Proton Minibeam Radiation Therapy (pMBRT): implementation at a clinical center

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Context of the study

- Conventional RT treatments remain unsatisfactory for:
  - ✓ some **radioresistant** tumours
  - ✓ some **paediatric** cancers
  - ✓ tumours close to a **sensitive organ**

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Innovative RT approaches being explored

↓

Minibeam Radiation Therapy
MBRT

Proton Therapy

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- Synchrotron radiation therapy technique (low energy x-rays)
- Combines **submillimetric field sizes** (500-700 µm) and **spatial fractionation of the dose** (inter-beam separation ≈ 1200 µm)

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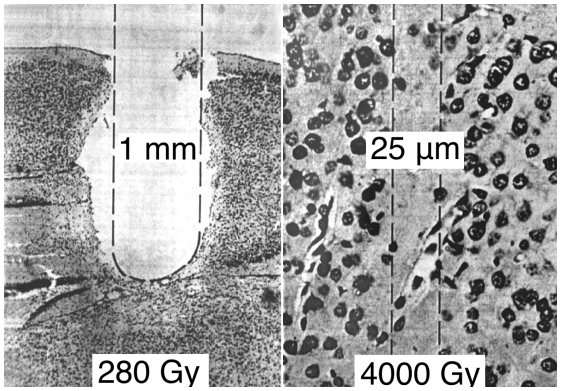

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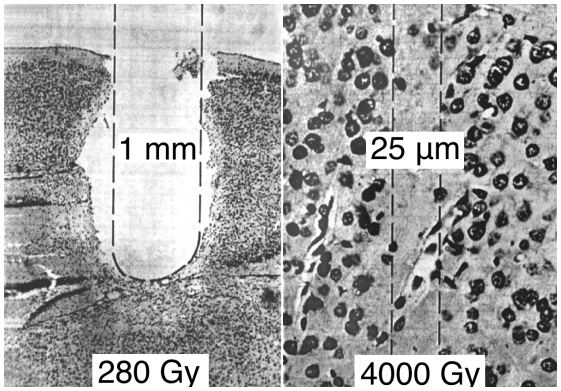

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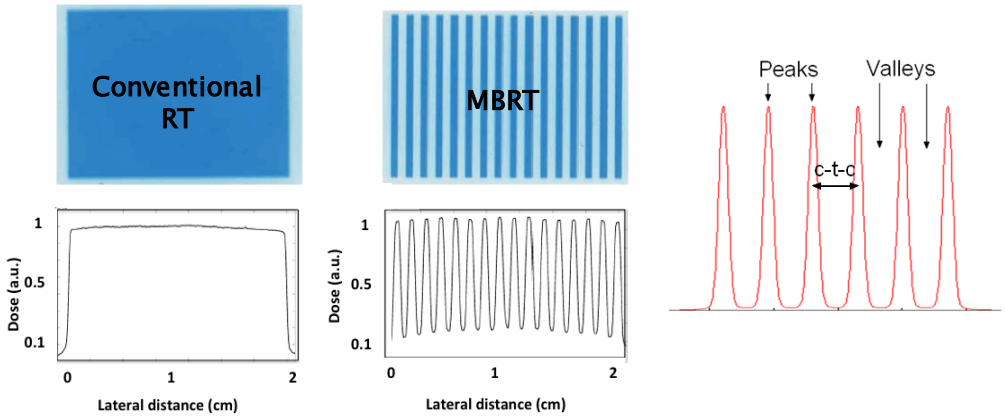

Pattern of peaks and valleys. Relevant dosimetric parameters: Peak and valley dose and Peak-to-Valley-Dose Ratio (PVDR). [Dilmanian 2002]

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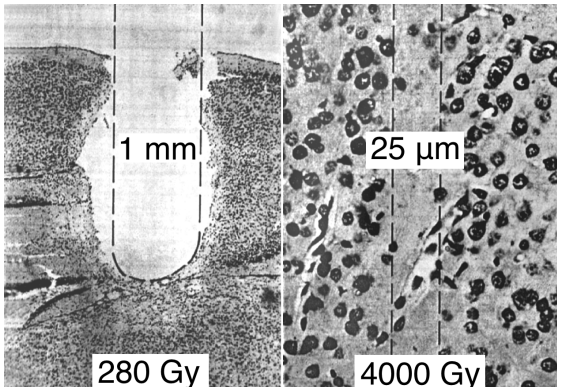

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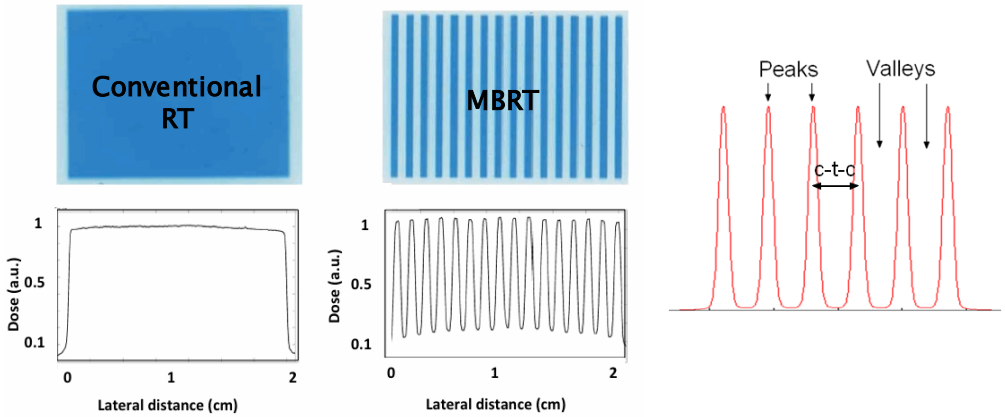

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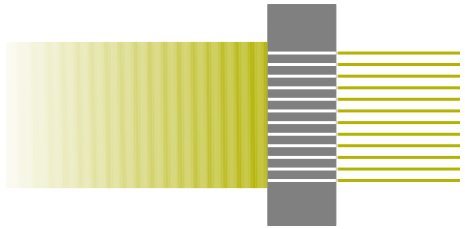
- **Biological studies with x-rays**:
  - ✓ Remarkable **normal brain resistance** to very high doses (up to 100 Gy): biological repair of microscopic lesions in peaks by minimally irradiated cells of valleys [Dilmanian 2006], [Deman 2012], [Prezado 2015]
  - ✓ Significant **tumour growth delay** [Prezado 2012], [Deman 2012]

pMBRT: a novel therapeutic approach

Advantages of spatial fractionation and small field sizes



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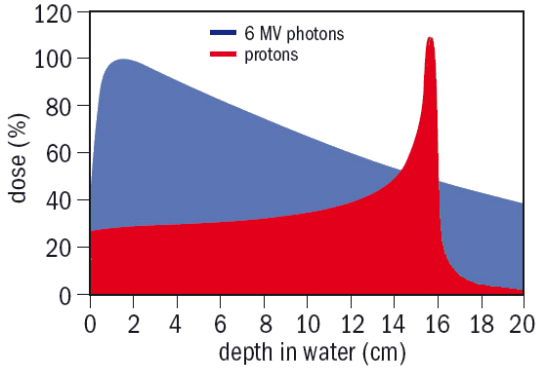
More precise ballistics of protons



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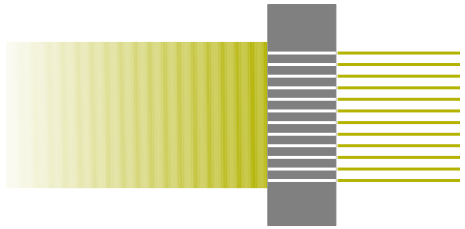

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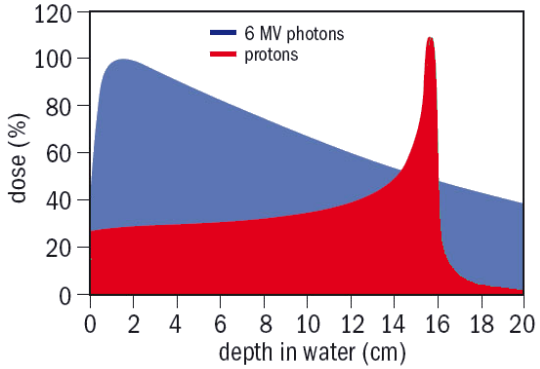
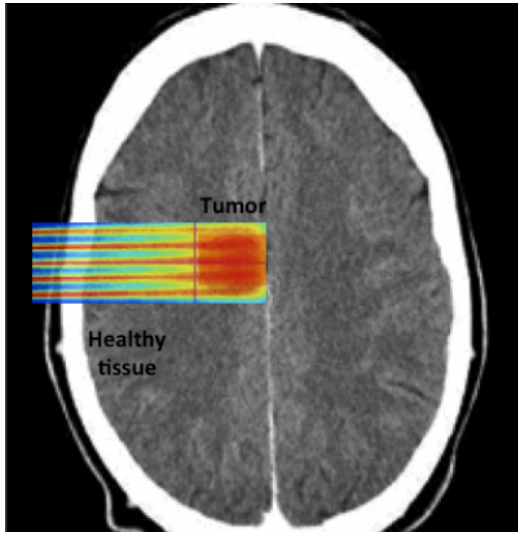


- In a recent work: Monte Carlo **proof of concept** suggested a **possible way to generate minibeams of protons** and highlighted advantages of this approach [Prezado 2013] :
  - ✓ Spatial fractionation in normal tissues
  - ✓ Homogeneous distribution at the Bragg peak location



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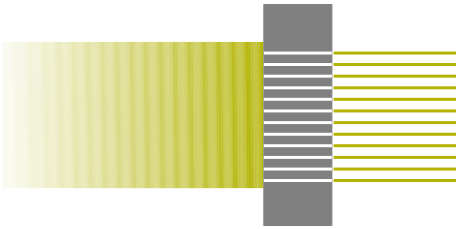

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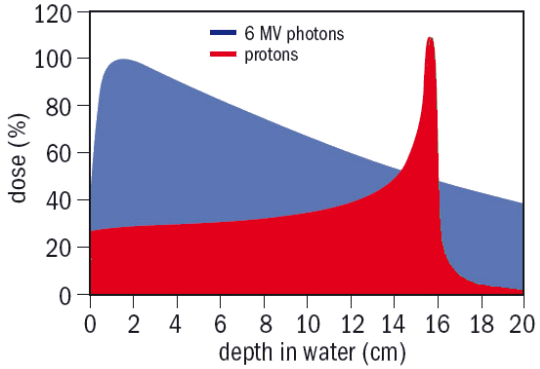

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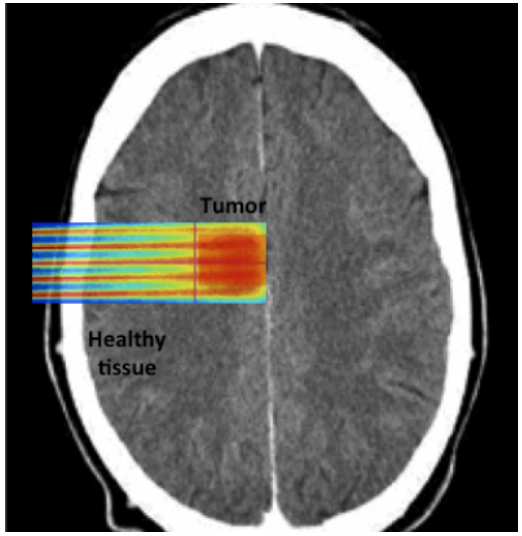
- In this study: Experimental proof of concept: **technical implementation and dosimetric evaluation** at a clinical center [Peucelle 2015]



Institut Curie – Proton Therapy Center in Orsay (ICPO), France

Evaluation at ICPO proton therapy facility

- **ICPO Y1 Beamline specifications**
  - ✓ IBA Isochronous Cyclotron
  - ✓ Fixed horizontal beamline – double scattering delivery mode
  - ✓ 201 MeV protons at the room entrance
    → degraded to 100 MeV with absorbers for pMBRT

- **Generation of proton minibeams with brass collimators**
  - ✓ Multislits collimators → 400 & 700 µm slits
    3200 & 3500 µm beam spacing

ICPO Y1 beamline
Intracranial treatments

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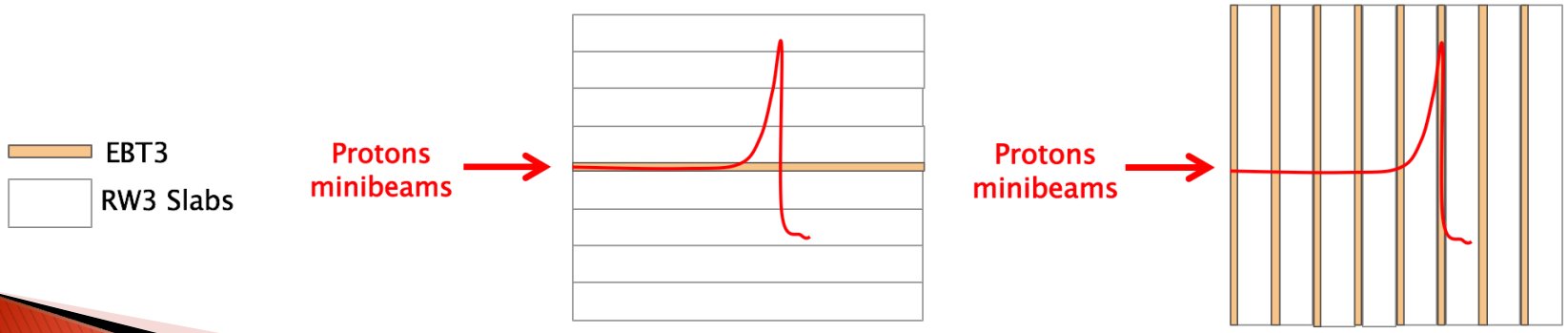
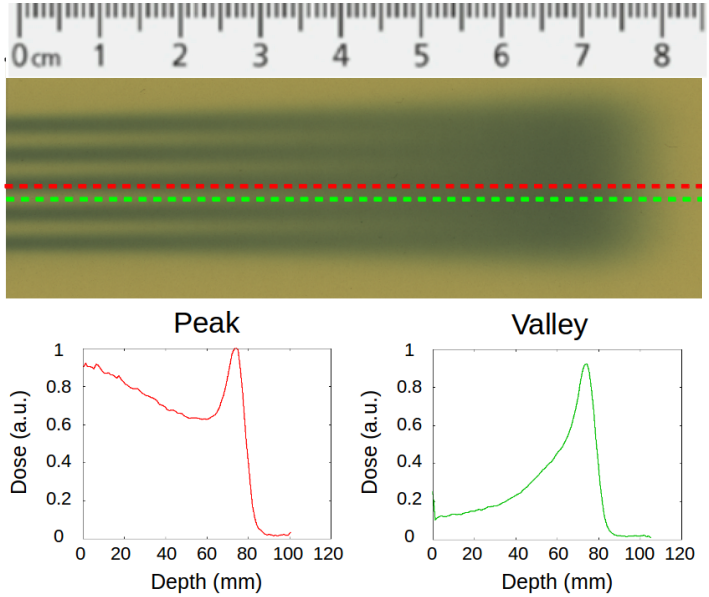
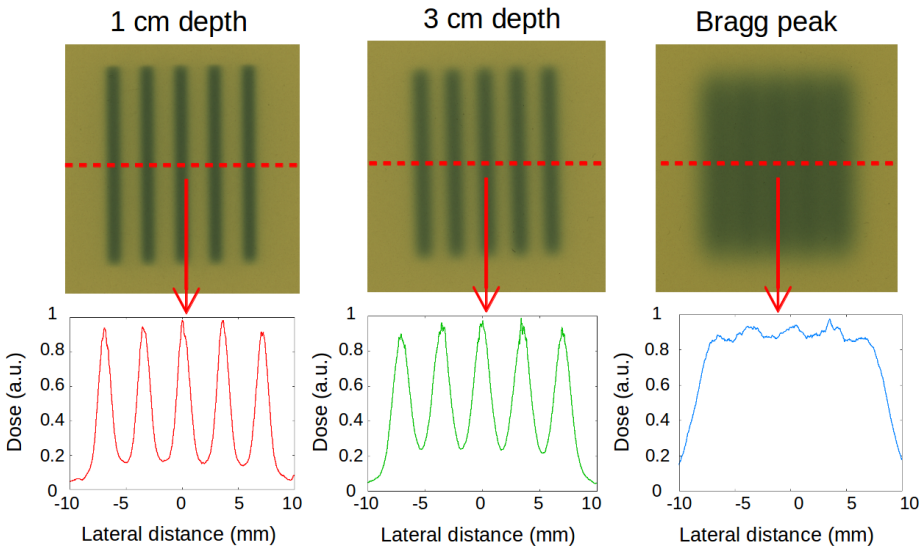
- **Irradiations of EBT3 films in RW3 slabs phantoms**
  - ✓ 10 Gy in reference conditions (broad-beam) – Absolute dosimetry performed with ion chamber
  - ✓ Films handling with AAPM TG 55 recommendations – correction factors (quenching, depth scaling)
  - ✓ Irradiations in two configurations:



Dose distributions extracted from EBT3 films (700 µm slits)

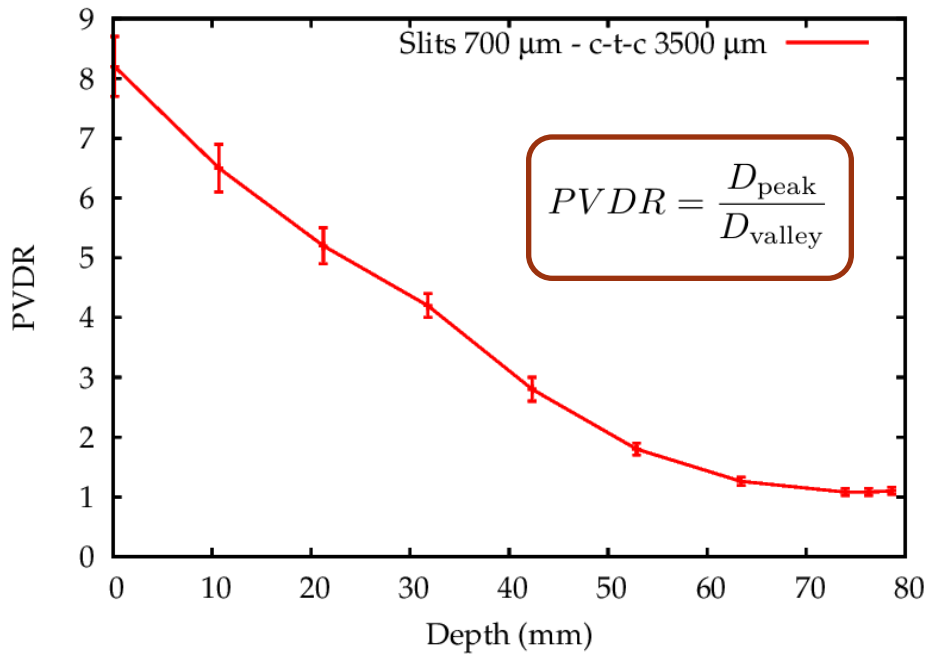




- **Depth dose distributions:**
  - ✓ **Peak shape differs from classical Bragg peak curve** due to the high ratio of lateral scattering compared to the dose deposited by primary beam
  - ✓ **Continuous increase of valley** in depth due to multiple Coulomb scattering (mcs)

- **Lateral dose profiles:**
  - ✓ **Spatial fractionation** of the dose in the proximal **normal tissues** while **quasi-homogeneous** dose distribution at the Bragg location due to mcs

Peak-to-valley dose ratios



- Continuous decrease of PVDR in depth due to multiple Coulomb scattering
- Values ranging from 8.2 ± 0.5 at the phantom entrance to 1.08 ± 0.06 at the Bragg peak location

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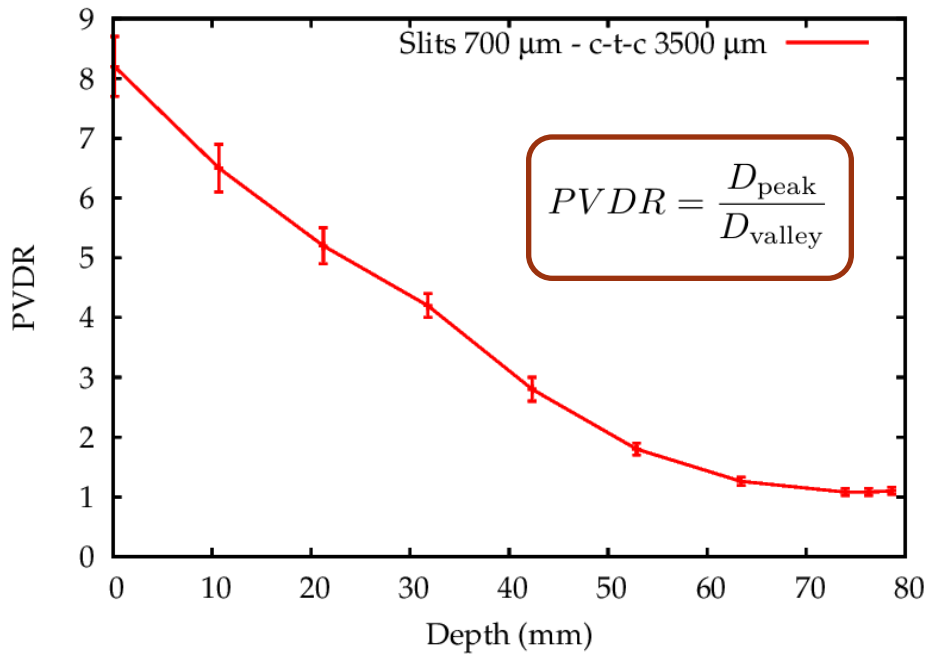

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→ Might offer a net gain in therapeutic index

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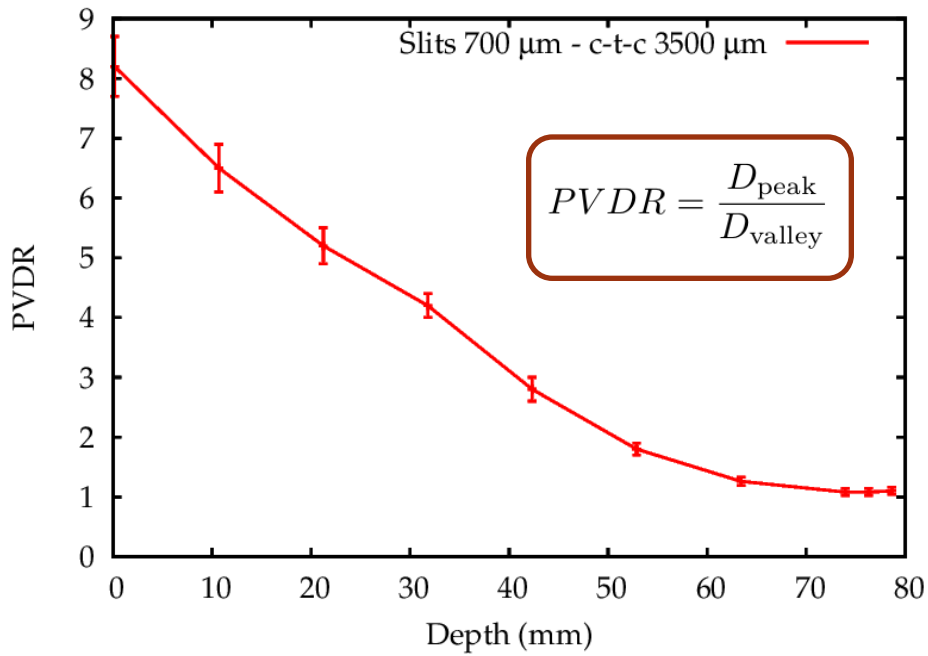

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C. Peucelle et al. Med. Phys. 42 (2015)

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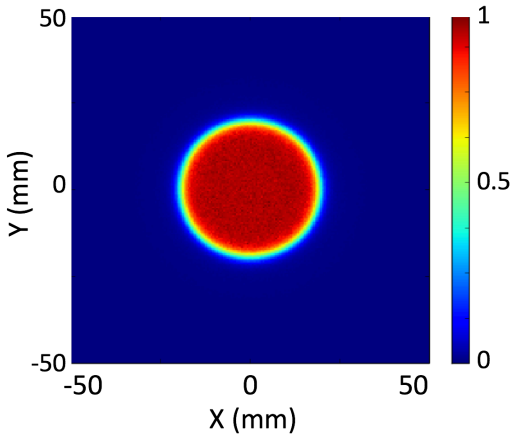
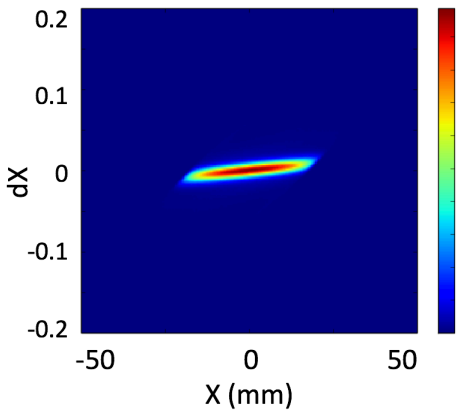
Ongoing Monte Carlo dose studies

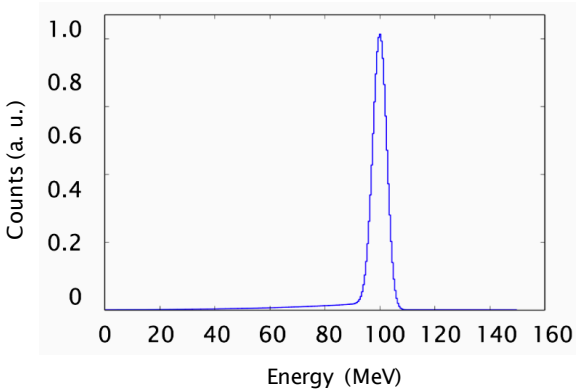
- **Modelling of the beamline** and **pMBRT collimators** (GATE/Geant4 platform)
- Computation of a ***Phase Space File*** at the end of the beamline



Probability density of protons position in the XoY plan



Correlation between protons position and direction



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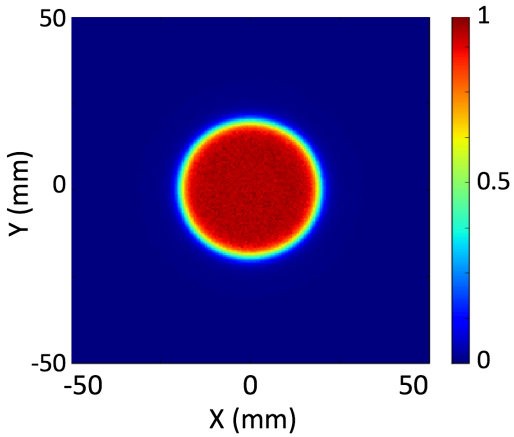

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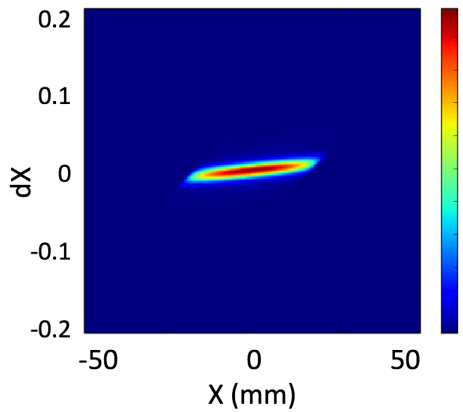

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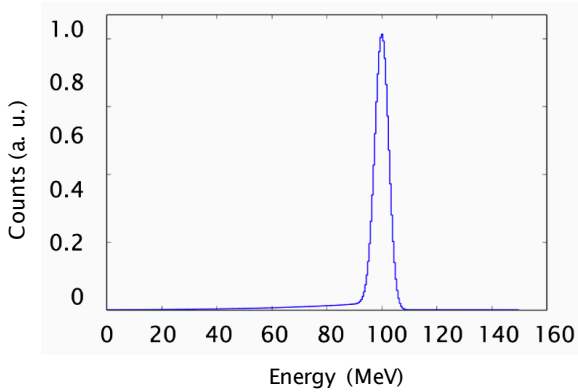

Energy distribution of protons

- Ongoing **development of a virtual source model** by:
  - ✓ Extracting phase space state variables of the particles reaching the end of the beamline
  - ✓ Using these data as input to create a source model in the GATE code (new GATE class)

FINAL PURPOSE

Development of a **pMBRT dose calculation engine**

First *in-vivo* experiments

- **Whole brain rats irradiations:**
  - ✓ 7 weeks **healthy** Fischer 344 rats
  - ✓ Irradiations with **broad beam** (conventional proton therapy) or **pMBRT** technique
  - ✓ Single fraction with same average dose (25 Gy) in both techniques
  - ✓ **Long term study**: histological and MRI studies 6 and 12 months after irradiations

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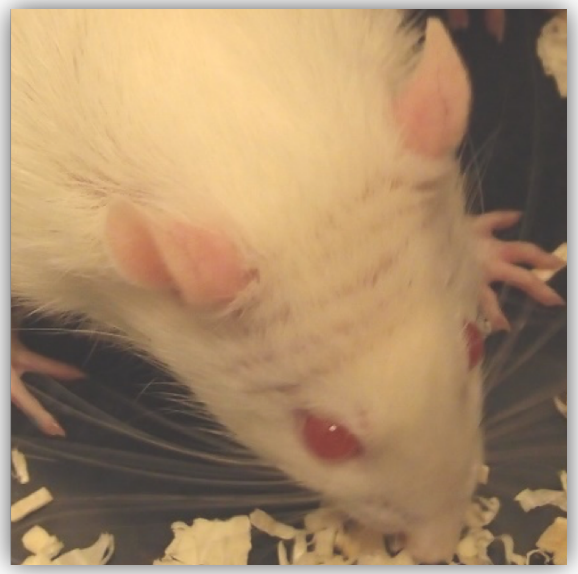
- **3 months follow-up:**
  - ✓ Broad beam: severe moist desquamation (grade 3)
  - ✓ pMBRT: no skin damage, probable reversible epilation, no behavioral changes or clinical symptoms

Broad beam irradiation
25 Gy



pMBRT irradiation
58 Gy (peak dose)

Conclusions

- **Experimental proof of concept** of pMBRT at a clinical proton therapy facility
- Complete **dosimetric database needed to guide ongoing** biological experiments is **available** (experiments started in October 2015)
- **Homogeneous** dose distribution in Bragg peak
  Spatial fractionation in normal tissues

  } Improvement of therapeutic index

Perspectives

- Development of a first **dose calculation engine dedicated to pMBRT**

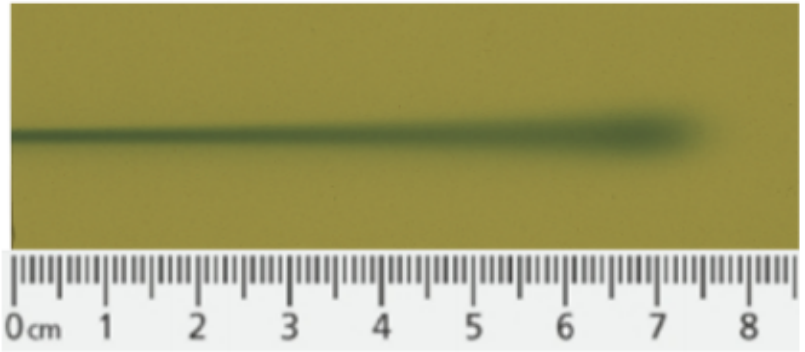
Thanks for your attention

EXTRA SLIDES

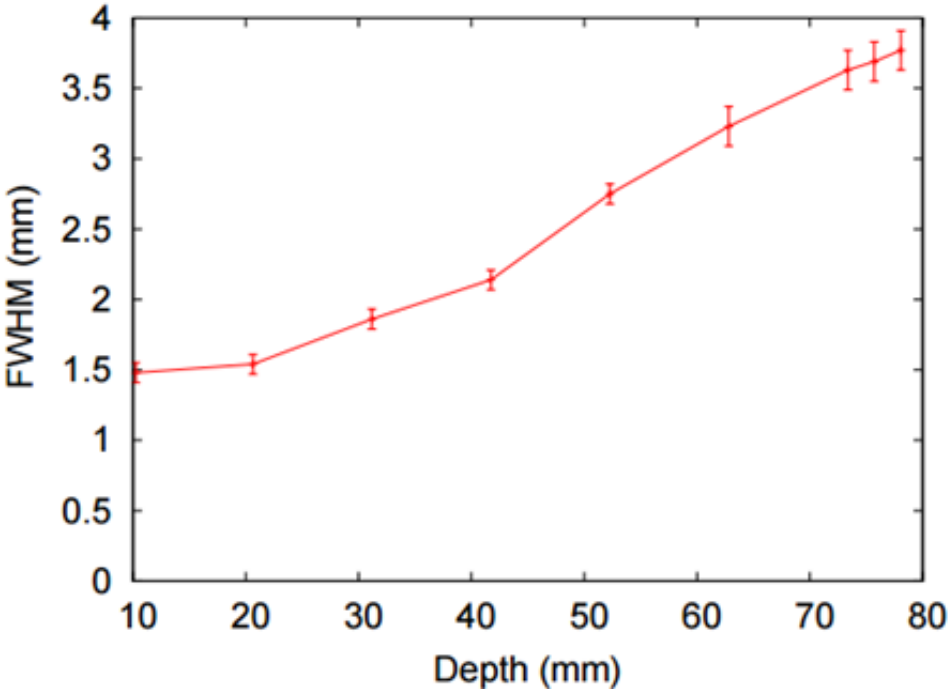
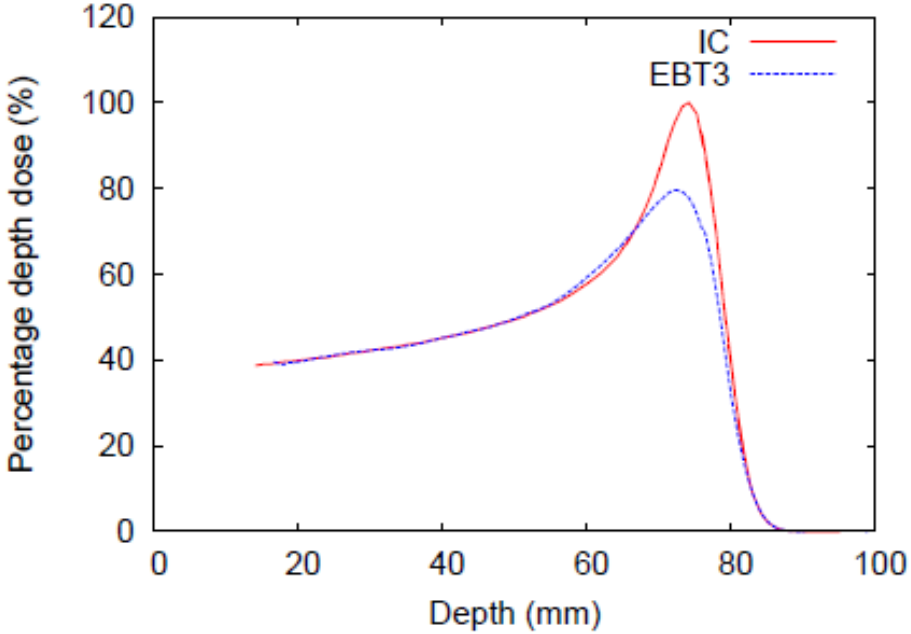
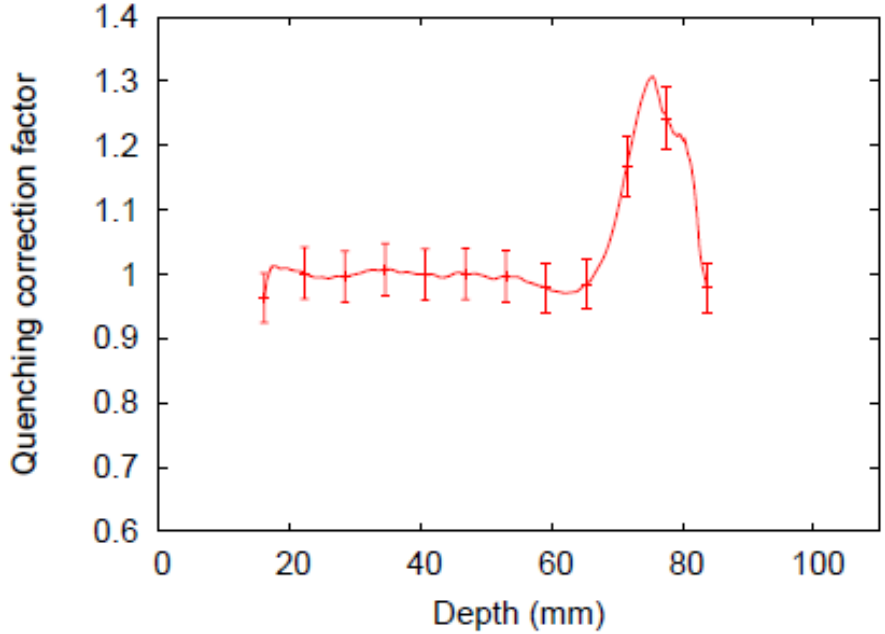
Increase of beam width in depth – FWHM

Single slit collimator

- **Increase of beam width** as a function of depth due to lateral scattering
  - → Visible on EBT3 film irradiated with single slit collimator



- **Quantification** thanks to **full width at half maximum** (**FWHM**):
  - → Values between 1.4 and 4 mm



Quenching Correction Factors (QCF)