Generation of clinical proton minibeams using magnetic focussing

Tim Schneider, IJCLab (ex IMNC), Orsay, France

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schneider@imnc.in2p3.fr

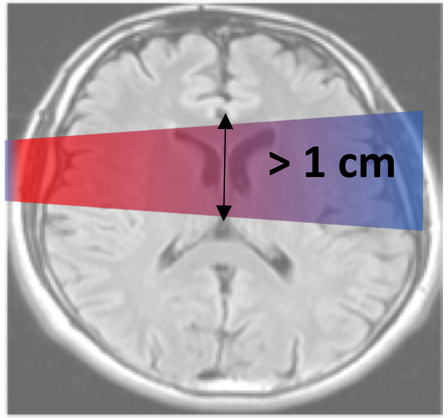
Context

- **proton minibeam radiation therapy** (pMBRT)
- **objective:** optimal implementation of proton minibeam RT in a clinical context
- **minibeams:** beams with small lateral size (FWHM ≤ 1 mm)
- conventional RT treatments can be limited by tolerance dose of normal tissue
- minibeam RT can increase tissue sparing/therapeutic index and widen therapeutic window
- potential fields of application: hypoxic tumours, glioma, …

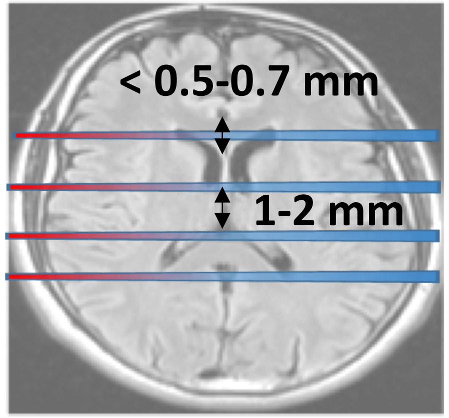
Spatially fractionated radiation therapy

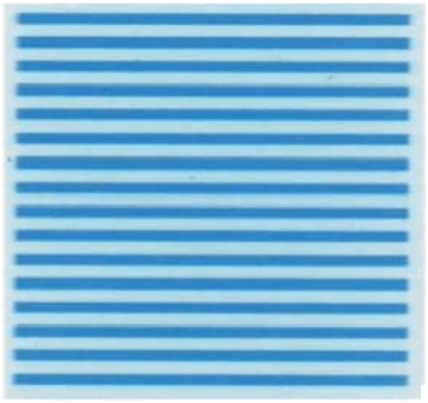
Standard RT

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

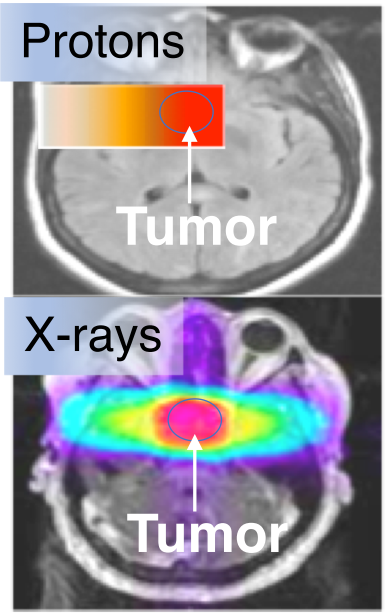
Proton minibeam radiation therapy (pMBRT)

Our proposal: a novel approach in disruption with standard RT

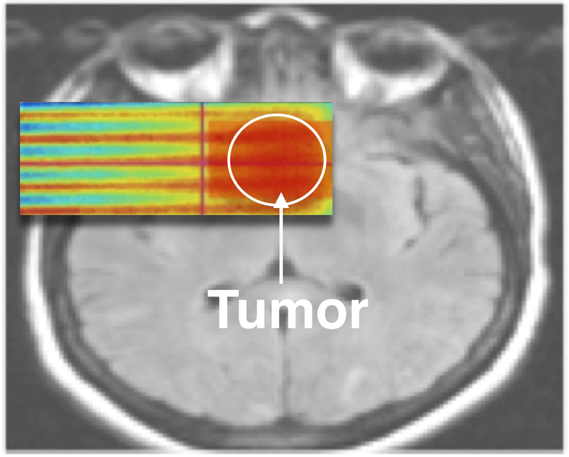
(Prezado et al., Med. Phys. 2013)

Minibeam radiation therapy (MBRT) **+** Different particle type, protons, and specific physics and biology

Standard RT



Proton minibeam radiation therapy (pMBRT)



Homogeneous dose in the tumour

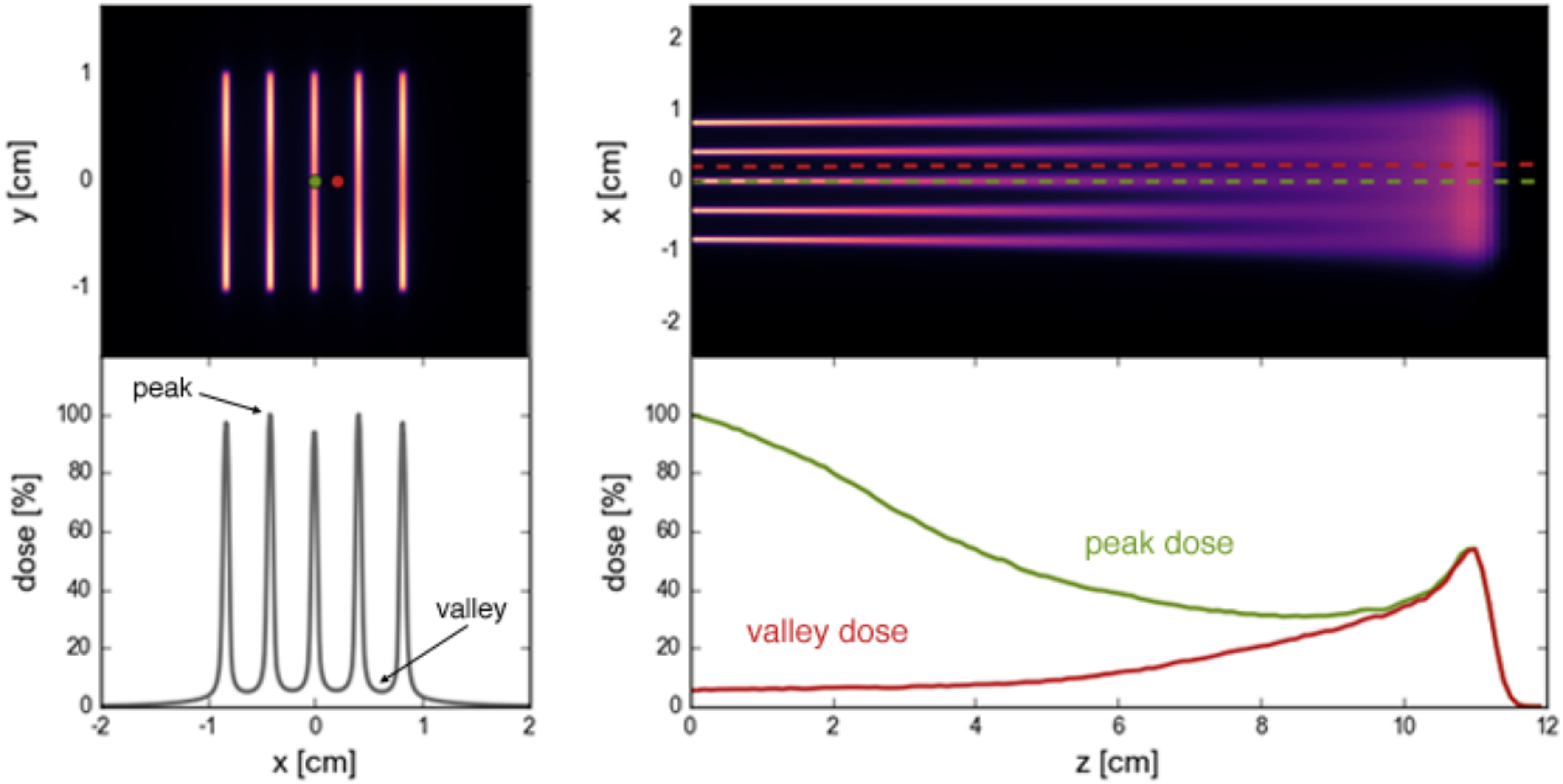
+

Spatial fractionation in normal tissue

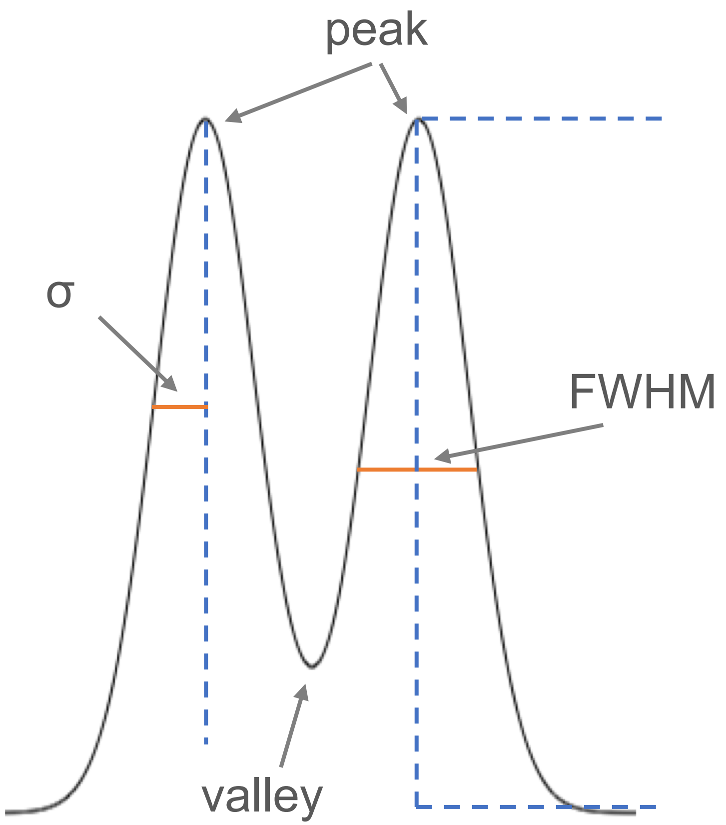
+

Biological advantages of protons

Proton minibeam radiation therapy (pMBRT) II



Proton minibeam radiation therapy (pMBRT) III



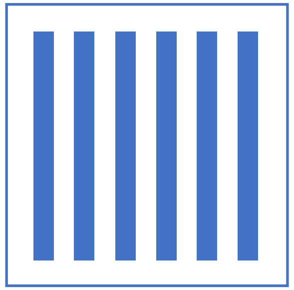
minibeam: FWHM ≤ 1 mm

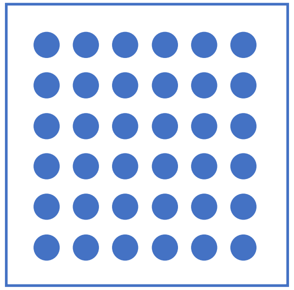
Important concepts

minibeam width
(σ, FWHM)

peak-to-valley dose ratio
(PVDR)

minibeam shape and pattern
- **array** of **planar** minibeams
- **grid** of **pencil-shaped** minibeams

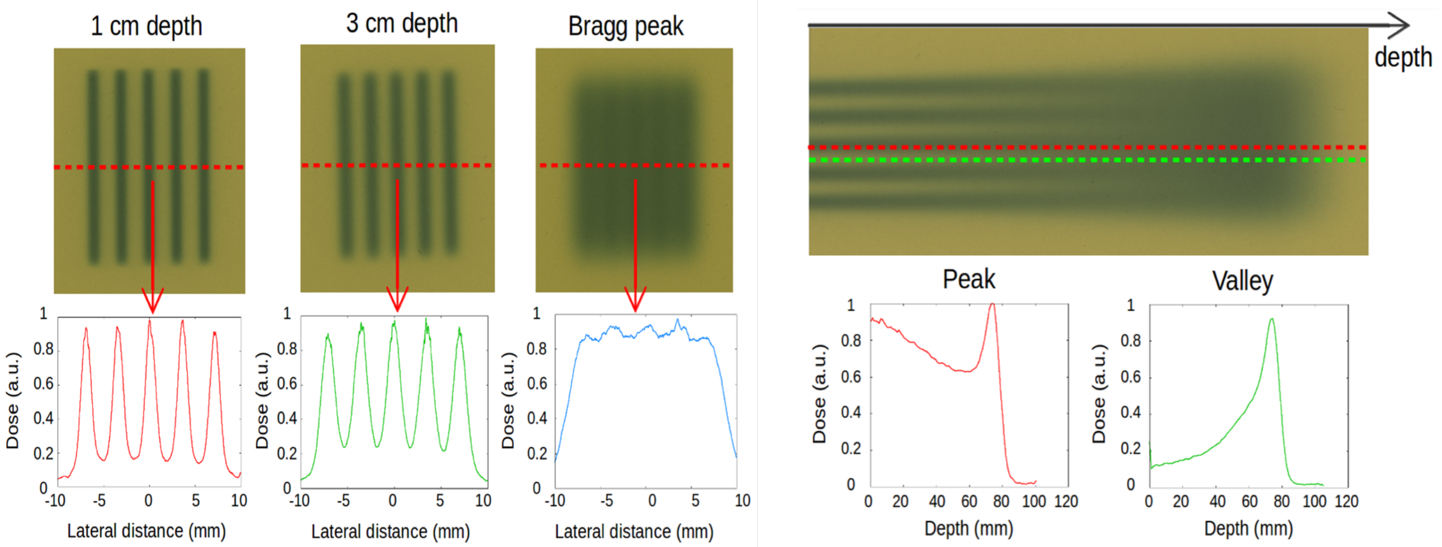


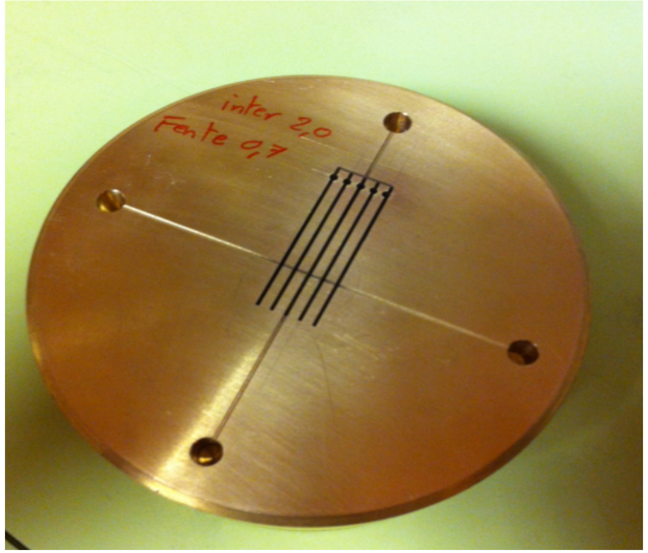


pMBRT – experimental results

- Minibeam generation: a first prototype with mechanical collimation
- Experimental proof of concept: dose distributions assessed with gafchromic films

(Peucelle et al, Med. Phys. 2015)





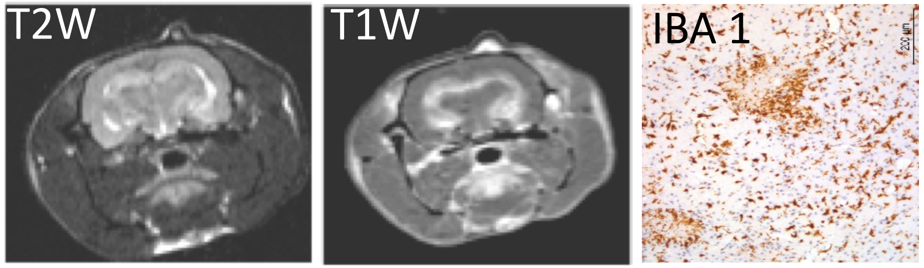
pMBRT – experimental results II

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

(Prezado et al., Sci. Rep. 2017)

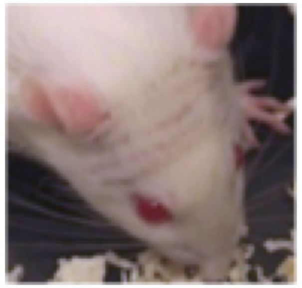
<u>Standard proton therapy</u>
<u>(25 Gy/one fraction, n=8)</u>

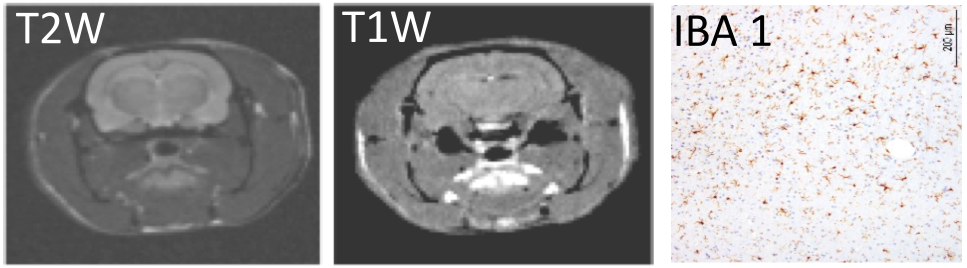
- Skin: moist desquamation
- Permanent epilation
- Important brain damage



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

- No skin damage
- Reversible epilation
- No brain damage observed



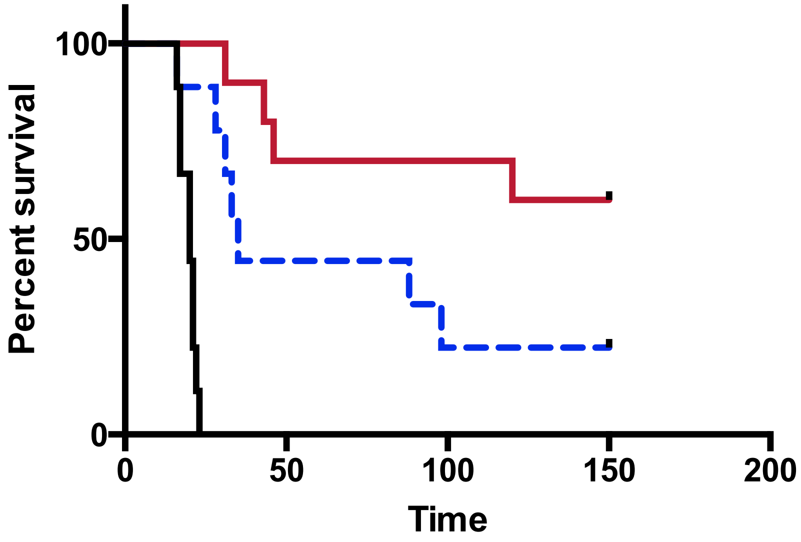


pMBRT offers a net gain in normal tissue resistance

pMBRT – experimental results III

Tumor control effectiveness in glioma (RG2) bearing rats
(Prezado et al., Int J Radiation Oncol Biol Phys 2019)

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

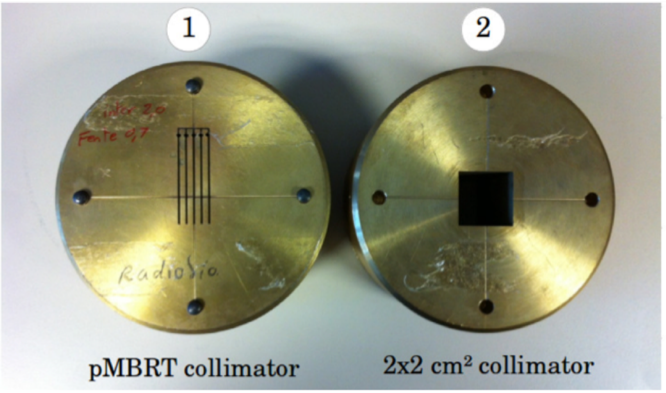
Controls 20 days

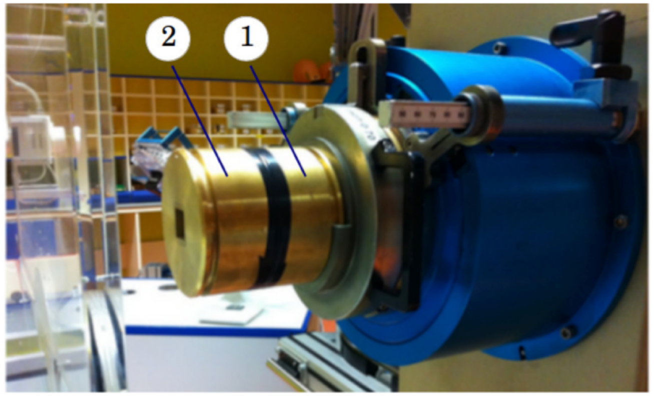
Standard 35 days   20 % long-term survivals (> 6 months)

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

Methods of minibeam generation

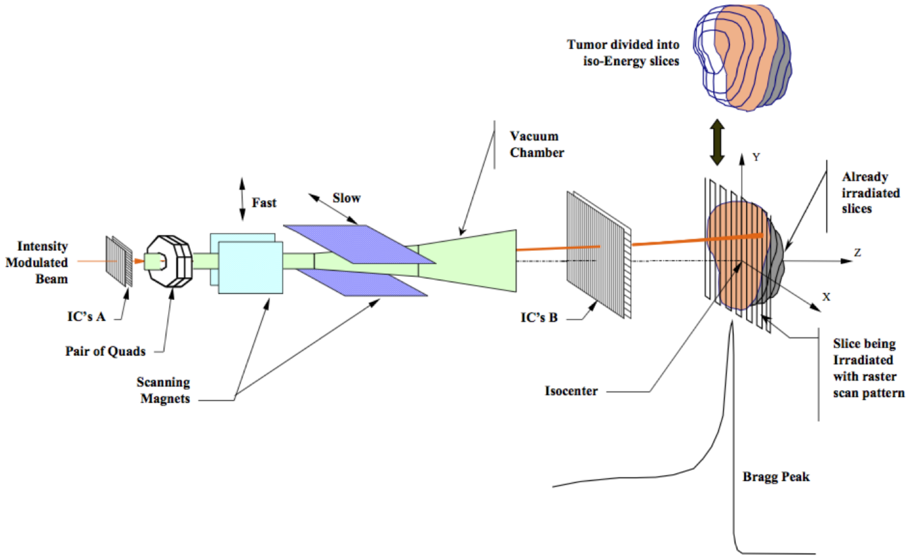
Mechanical collimation





Source: Peucelle, *Spatial fractionation of the dose in charged particle therapy*, PhD thesis

Magnetic focussing



schematic of a
PBS (pencil beam scanning) nozzle

Source: Marchand et al., *IBA proton pencil beam scanning: an innovative solution for cancer treatment*, Proceedings of EPAC, Vienna, 2000.

Methods of minibeam generation II

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 doses can be administered
- higher PVDR expected
- basically like PBS but beam 10x smaller

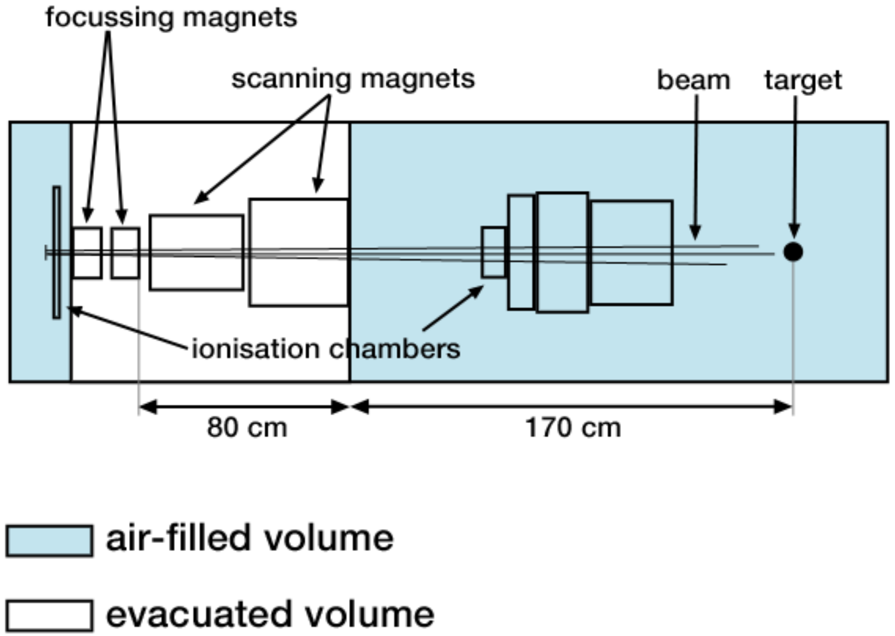
↳ **main challenge:** generate minibeams in a clinical context (energy, accelerator, beamline)

(existing facilities are designed to deliver beam spots ≥ 1 cm FWHM)

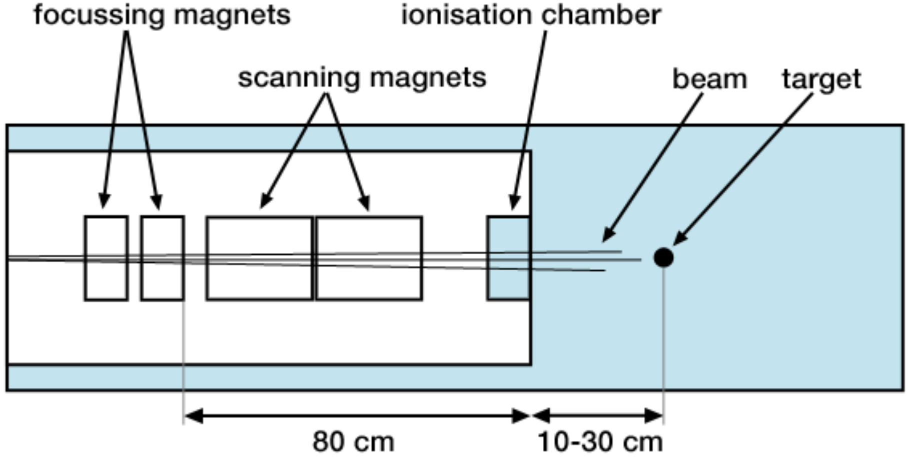
Magnetically focussed proton minibeams

A clinical nozzle for magnetically focussed proton minibeams (Schneider et al., Sci. Rep. 2020)

conventional PBS nozzle



our minibeam nozzle design



- same elements as conventional PBS nozzle
- more compact
- less propagation in air

Minibeam nozzle + LhARA proton beam

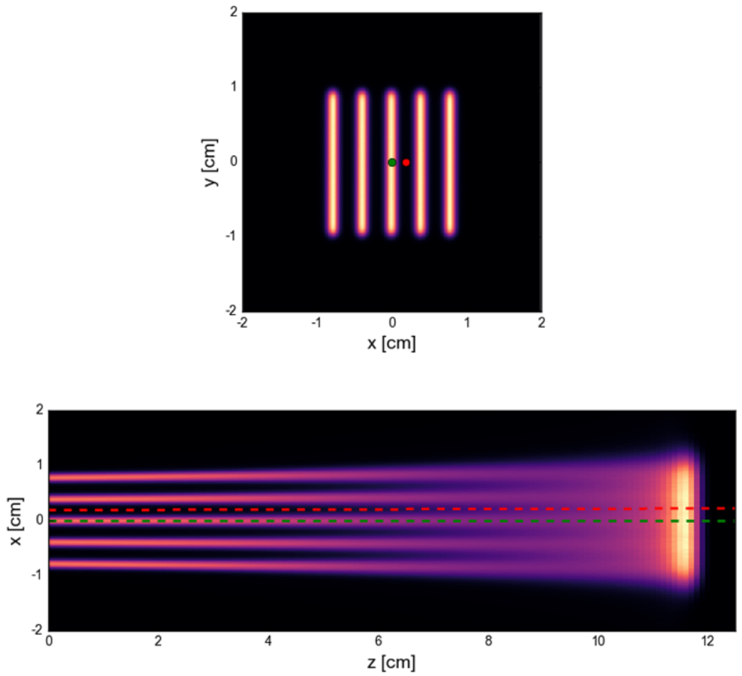
- Monte Carlo simulations with TOPAS v3.2
- two cases for air gap: 10 and 30 cm
- beam parametrisation at nozzle entrance:
  - Gaussian distribution for size, angular spread and energy spread
  - energy: 127 MeV
  - energy spread (σ): 0.2%
  - size (σ): 2.5 mm
  - divergence (σ): 0.55 mrad
  - emittance: 0.43 mrad*mm (0.137 π mrad*mm)

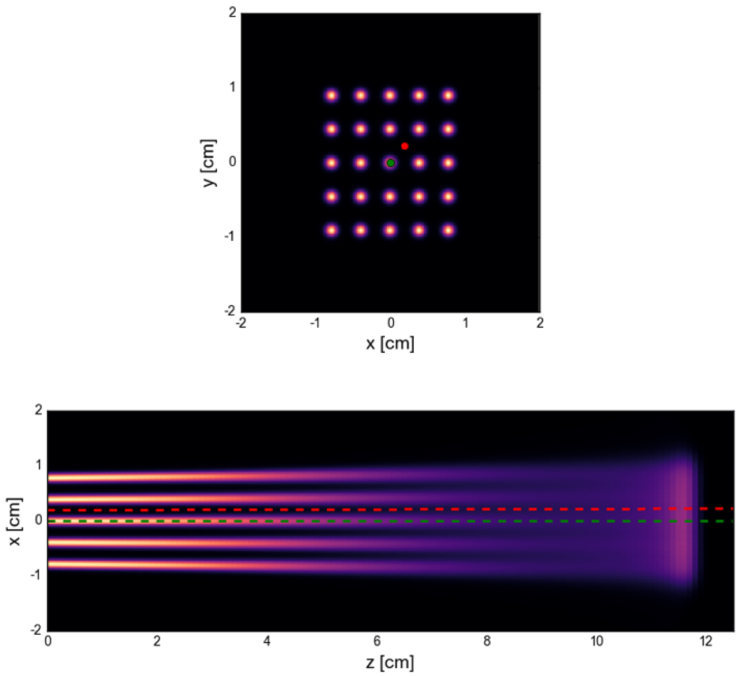
- resulting beam size at target:

Air gap [cm]	FWHM (x) [mm]	FWHM (y) [mm]	Diverg. (x) [mrad]	Diverg. (y) [mrad]
10	**0.57**	**0.54**	2.3	4.5
30	1.37	1.34	2.4	3.9

Minibeam nozzle + LhARA proton beam II

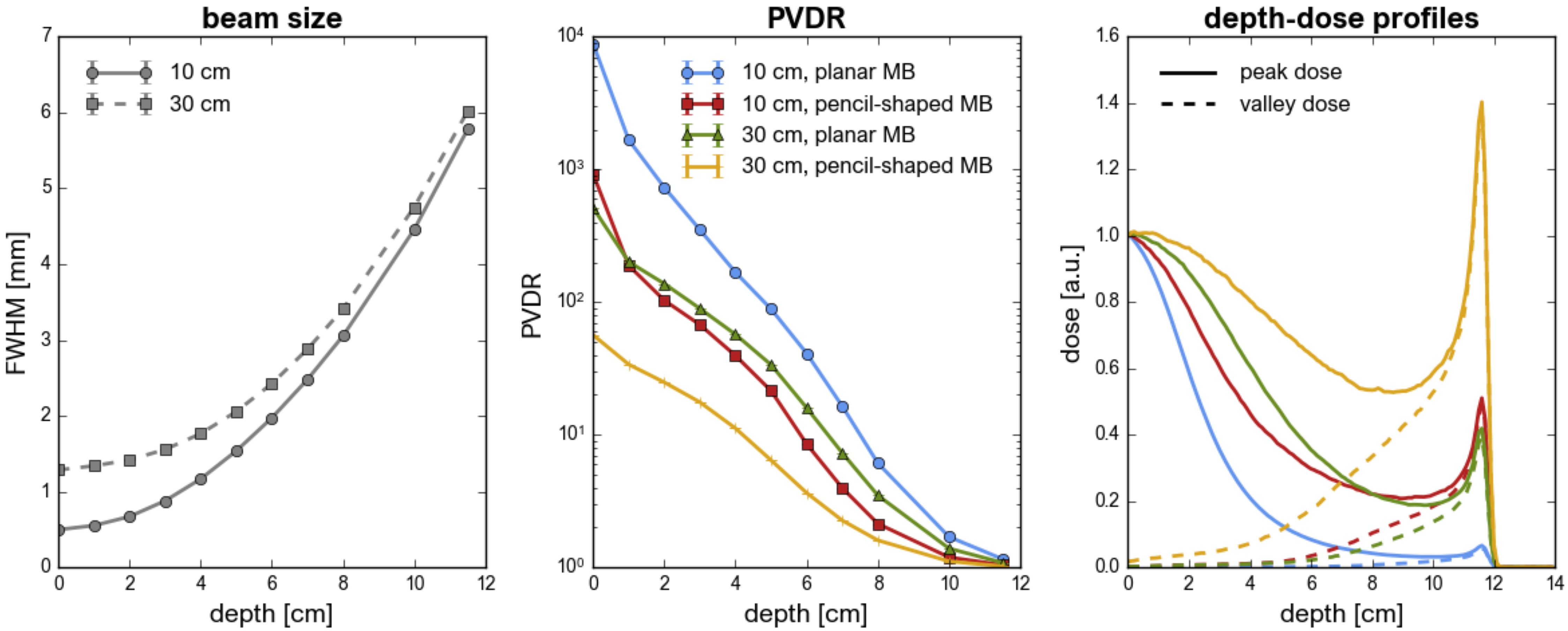
- simulation of dose deposition in water phantom
- two patterns:
  - array of 5 planar minibeams (continuously scanned beam spot)
  - grid of 5x5 pencil-shaped minibeams





Minibeam nozzle + LhARA proton beam III

- both patterns evaluated for cases of 10 and 30 cm air gap



Minibeam nozzle + LhARA proton beam IV

Conclusion

- very promising results
- excellent beam sizes
- excellent PVDR
- high dose rate very interesting (minibeams + FLASH?)