The Henryk Niewodniczański Institute of Nuclear Physics Polish Academy of Sciences

Investigations on physical and biological range uncertainties in Krakow proton beam therapy centre

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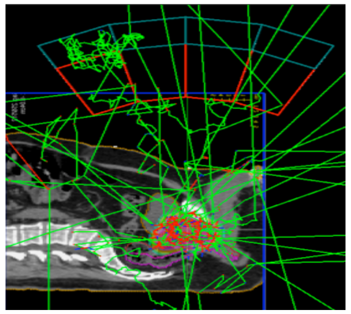
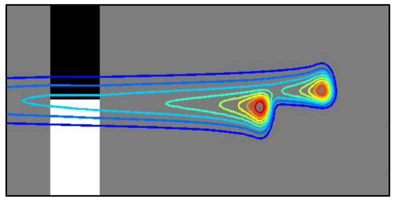
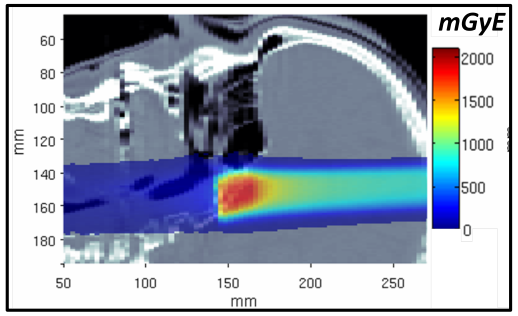
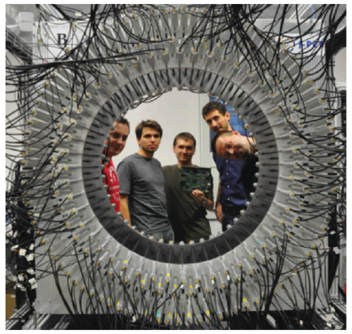
The National Centre for Research and Development
LIDER
European Funds Smart Growth
Republic of Poland
FNP Foundation for Polish Science
European Union European Regional Development Fund

Outline









GPU accelerated Monte Carlo code **FRED** for

- Treatment planning, biological dose modeling with variable RBE, quality assurance

J-PET for

- Proton therapy range monitoring by means of PET-gamma detection

- Research
- Translation
- Interdyscyplinary collaboration

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Photons
TCP/NTCP

$$D_{bio} = D_{phys} \cdot RBE$$

Protons
TCP/NTCP

Physical

Biological

range uncertainties

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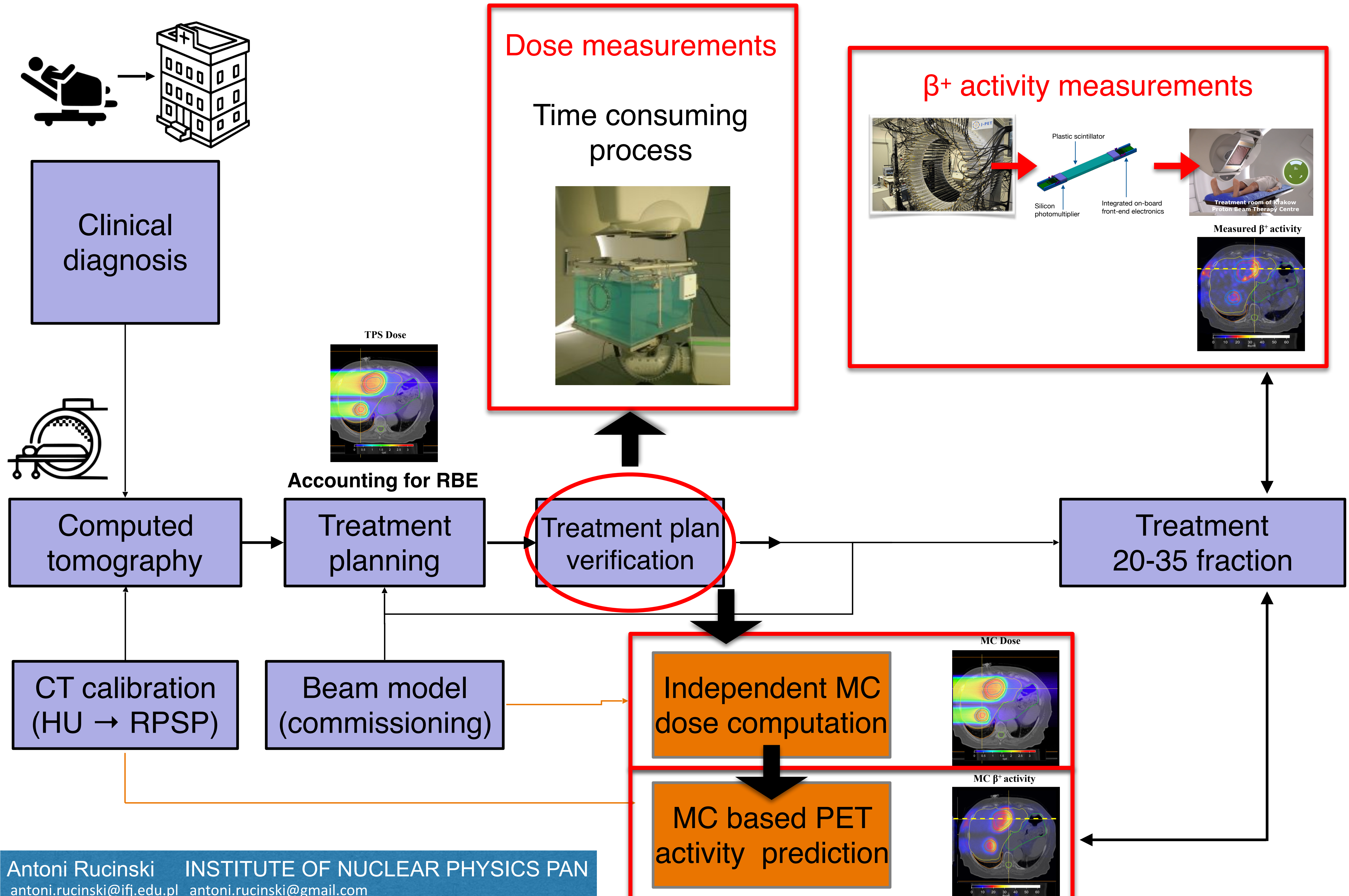
Proton therapy treatment



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Fred MC: the power of GPU

Validation vs. FLUKA and measurements @ CNAO (Schiavi et al. PMB 2017)

acc. x1000 wrt. full MC code

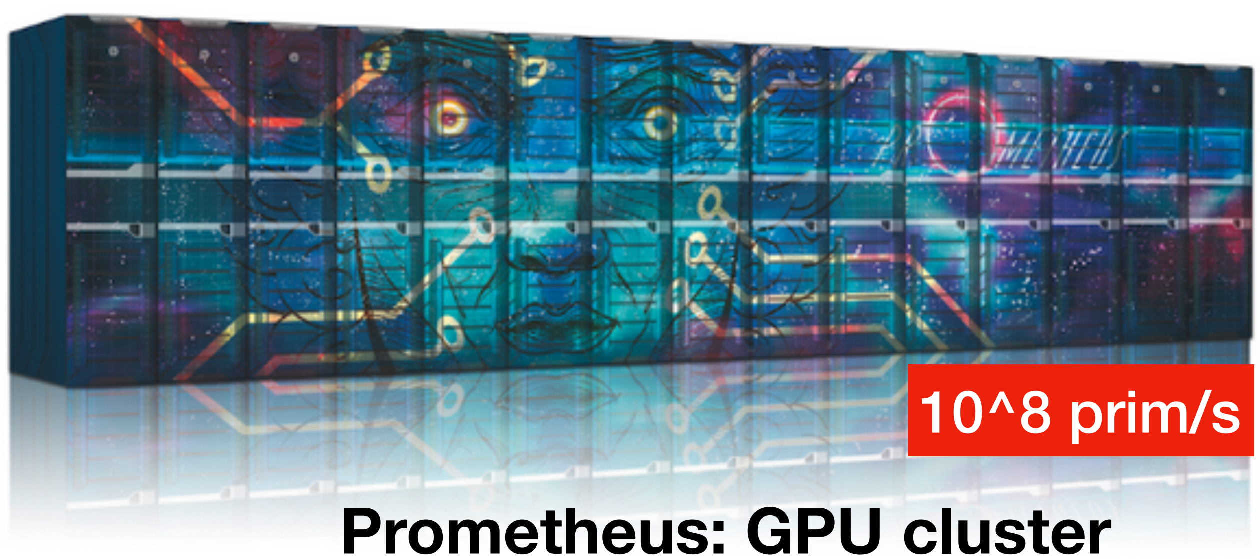
Accuracy
Flexibility
Efficiency

- MC for protons in voxel geometry
- condensed history for continuous processes (dE/dx, MCS, energy loss fluctuations),
- single steps for nuclear events: elastic and inelastic; fragmentation; local deposition of heavy ions; tracking of secondary protons and deuterons
- HU to density conversion (Schneider) and stopping power calibration
- dose optimisation using Dose Difference Optimisation (DDO; Lomax)
- RBE = 1.1 for protons and variable RBE calculations…

+

10^6 prim/s

Local computation unit



10^8 prim/s

Prometheus: GPU cluster

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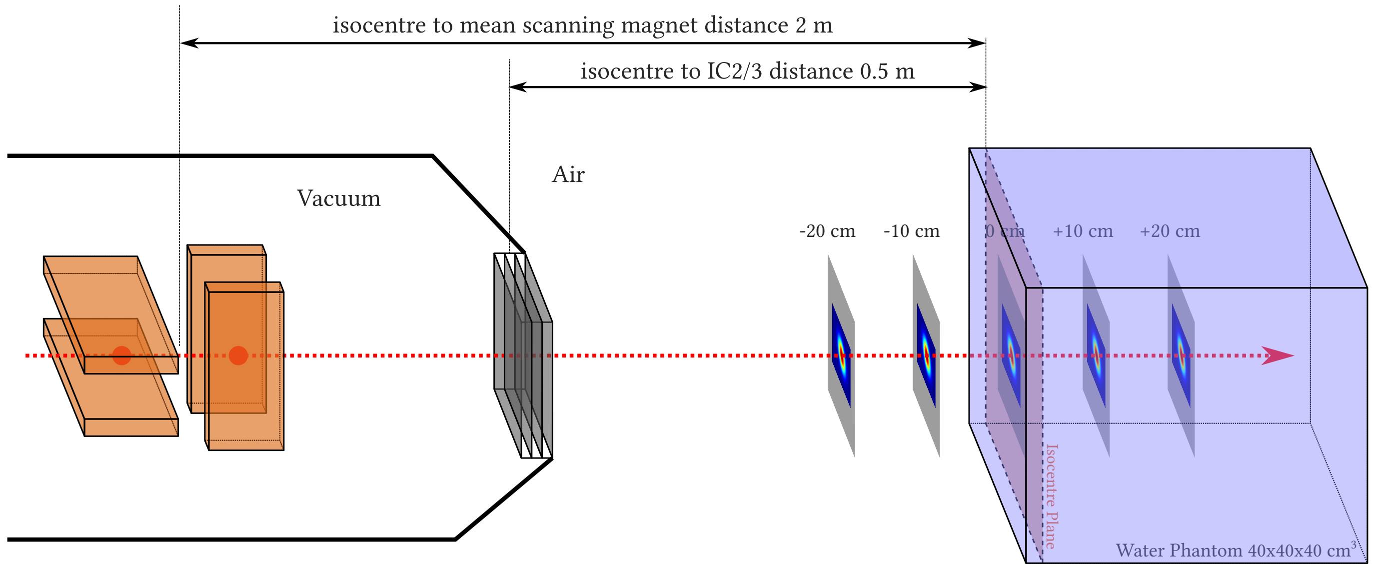
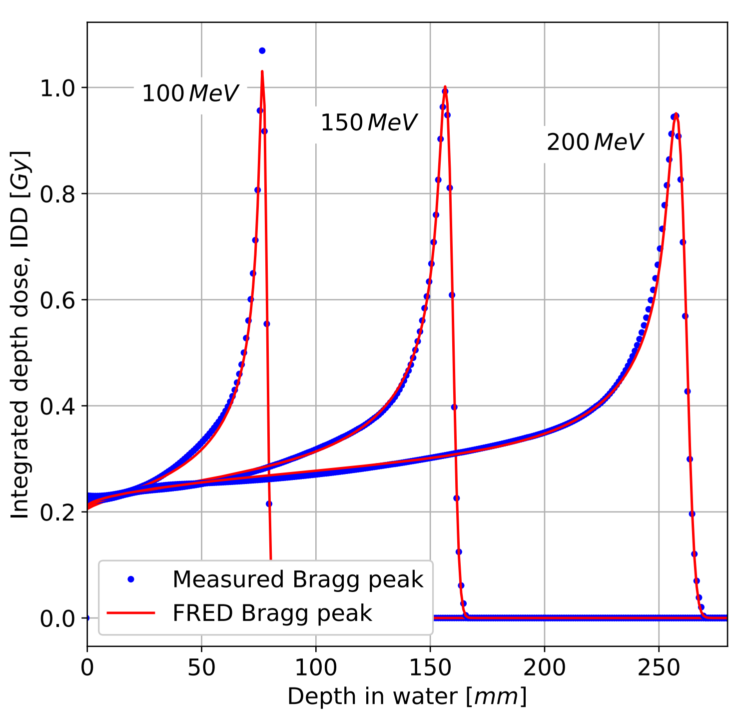
New developments of FRED

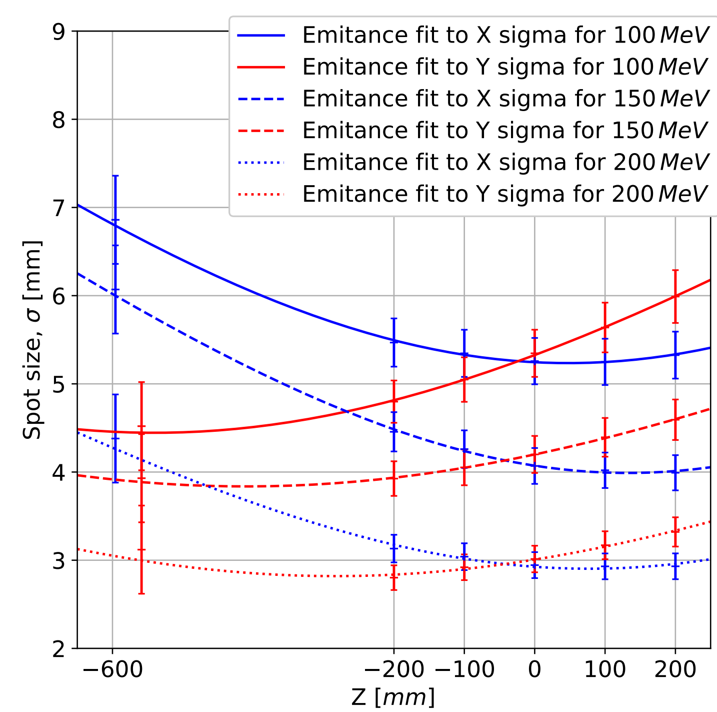
- Proton radiography (Lyon, Maastricht)
- Implementation of scoring in multiple regions with arbitrary orientation
- Application of range shifter, dynamic aperture or detector development for range monitoring in PBT
- Slicer 3D interface
- FRED kernel developments/implementations
    - photon interactions
    - nuclear models for light ions in particle therapy (e.g. carbon, helium, oxygen).

Commissioning - physics

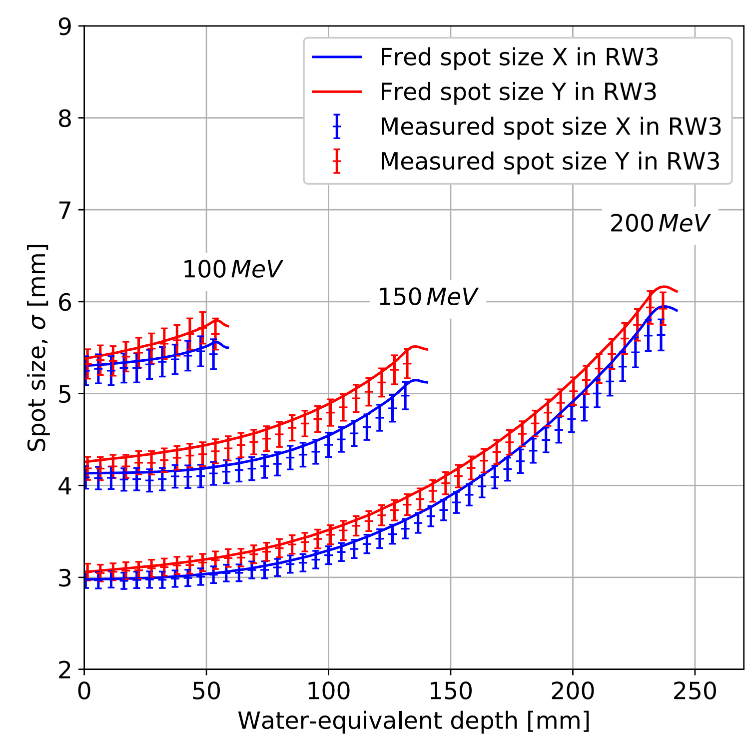




Range



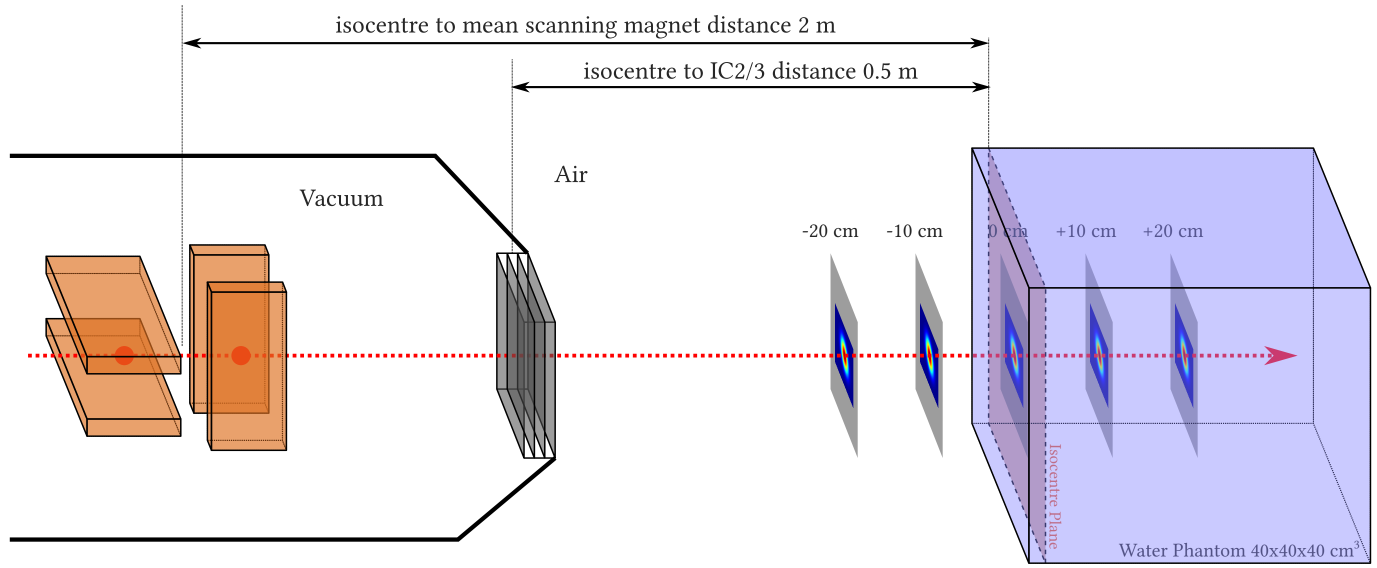
Lateral profiles in air

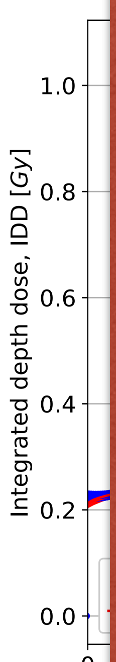


Lateral profiles in RW3

Submillimetre agreement, with and without range shifter

Commissioning - physics





9 parameters of beam model for each 17 energies
(E + σE + 6 emittance param. + MU scaling factor)

Beam model based on commissioning measurements
or up-to-date QA data

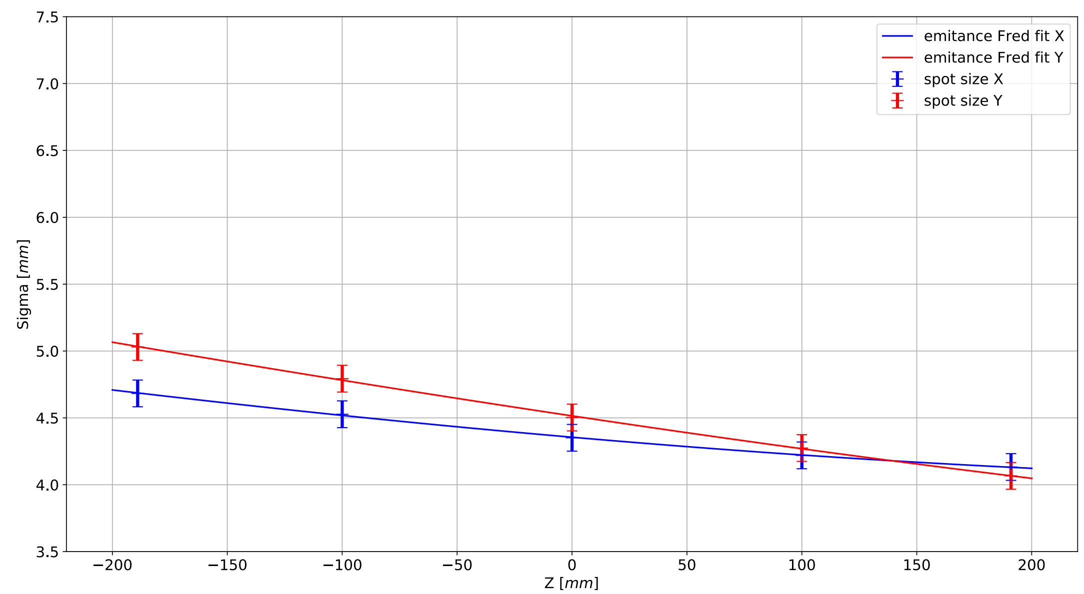
Beam model preparation time ~12h (fully automated)

Range **Lateral profiles in air** **Lateral profiles in water**

Submillimetre agreement, with and without range shifter

VARIAN medical systems

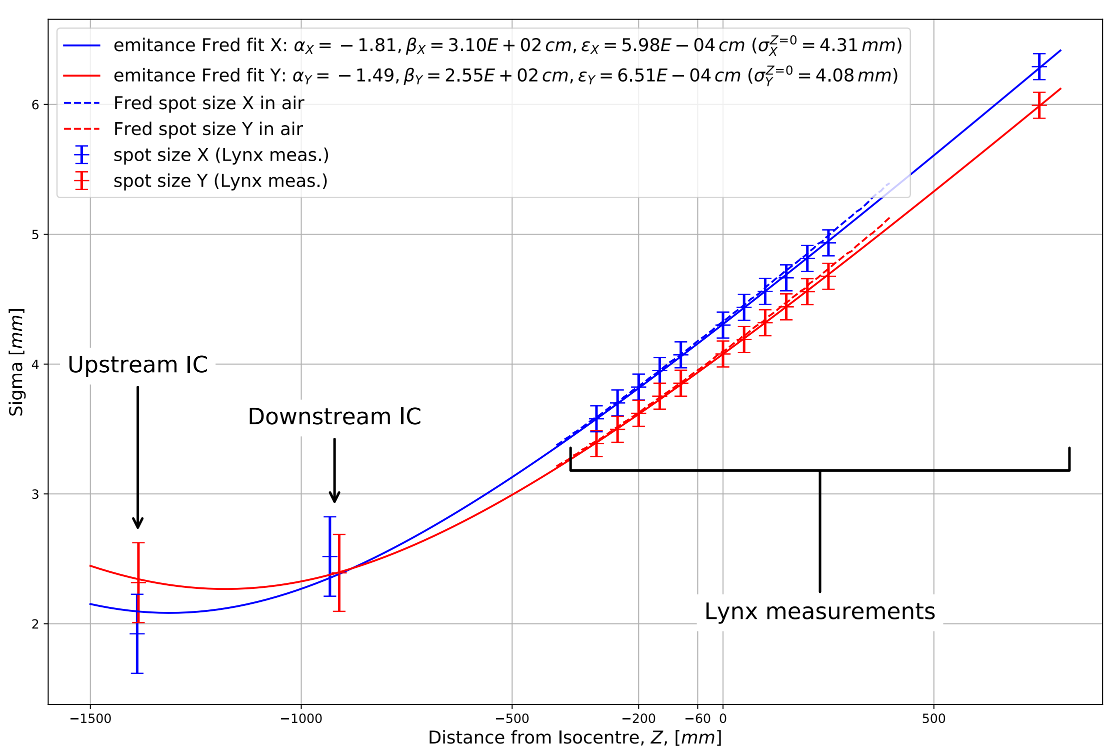
E200



MEVION medical systems

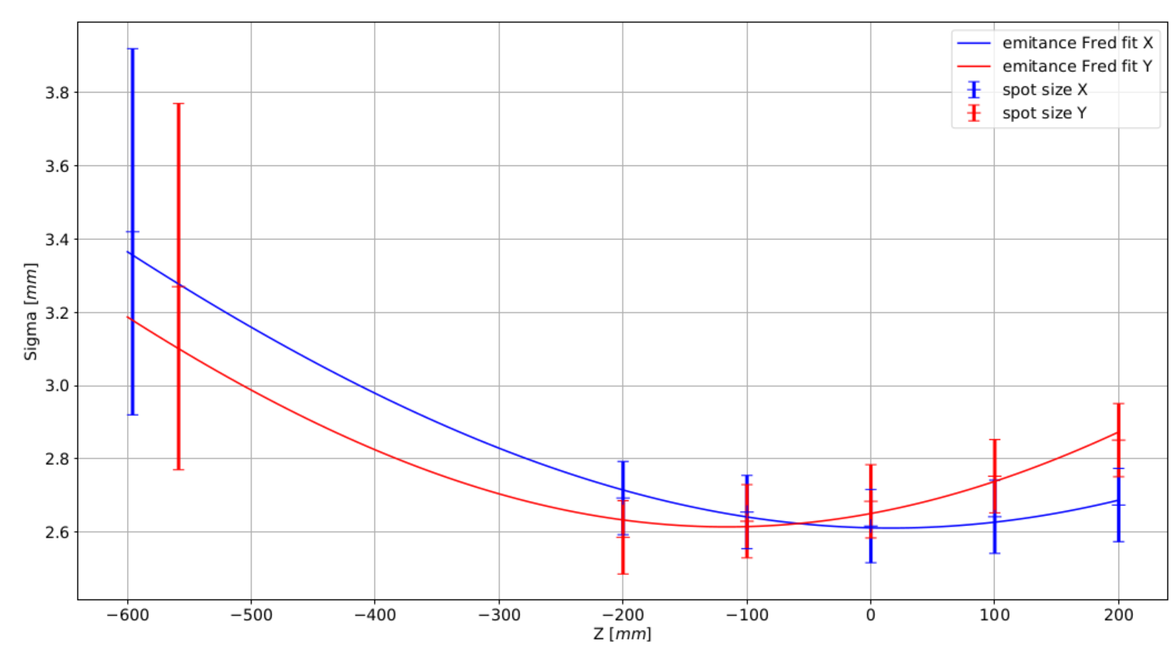
MAASTRO CLINIC

E227

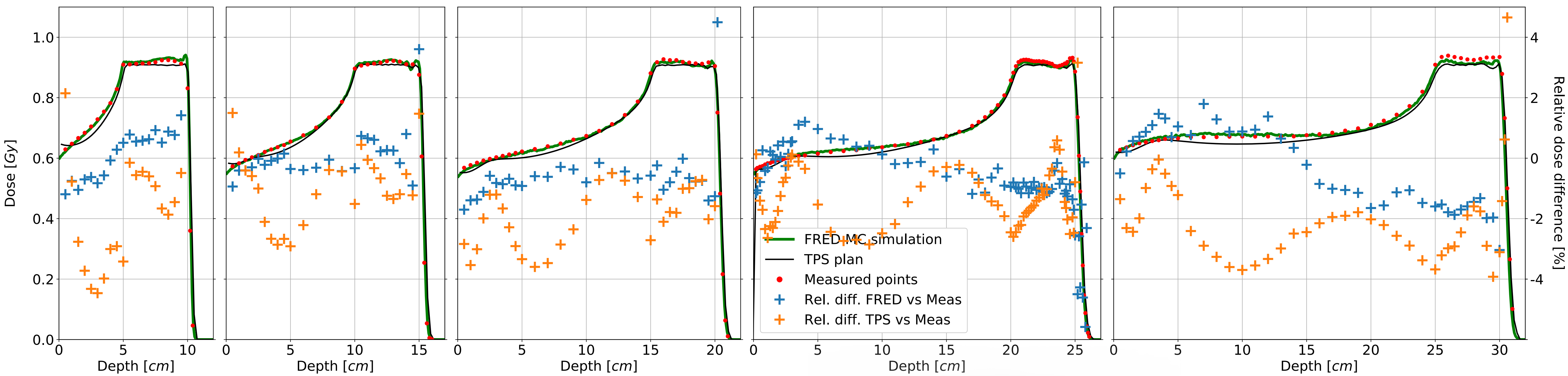


CCB

E200

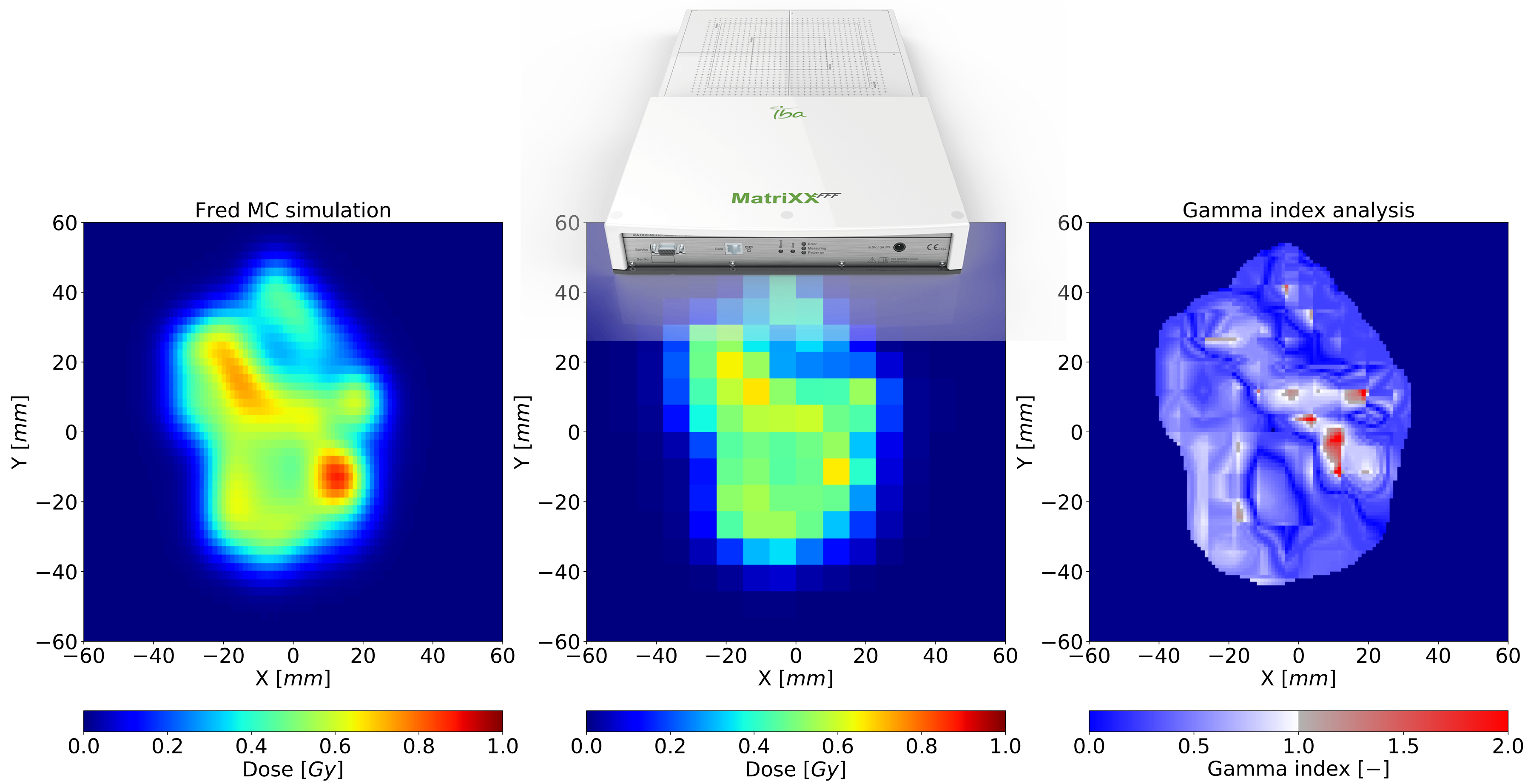


Validation in water

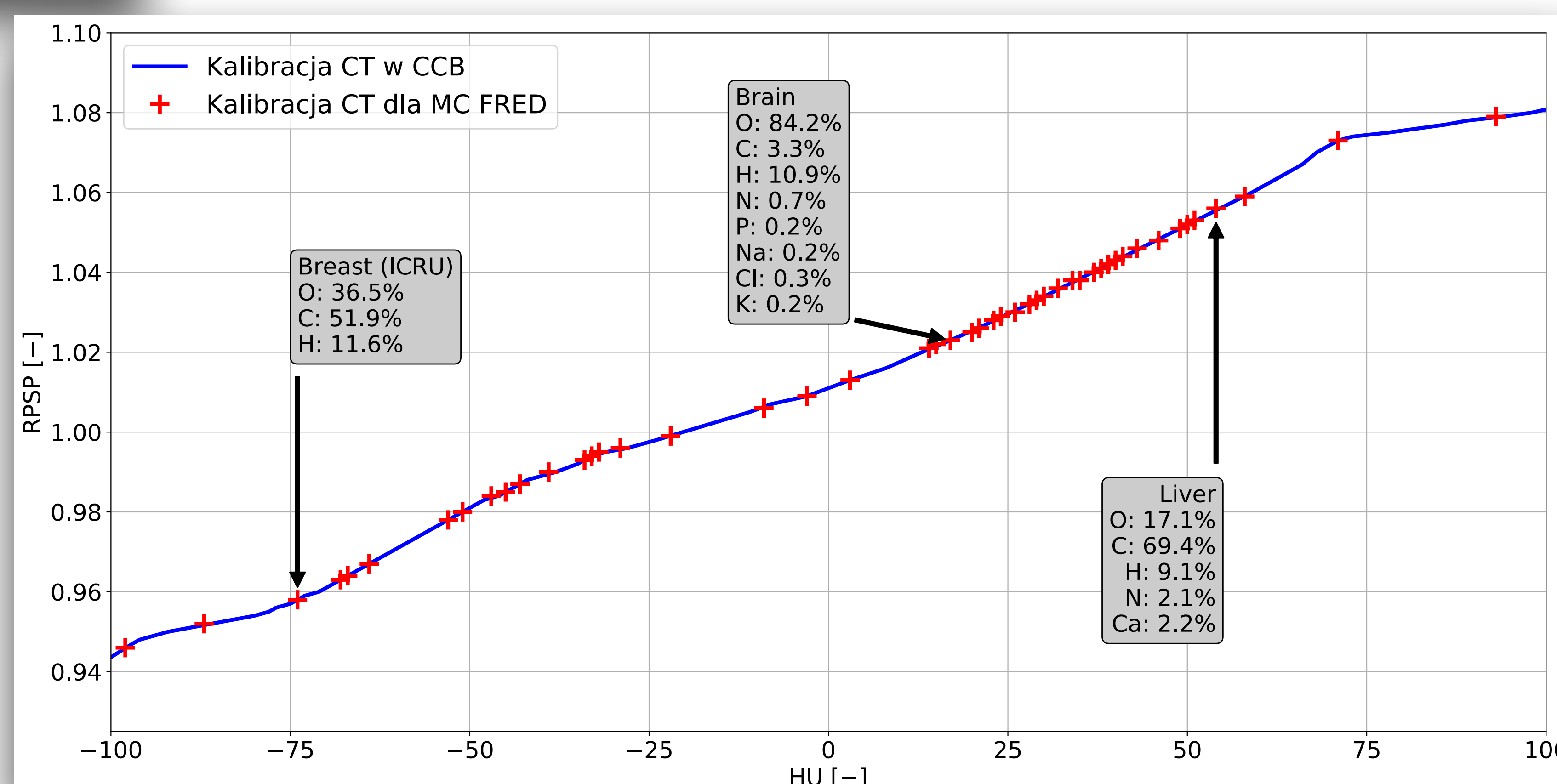


182 QA measurements with MatriX

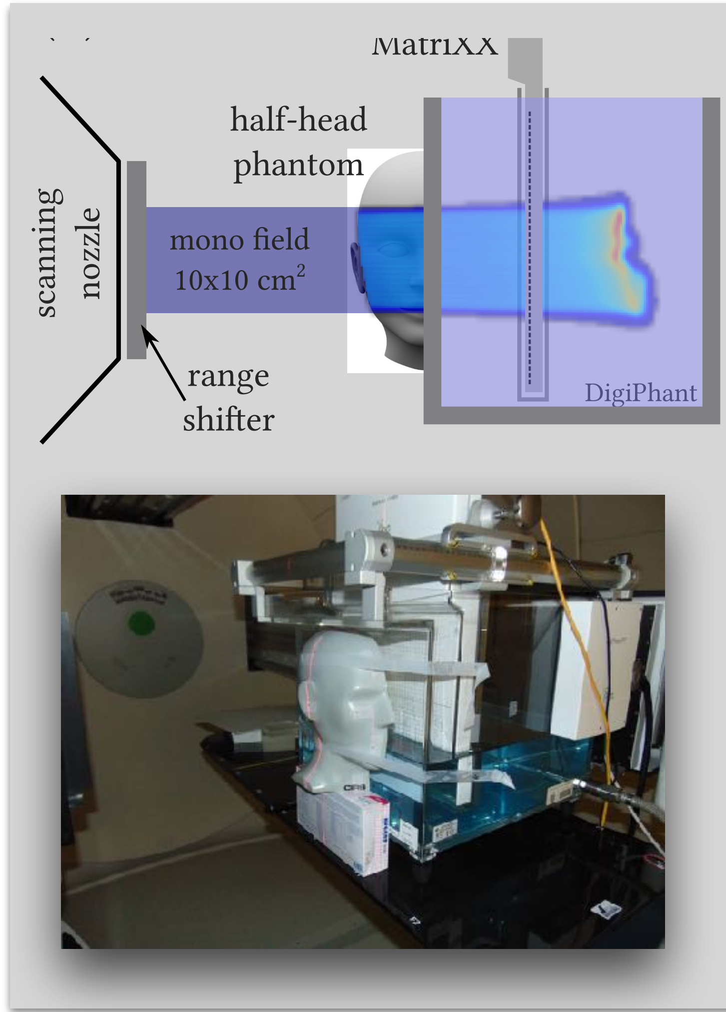
Gamma Index
(2mm/3%, CCB workflow)
FRED: 94.6(10.4)% (1σ)
TPS: 91.3(13.6)% (1σ)



CT calibration

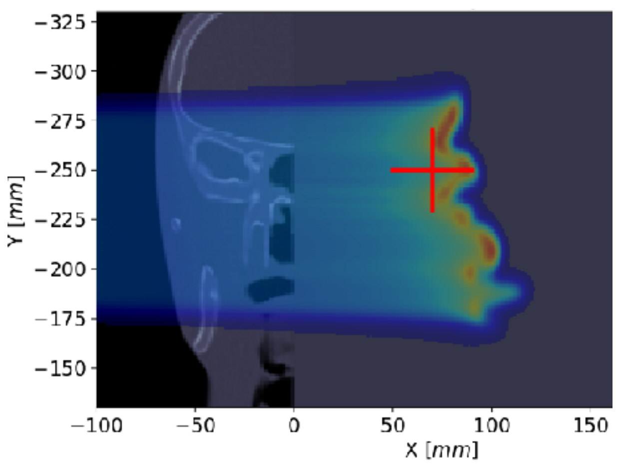


Validation in head phantom

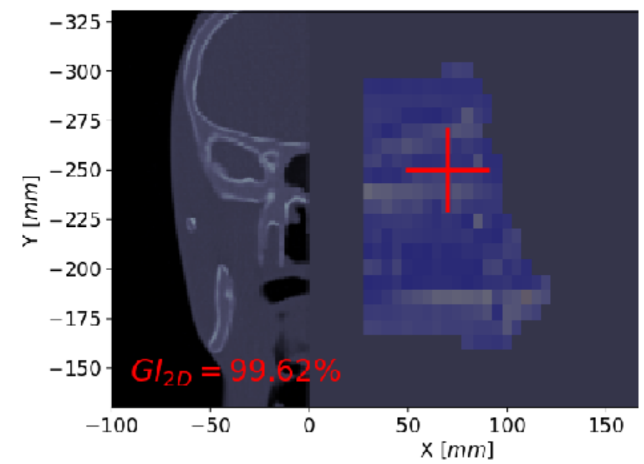


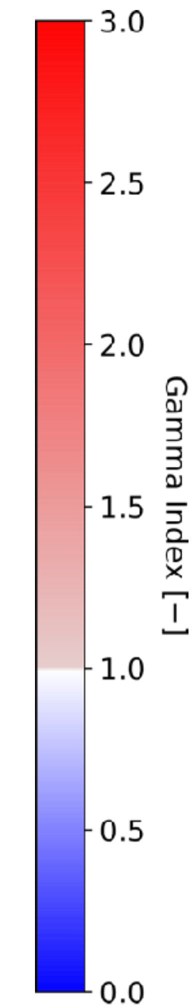
Gamma Index

FRED

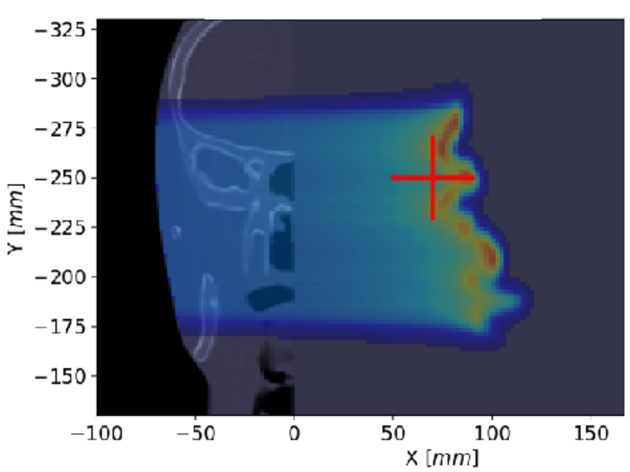


FRED vs MatriXX

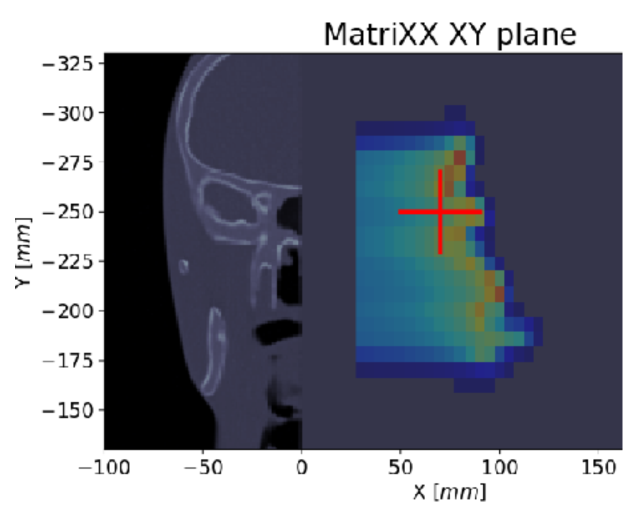




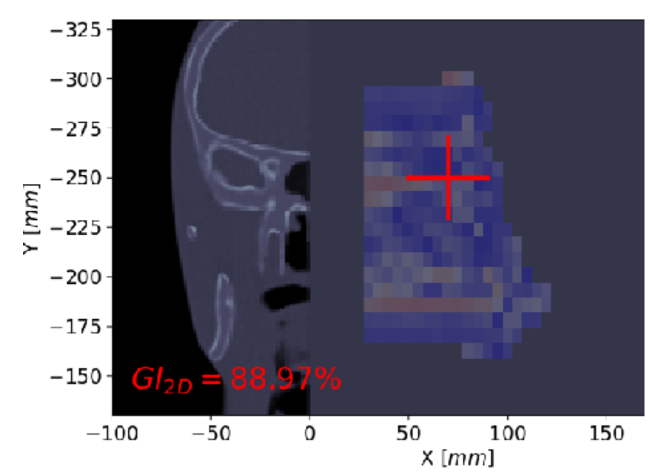
TPS



MatriXX



TPS vs MatriXX



Uniform, mono-energetic field, 150 MeV, 10x10 cm

Photons
TCP/NTCP

$$D_{bio} = D_{phys} \cdot RBE$$

Protons
TCP/NTCP

Physical range uncertainties

Biological range uncertainties

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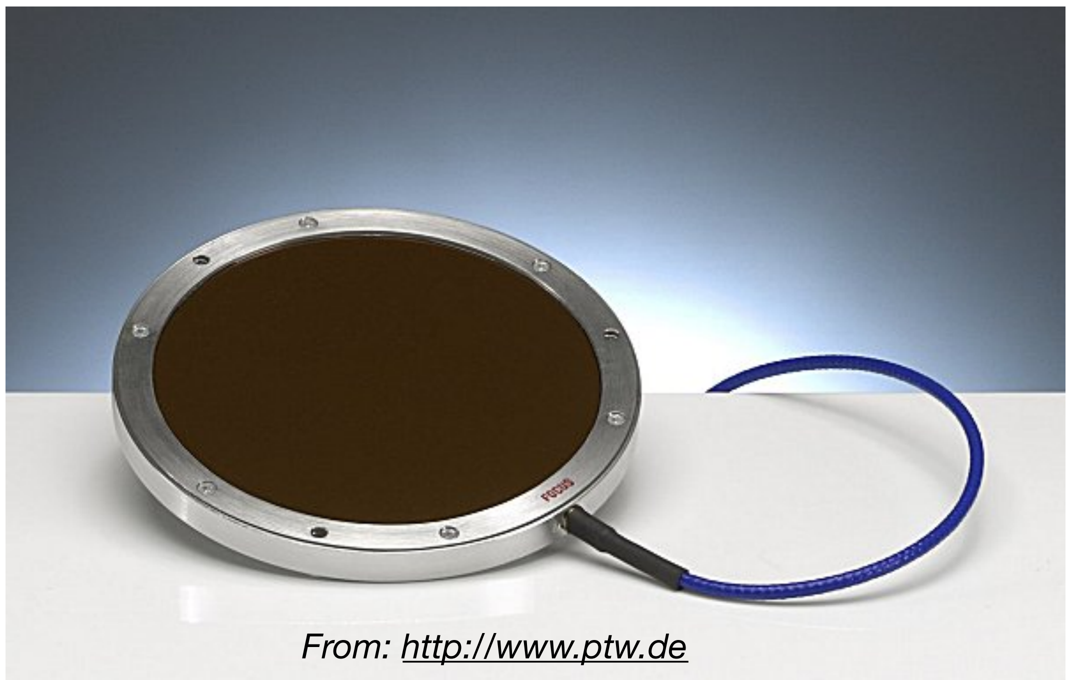
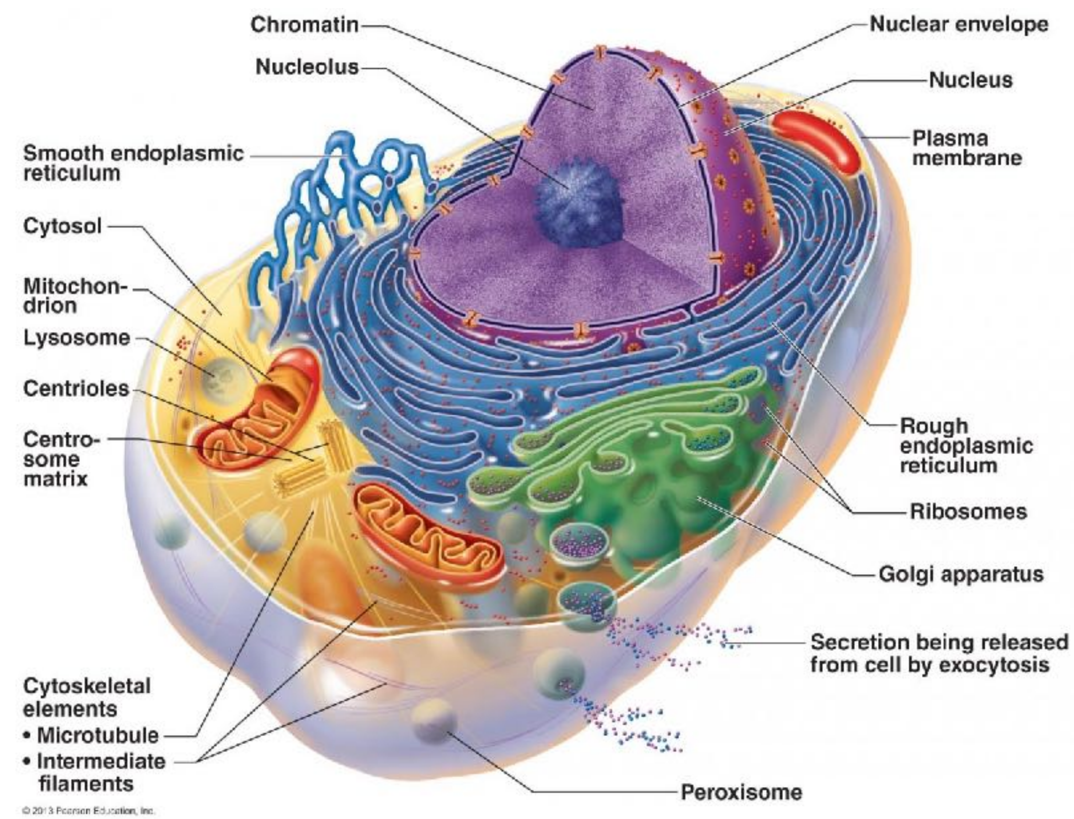
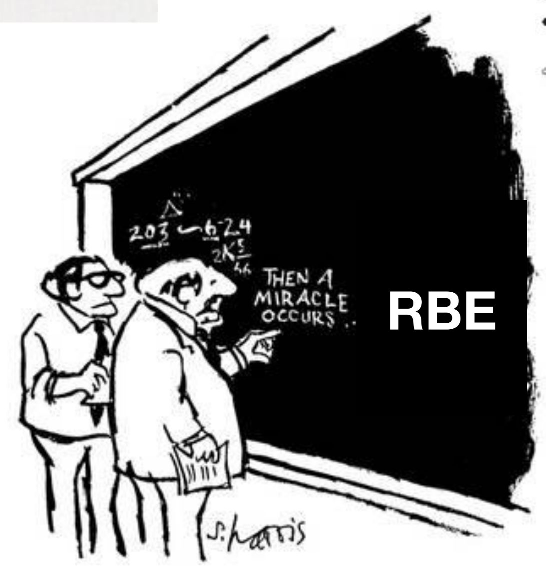
Radiobiological modeling

Dose: Macroscopic concept ? **Cell damage: Microscopic concept**





RBE modeling



"I think you should be more explicit here in step two."

RBE modeling:
- Phenomenoligical
- Microdosiemtric
- Mechanistic

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Constant RBE proton therapy routine

$$D_{bio} = D_{phys} \cdot RBE$$

Average RBE is ~1.1

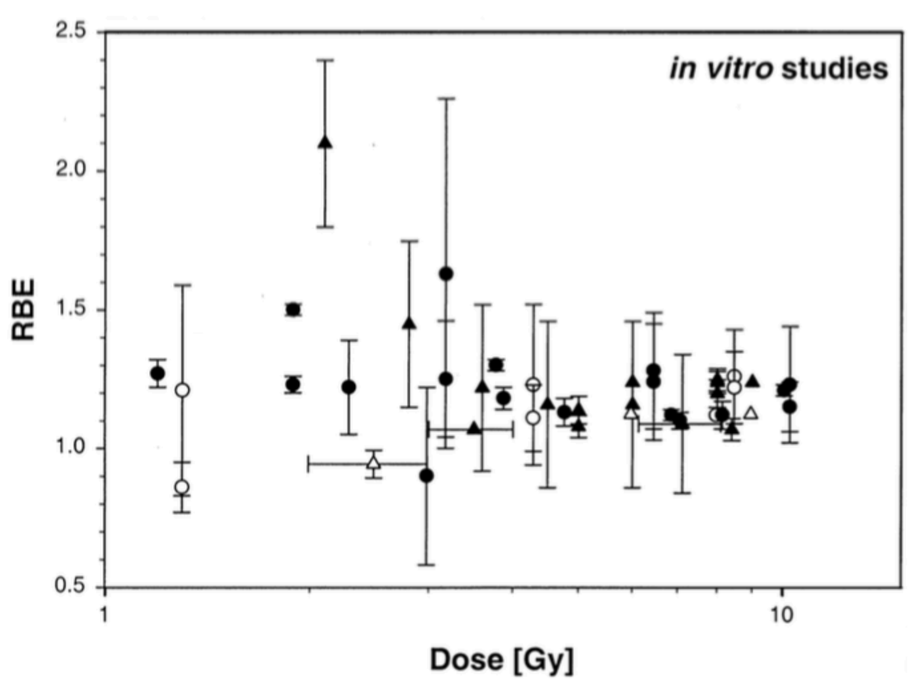
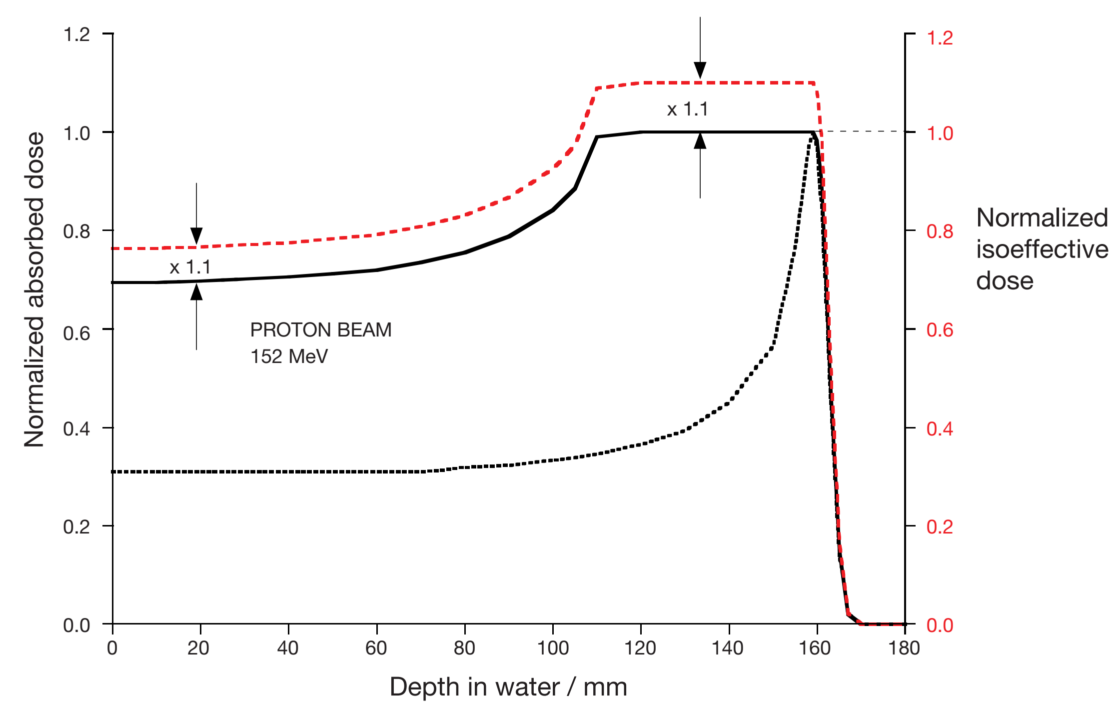


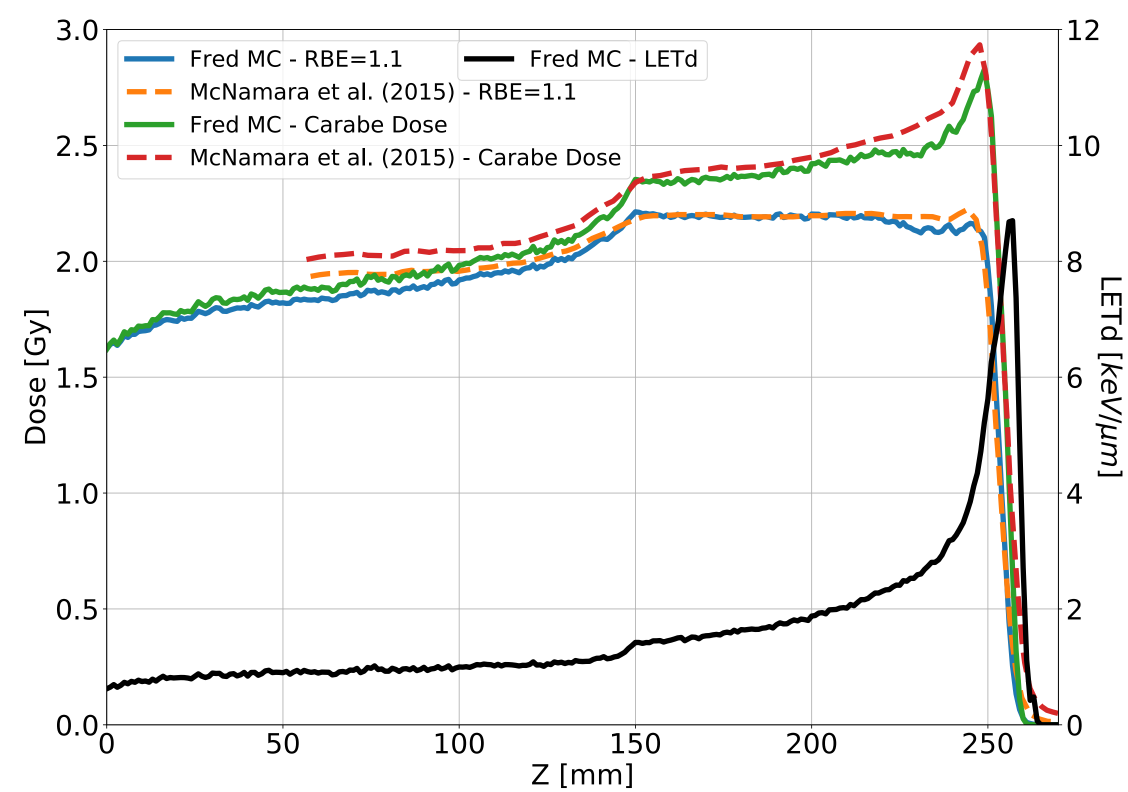
Fig. 1. Experimental proton RBE values (relative to ^{60}Co) as a function of dose/fraction for cell inactivation measured *in vitro* in the center of a SOBP. Closed symbols show measurements using Chinese Hamster cell lines; open symbols stand for other cell lines. Circles represent RBEs for <100-MeV beams and triangles for >100-MeV beams.



Variable RBE hypothesis in proton therapy

$$D_{bio} = D_{phys} \cdot RBE$$

- **RBE depends on**
  - dose/fractionation scheme
  - biological endpoint
  - LET (depth, particle type)
  - Dose rate (FLASH)

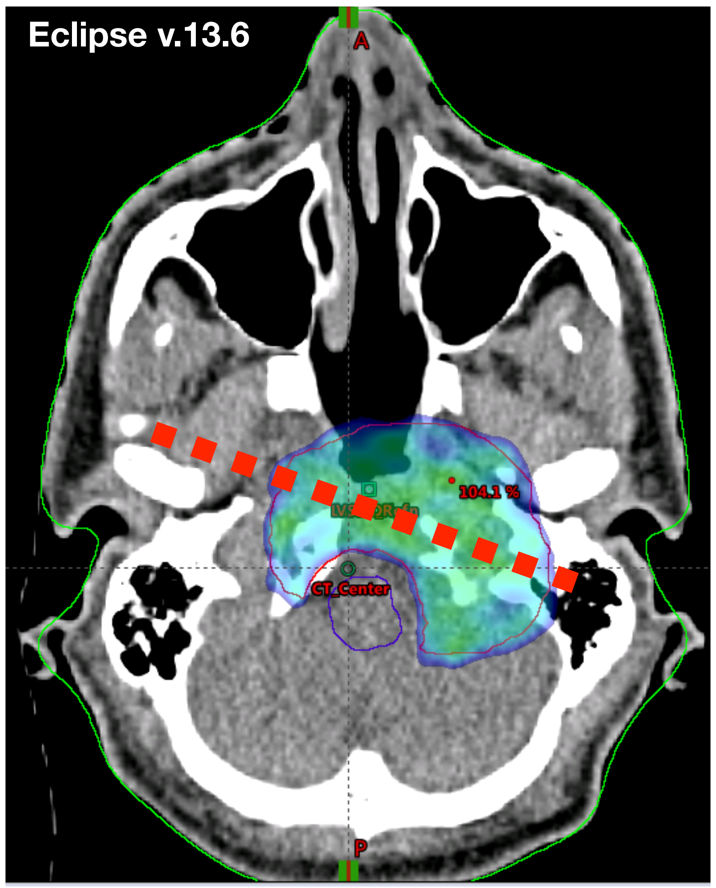


LQ model based

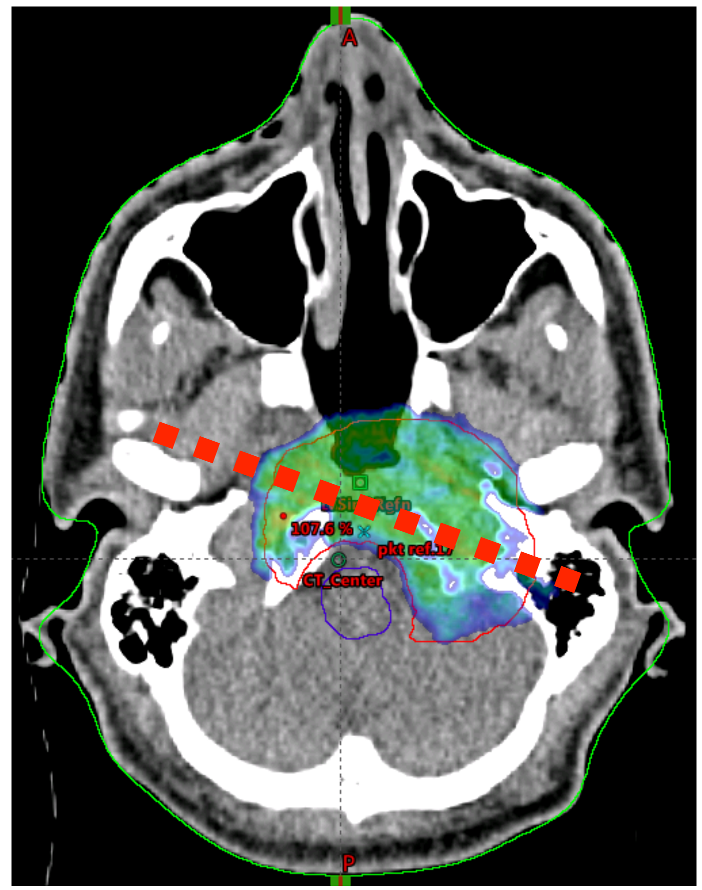
$$RBE\left(D_p, \frac{\alpha_p}{\alpha_x}, \frac{\beta_p}{\beta_x}, \left(\frac{\alpha}{\beta}\right)_x\right) = \frac{D_x}{D_p} = \frac{\sqrt{\left(\frac{\alpha}{\beta}\right)_x^2 + 4\frac{\alpha_p}{\alpha_x}\left(\frac{\alpha}{\beta}\right)_x D_p + 4\frac{\beta_p}{\beta_x} D_p^2} - \left(\frac{\alpha}{\beta}\right)_x}{2D_p}.$$

Variable RBE for CCB patient

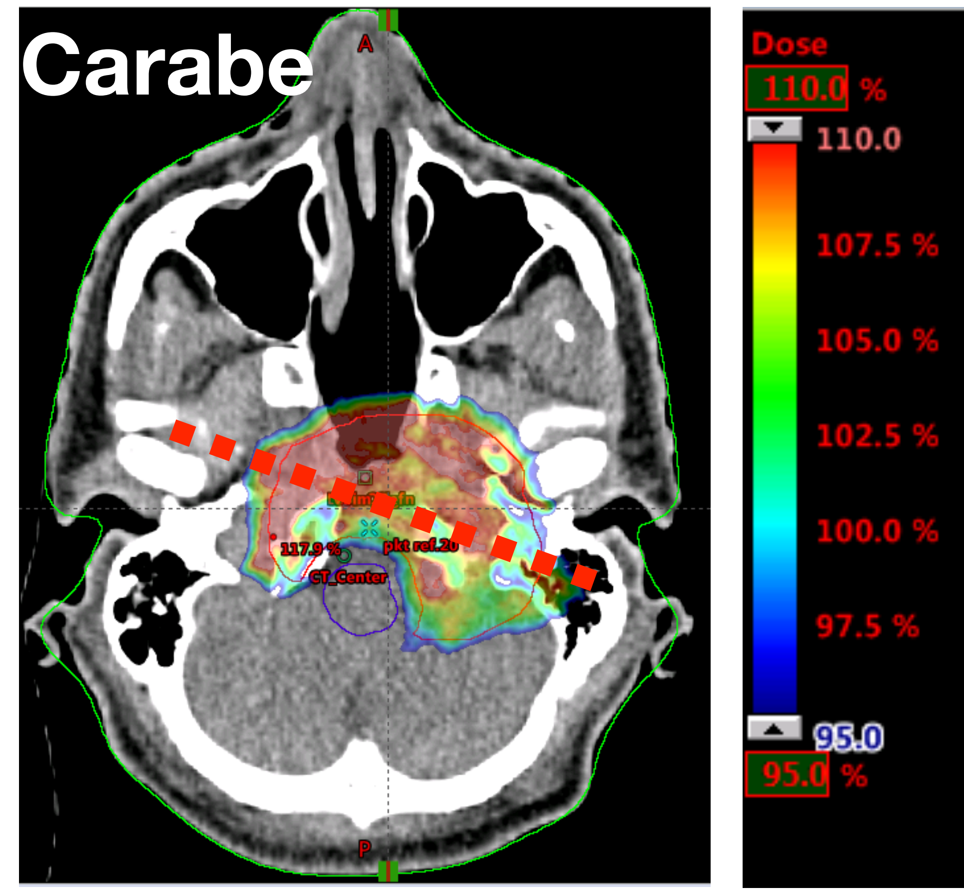
Radiobiological dose
TPS RBE=1.1

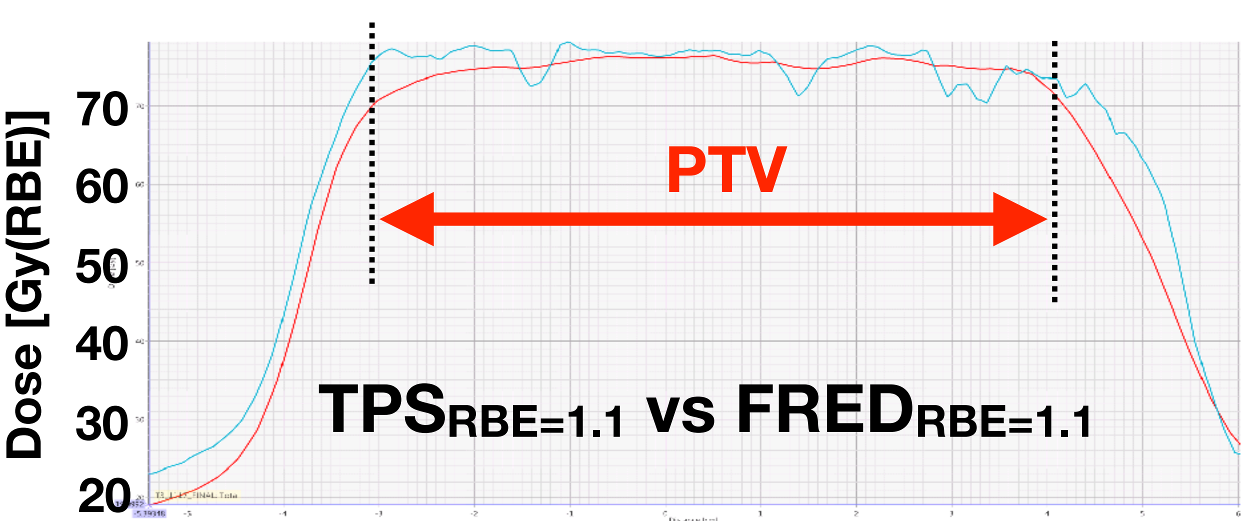


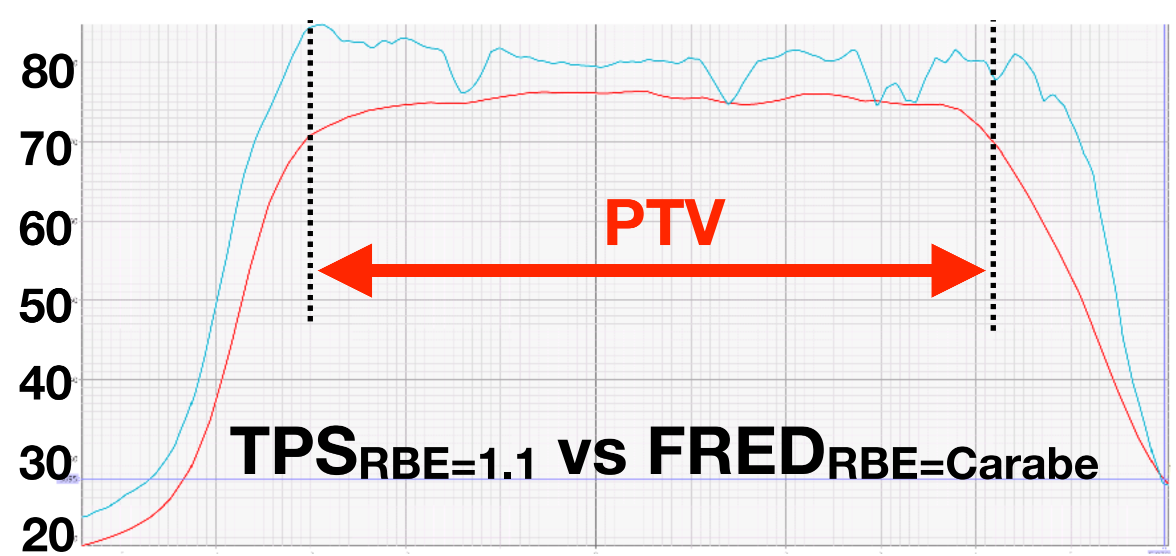
Radiobiological dose
FRED RBE=1.1



Radiobiological dose
FRED variable RBE

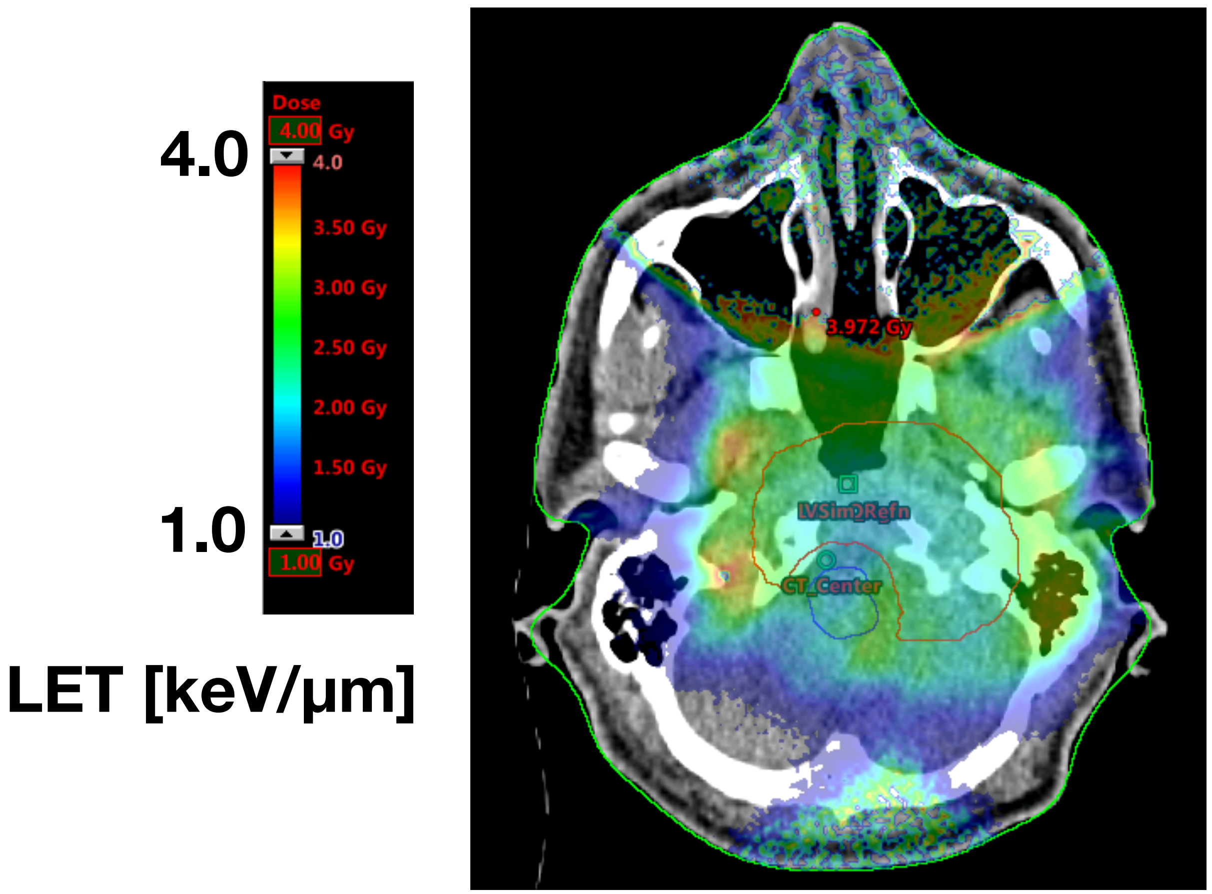




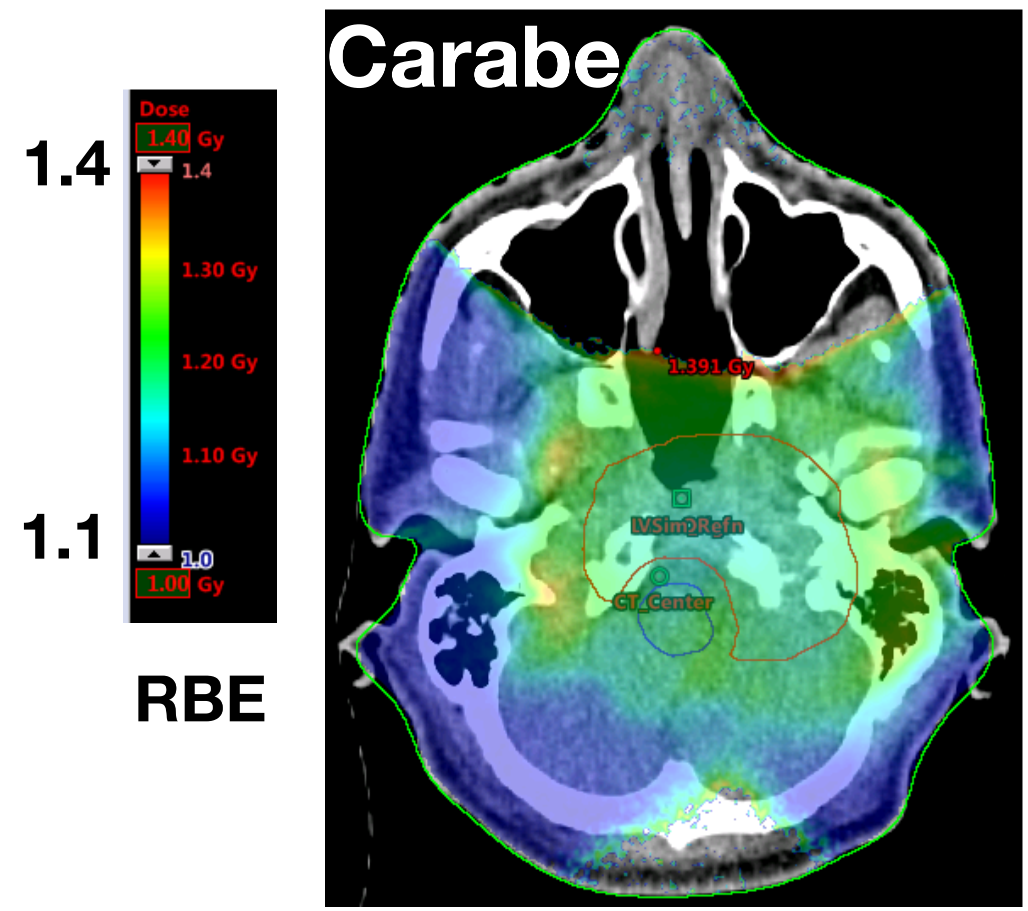


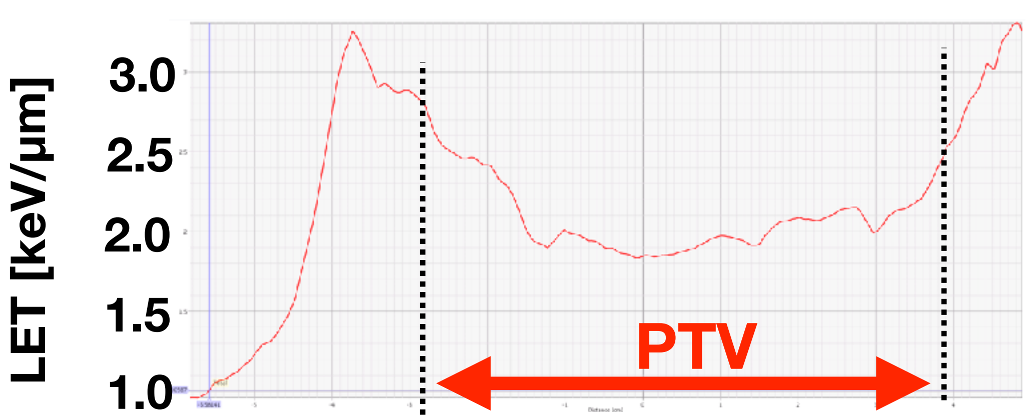
Variable RBE for CCB patient

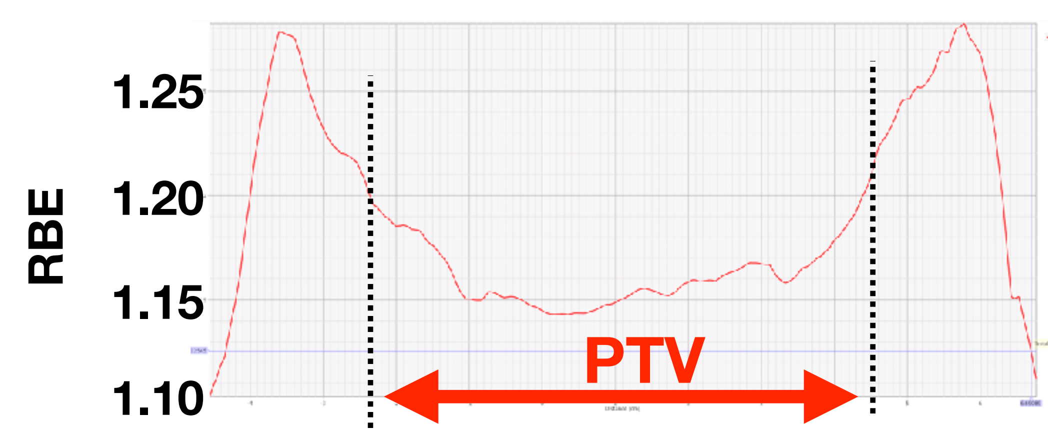
LET distribution



RBE distribution







FRED MC in CCB

- **Research**
    - Retrospective treatment planning studies of RBE dose in patients (A. Skrzypek & M. Garbacz)
      Collaboration with clinicians, MPs, and radiobiologists
- **Translation**
    - Installation of FRED computation unit in CCB
    - Physical dose QA
    - RBE dose

Photons
TCP/NTCP

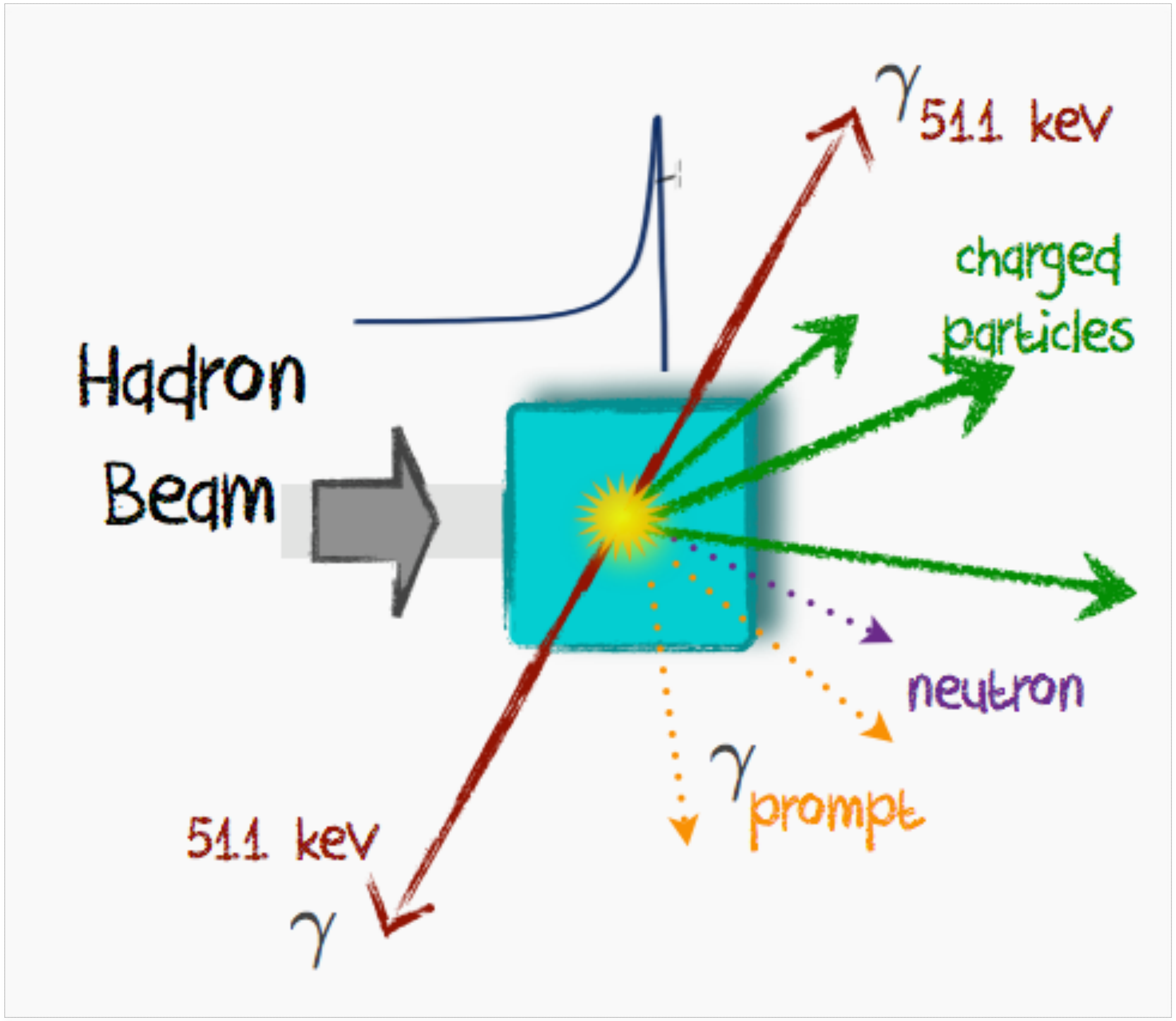
$$D_{bio} = D_{phys} \cdot RBE$$

Protons
TCP/NTCP

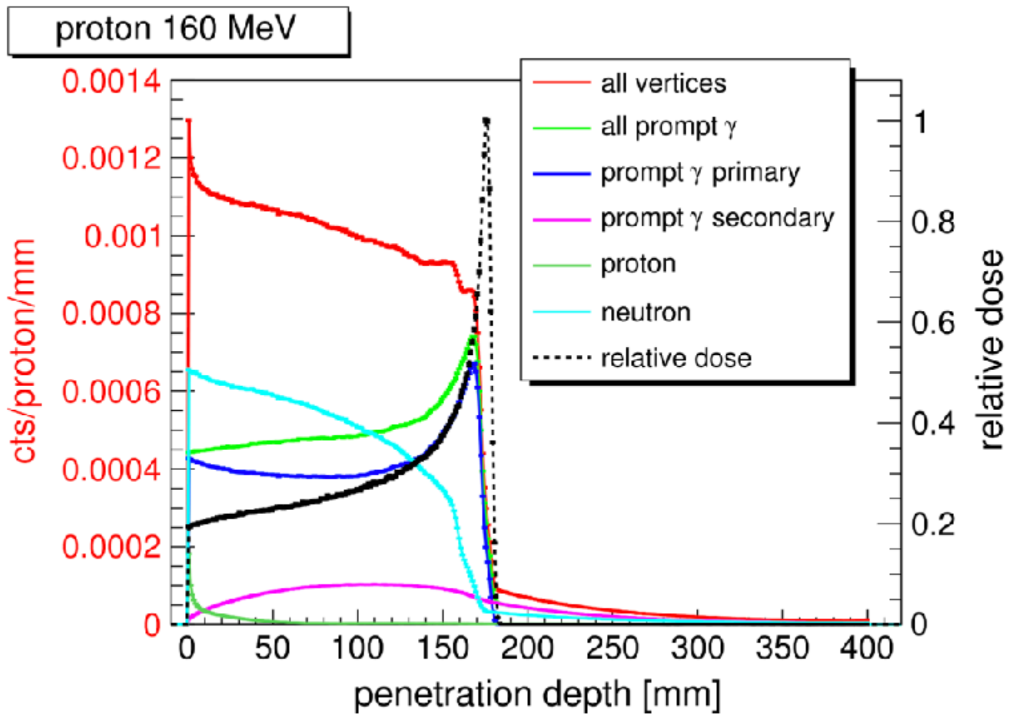
Physical range uncertainties

Biological range uncertainties

Secondary radiation & range monitoring



Signal is patient & particle type specific

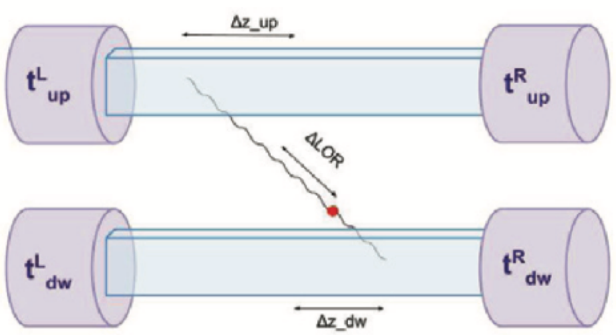


Krimmer et al. Nuclear Inst. and Methods in Physics Research, A 878 (2018) 58–73

Jagiellonian-PET (J-PET)

Cost effective method for the Total-body PET

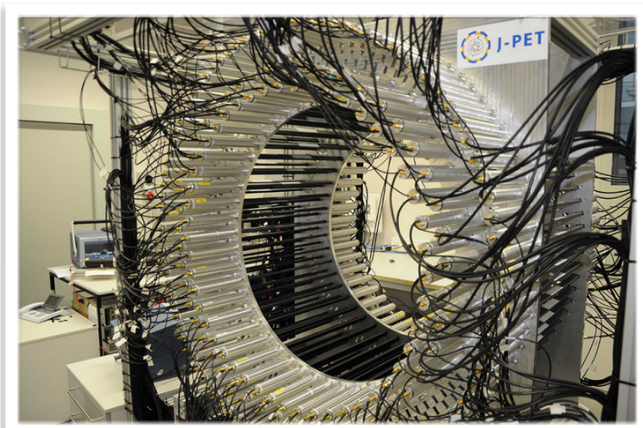
Principle



CRT = 0.266 ns.

$$t_{hit}=(t^L+t^R)/2$$
$$\Delta LOR=(t_{hit}^{up}-t_{hit}^{dw})c/2$$

Prototype

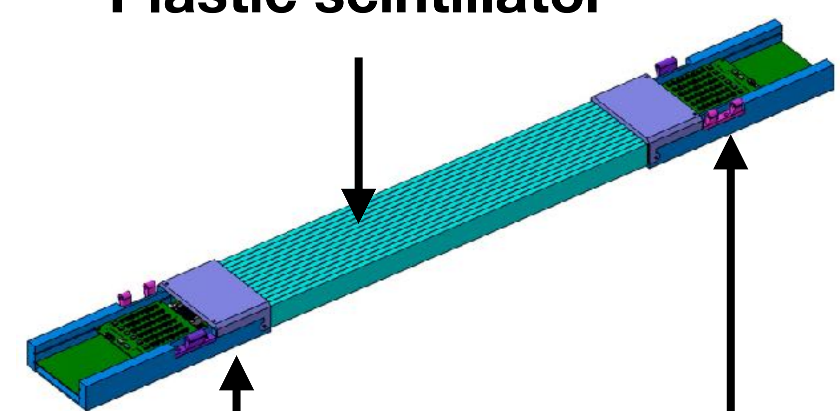


- Three cylindrical layers of EJ-230 plastic scintillator strips (7×19×500mm3)
- Vacuum tube photomultipliers

Modular Prototype

light weight, portable, reconfigurable

Plastic scintillator



Silicon photomultiplier

Integrated on-board front-end electronics

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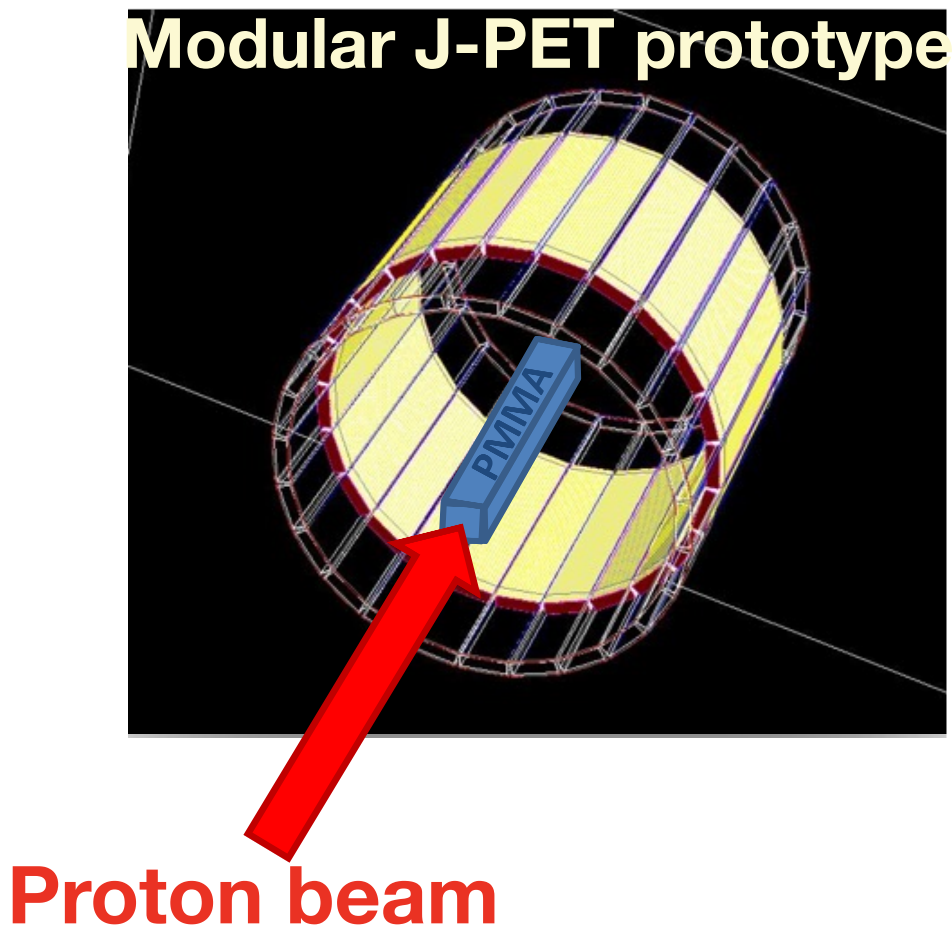
Simulation setup

J. Baran & M. Pawlik-Niedźwiecka



Settings:

- GATE/Geant4
- Physics list: QGSP_BIC_HP_EMY
- Full simulation
- in-room design
  (in-beam in the future)
- PMMA phantom 10x10x40cm^3
- Protons at 150 MeV
- 10^7 primary protons
- Clinical proton beam model
  used in Krakow for patient treatment

Scoring:

- # of annihilations in the PMMA
- # of detected singles
- # of detected coincidences

Signal / efficiency

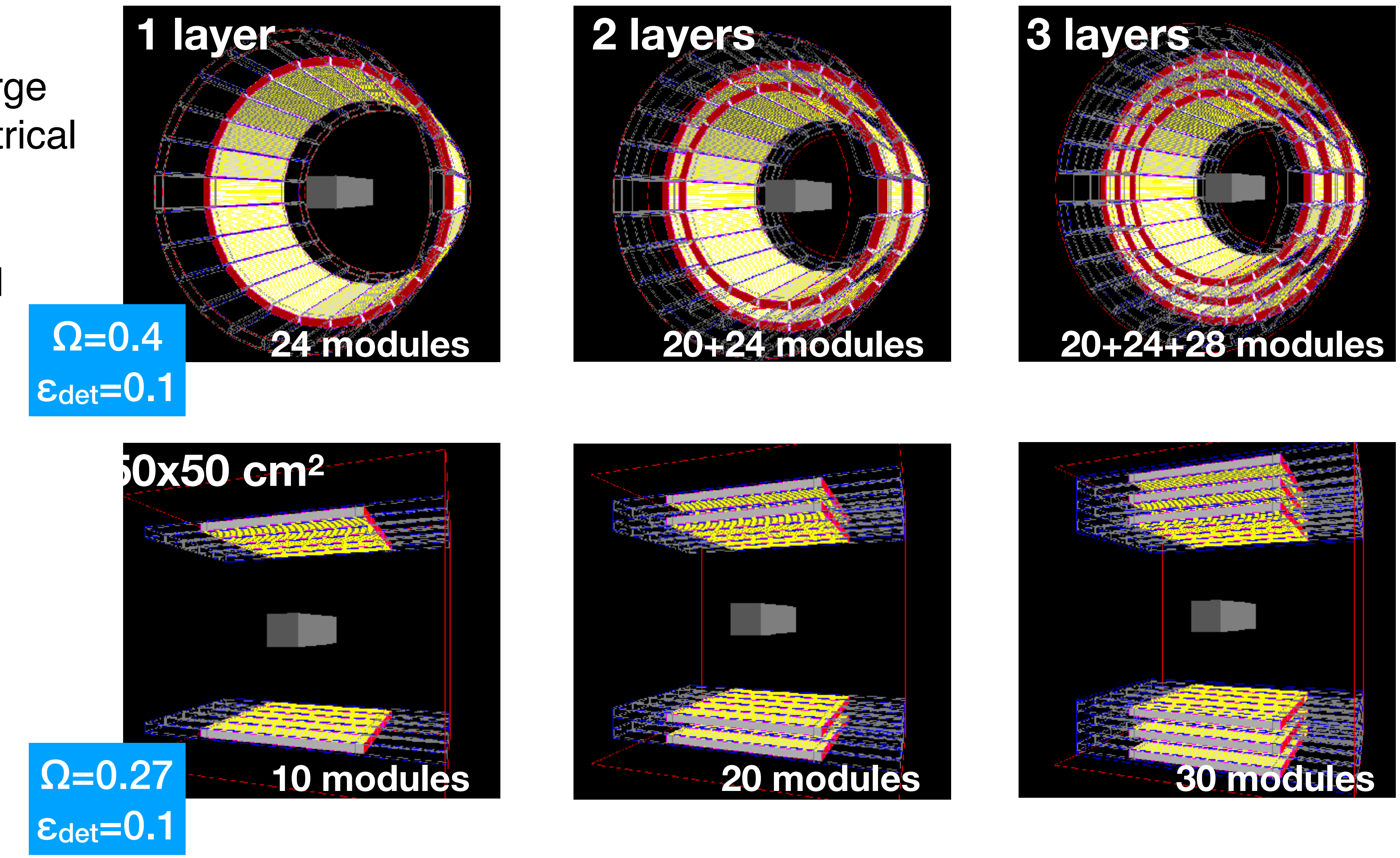
- $\varepsilon_{total} = \varepsilon_{back\text{-}to\text{-}back} * \varepsilon_{det} * \Omega$ $\varepsilon_{det}=0.1$, $\Omega_{barrel}=0.44$
- Monte Carlo simulations:
  - What counts for proton therapy is:

    ε_{total} = # of coincidences / # of primary protons

    …accounting for the annihilation production distribution in the target

Design

- The modular J-PET gives large freedom of choice of geometrical arrangement
- The number of layers should improve the efficiency
- Barrel could be integrated away from the gantry using e.g. rail-system
- Dual head can be integrated in the treatment position (studied in GSI and CNAO)

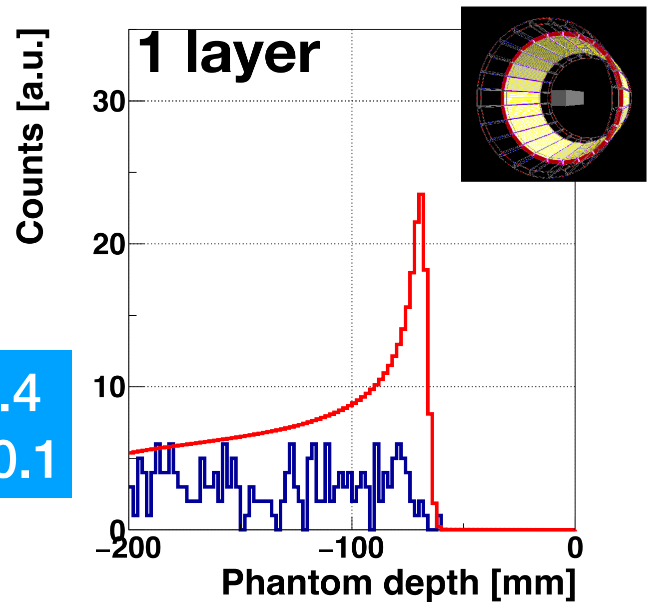


Signal

coincidences per primary:

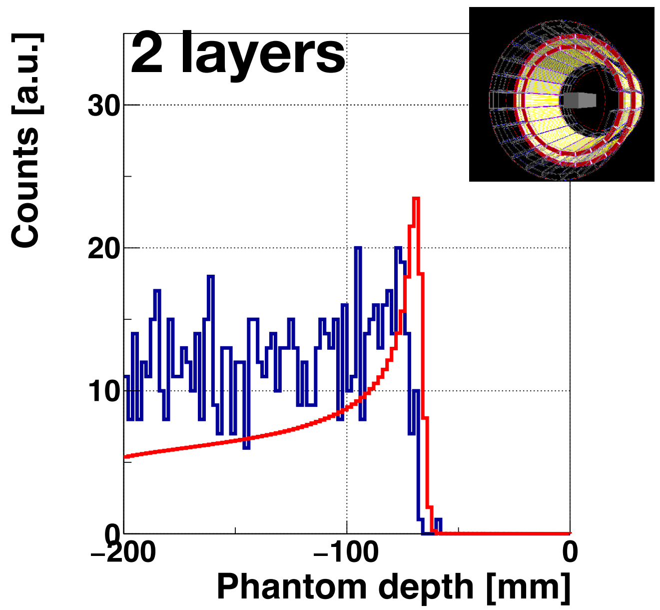
Ω=0.4
ε_{det}=0.1

24 modules



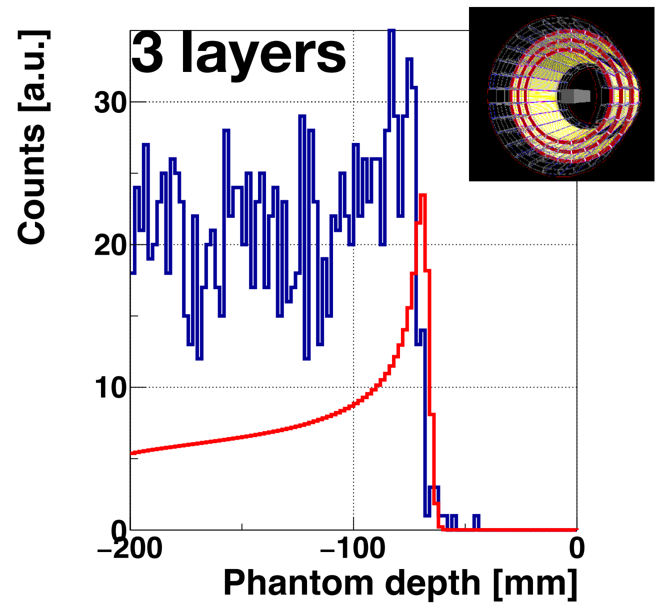
3.5E-05

20+24 modules



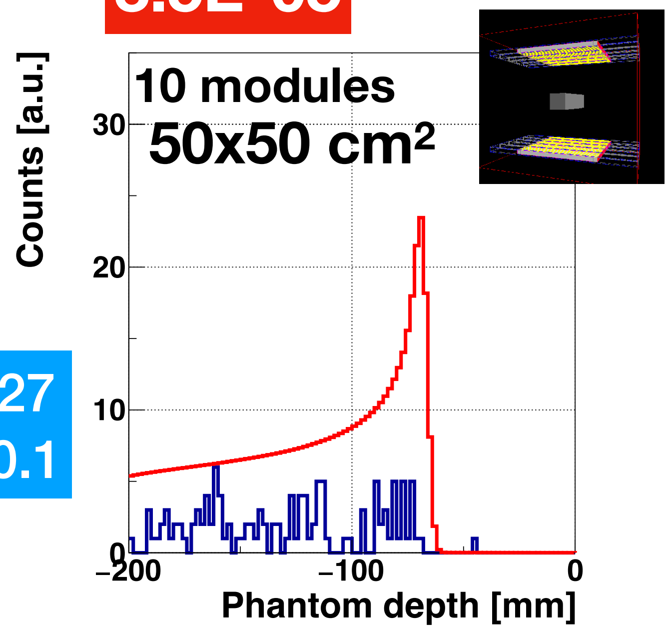
1.4E-04

20+24+28 modules

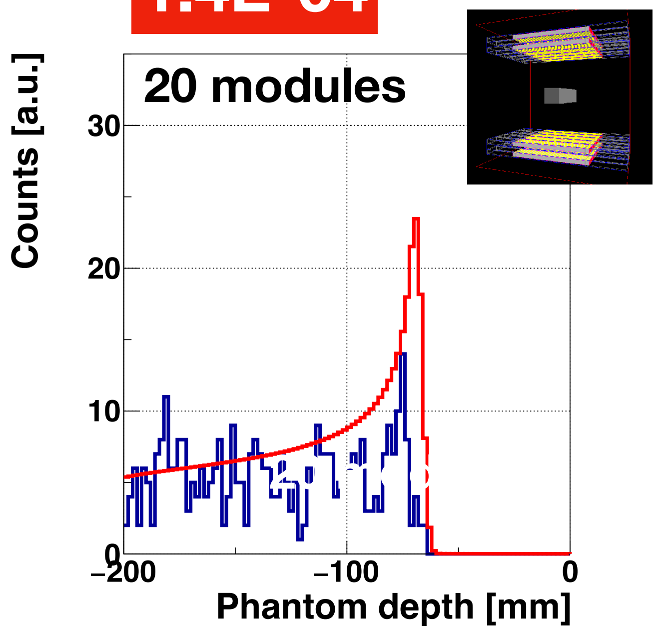


2.5E-04

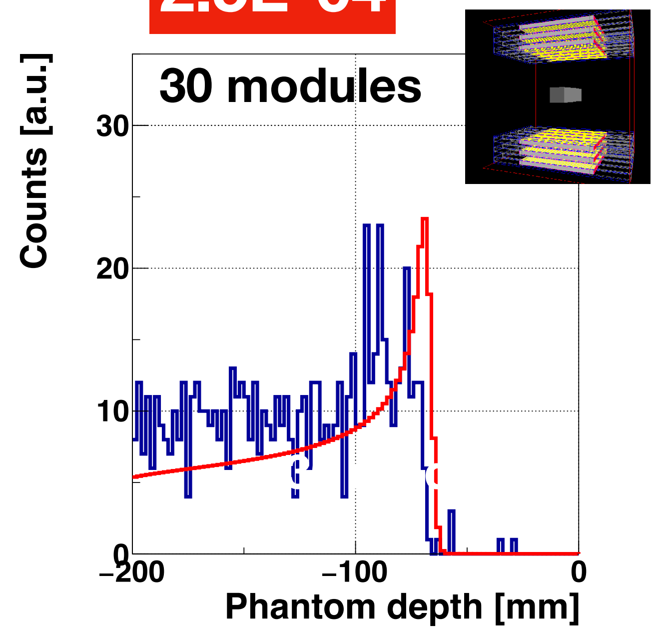
Ω=0.27
ε_{det}=0.1



1.9E-05



5.4E-05



1.0E-04

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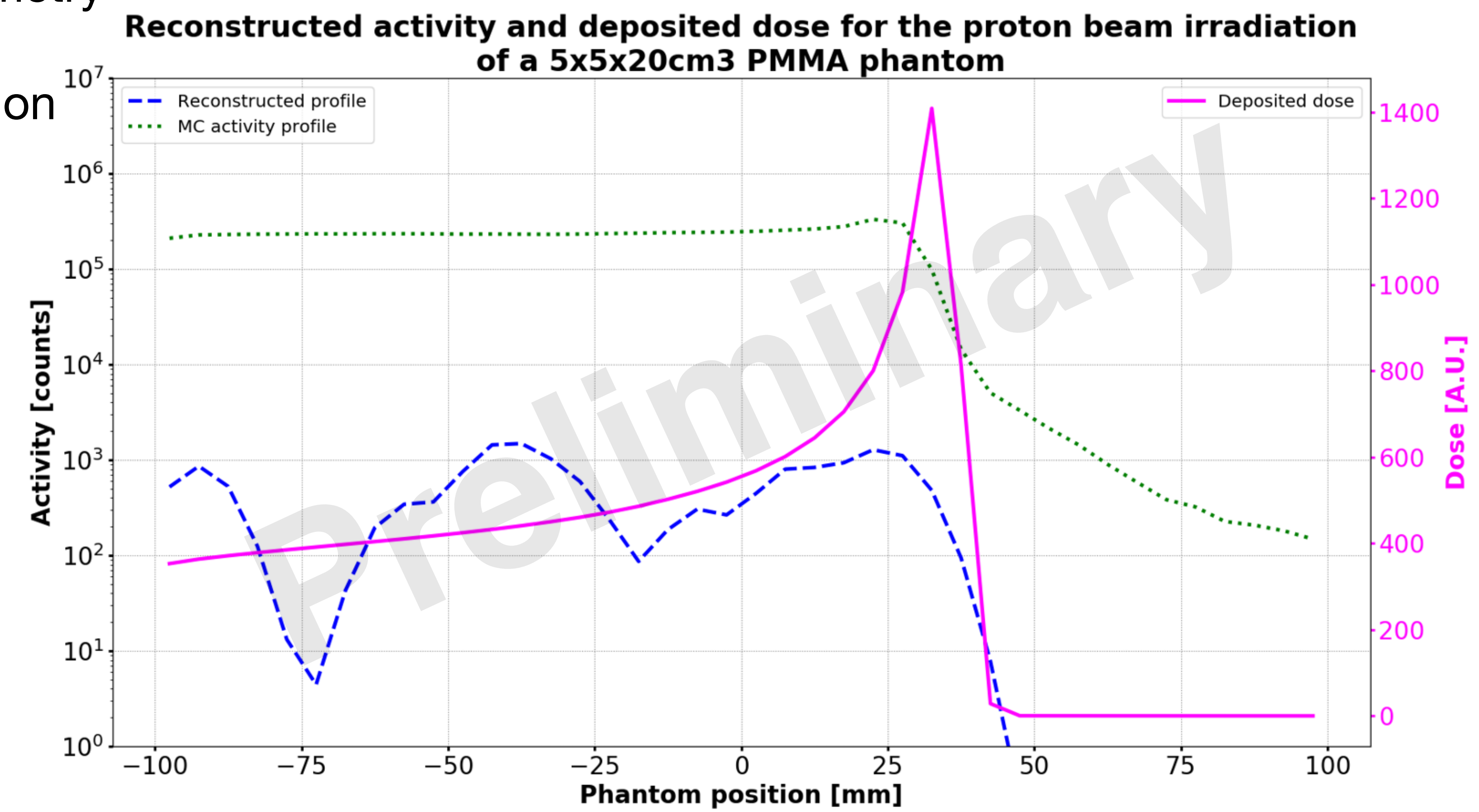
CASTOR for the J-PET image reconstruction

- **Reconstruction requirements for the J-PET**
- long axial FOV (2m)
- multi-layer, non-cylindrical geometry
- inclusion of TOF
- continuous position determination along the axial direction



- **The currently ongoing work**
    - Simulations of the system matrix
    - Reconstruction of PET images

Experimental validation

- First experiment of the J-PET in the proton beam is planned in the first week of July
- It aims to investigate the secondary radiation counting rate of the J-PET detector by
  - parallel measurements of secondary radiation with J-PET and Time-Pix (ADVACAM)
  - GATE Monte Carlo simulations of the experimental setup

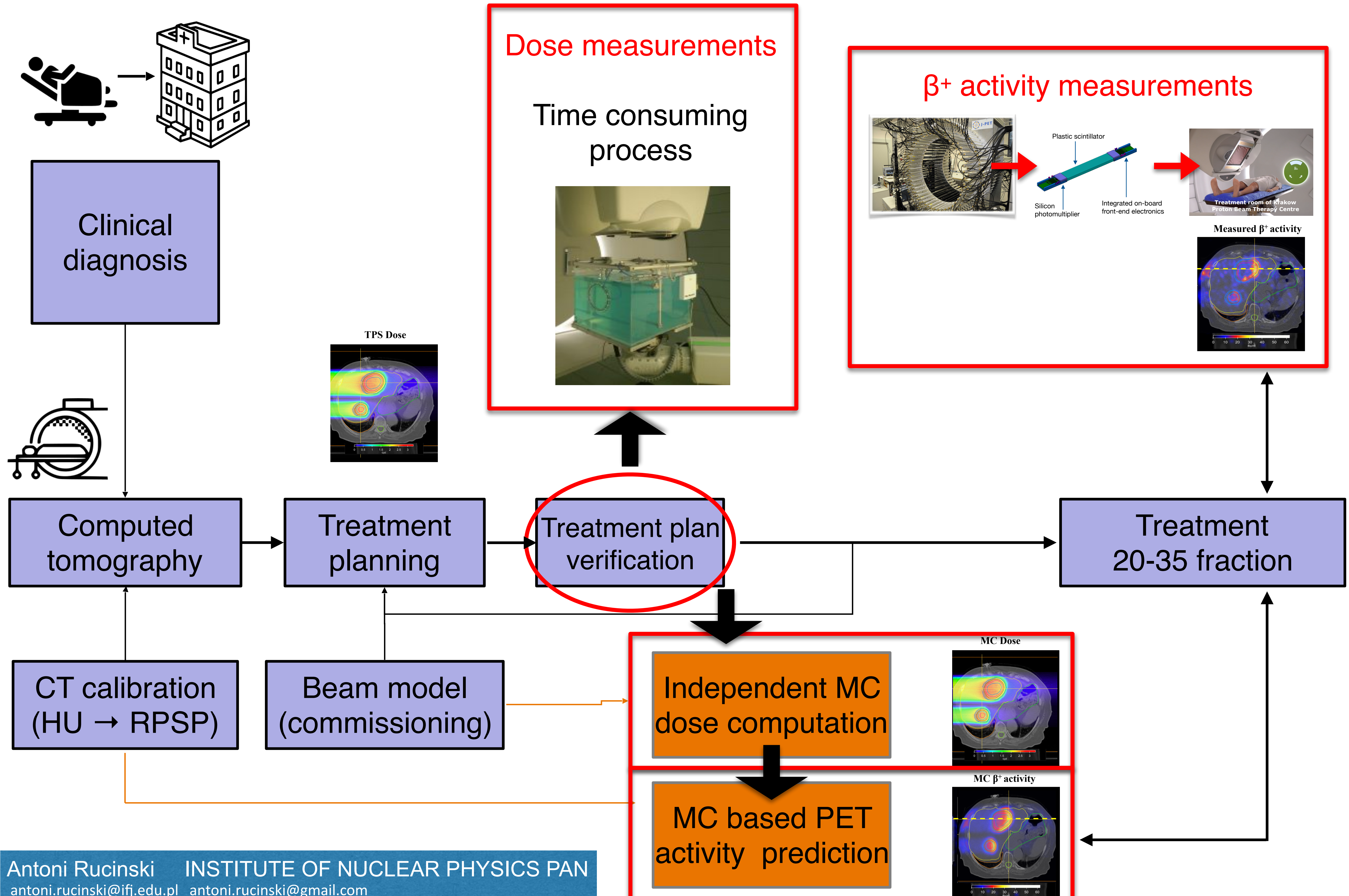
Photons
TCP/NTCP

$$D_{bio} = D_{phys} \cdot RBE$$

Protons
TCP/NTCP

Physical Biological
range uncertainties

Proton therapy treatment



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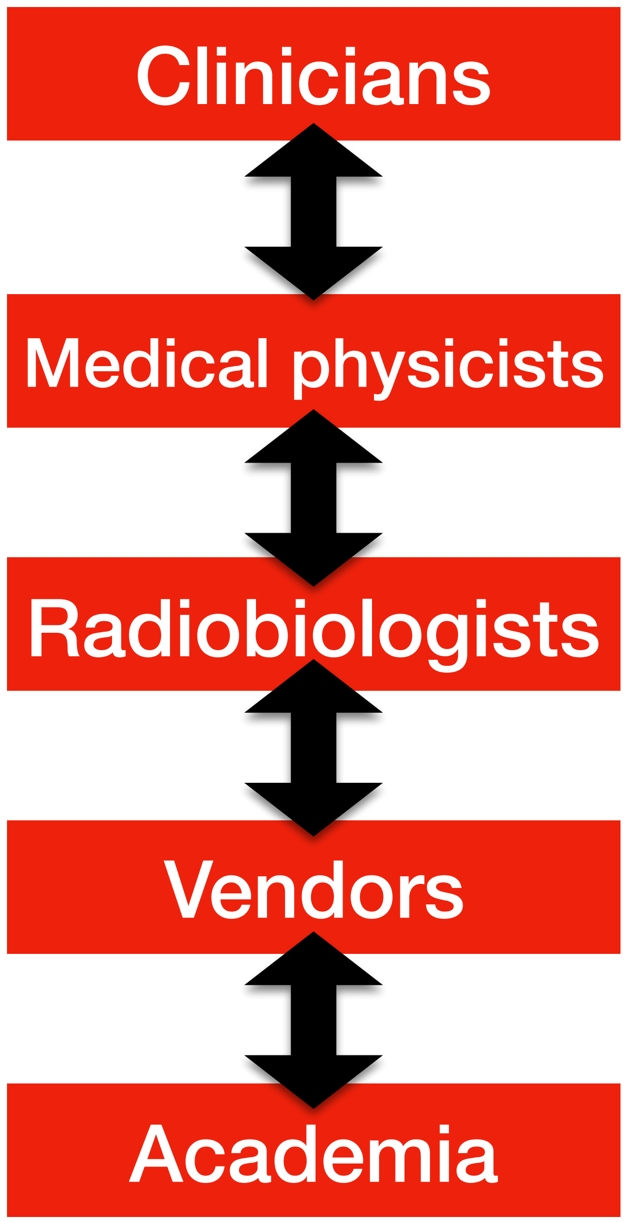
A lot of work to do…

- Clinical trials (evidence)
- New treatment protocols (standardisation)
- Robust treatment planing
- Treatment of moving targets
- Range uncertainties/new imaging methods
- HU-RSP conversion/proton radiography & CT
- Understanding radiobiology
- Cost reduction



Thank you

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