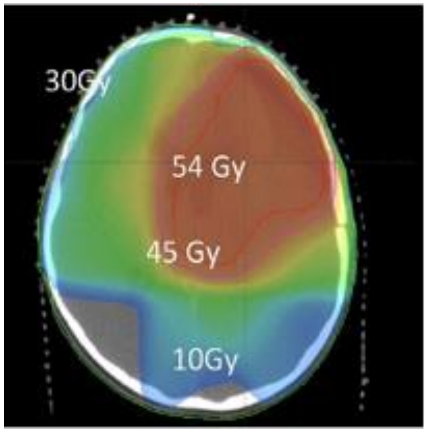
protons/ions

exhibit *Bragg peak*

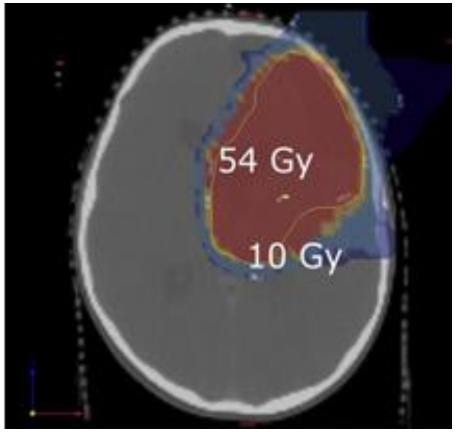
Proton therapy

- more targeted dose distribution (Bragg peak)
- combine multiple pristine Bragg peaks to form a spread-out Bragg peak





irradiating a brain tumor with X-rays



irradiating a brain tumor with protons

Source: Newhauser and Zhang, *The physics of proton therapy*, Phys Med Biol 2015

Clinical proton minibeams

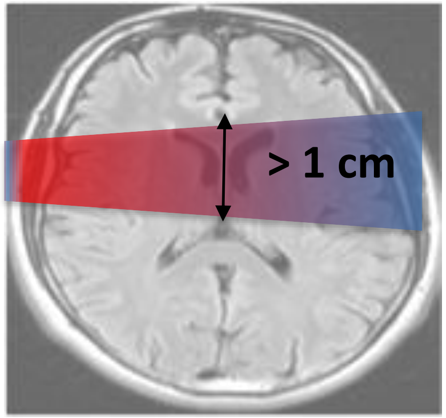
are used for

proton <u>minibeam</u> radiation therapy.

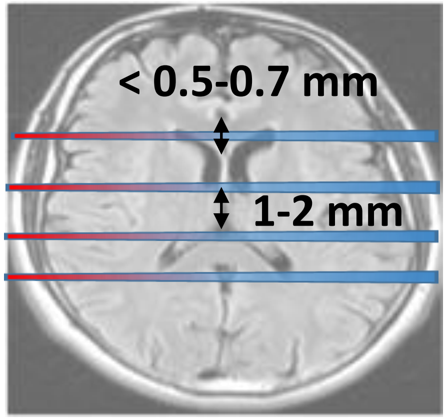
Spatially fractionated RT (SFRT)

Standard RT

large beam sizes
(> 1 cm^2)
+
homogeneous
dose distributions



Spatially fractionated RT

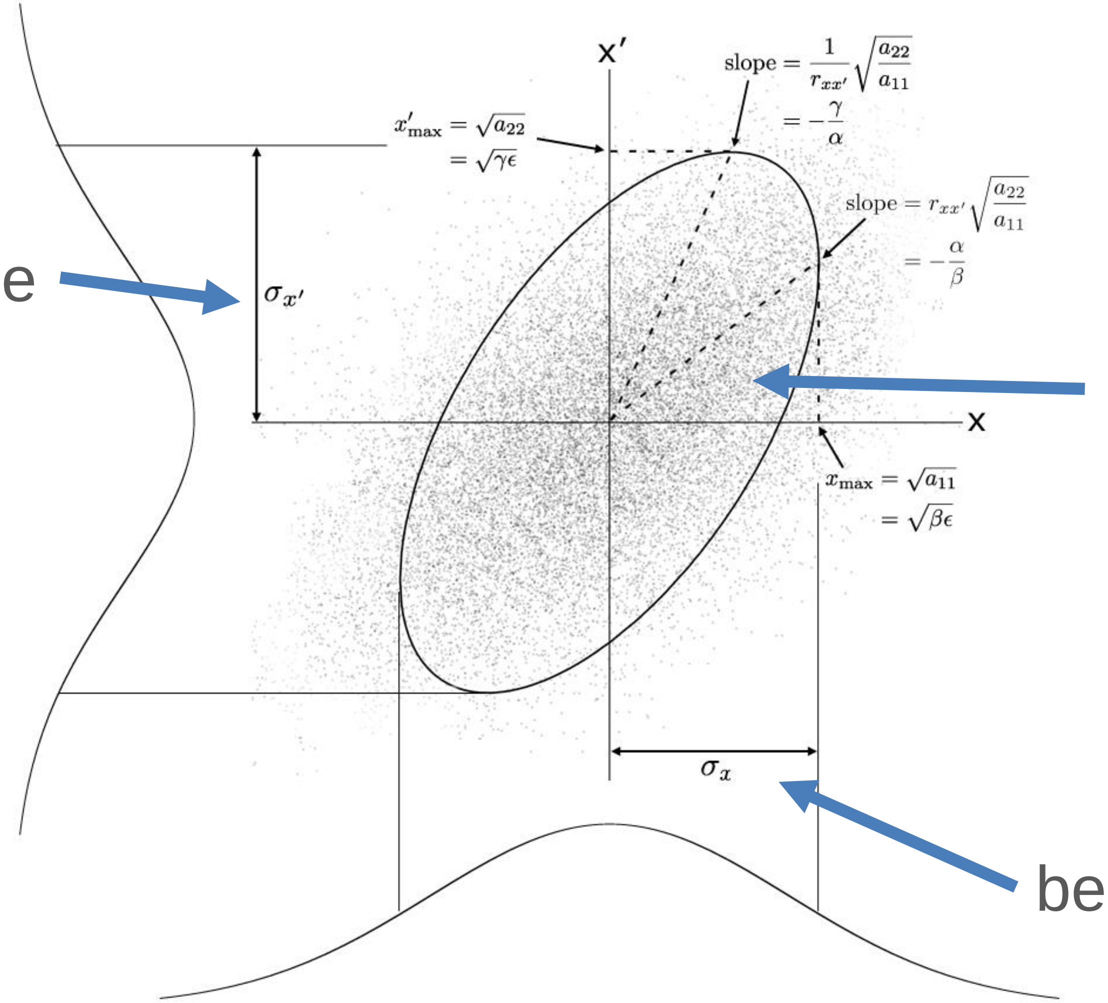


very narrow beam sizes
separated by
areas of low dose
+
heterogeneous
distributions

→ tolerance of normal tissue increases

Some vocabulary

Beam ellipse in phase space



divergence

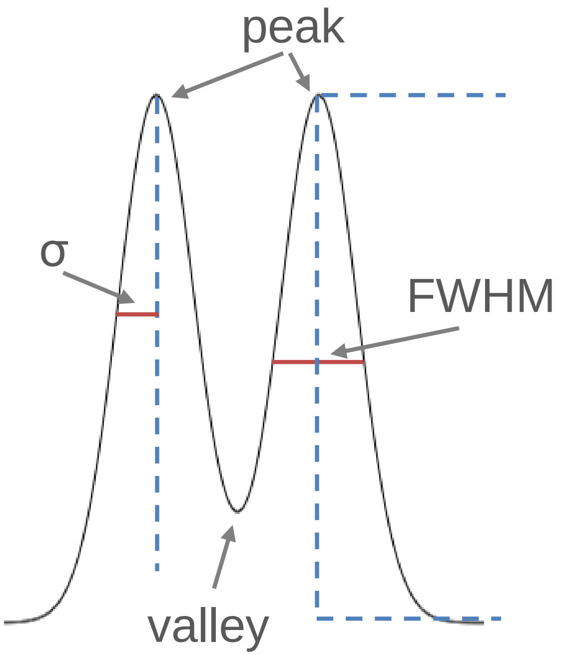
individual particles

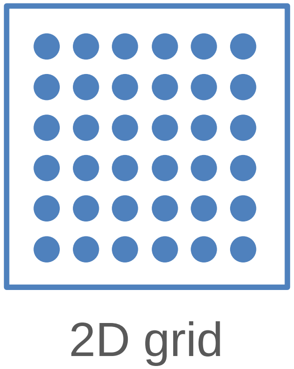
beam size

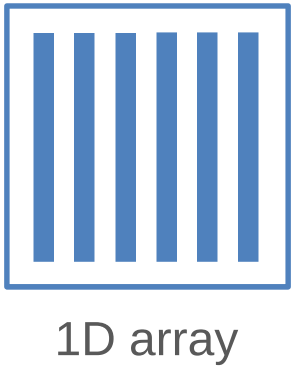
Some vocabulary

Vocabulary for SFRT:

- peaks and valleys: peak-to-valley dose ratio (**PVDR**)
- beam width: σ, full width at half maximum (**FWHM**)
- GRID therapy
  - 2D “grid” of beams
- microbeam RT (MRT)
  - 1D “array” of beams
  - beam width 25 – 75 µm
- **minibeam RT (MBRT)**
  - 1D “array” of beams
  - beam width 300 µm – 1 mm







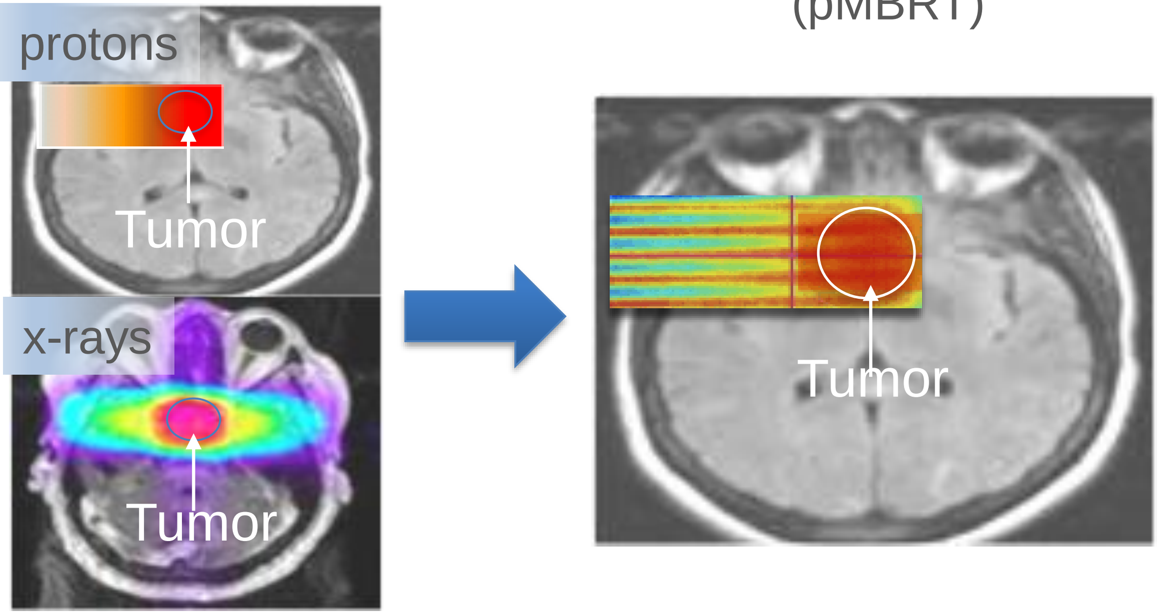
Proton minibeam RT (pMBRT)

Our proposal: a novel approach in disruption with standard RT *(Prezado et al 2013)*

MBRT **+** **superior dose distribution of protons**

Standard

Proton minibeam radiation therapy (pMBRT)



Homogeneous dose in the tumour

+

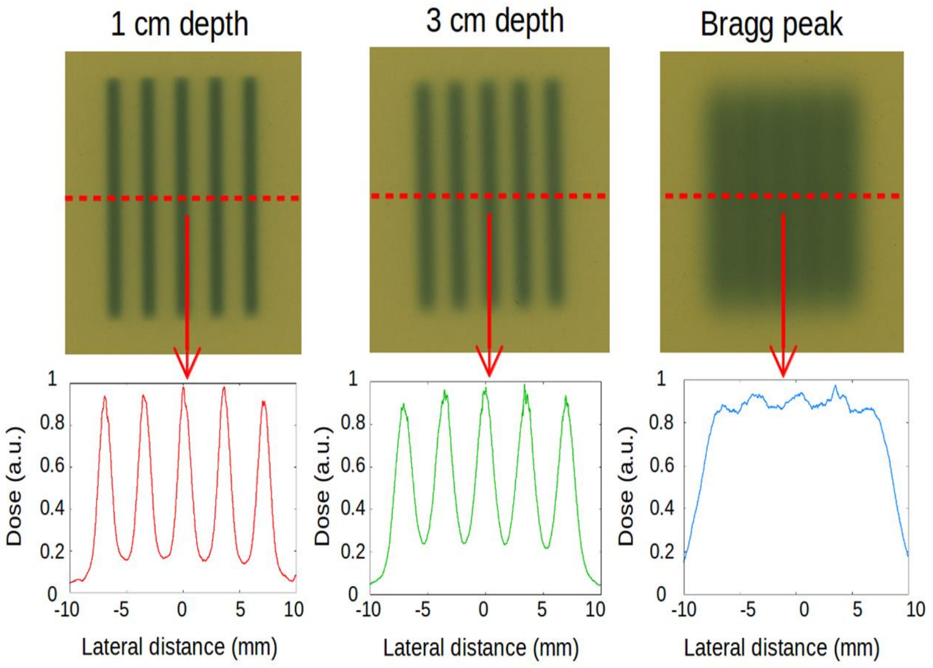
Spatial fractionation in normal tissue

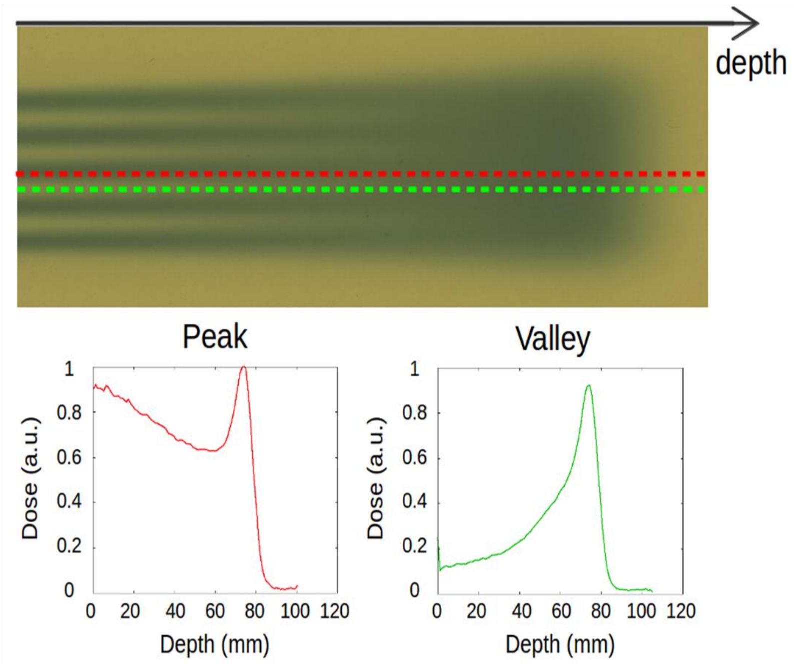
+

Biological advantages of protons

pMBRT - first results

- experimental proof of concept: dose distributions assessed with gafchromic films (Peucelle et al, Med. Phys. 2015)
- minibeam generation: a first prototype with mechanical collimation

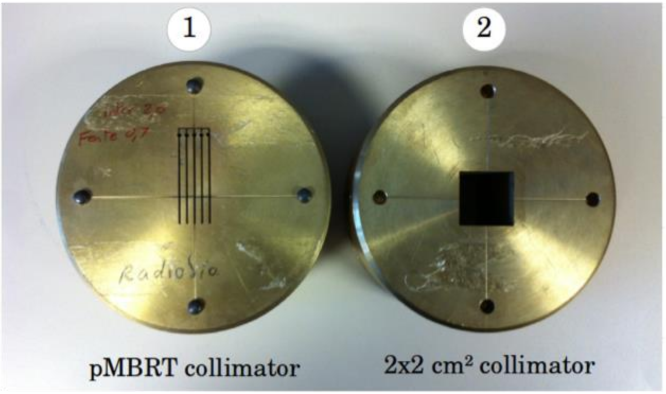


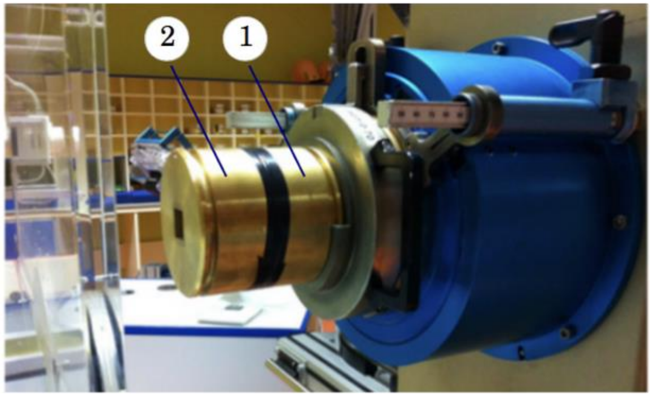


Source: Peucelle et al., Proton minibeam radiation therapy: Experimental dosimetry evaluation, Med Phys 2015

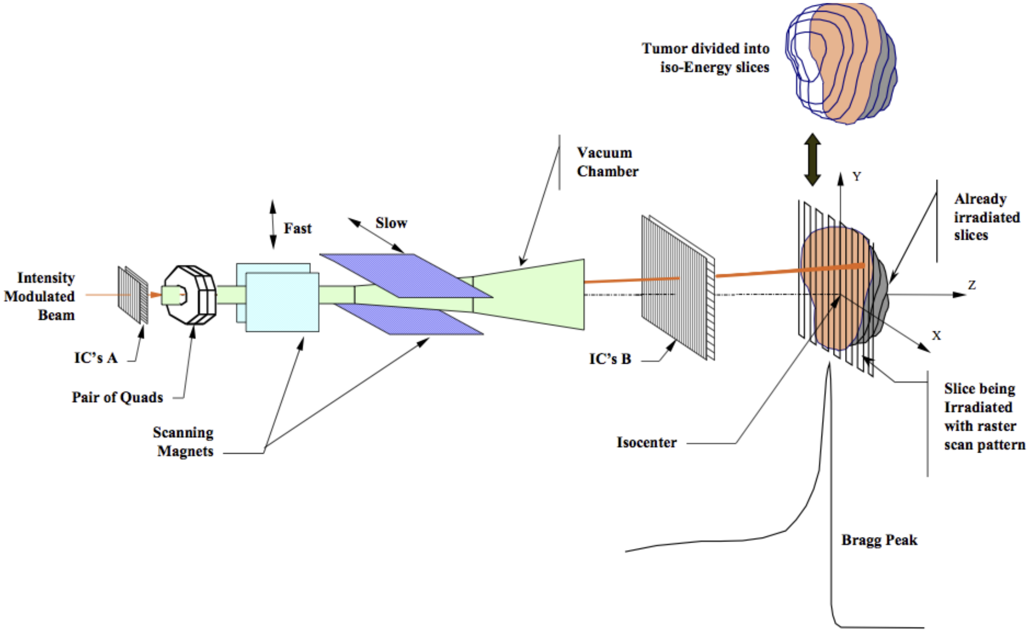
Generation of proton minibeams

Mechanical collimation





Magnetic focussing



schematic of a
PBS (pencil beam scanning) nozzle

Source: Peucelle, *Spatial fractionation of the dose in charged particle therapy*, PhD thesis; Marchand et al., *IBA proton pencil beam scanning: an innovative solution for cancer treatment*, Proceedings of EPAC, Vienna, 2000.

Mechanical vs magnetic collimation

Mechanical collimation

- inefficient
- inflexible (possibly new collimator for different tumors and different energies)
- production of harmful secondary particles (neutrons) close to patient

Magnetic focussing

- full beam used to irradiate tumor
- higher dose rate
- higher PVDR expected
- basically like PBS

  BUT beam much (>10x) smaller

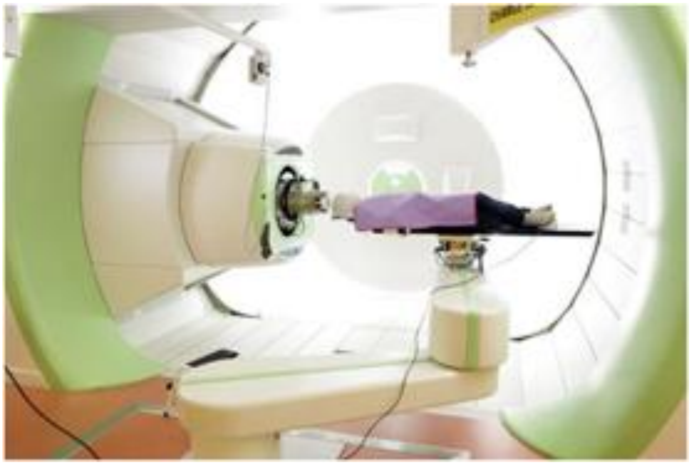
➢ *main challenge:*

generate (sub-)millimetric beams at clinical energies/accelerators and beamlines (existing facilities are designed to deliver beam spots ≥ 1 cm FWHM)

PBS nozzle at CPO

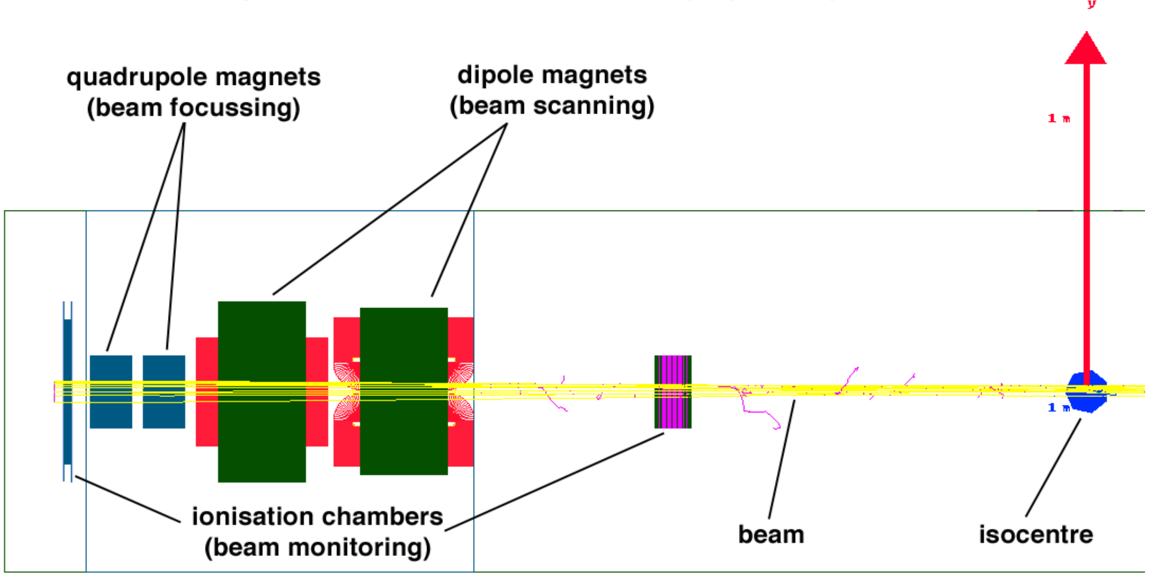
Centre de protonthérapie d’Orsay (CPO)

- more than 7700 patients treated since 1991
- IBA 230 MeV cyclotron
- treat with 70 to 230 MeV proton beams



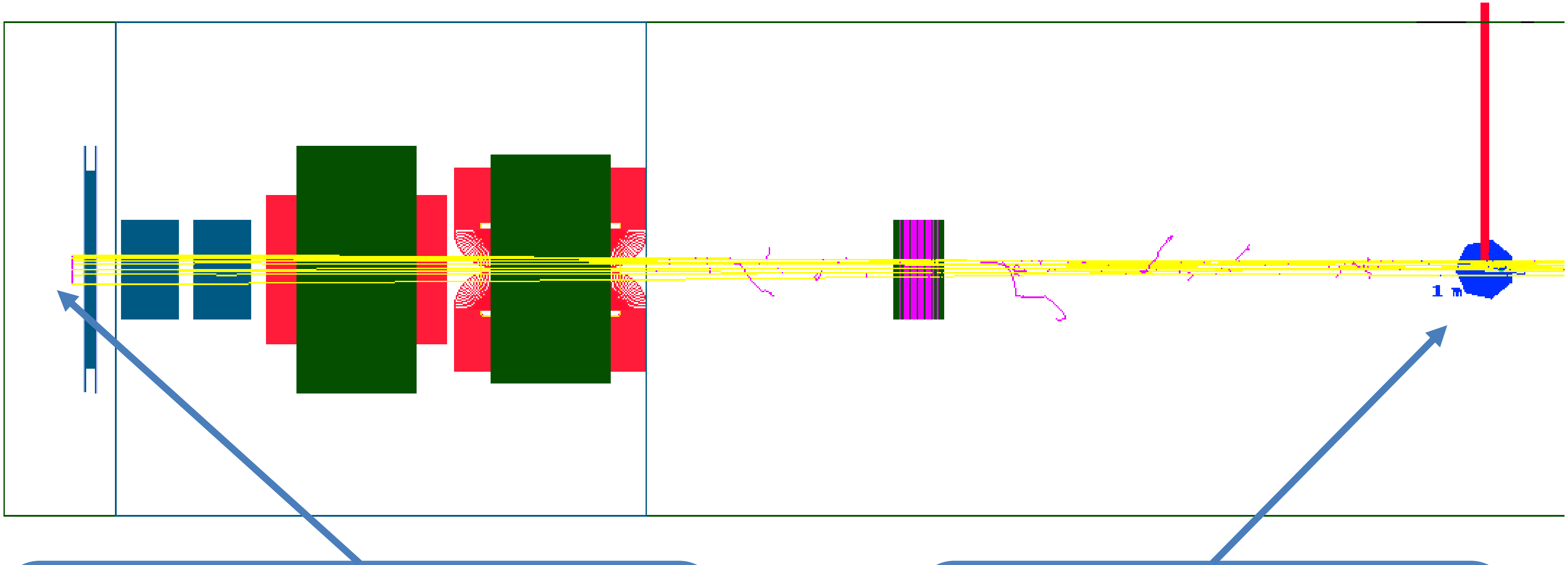
Source: Centre de protonthérapie d’Orsay

Schematic of pencil beam scanning (PBS) nozzle



PBS nozzle at CPO

Current beam sizes at CPO



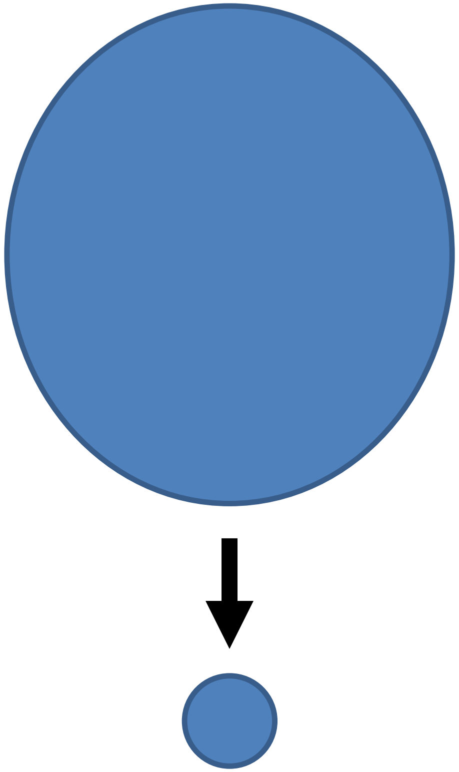
Beam FWHM at nozzle entrance
100 MeV: 20.9 / 30.6 mm
200 MeV: 9.3 / 13.3 mm

Beam FWHM at isocentre
100 MeV: 18.2 / 17.6 mm
200 MeV: 10.5 / 9.9 mm

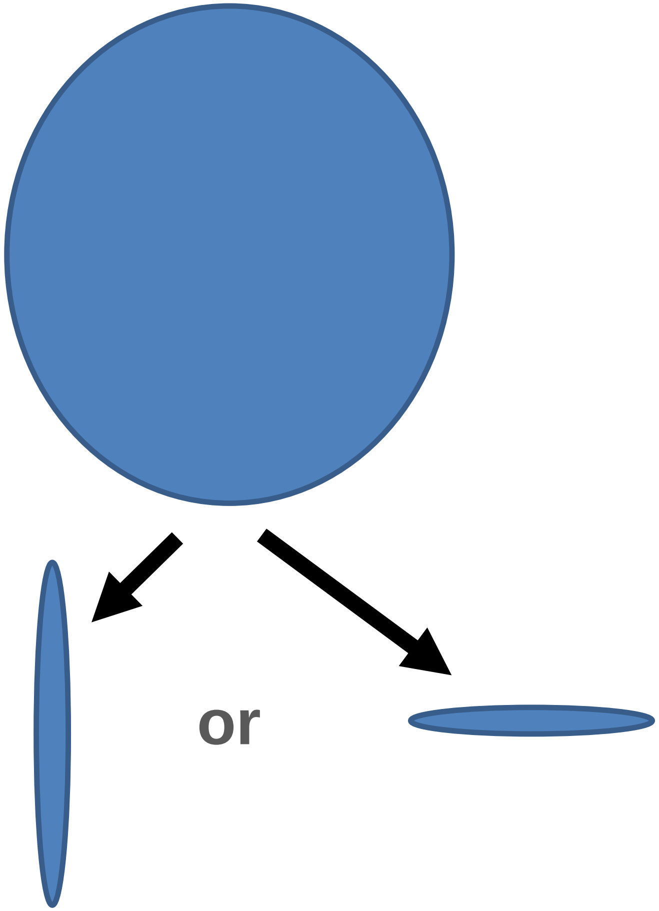
Reduction by a factor 10-20 required!

What’s a small beam?

symmetrically small



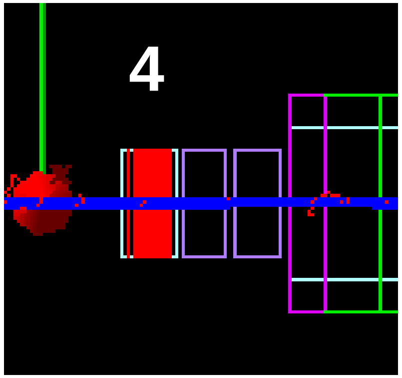
unidirectionally small

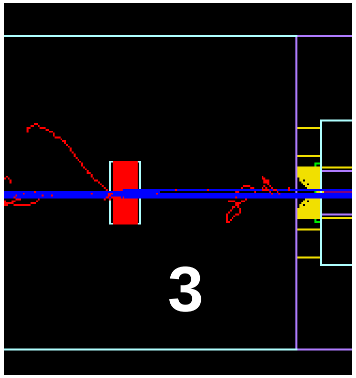


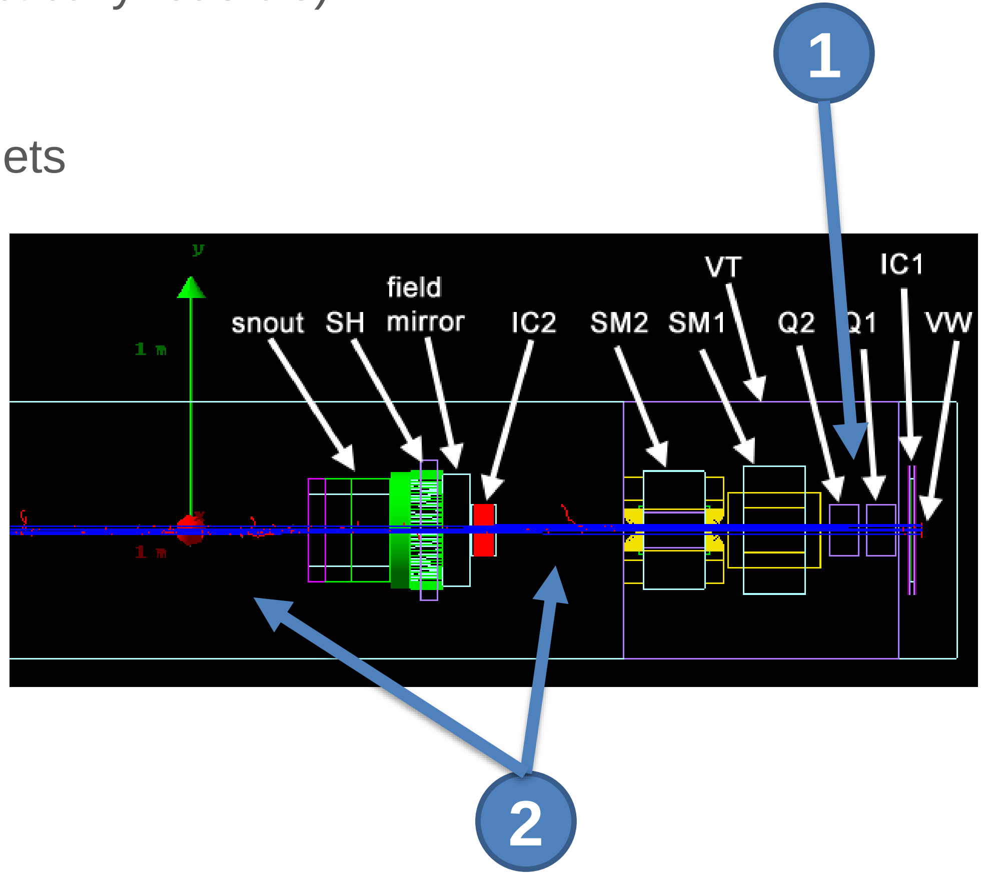
Approaches for beam size reduction

starting from PBS nozzle at CPO:

1) change magnetic fields (quadrupoles)
2) remove air from beam path (not practically feasible)
3) reduce distance to target
4) introduce additional focussing magnets

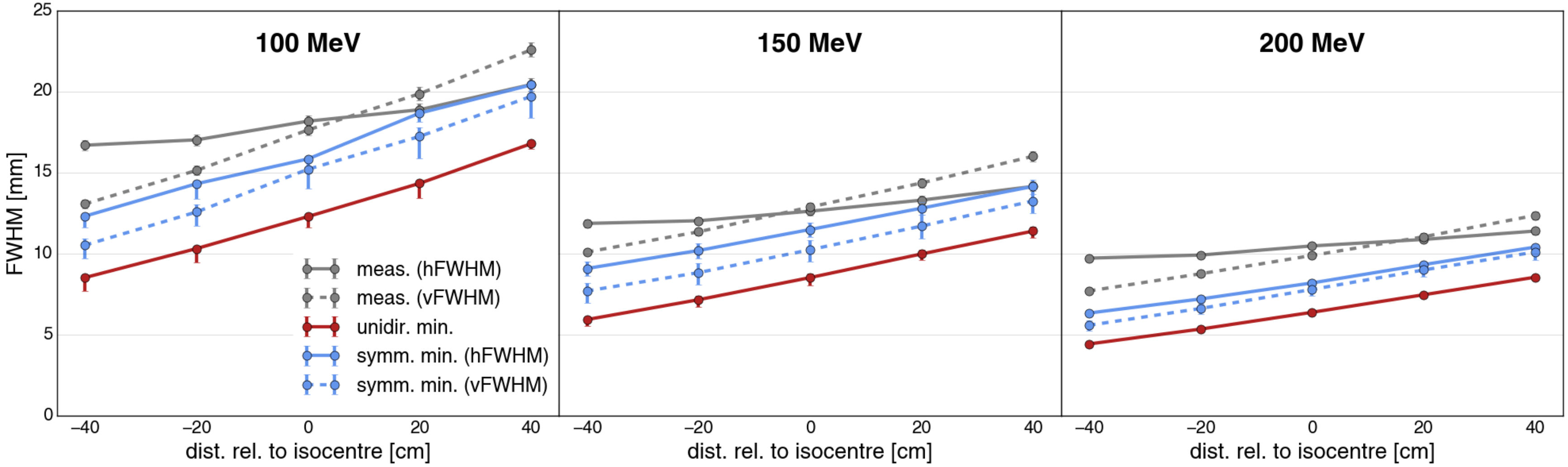




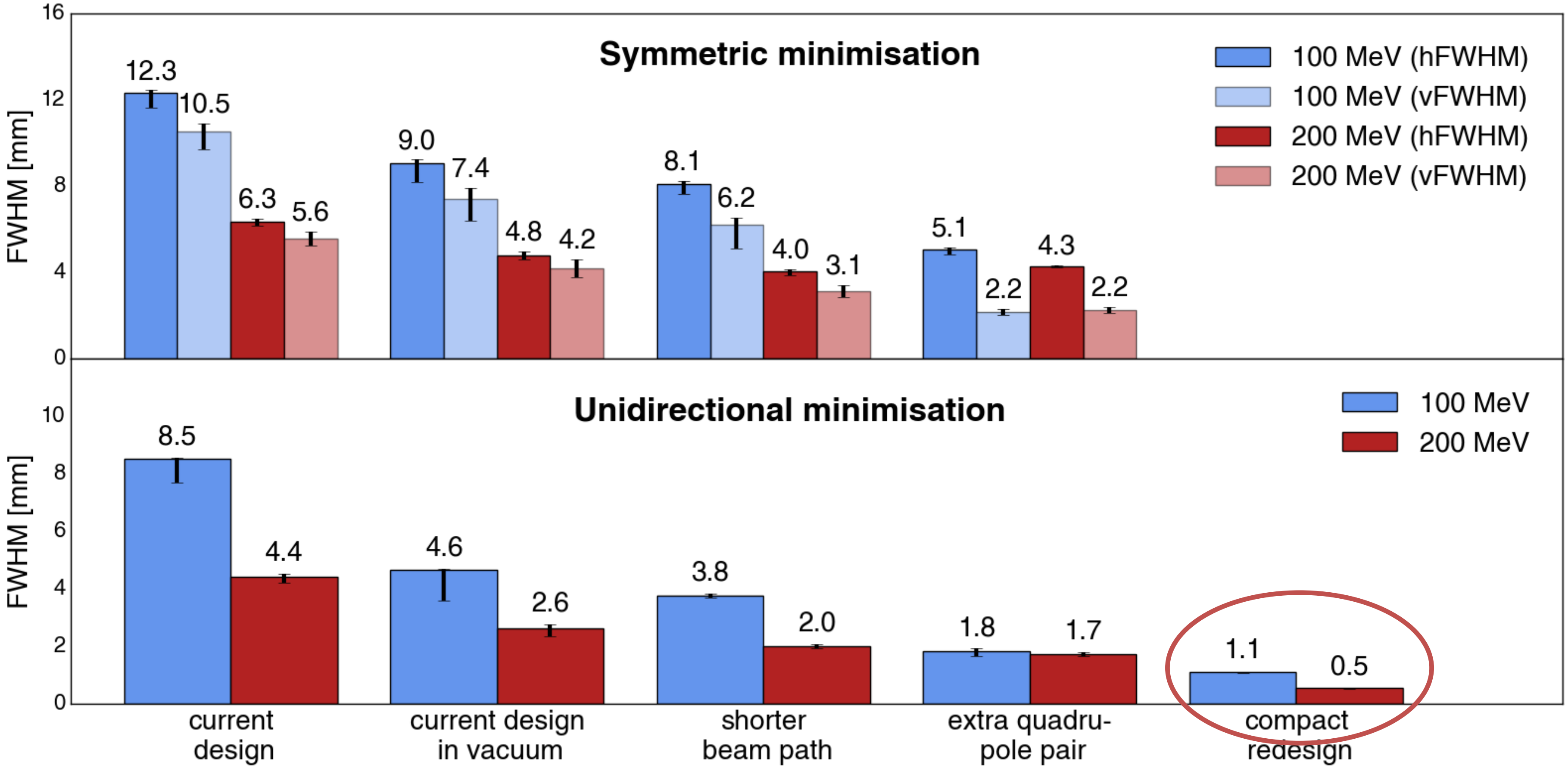


Results

same nozzle, changing only quadrupole fields (1)



Results



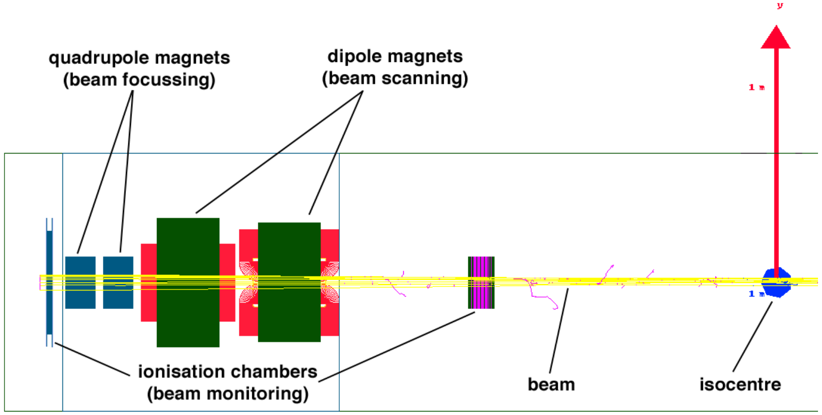
(1) (2) (3) (4)

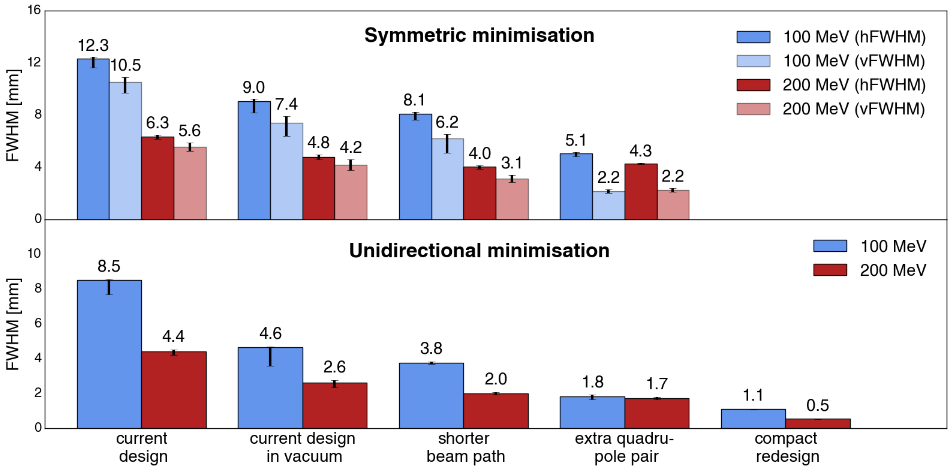
getting there,
but not really satisfactory

What’s next?

- design a new nozzle (more compact, shorter distance to patient)
- define requirements for beam entering nozzle
- check compatibility with existing accelerators/beamlines
- build prototype?

Thank you for your attention!



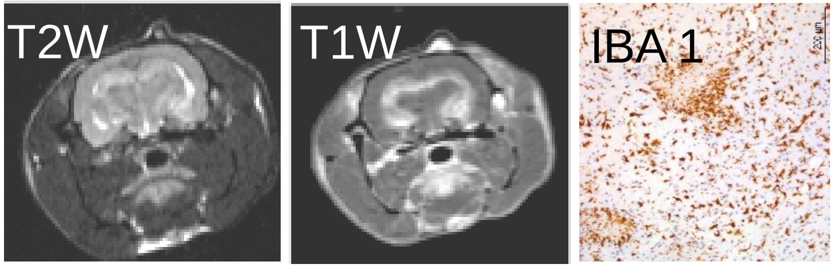


pMBRT - first results

Whole normal rat brain irradiations (6 months follow up) with 100 MeV proton minibeams

Standard proton therapy
(25 Gy/one fraction, n=8)

- skin: moist desquamation
- permanent epilation
- important brain damage



pMBRT
(58 Gy peak dose/one fraction, n=8)

- no skin damage
- reversible epilation
- no brain damage observed

pMBRT offers a net gain in normal tissue resistance

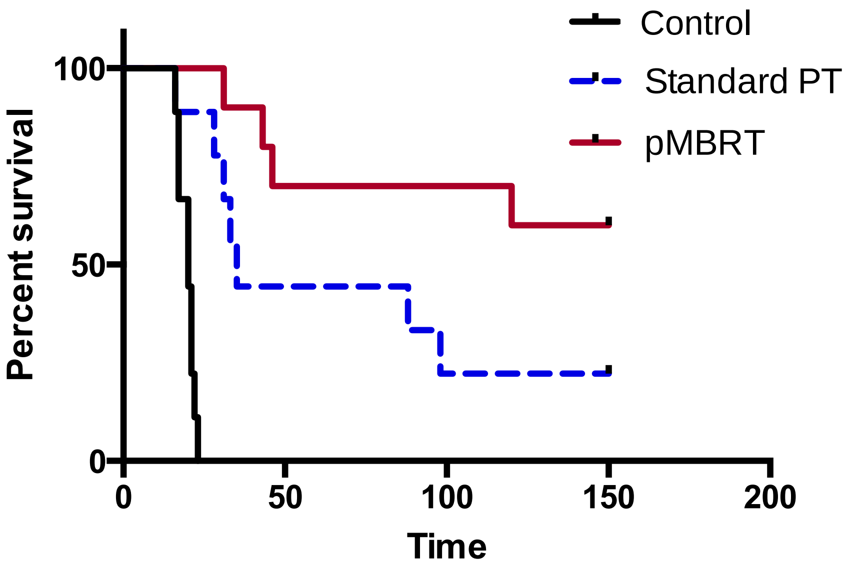
Prezado et al. Scie. Reports 2017

Tumor control effectiveness in glioma (RG2) bearing rats

Three groups

- Control (n=9)
- Standard PT (n=9) 25 Gy
- pMBRT (n=9) 25 Gy

IR 4 days after implantation
5000 cells RG2



Median survival

Controls 20 days

Standard 35 days 20 % of long-term survivals (> 6 months)

pMBRT >150 days 60 % of long term survivals (> 6 months)