Proton minibeam radiation therapy: a new approach in radiotherapy

Yolanda Prezado

Laboratoire Imagerie et Modelisation pour la Neurobiologie et la Cancérologie (IMNC)-CNRS

Index

1. Introduction

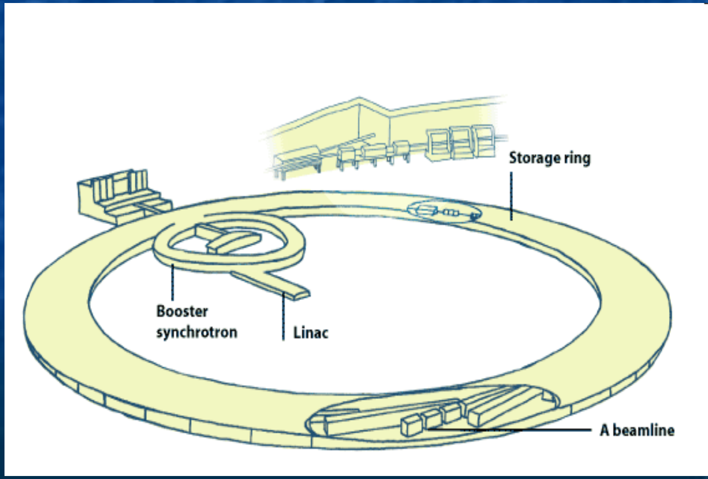
2. Synchrotron Radiation Therapy.

   -Spatial fractionation of the dose: Minibeam radiation Therapy

3. Proton minibeam radiation therapy :

   a new approach

4. Perspectives



Despite the important development of RT in the last decades

- There are radioresistant tumors, like gliomas, for which there is no effective treatment

- The treatment of pediatric cancers is very limited due to serious complications in the development of the child

- The management of tumors close to an organ at risk, like the spinal cord, is also very restricted

- There is still a non negligible risk of secondary cancers in some treatments

MAJOR LIMITATION of RT: high morbidity of the nearby healthy tissues

Radiation Therapy

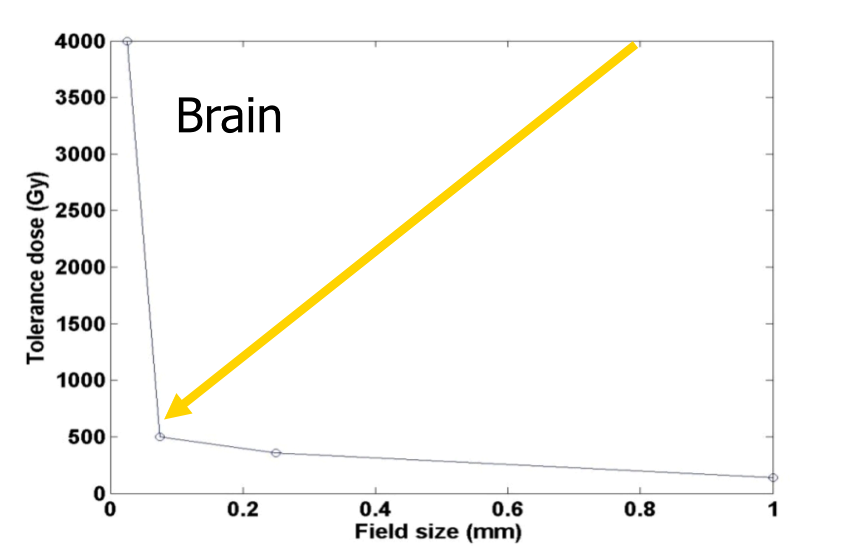
Physical dose → Biological dose

Biological effect

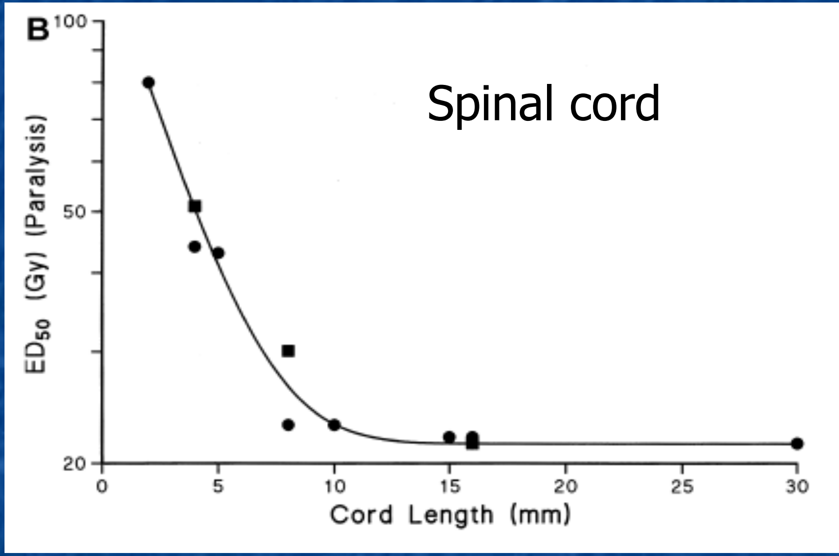
- Type of radiation γ, α, β, p, ^{12}C
- Energy of the beam
- Delivery mode:
  - -dose rate
  - -spatial/temporal fractionation-field sizes
  - -etc.

The importance of field size: dose-volume effects

The smaller the field size, the higher the tolerance of the healthy tissues



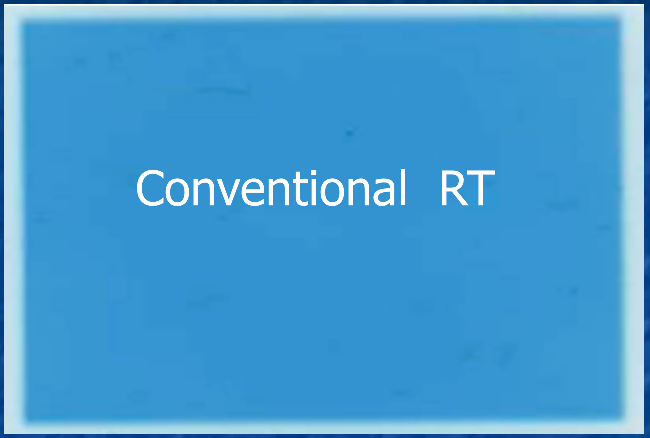
Zeman et al., Science (1959)

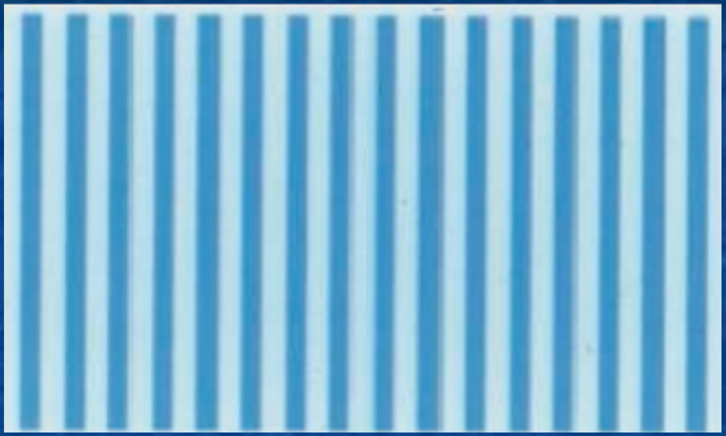


Hopewell et al., Radioth. Oncol. (2000)

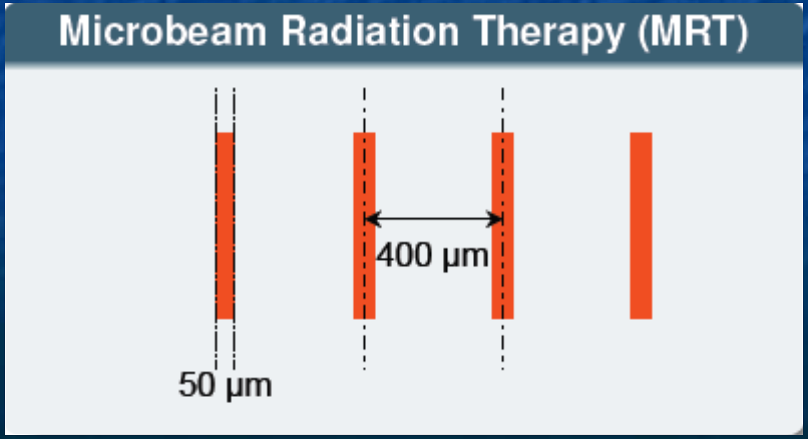
➢The stem-cell depletion hypothesis→ for each organ it exits a limiting critical volume, which can be repopulated by a single surviving stem cell and for which damage can be repaired by repopulation (Yaes & Kalend, 1988; Yaes et al, 1988).

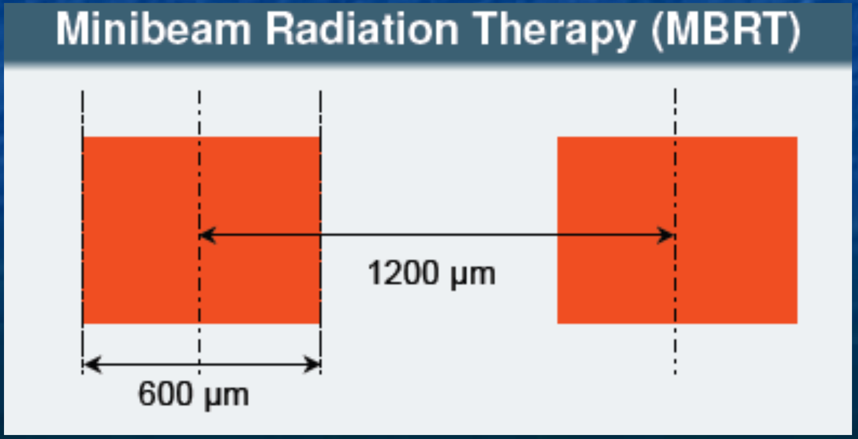
Spatial fractionation of the dose





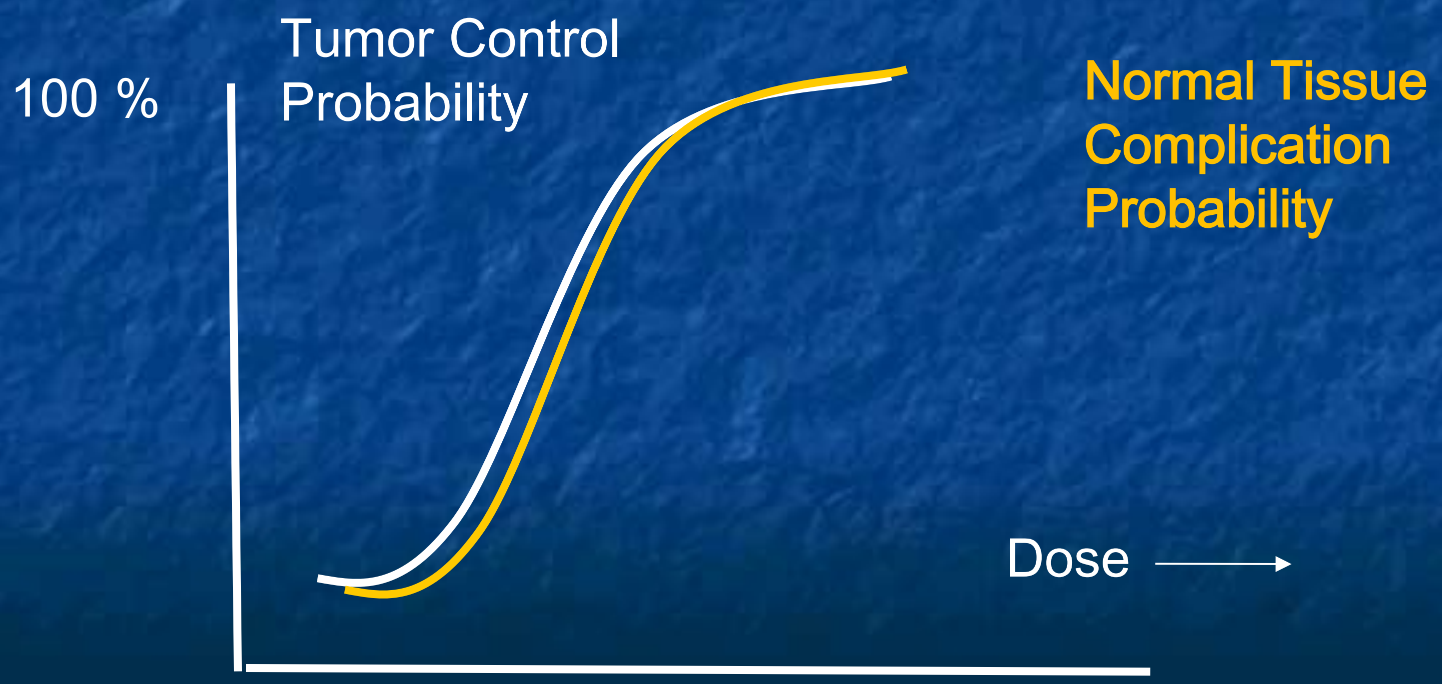
Spatially fractionated RT synchrotron tecnhiques





Preclinical studies

- Dose-volume effects → exponential increase of healthy tissue tolerances
- Spatial fractionation→gain in healthy tissue recovery → increase of healthy tissue tolerances



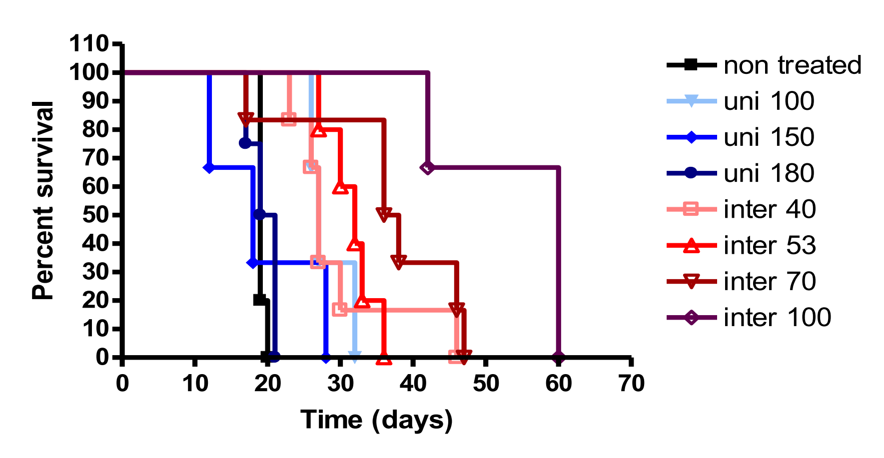
MBRT: a promising RT technique

1. Extremely high resistance of healthy rat brain to MBRT

Doses as high as 100 Gy in one session are still tolerated by the rat brain in comparison with 30 Gy in hospital RT.

Y. Prezado et al., paper in preparation

2. Increase of lifespan of glioma bearing rats after MBRT



A factor 3 increase in mean survival time

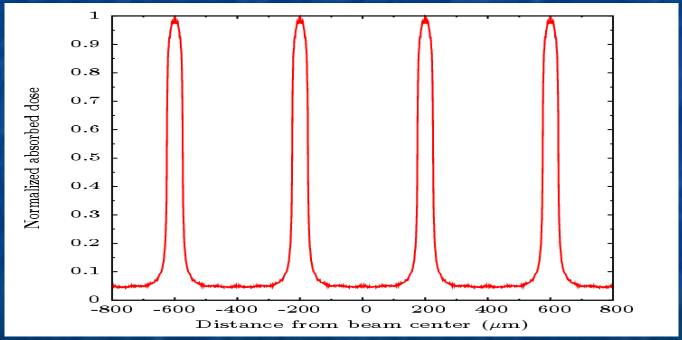
Y. Prezado et al. Enhancement of lifespan of glioma bearing rats after MBRT, J. Synchr. Radiat. 2012

3. It can be potentially transferred outside synchrotron sources with a cost-effective equipment (Project Physics for Cancer)

Differential effect tumor/healthy tissues

- It is possible to ablate gliomas without killing all tumoral cells. Spatial fractionation of the dose might involve other mechanisms than a direct ionizing radiation effects on tumoral cells like :
  - poor regenerative capacity of tumoral vessels after radiation exposure
  - abscopal effects

- Valley doses : the main responsible of healthy tissue sparing



To guarantee the repair mechanisms the valley dose should remain below the tolerances for each type of tissue for broad beam irradiation

Peak-to-Valley Dose Ratio $PVDR = \frac{\text{Peak dose}}{\text{Valley dose}}$ high for tissue sparing

Radiation Therapy

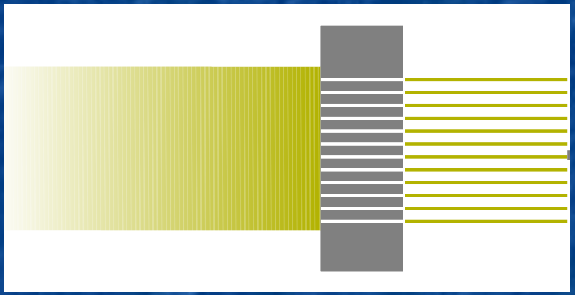
Physical dose → Biological dose

Biological effect

- Type of radiation γ, α, β, p, ^{12}C
- Energy of the beam
- Delivery mode:
  - -dose rate
  - -spatial/temporal fractionation-field sizes
  - -etc.

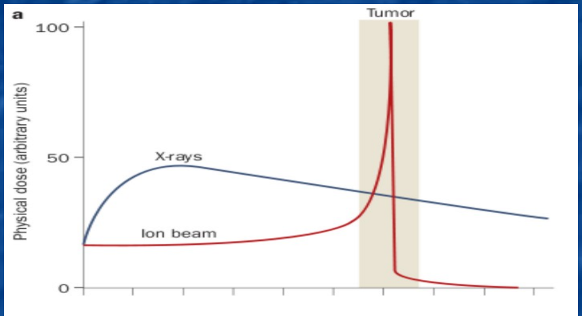
Proton-minibeam radiation therapy: a proof of concept

Spatial fractionation of the dose



+

Selective energy deposition of protons



Monte Carlo simulations (GATE)

-Water cylinder (16 cm diameter/ 16 cm height)

-Proton-minibeams: -700 µm wide

-1400, 2800, 3500 µm center-to-center (c-t-c) distance

-Beam energy: 105 MeV and 1 GeV (PNPI Saint Petersbourg)

-Tumor center at 8 cm.

-Covering an area of 2 x 2 cm^2

-Mechanical collimation: 5 cm thick brass block (105 MeV)
70 cm thick lead block (1 GeV)

Magnetic shaping of the beam by using several sets of quadrupoles magnets

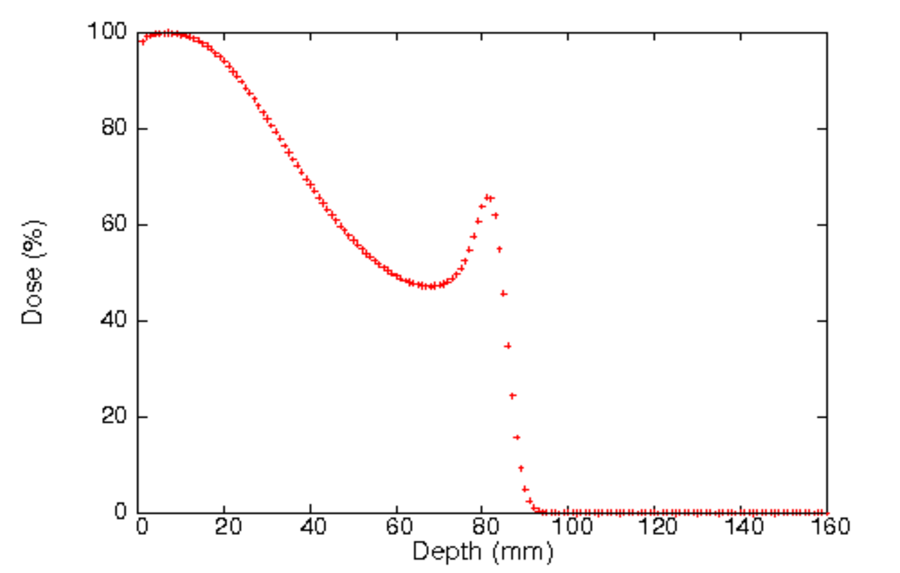
-Realistic beam divergence (3 mrad) and spot size 3 mm FWHM.

Figure of merit: Peak-to-valley dose ratio (PVDR) & penumbras

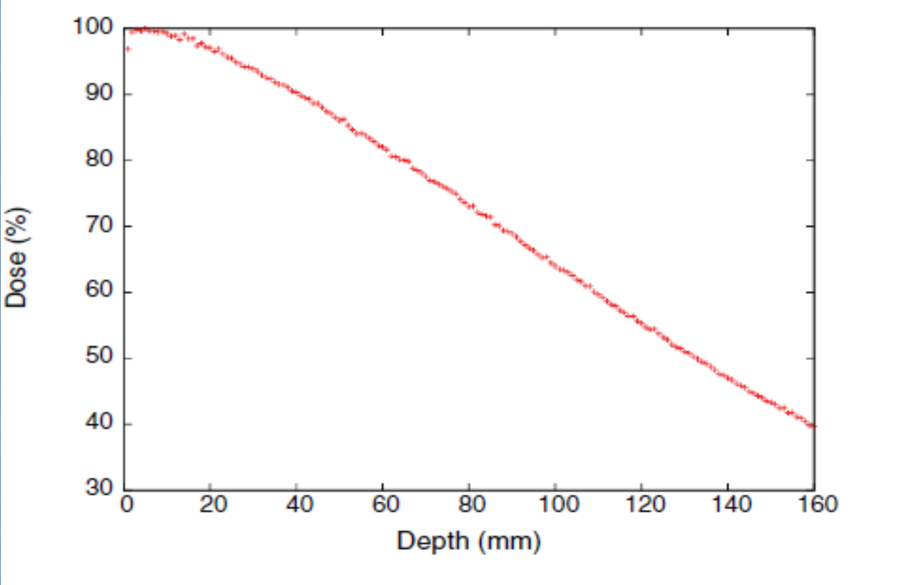
For healthy tissue sparing → high PVDR
narrow penumbras

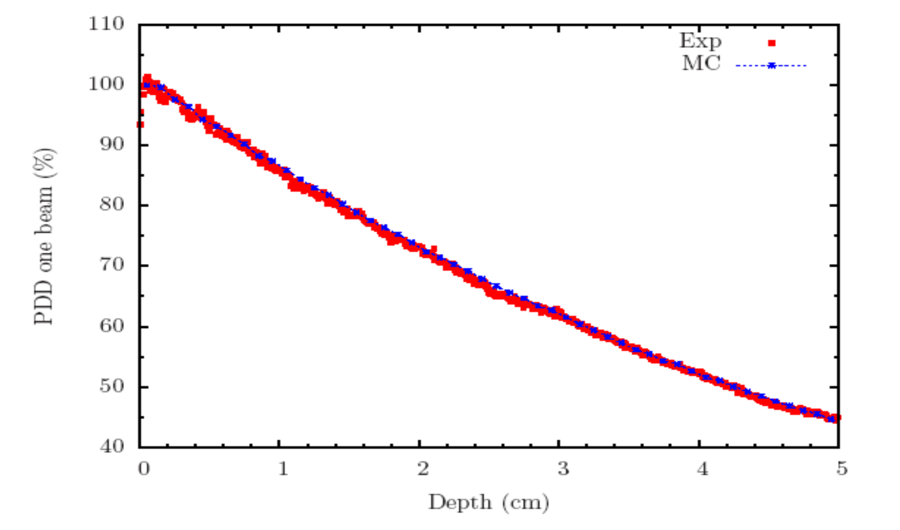
Dose distributions: percentage depth dose curves

105 MeV pMBRT



1 GeV pMBRT

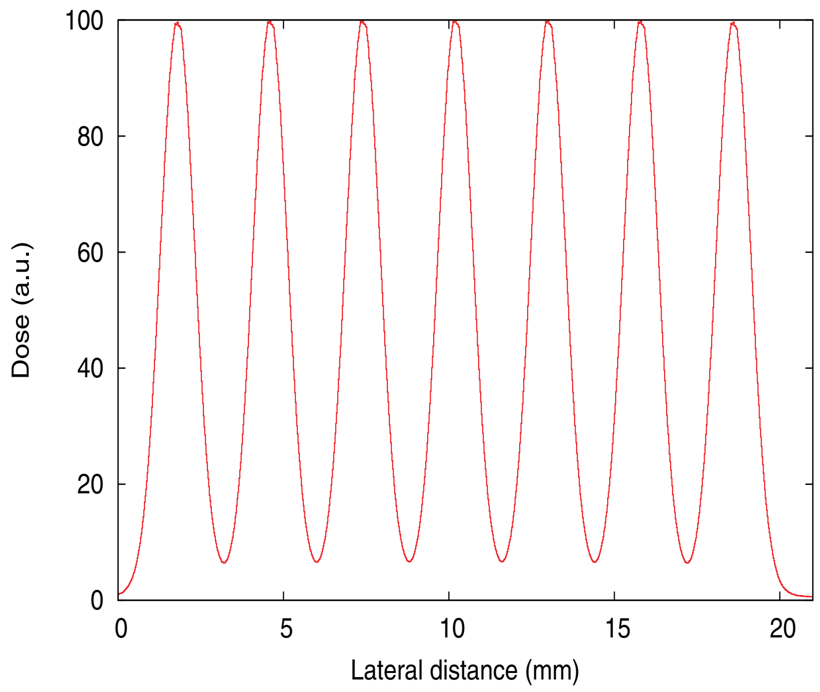




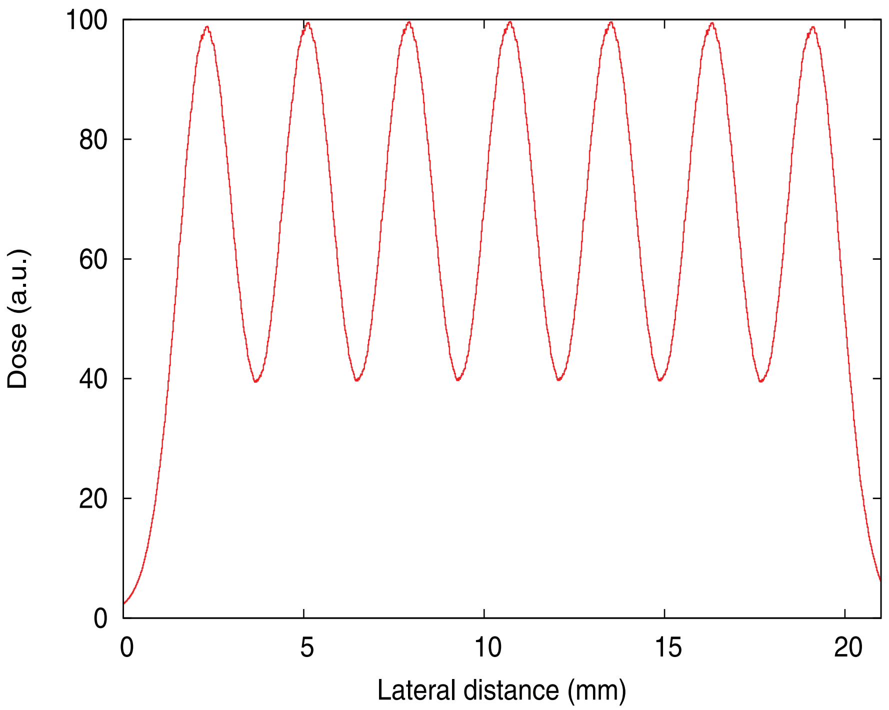
X-ray MBRT

Dose distributions: lateral dose profiles

3 cm depth



5 cm depth



Lateral dose profiles: PVDR

105 MeV pMBRT, c-t-c 3.5 mm

Depth (cm)	Magnetic coll.	Mechanical coll.	X-rays MBRT
1	162 ± 8	15.6 ± 0.8	10.1 ± 0.5
3	53 ± 3	14.8 ± 0.7	8.4 ± 0.4
5	11 ± 0.6	6.5 ± 0.3	7.4 ± 0.4
7	1.9 ± 0.1	1.55 ± 0.08	7.1 ± 0.4
8.2	1.22 ± 0.06	1.07 ± 0.05	6.8 ± 0.3

PVDR promising results. Biological experiments warranted.

Y. Prezado and G. Fois, Proton-minibeam radiation therapy: a proof of concept, Med. Phys. 2013

Lateral dose profiles: PVDR

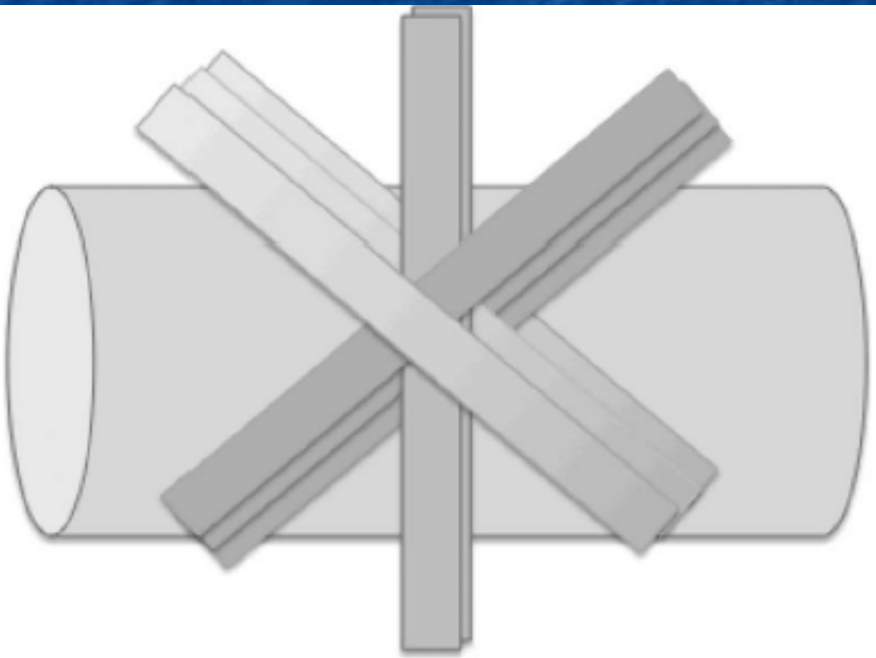
1 GeV pMBRT, c-t-c 3.5 mm

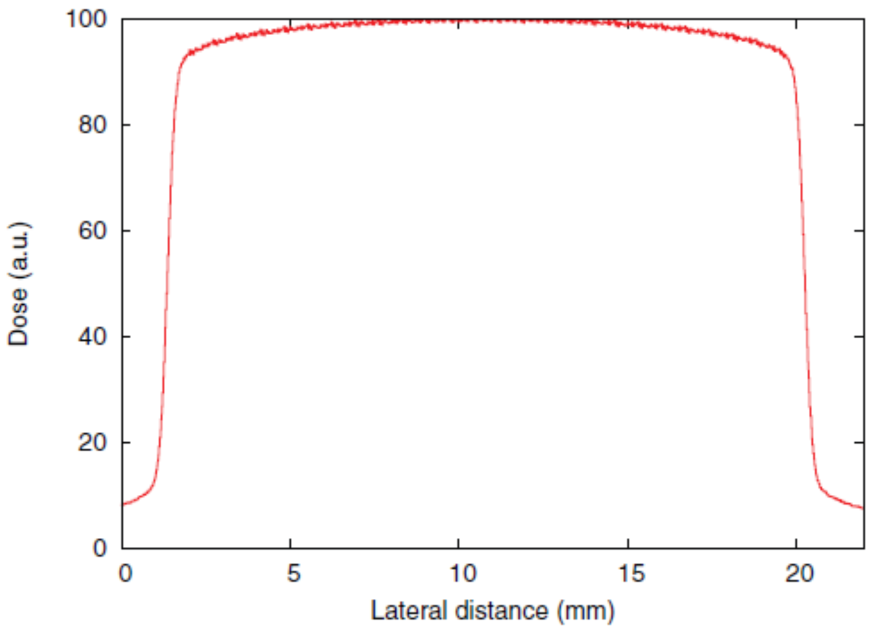
Depth (cm)	Magnetic coll.	Mechanical coll.	X-rays MBRT
1	41 ± 2	23.3 ± 1.1	10.1 ± 0.5
3	27.0 ± 1.3	16.7 ± 0.8	8.4 ± 0.4
5	26.4 ± 1.2	16.6 ± 0.8	7.4 ± 0.4
7	23.8 ± 1.1	16.3 ± 0.8	7.1 ± 0.4
8.2	22.8 ± 0.9	15.2 ± 0.7	6.8 ± 0.3

PVDR promising results. Biological experiments warranted.

Y. Prezado and G. Fois, Proton-minibeam radiation therapy: a proof of concept, Med. Phys. 2013

Interlaced minibeams (1 GeV)





Penumbra values

Depth	Penumbra 105 MeV (μm)		Penumbra 1 GeV (μm)		GK
(cm)	Magnetic	Mechanical	Magnetic	Mechanical	(μm)
1	492 ± 25	212 ± 11	459 ± 23	261 ± 13	3444 ± 172
3	588 ± 29	484 ± 24	461 ± 23	301 ± 15	3596 ± 179
5	920 ± 46	905 ± 45	480 ± 24	310 ± 15	3640 ± 180
7	1343 ± 67	1228 ± 61	519 ± 26	340 ± 17	3648 ± 180
8.2	1705 ± 85	1628 ± 81	585 ± 29	385 ± 19	3670 ± 183
13	NA	NA	658 ± 33	509 ± 25	3872 ± 194
15	NA	NA	756 ± 38	635 ± 32	4077 ± 204

Significantly narrower than in Gammaknife radiosurgery

Conclusions

Promising dose distributions for healthy tissue sparing

-1 GeV beams→ very low penumbras→ideal for radiosurgery
-105 MeV→ not need for interlacing
-Magnetic shaping → higher penumbras than mechanical collimator but lower neutron yield

Biological experiments warranted

Perspectives: technical implementation at CPO (Orsay)

Challenge: small field dosimetry for protons


Thanks for you attention
prezado@imnc.in2p3.fr