A versatile treatment planning system for microbeam radiation therapy

Validation and biological dosimetry

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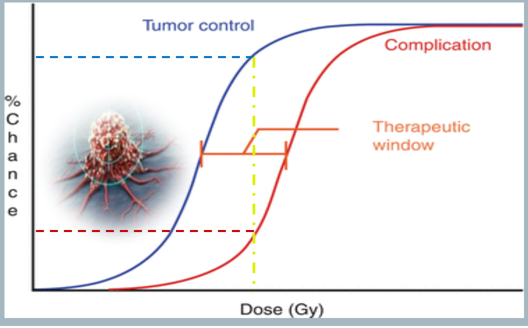
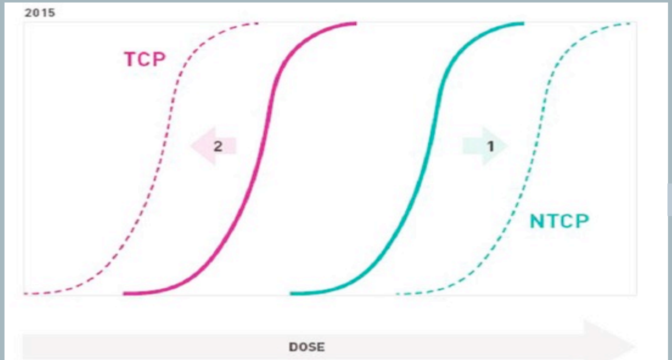
ESRF
The European Synchrotron

LABEX PRIMES
UNIVERSITÉ DE LYON

CHU GRENOBLE ALPES

Holthusen (*1936*): probability of tumor control and of developing normal tissue complications after radiotherapy





C. Chargari *et al.* / Cancer Treatment Reviews 45 (2016) 58–67

- Aim: Increasing tumor control
- Quest for possible ways of improving the therapeutic index
- Optimization of therapeutic window

Optimization of treatment

- Induce a more efficient tumoral irradiation
  - Particle / energy
  - Targeted radiotherapy/ nanoparticles
- Preserve the healthy tissues
  - Particle/energy (hadron/VHEE)
  - Dose delivery: Spatial fractionation of dose and FLASH

Optimization of treatment

Induce a more efficient tumoral irradiation

Preserve the healthy tissues

Particle/ energy

Targeted radiotherapy/ nanoparticles

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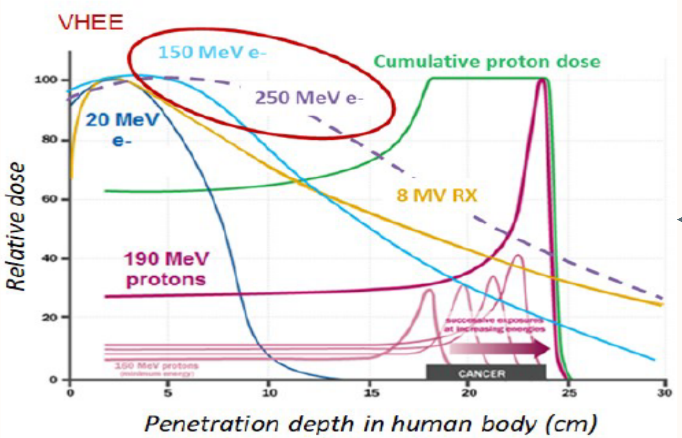
Dose delivery: Spatial fractionation of dose and FLASH

Rachel Delorme, Yolanda Prezado



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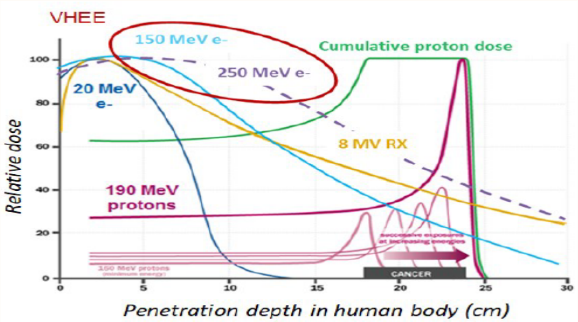
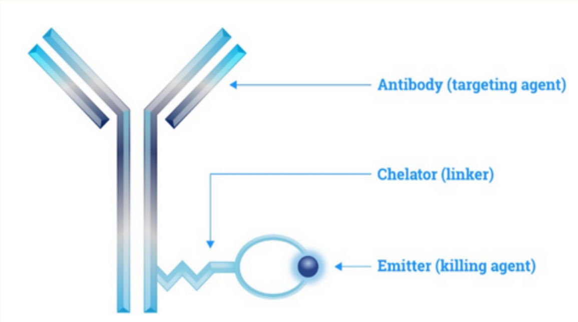


Rachel Delorme, Yolanda Prezado



https://www.actiniumpharma.com

S. Pandeti *et al.*; RSC Advances, 2017

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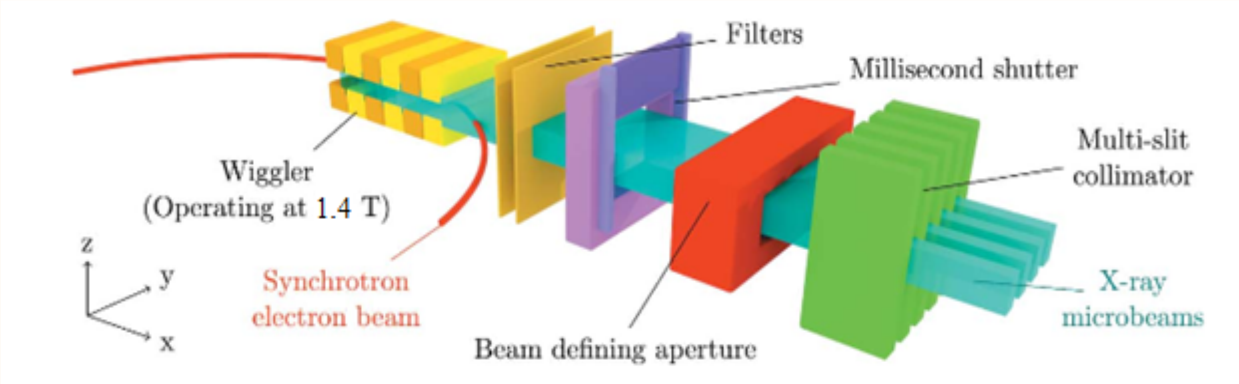

J. Archer *et al.*; JSR, 2018.

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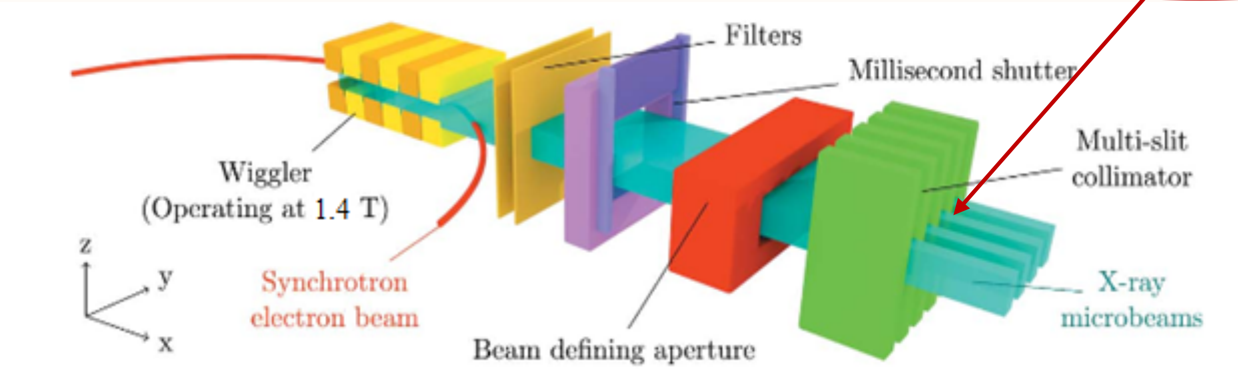
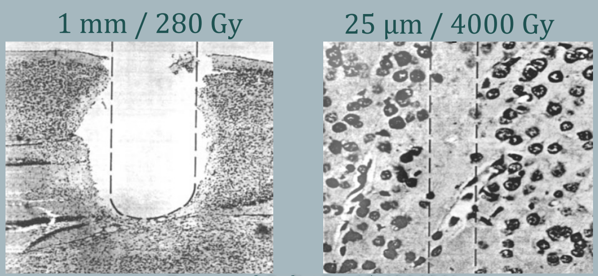
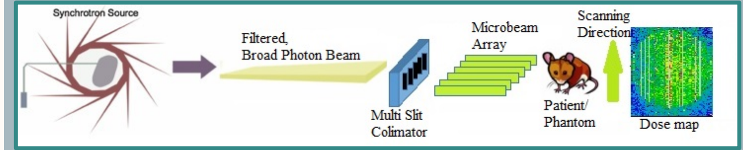


J. Archer *et al.*; JSR, 2018.



Zeman *et al,* Radiat Res 15, 496,1961
Curtis, H. J., Radiat. Res., Suppl. 7, 1967

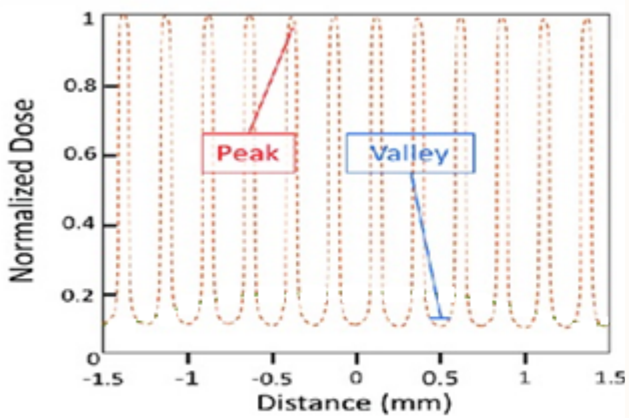


Anderson *et al.*, Phys Med Biol, 2012.

- Spatial fractionation as a technique to induce dose-volume effect.
- Microbeam Radiation Therapy (MRT) is based on dose-volume effect.
- First observation in *1909* by *Alban Köhler.*
- MRT combines spatial fractionation with FLASH effect.

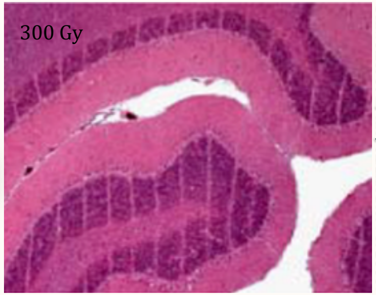
- X-ray beams of 50 μm (Peaks)
- Separation of 400 μm (Valleys)
- Peak to valley dose ratio (PVDR) determines the biological response.

PVDR ↗ Tolerance of normal tissue ↗ Therapeutic index ↗



S. Bazyar, PhD thesis, Chapel Hill, 2018.

- Radiotoxic dose is confined to narrow microbeam passage area.



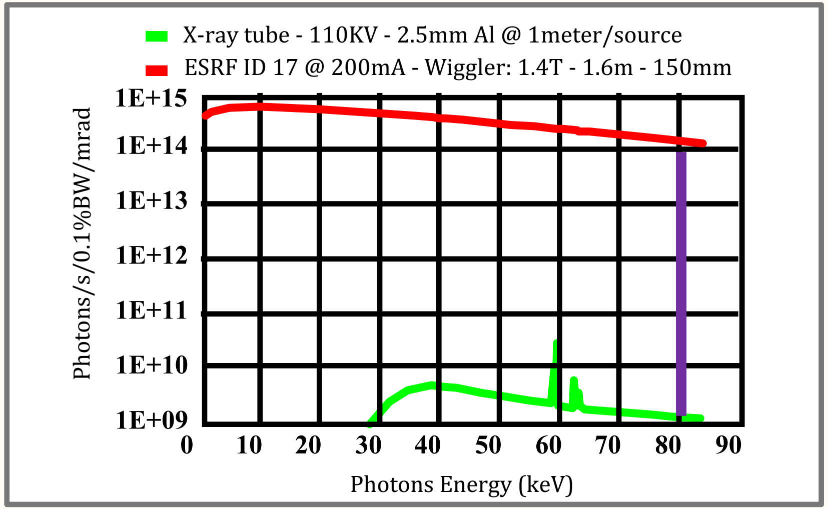
Schweizer *et al*, Int J Radiat Biol 76. 2000.

Cervelet piglet (15 months after ir.)

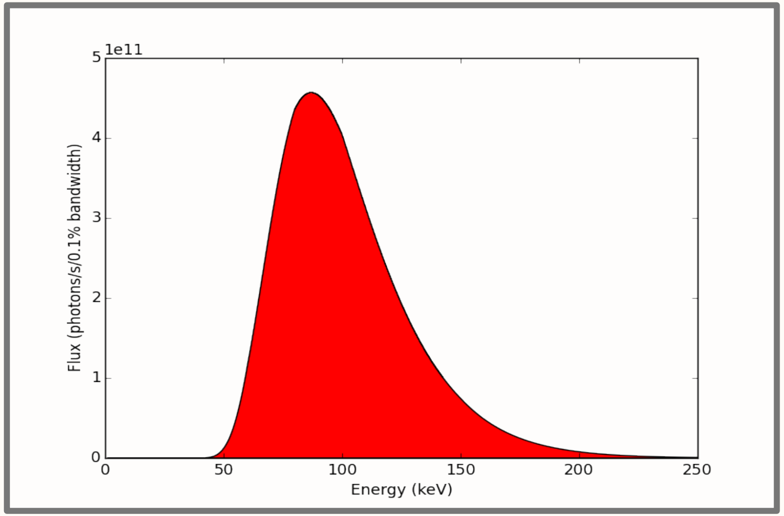
- Low divergence
- High dose rate
- Steep penumbra

As an ideal irradiation source:

3^{th} generation of synchrotron
Like ESRF, Grenoble, France



Energy spectrum ID17 (ESRF)



15 $kGy.s^{-1}$ in synchrotron

To avoid smearing out microbeams attributable to the organ motion

- Challenges in MRT
  - Experimental dosimetry
  - Dose calculation

- Challenges in MRT

Experimental dosimetry

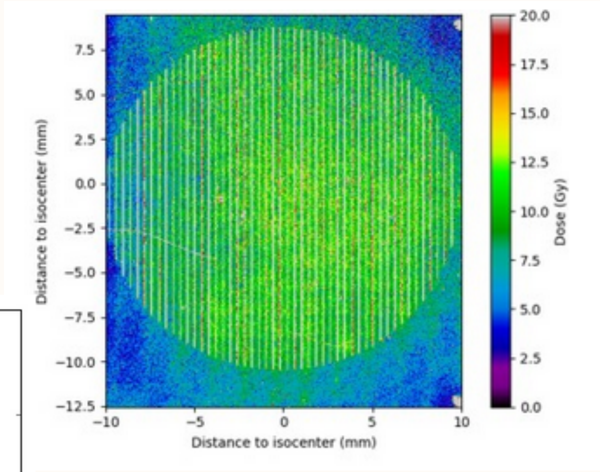
Dose calculation

- High dose rate 15 $kGy.s^{-1}$
- Micrometric resolution
- Dynamic dose range from 1 Gy to 1000 Gy
- Water equivalency of dosimeter

Potential dosimeters for MRT:

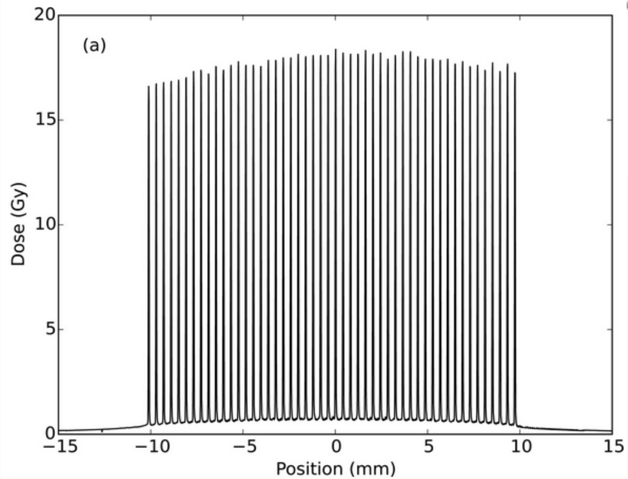
- Proportional counters TEPC
- Solid state MOSFET
- Fluorscent nuclear track detector (FNTD)
- Thermoluminescent Dosimeter (TLD)
- Silicon strip detector
- Doped optical fibers
- MRI gel dosimeters
- Diamond detector
- Gafchromic films

Gafchromic (HD-V2)



A. Ocadiz *et al*. Physica Medica; 2019.

MicroDiamond 60019



J. Livingstone *et al.*, Med. Phys, 2016.

- Challenges in MRT

Experimental dosimetry

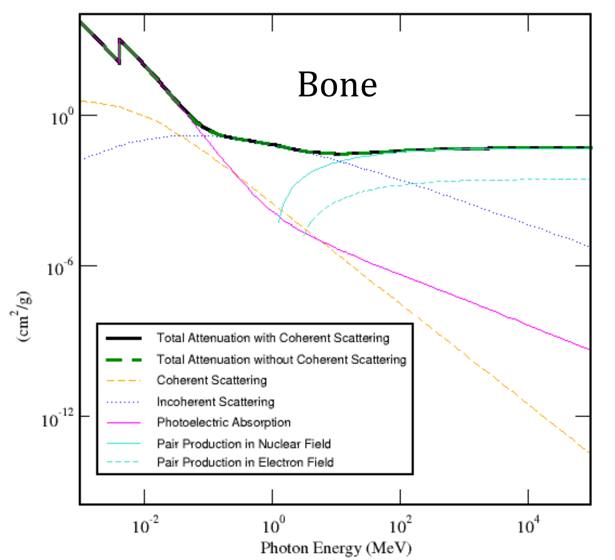
Dose calculation

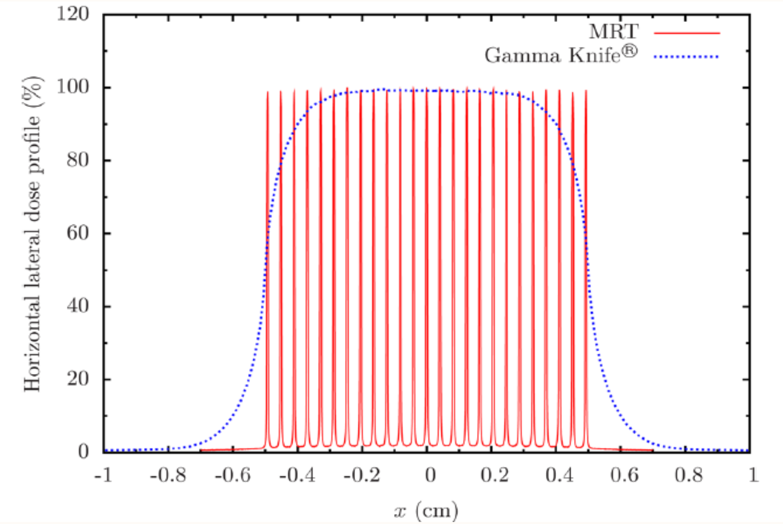
Dose calculation in MRT is different from conventional RT

Energy spectrum

Spatial dose distribution pattern

XCOM/Nist





I. Martinze-Rovira. et al, Med. Phys. 2012.

- At kV energies, photoelectric effect induces a strong atomic number dependence.

Three dose calculation algorithms in MRT

- Convolution/superposition
- Monte Carlo
- Hybrid

Three dose calculation algorithms in MRT

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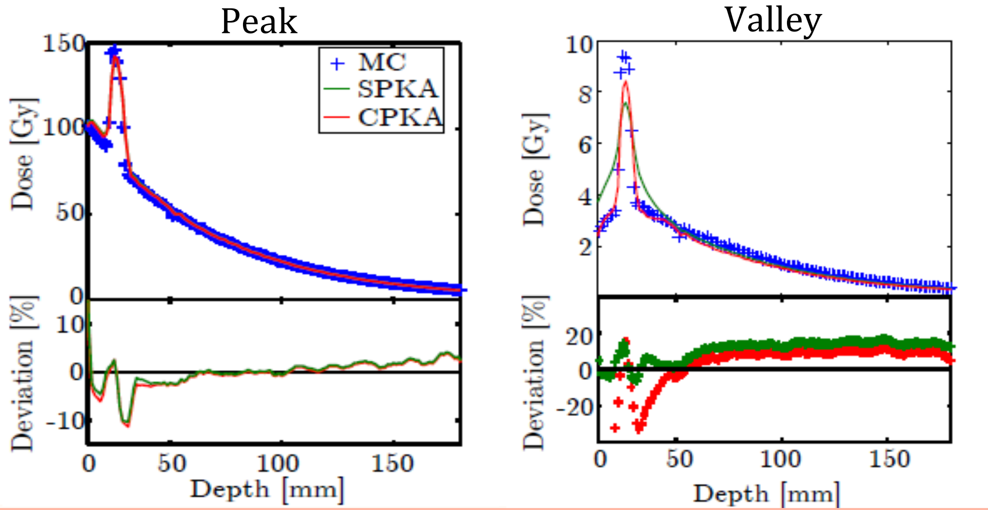
Convolution of TERMA and analytical dose kernel:

- Uncertainty in heterogeneities.
- Lack of consideration the photon polarization.

Percentage depth dose



S. Bartzsch, PhD thesis, 2014.

Three dose calculation algorithms in MRT

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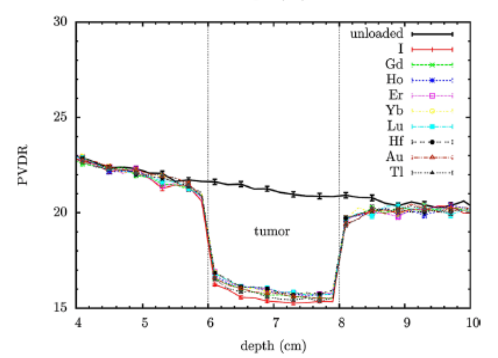
PVDR calculated by PENELOPE



I. Martinze-Rovira. et al, Med. Phys. 2011.

- Time consuming
- Micrometric grid
- Consideration of photon polarization

The only option to reproduce correctly the propagation of scattered orthovoltage photons on a heterogeneous geometry

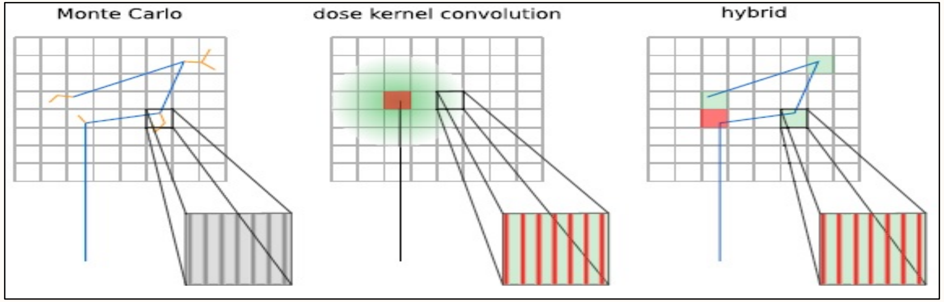
Three dose calculation algorithms in MRT

Convolution/superposition

Monte Carlo

Hybrid

- Inherits photon transport from MC and electron transport convolution based method.

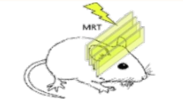


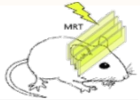
M.Donzelli, *et al*; Phys Med Biol. 2018.

Based on several approximations with:
Advantage: Rapidity
Disadvantage: Potential uncertainty

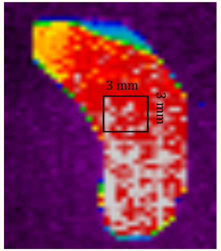
Experimental validation of hybrid algorithm using EBT-3 and HD-V2 Gafchromic films

MRT 373 Gy

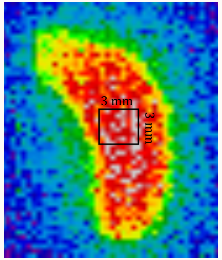
	**Relative difference**
Peak (2cm)	-33.46%
Peak (7cm)	-5.78%

	**Relative difference**
Valley (2cm)	19.05%
Valley (7cm)	45.78%

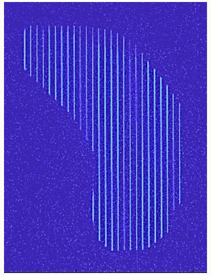
Peak dose map



Valley dose map



Peaks & valleys



Potential explanations

Hybrid algorithm uncertainties

- Polarized Livermore as physics list
- Field shape complexity
- Energy spectrum
- No scattering in collimator

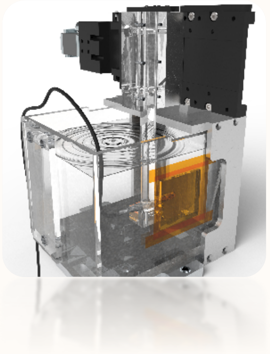
Film dosimetry uncertainties

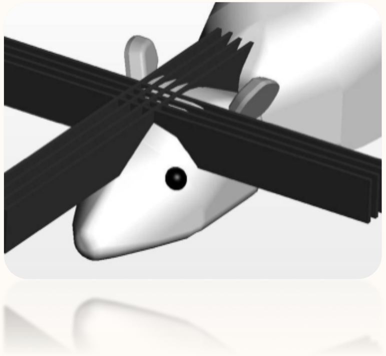
- Statistical noise
- Film inhomogeneities
- Calibration uncertainties

Developing a new hybrid calculation engine for MRT which is able to consider:

- Beam and beam modifier properties, photon polarization and irradiation geometries.
- Dose metrics adapted to MRT and biological equivalent doses.

Benchmarking and validation the TPS using in-vitro and in vivo trials.





Thank you for your attention

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