UniversitätsKlinikum Heidelberg

Heidelberg Ionenstrahl-Therapie Centrum

Proton and helium beams: the present and the future of light ion beam therapy

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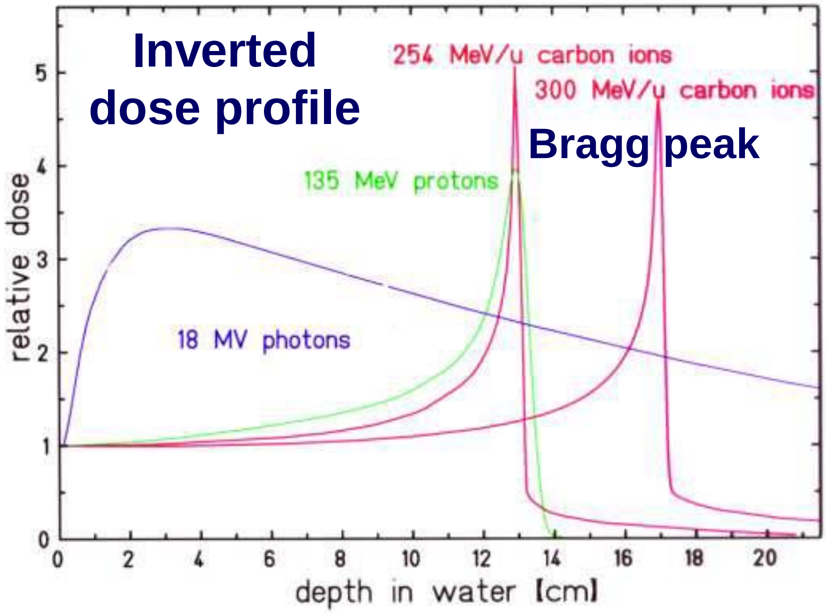
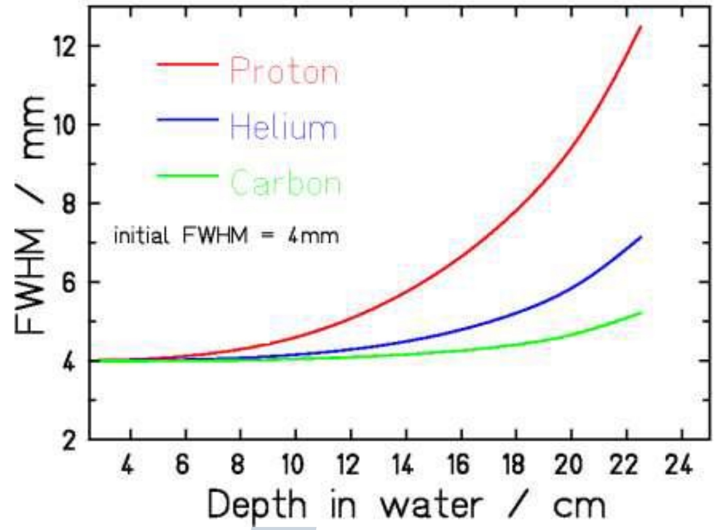
03/05/2018 Dresden

Rationale for proton and ion beam therapy

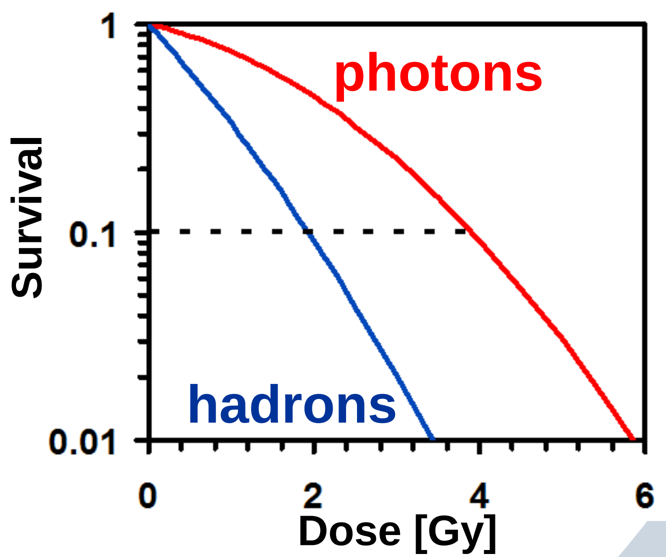
Physics



Lateral scattering



Biology



RBE (relative biological effectiveness):

$RBE = D_{photon} / D_{hadron}$
for the same biological effect

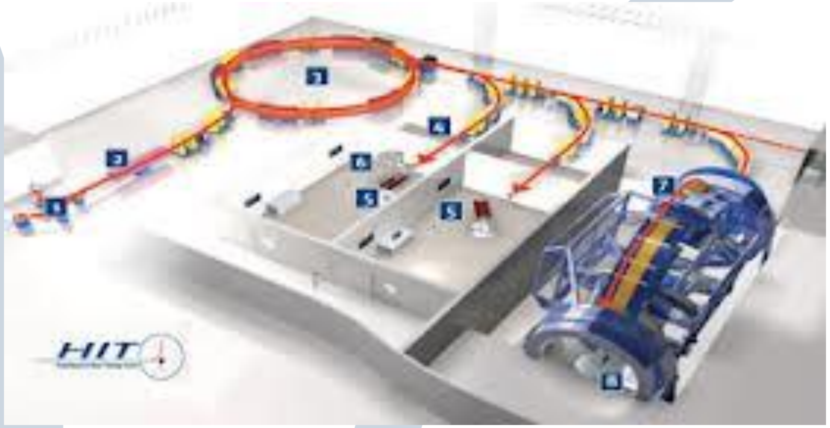
The RBE depends on:

- **particle type (p, ^{12}C, …), LET / local energy spectrum, dose**
- **tissue type, biological endpoint**

In clinic: p RBE = 1.1
^{12}C RBE models

How do we bring particle beams to clinics?

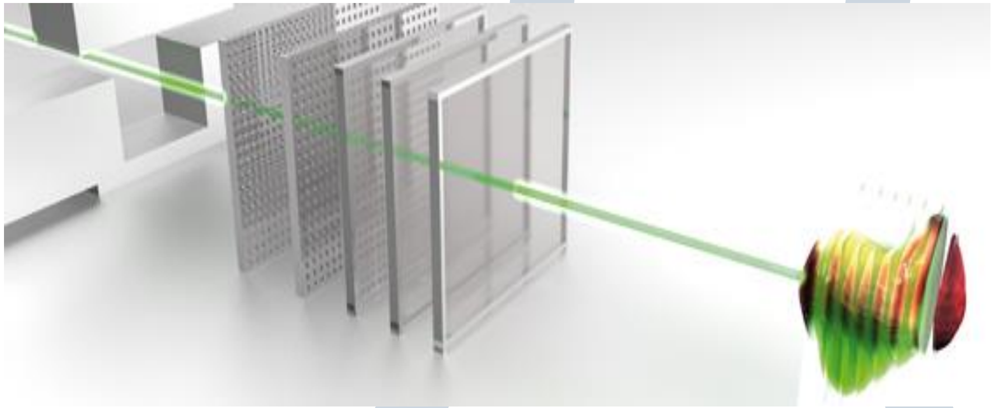
Heidelberg Ion Beam Therapy Center (HIT)



Synchrotron-based facility[1]
Active beam scanning delivery[2]

^{1}H and ^{12}C beams in **clinics**
^{4}He and ^{16}O beams for **research**

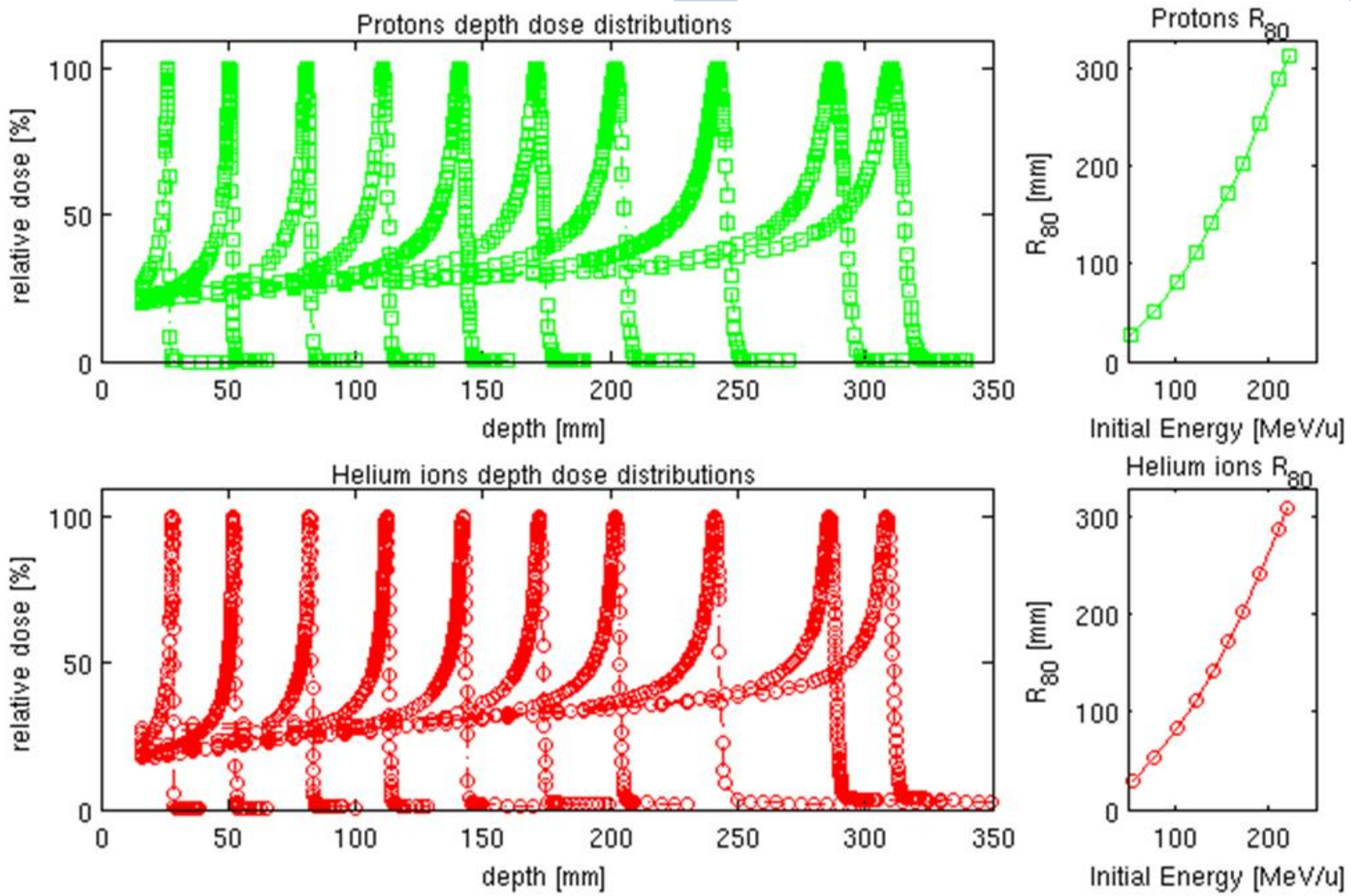
Active Beam Scanning delivery with Synchrotron



Key: accurate dosimetric characterization of the pencil beams

[1,2] Haberer et al. Radiother Oncol. 2004, 73, 186-190, NIM A 1993, 330, 296-305

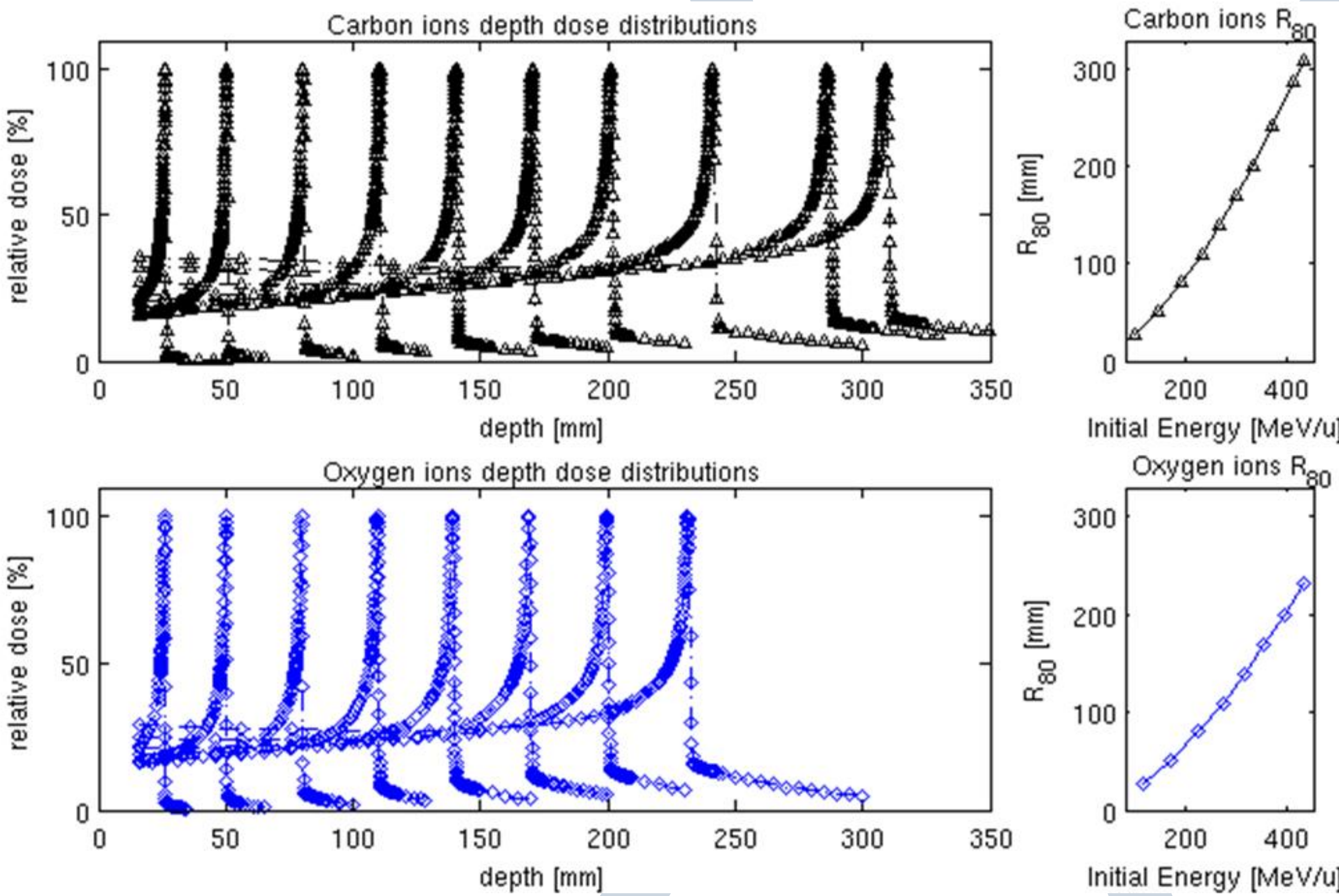
Depth-dose distributions at HIT



Depth dose distributions results for protons, helium, carbon and oxygen ions, respectively, from the top to the bottom panels. In the left panels the *ddds* of the ions in water, in the right panels, the dependence of R_{80} as a function of the ion energy.

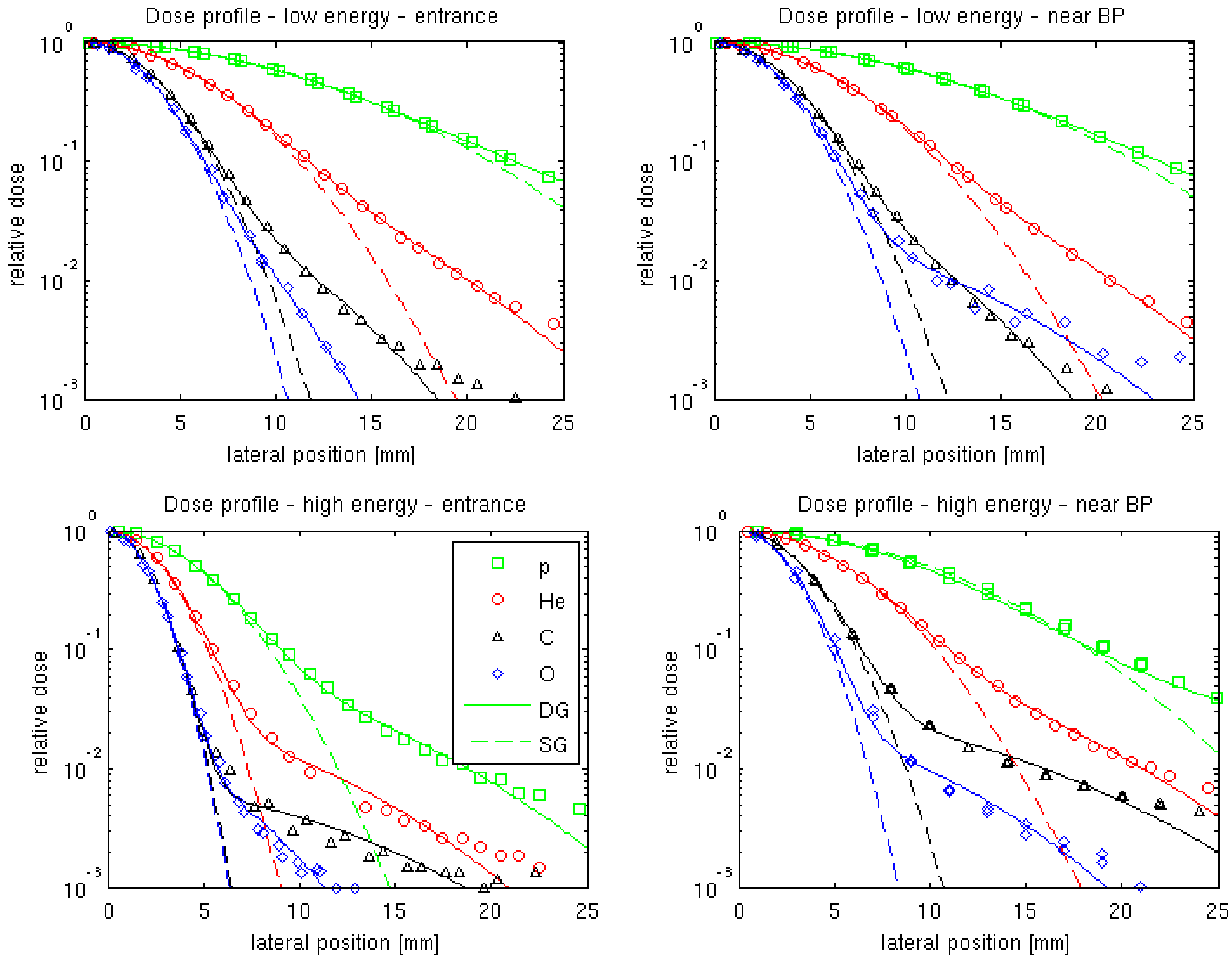
T Tessonnier , A. Mairani, et al Physics in Medicine Biology, 2016, 62(10):3958-3982

Depth-dose distributions at HIT



Depth dose distributions results for protons, helium, carbon and oxygen ions, respectively, from the top to the bottom panels. In the left panels the *ddds* of the ions in water, in the right panels, the dependence of R_{80} as a function of the ion energy.

Lateral dose distributions in water at HIT



Lateral dose distribution: Protons are represented with squares, helium ions with circles, carbon ions with triangles and oxygen ions with diamonds. In solid line, the double Gaussian (DG) fits are shown, and in dashed line the simple Gaussian (SG) fits.

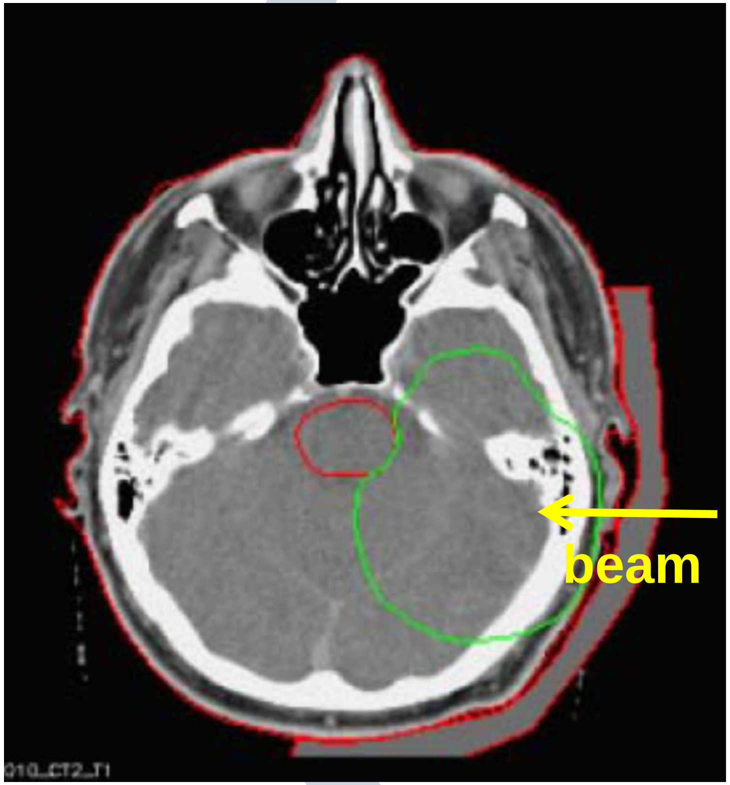
T Tessonnier , A. Mairani, et al Physics in Medicine Biology, 2016, 62(10):3958-3982

Treatment planning system (TPS)

- Acquisition of imaging data (CT, MRI)
- Delineation of regions of interest
- Selection of proton/ion beam directions
- Design of each beam
- Optimization of the plan

main input for dose calculation:

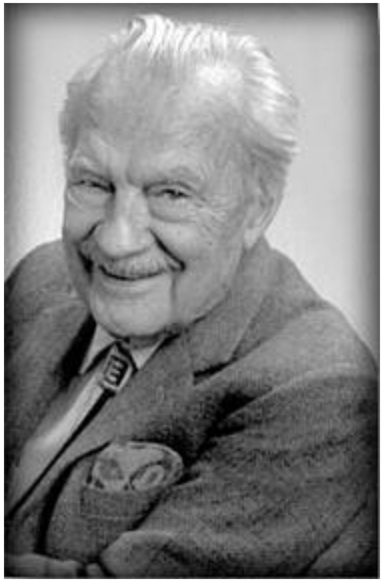
dosimetric description of the interaction of the beam in water



Advanced calculation approaches

The Monte Carlo (MC) method

Invented by John von Neumann, Stanislaw Ulam and Nicholas Metropolis (who gave it its name), and independently by Enrico Fermi



http://en.wikipedia.org/wiki/Nicholas_Metropolis#/media/File:Nicholas_Metropolis_cropped.PNG

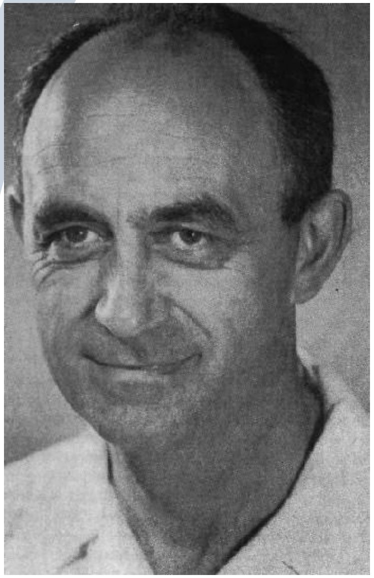
N. Metropolis

http://www.atomicarchive.com/History/hbomb/images/ulam_stanislaw_s.jpg

S. Ulam

http://http://upload.wikimedia.org/wikipedia/commons/5/5e/JohnvonNeumann-LosAlamos.gif

J. von Neumann



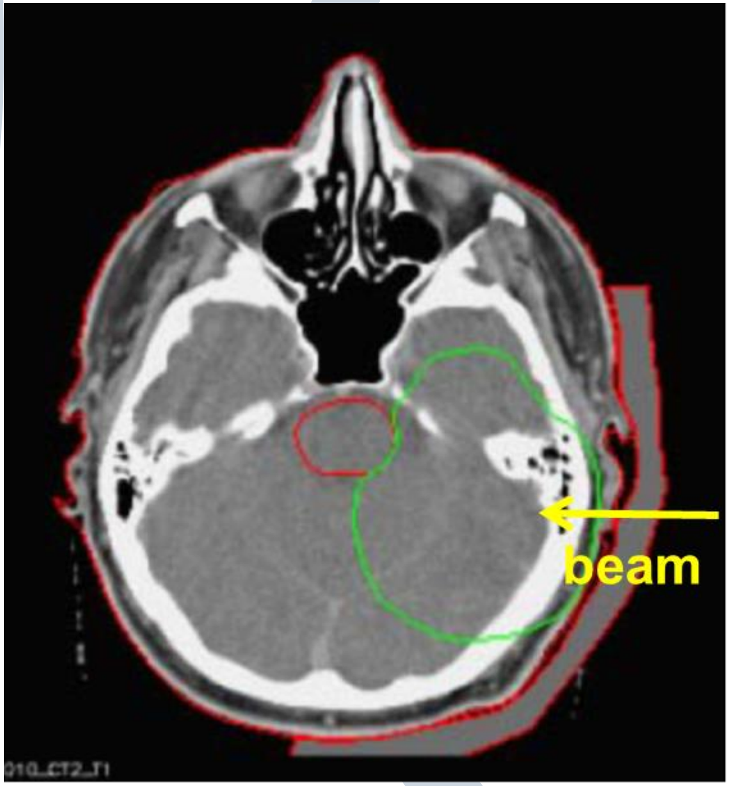
http://steppforcongress.blogspot.de/2011/01/enrico-fermi-immigrant-of-day.html

E. Fermi

Advantages/disadvantages of MC simulations for particle therapy

+ Detailed description of particle transport and interactions
+ Patients density and elemental composition in account
+ Flexibility

- Long computational time
- Programming skills needed
- Dedicated hardware

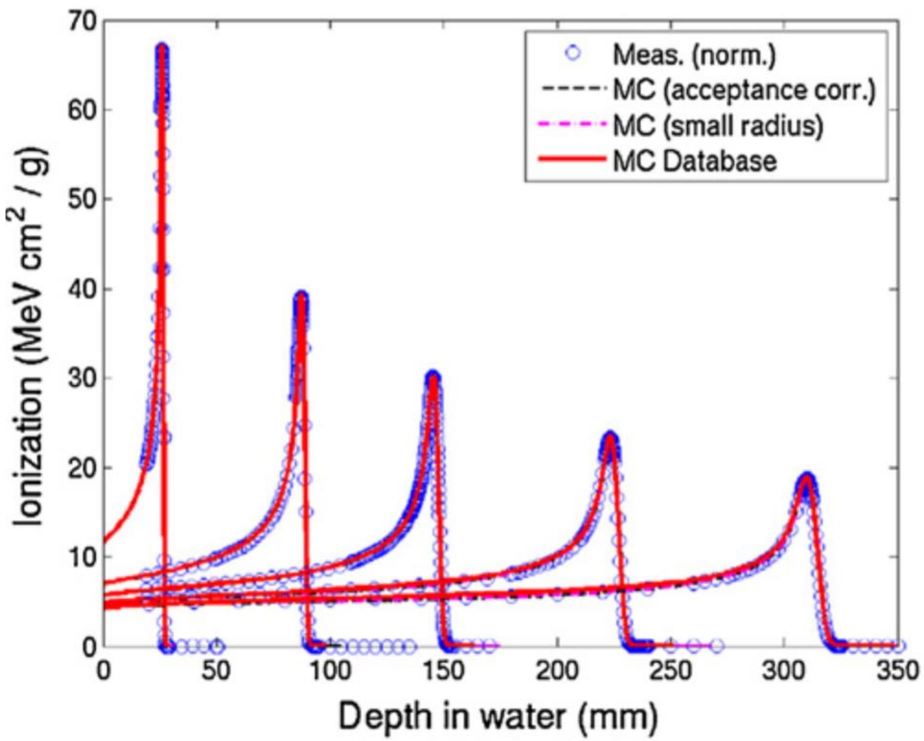


…back to clinics

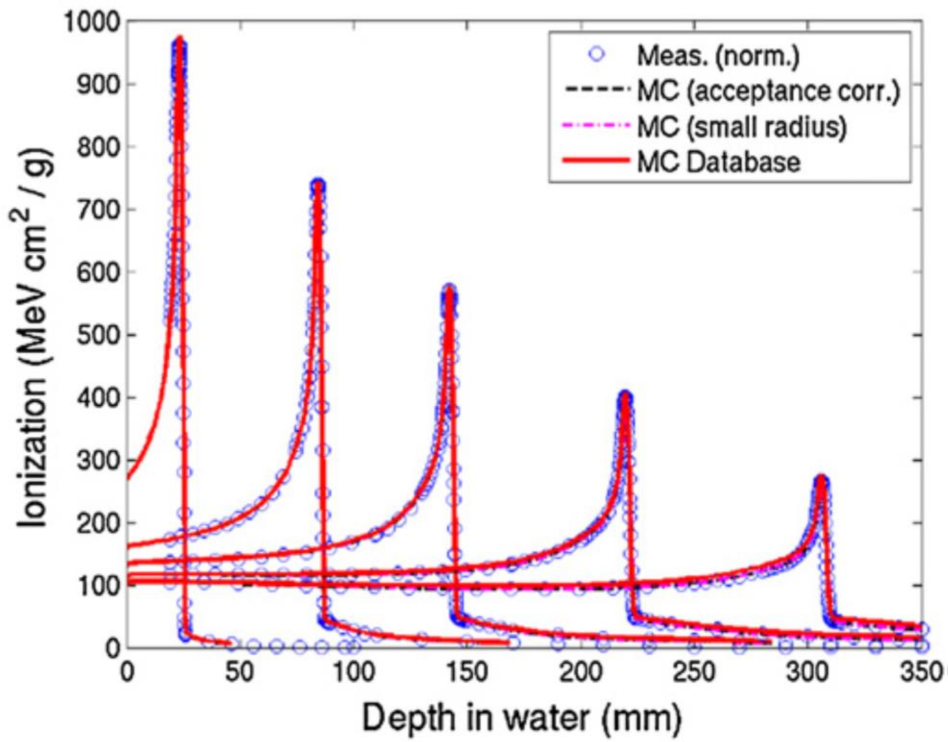
Input dosimetric data for clinical treatment planning

Depth-dose distributions for p (left panel) and carbon ions (right panel)

p



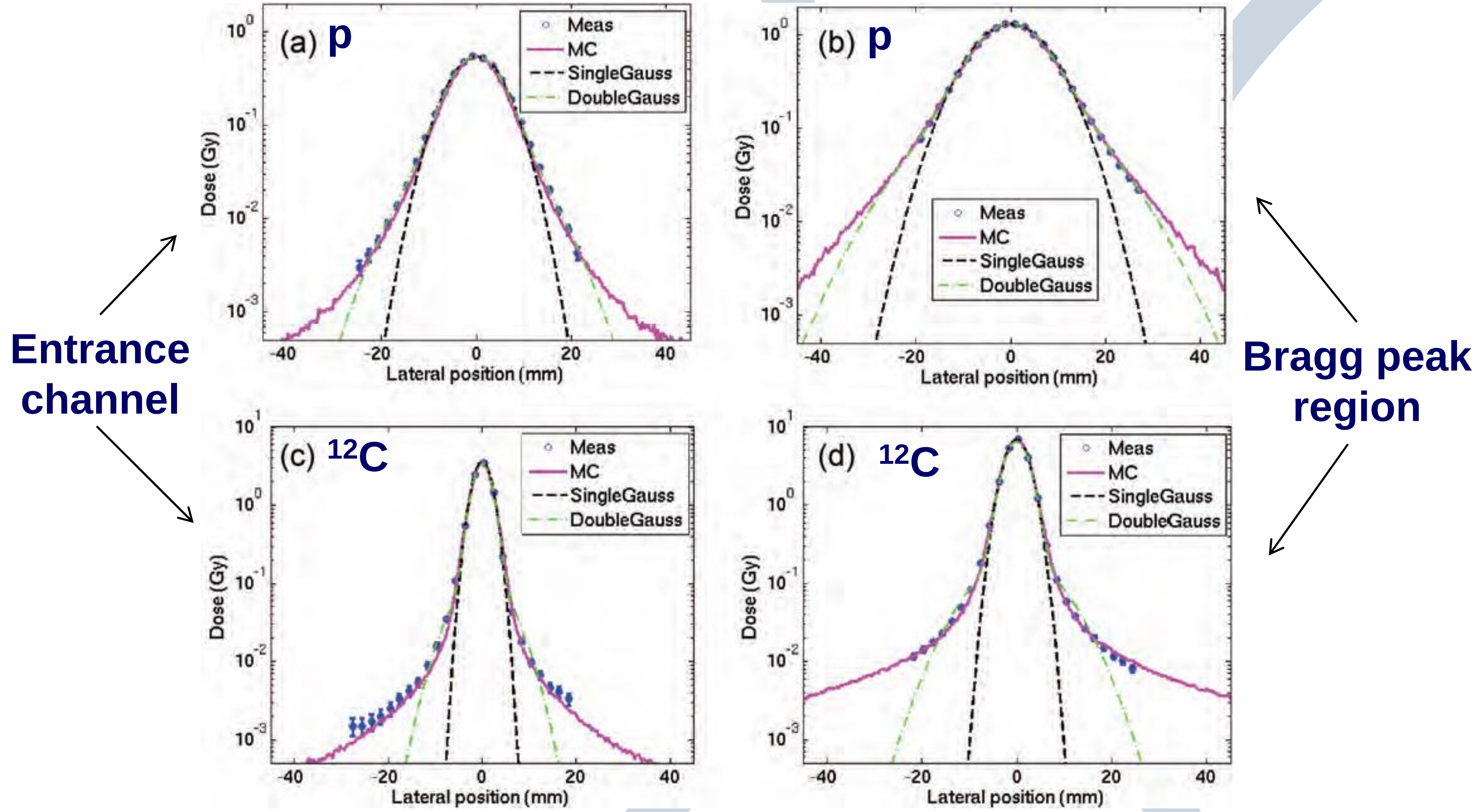
^{12}C



K. Parodi, A. Mairani, et al Physics in Medicine and Biology 2012, 57, 3759-3784

Input dosimetric data for clinical treatment planning

Lateral dose distributions for p (upper panels) and carbon ions (lower panels)



F. Sommerer, A. Mairani, K. Parodi, Radiation Research, 2013, 54, i91–i96

Input dosimetric data for clinical treatment planning: proton database HIT vs CNAO

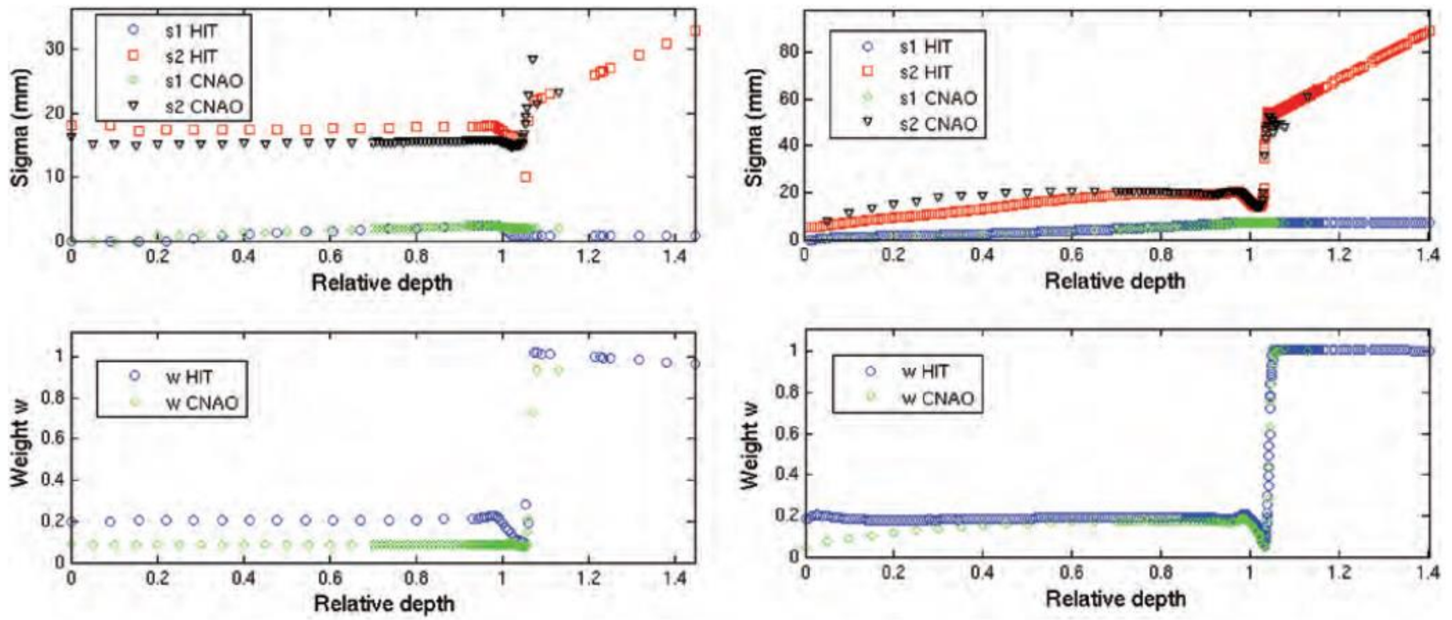


Fig. 6. Comparison of the HIT basic data input in both the HIT and CNAO TPS, with respect to the parameters deduced using the same fitting procedure described in this work, however applied to FLUKA MC simulations of lateral beam broadening in water using a detailed modelling of the CNAO beamline for proton beams [11]. Two similar energies of approximately 60 MeV/u (left) and 221 MeV/u (right) were considered. While the sigma parameters match fairly well, some discrepancies are observed in the weight factor *w* directly related to the broad Gaussian component, especially for low-energy proton beams. This is likely ascribed to less large-angle scattering material in the CNAO beamline.

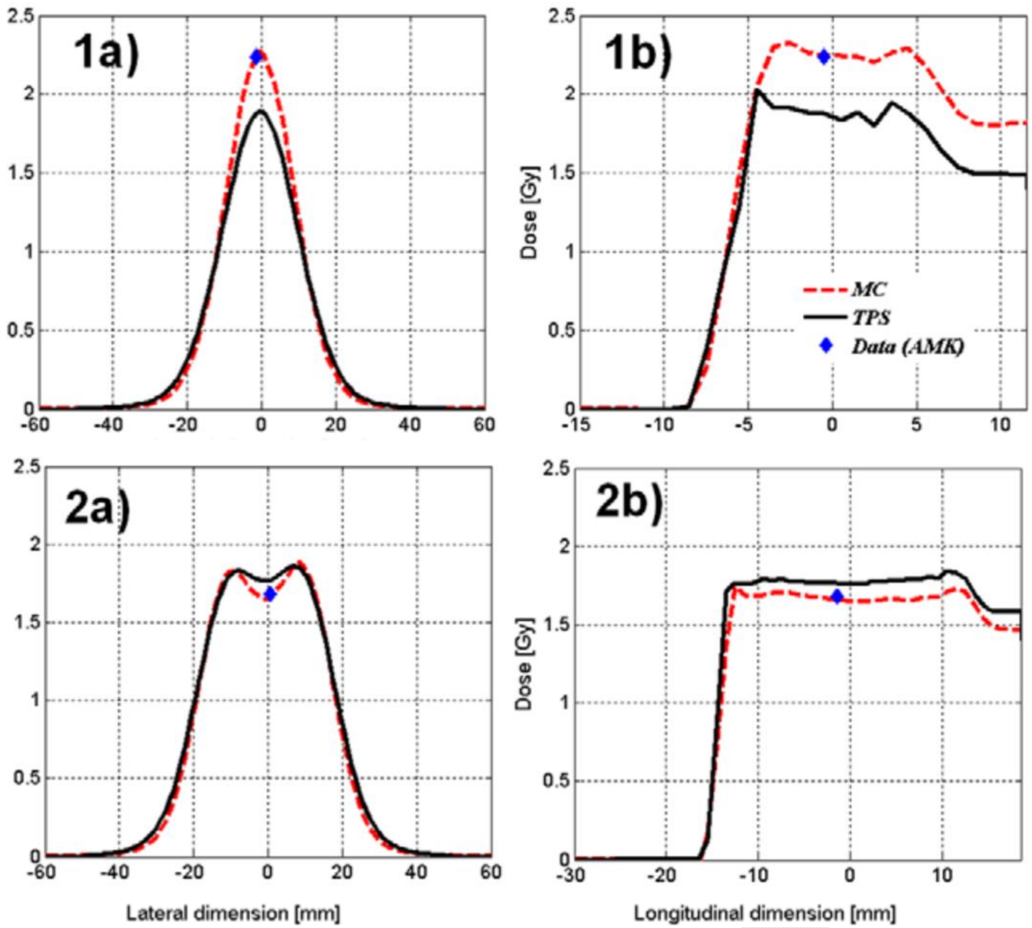
F. Sommerer, A. Mairani, K. Parodi, Radiation Research, 2013, 54, i91–i96

Current clinical applications of MC

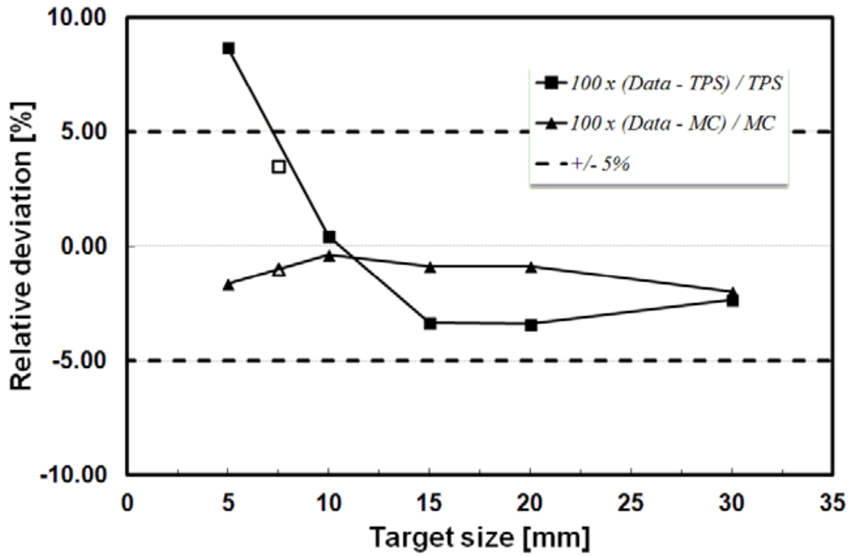
Dosimetric comparisons

Proton extended fields in water: MC vs TPS vs experimental data

1) 5 mm side cube at 5 mm depth
2) 20 mm side cube at 30 mm depth

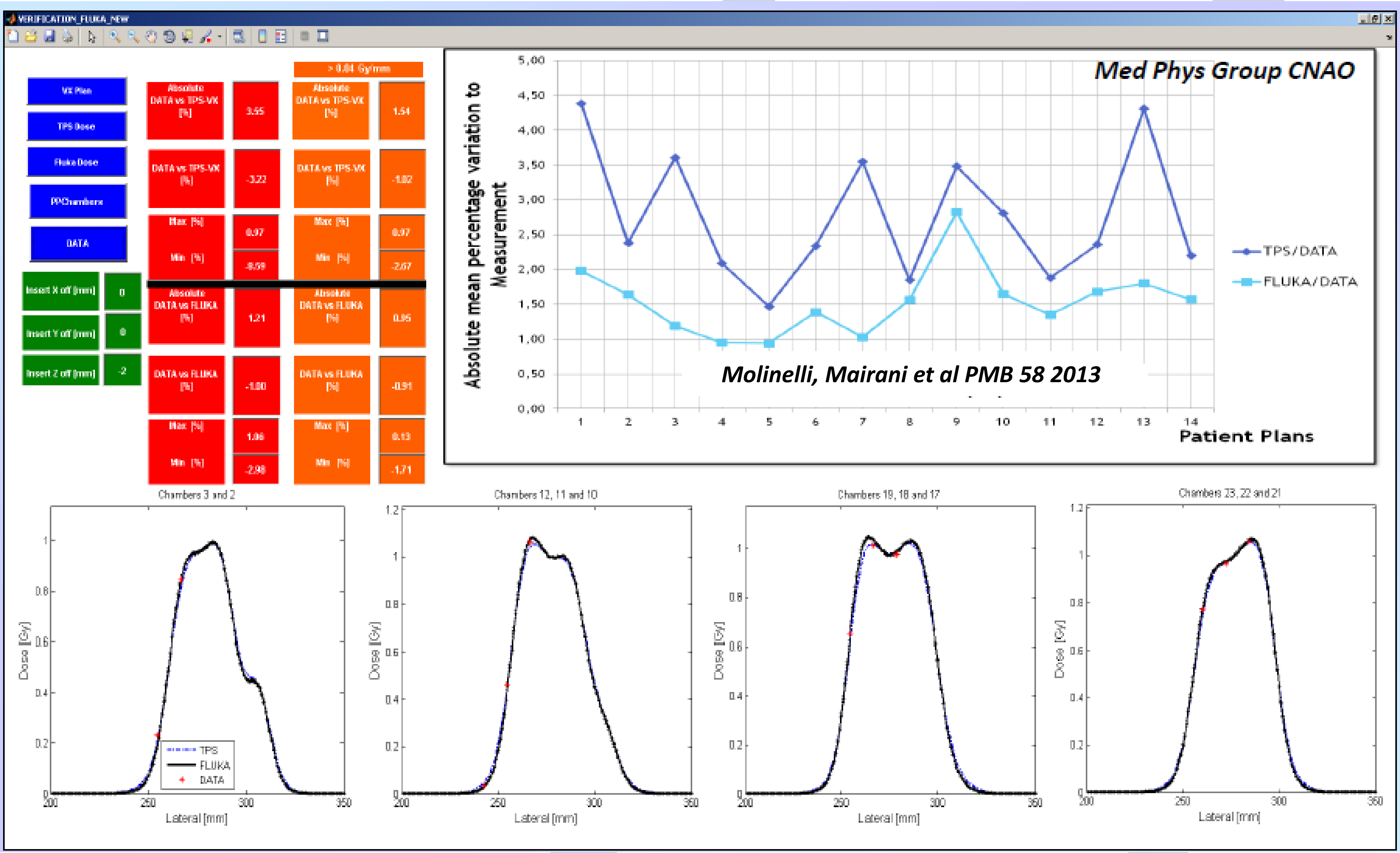


Dosimetric accuracy as a function of the target size

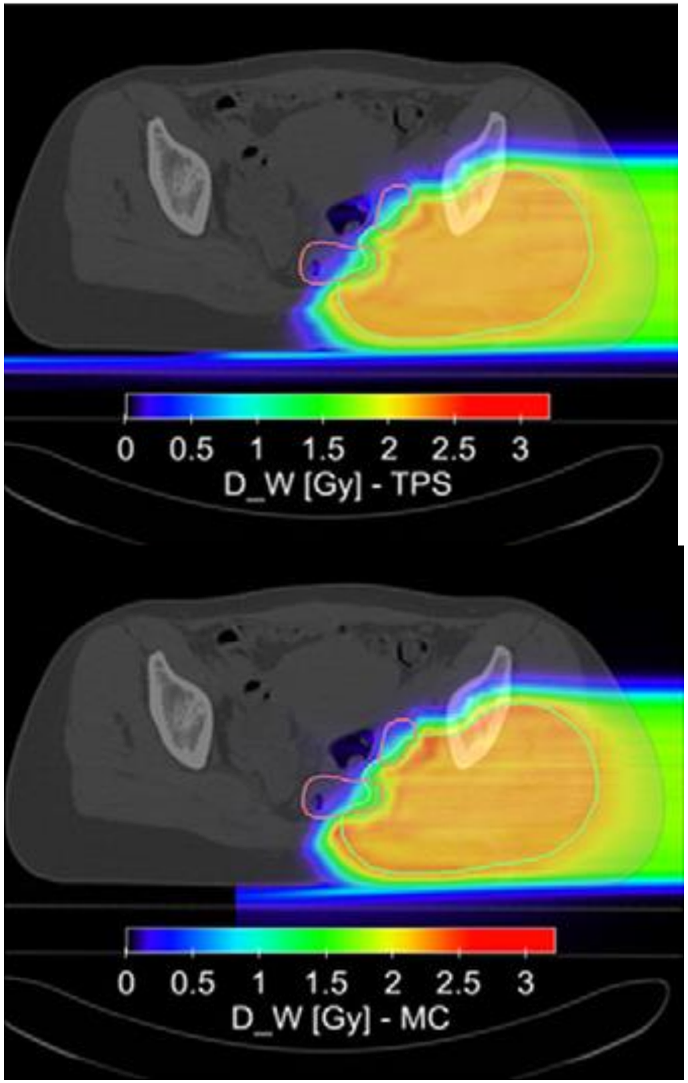


G. Magro, S. Molinelli, A. Mairani, et al
Physics in Medicine Biology, 2015, 60, 6865

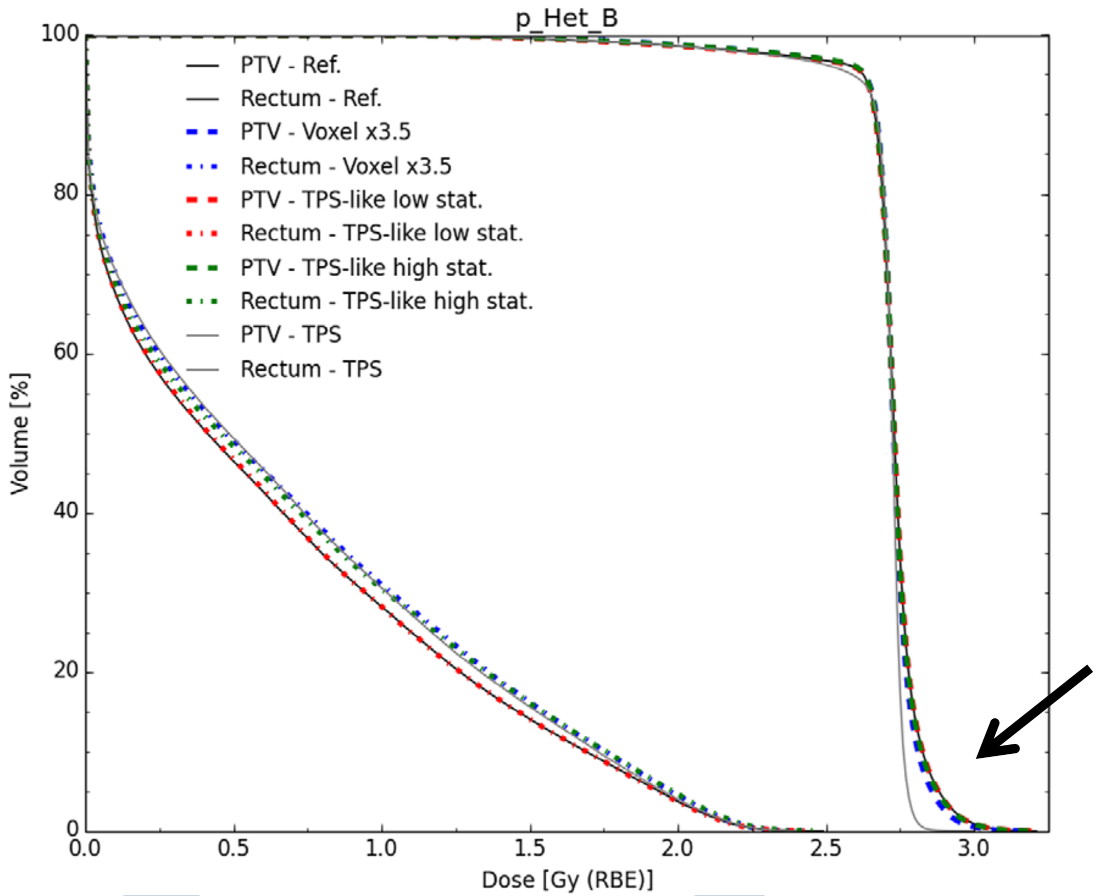
Patient Plan Verification



Re-calculations of patient dose distributions



Deep-seated sacral tumor irradiated with **p**

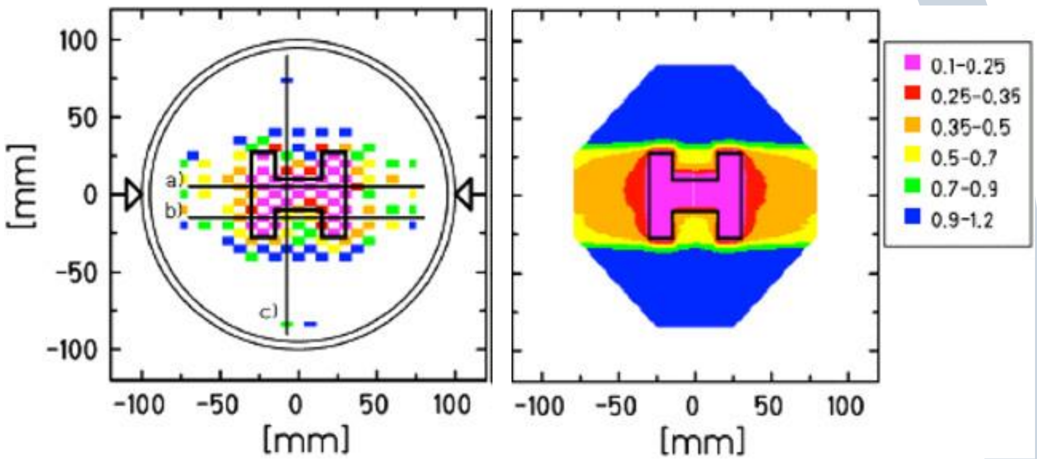


J. Bauer, F. Sommerer, A. Mairani, et al Physics in Medicine Biology, 2014, 59, 4635

Biological calculations in carbon ion therapy

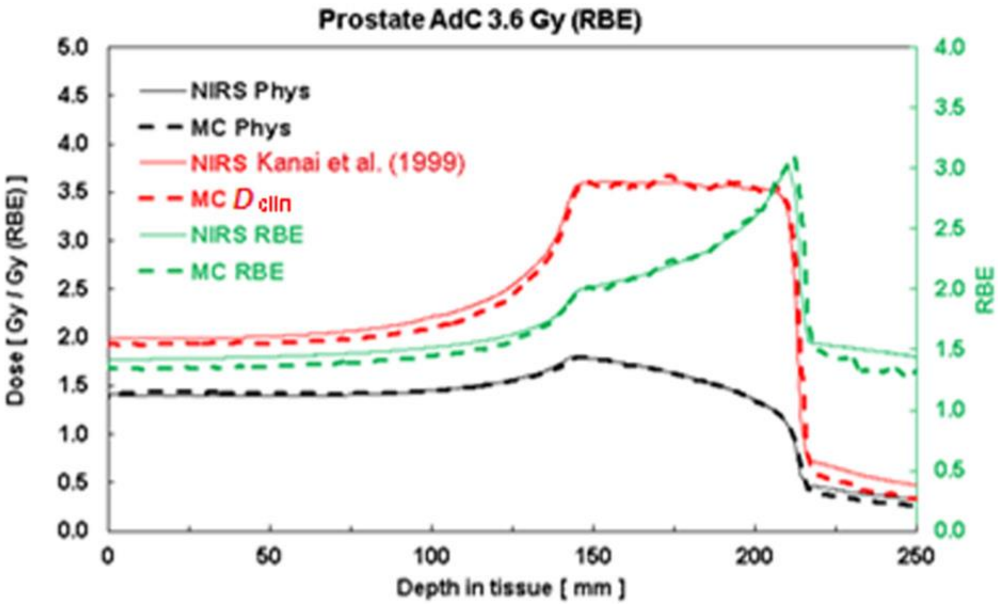
in vitro **data** **predictions**

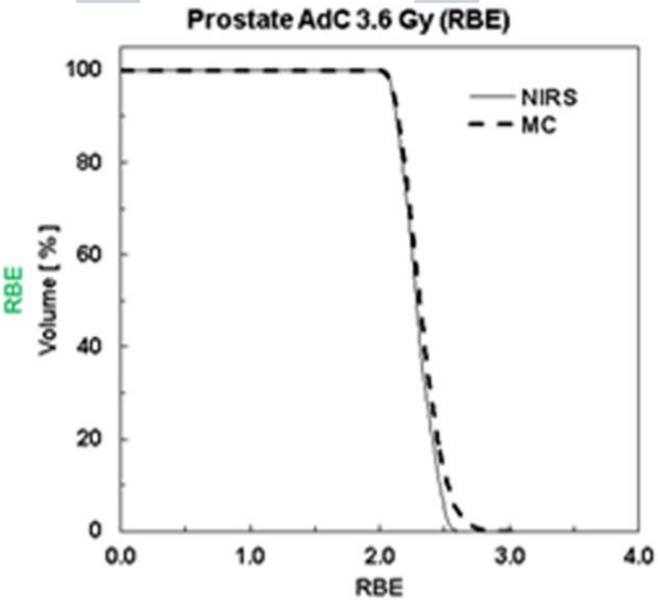
A. Mairani, et al Physics in Medicine and Biology 2010, 55, 4273–4289



MC + LEM model

MC + NIRS approach

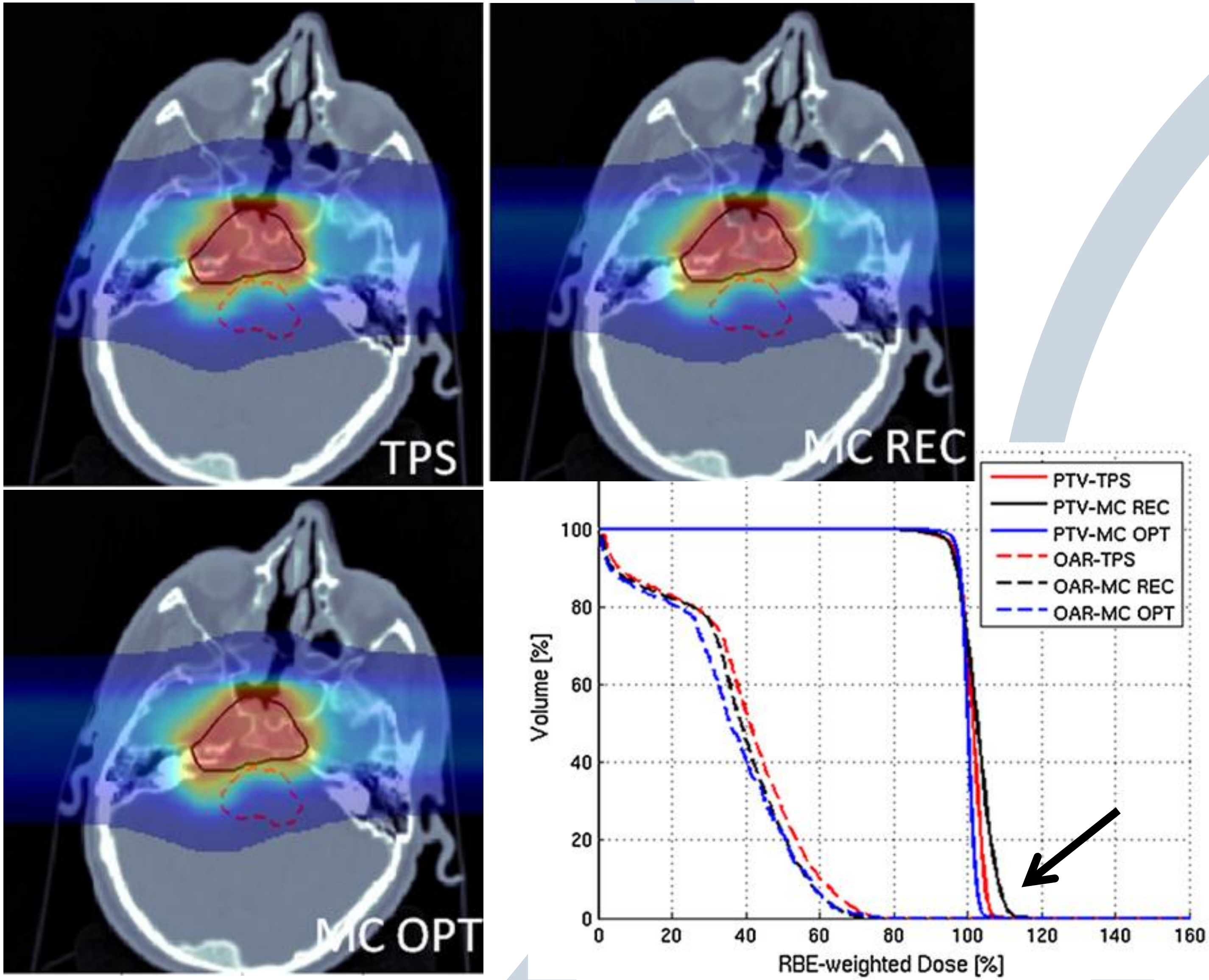




G. Magro,…,A.Mairani Physics in Medicine and Biology 2017, 56, 3814–3827

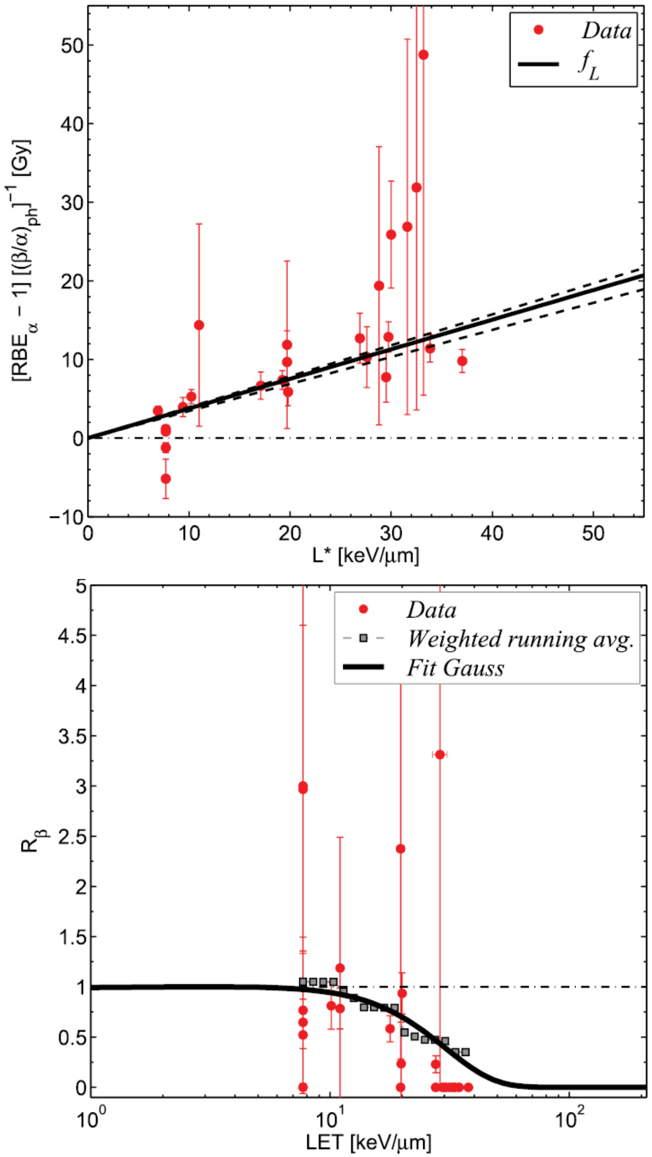
Future clinical applications: overcoming TPS limitations

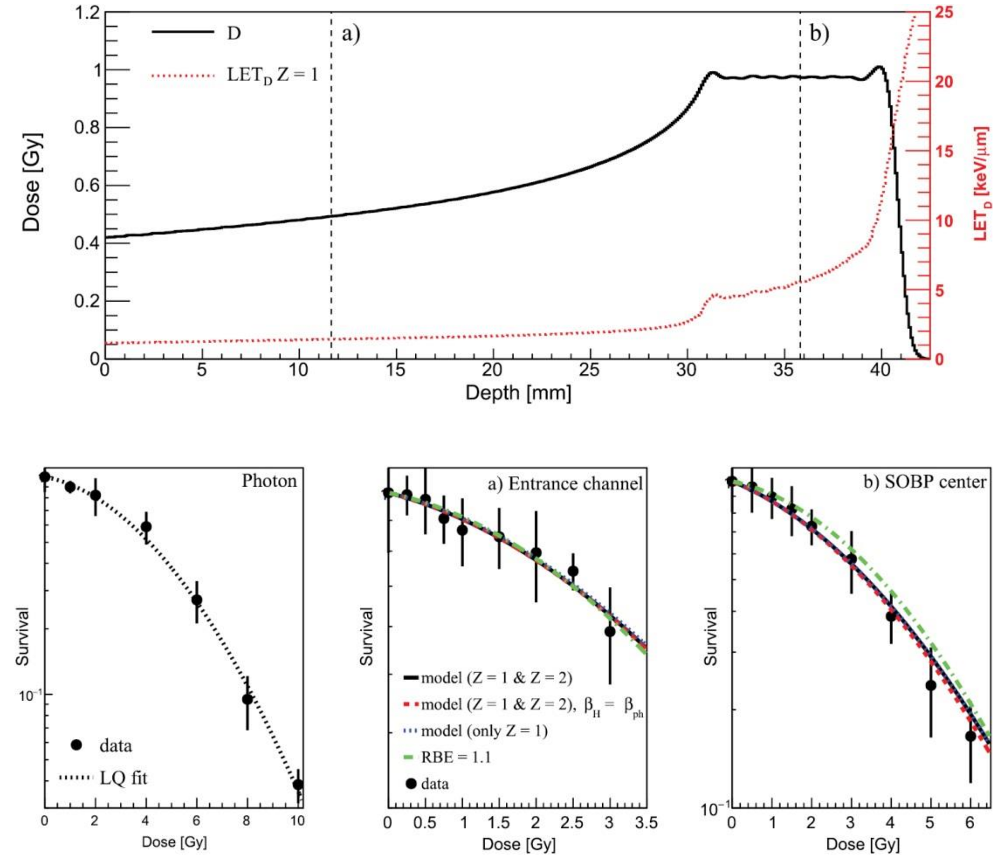
Monte Carlo-based Treatment Planning Tool



A. Mairani, et al. Physics in Medicine and Biology 58 (2013) 2471–2490

Beyond the TPS: variable RBE in proton therapy

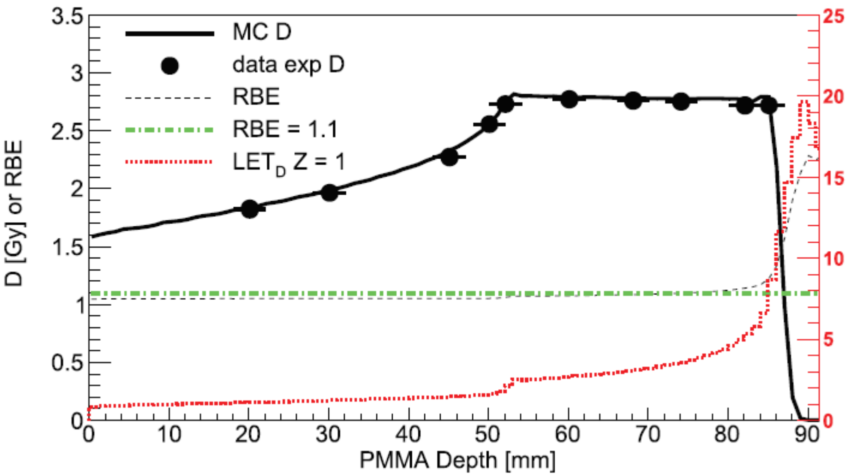


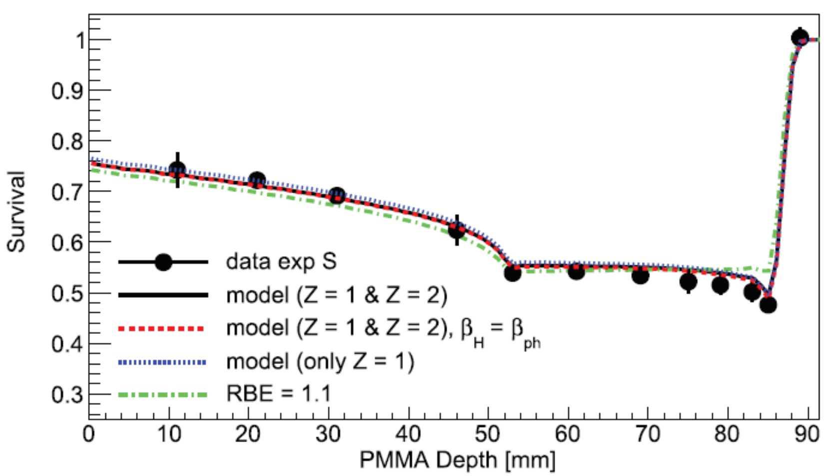


A. Mairani, et al Physics in Medicine and Biology 2017 61: 1378–1395

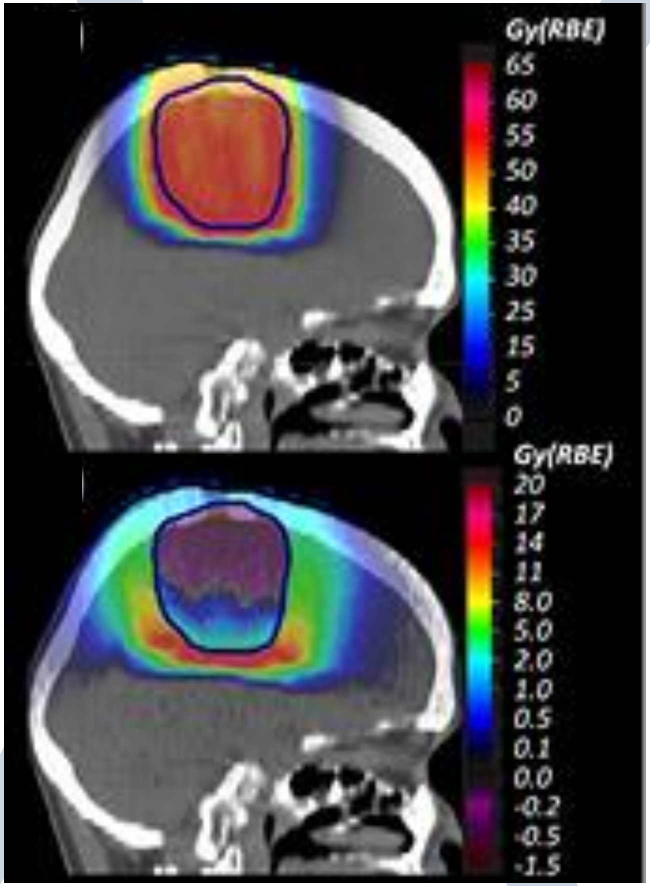
Beyond the TPS: variable RBE in proton therapy

Dosimetric and *in vitro* cell stack experiment: model vs data





Calculation of patient plans with variable RBE (varRBE) models



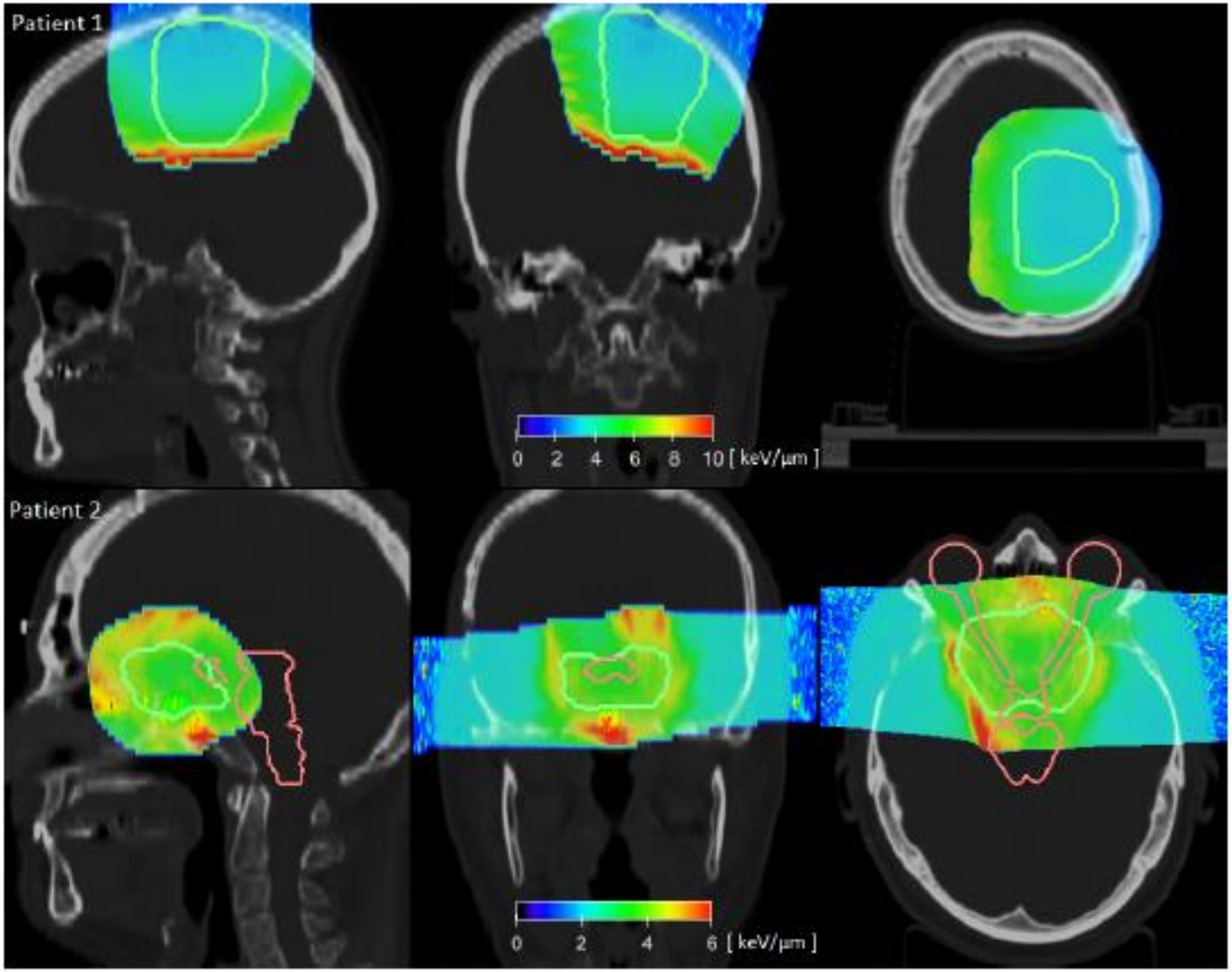
D_{varRBE} assuming varRBE

Dose difference:

D_{varRBE} – $D_{RBE=1.1}$

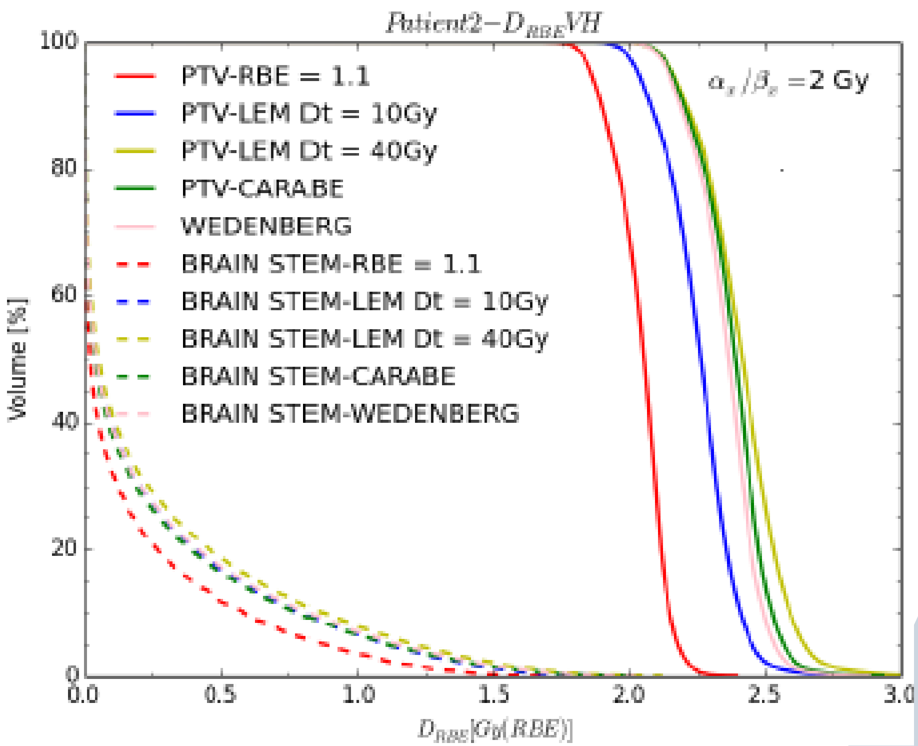
A. Mairani, et al Physics in Medicine and Biology 2017 61: 1378–1395

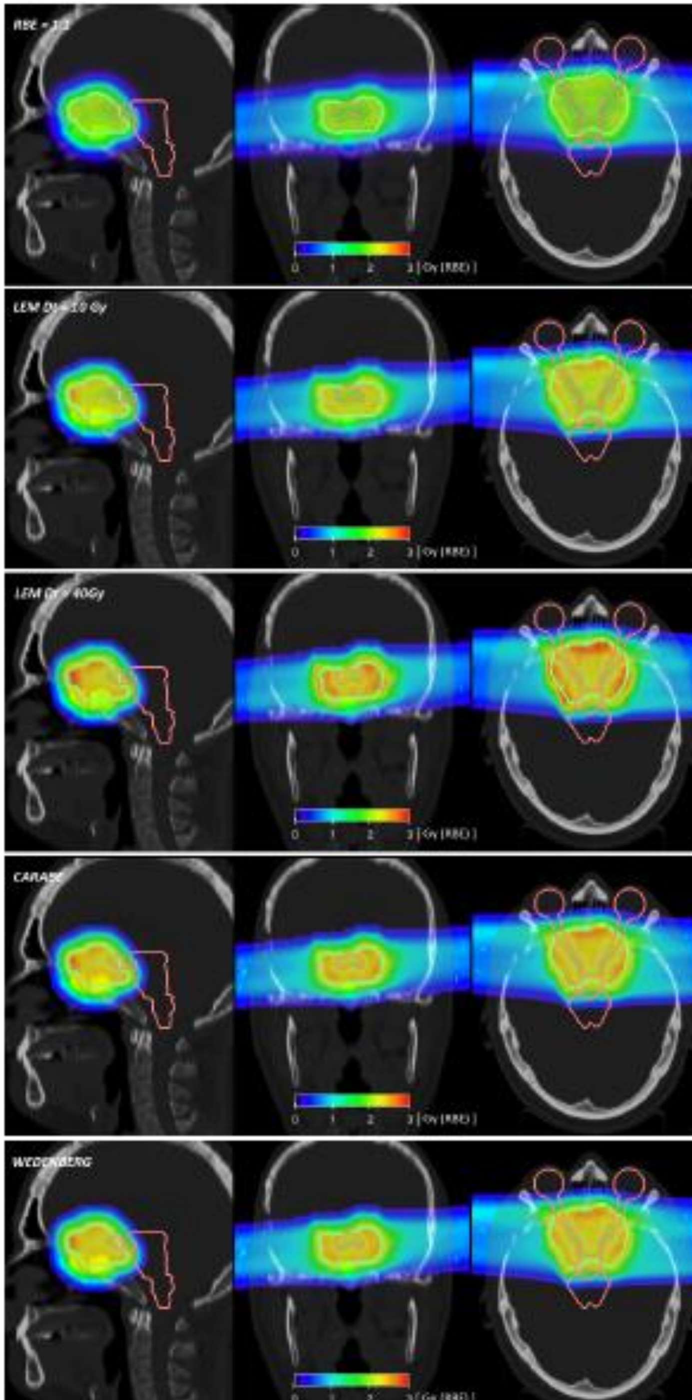
Beyond RBE 1.1 in proton therapy: LET distributions in clinical-like scenario



G. Giovannini,...A. Mairani, K. Parodi Radiation Oncology (2016) 11:68

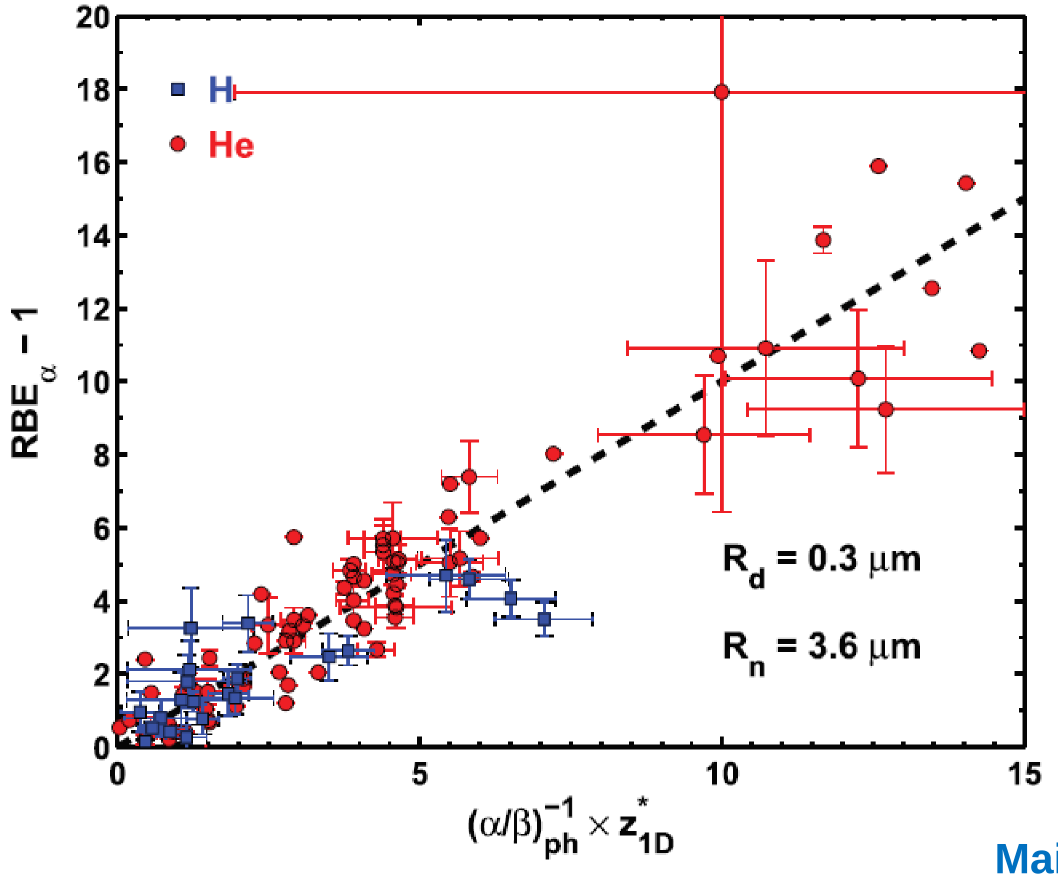
D_{RBE} distributions in clinical-like scenario with $(\alpha/\beta)_{ph}$ = 2 Gy





G. Giovannini,...A. Mairani, K. Parodi
Radiation Oncology (2016) 11:68

Beyond the TPS: variable RBE in proton (and He) therapy tuning MKM input parameters



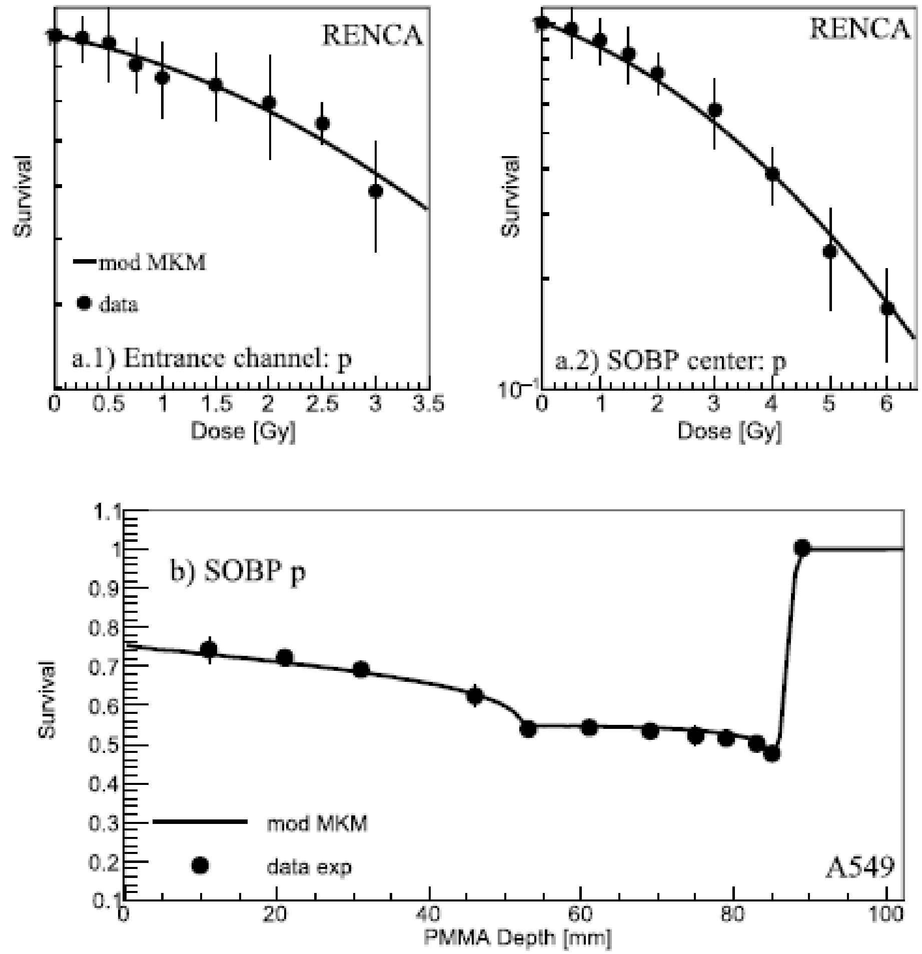
$$\mathrm{RBE}_\alpha \equiv \frac{\alpha_{\mathrm{ion}}}{\alpha_{\mathrm{ph}}} = 1 + \left(\frac{\alpha}{\beta}\right)^{-1}_{\mathrm{ph}} \cdot z^*_{1\mathrm{D}} ,$$

$$\mathrm{R}_\beta \equiv \frac{\beta_{\mathrm{ion}}}{\beta_{\mathrm{ph}}} = 1.$$

Mairani et al PMB (2017) 62: N244

Figure 1. Experimental $\mathrm{RBE}_\alpha - 1$ (points with error bars) as a function of $z^*_{1\mathrm{D}} \cdot (\alpha/\beta)^{-1}_{\mathrm{ph}}$. $z^*_{1\mathrm{D}}$ values have been calculated using the best fit parameters $R_d = 0.3$ μm and $R_n = 3.6$ μm. The slope of the dashed line graphically displays a 1:1 dependence.

Beyond the TPS: variable RBE in proton (and He) therapy tuning MKM input parameters



Mairani et al PMB (2017) 62: N244

Novel ions at HIT:

^{4}He ion beams

Dosimetric comparisons

^{4}He as a good candidate for further particle therapy **improvements** :

- Favorable physical characteristics
- Smaller lateral scattering than p , Fall-off distal / lateral
- Very low tail-to-peak ratio compared to ^{12}C or ^{16}O

- Comparisons MC-FLUKA[6,7,8] / dosimetric measurements

→ **Beam Modelling (DDD + Lateral profile + SOBP)**

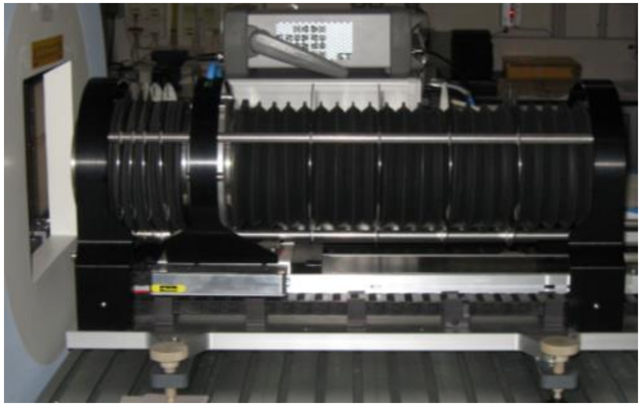
[6] Böhlen *et al.* (2014)
[7] Ferrari *et al*. (2005)
[8] Battistoni *et al.* (2016)

MC - Beam Modelling

Depth Dose Distribution

Measurements

- **10 energies** (56.44-220.51 MeV/u, ~2.5-31 cm)
- **PeakFinder** (PTW) water column
- Delivery of a quasi-**monoenergetic** pencil-like beam in the central axis
- Step size in the peak region ~ 50µm
- w/wo Ripple Filter (**RiFi**)



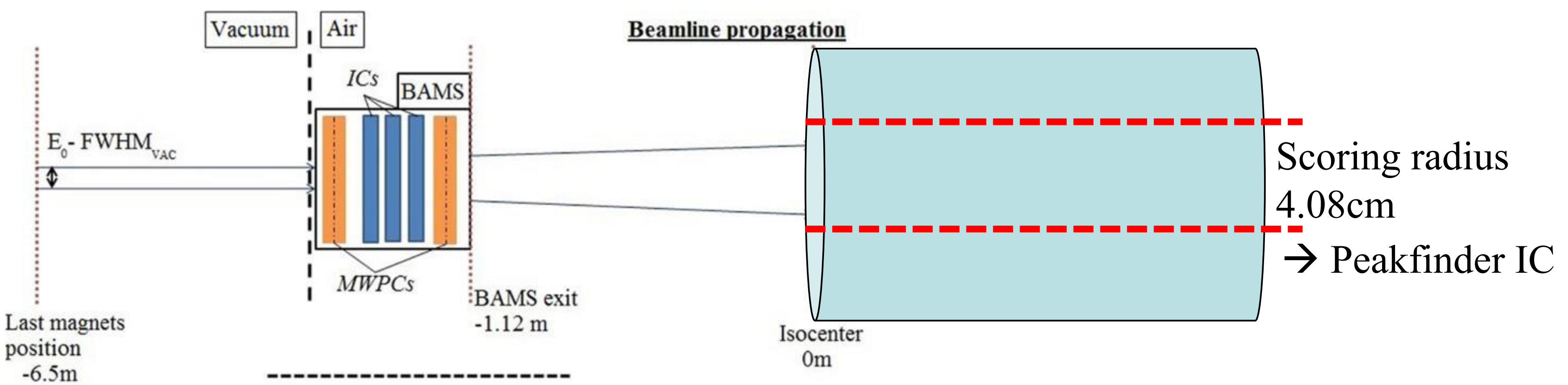
PeakFinder Water column

MC - Beam Modelling

Depth Dose Distribution

Simulations

- **Detailed model** of the HIT beamline[9]
- Binning of 25µm (radius=4.08cm) - + WATER
- 10^6 primary histories



- **Density ?**
- **Ionization Potential ?**
- **Momentum spread ?**

MC - Beam Modelling

Depth Dose Distribution

Simulations

- **Detailed model** of the HIT beamline[9]
- Binning of 25µm (radius=4.08cm)
- + WATER
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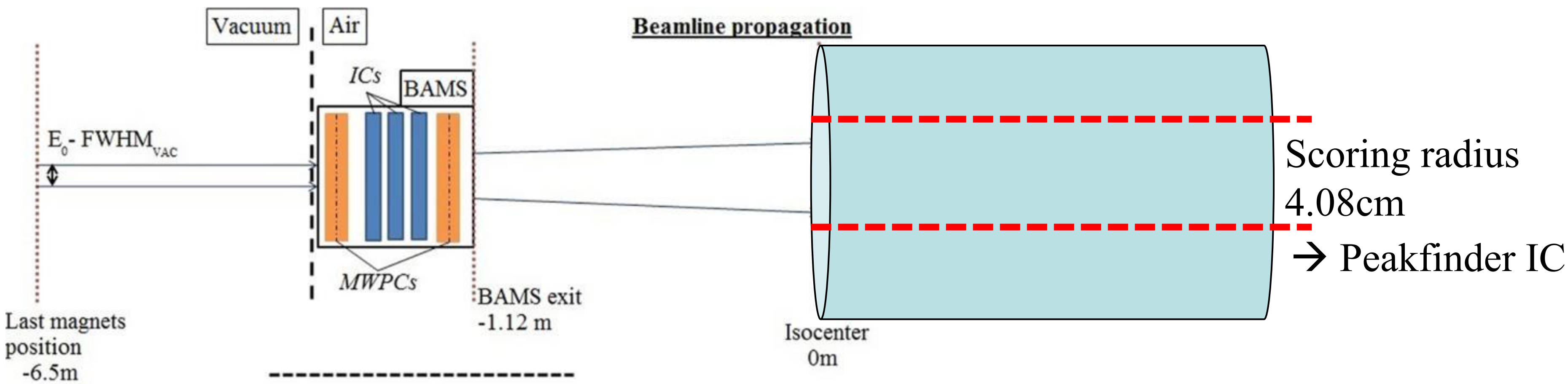


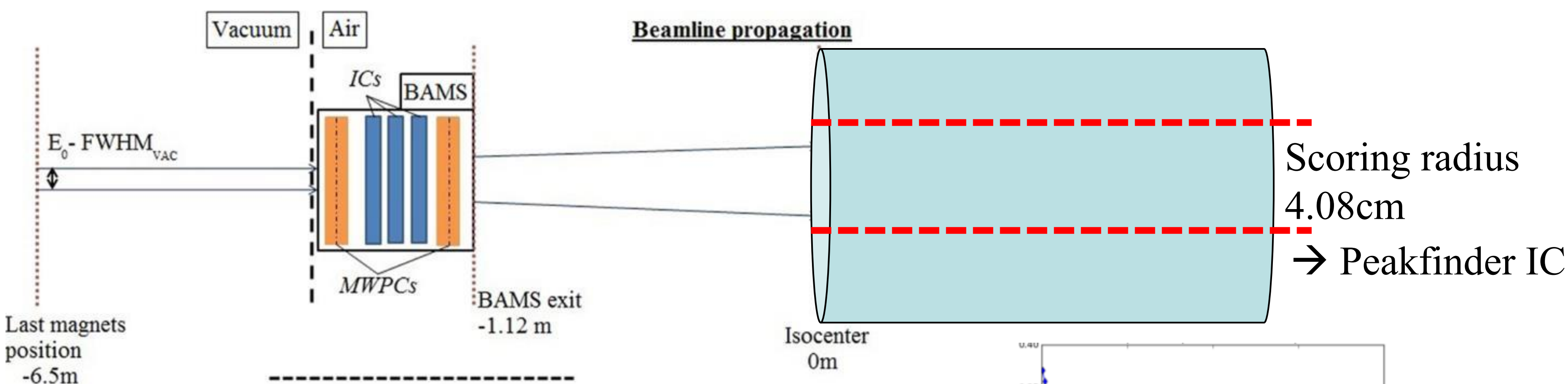
- **Density ?** → **0.998 g.cm^{-3} (Exp. Conditions)**
- **Ionization Potential ?** → **Trial and errors : Range comparisons**
- **Momentum spread ?** → **Trial and errors : Bragg Curve similitude (χ^2 red.)**

MC - Beam Modelling

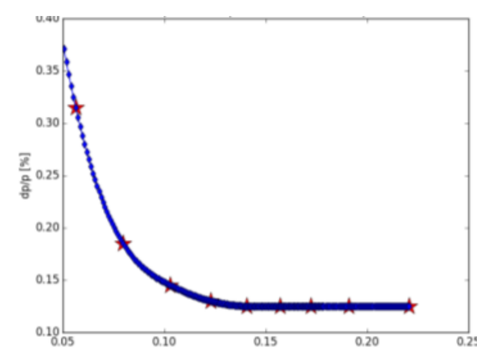
Depth Dose Distribution

Simulations

- **Detailed model** of the HIT beamline[9]
- Binning of 25µm (radius=4.08cm) - + WATER
- 10^6 primary histories



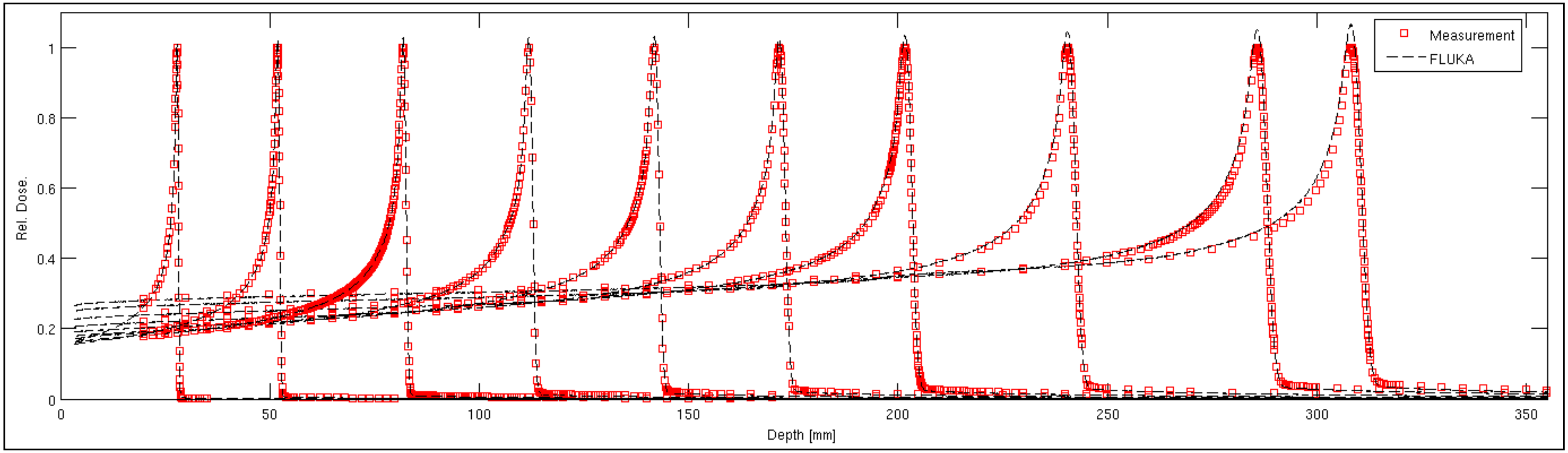
- **Density ?** → **0.998 g.cm^{-3}**
- **Ionization Potential ?** → **76.8 eV**
- **Momentum spread ?** → **dp/p=f(E)**



MC - Beam Modelling

Depth Dose Distribution

Results



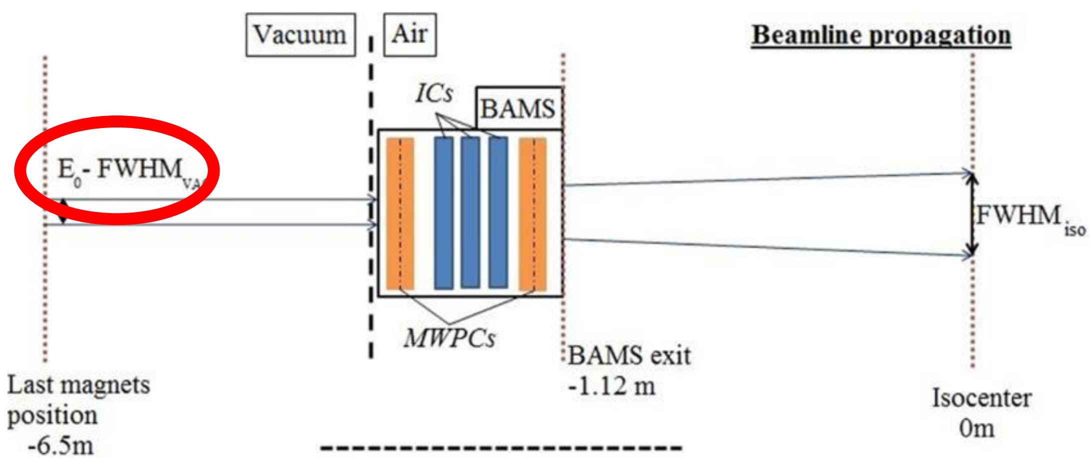
- Overall **good agreement** between simulations and measurements (w/wo RiFi)
- Range differences **< 0.10 mm**
- Dose differences **from 0.5 to 6%** in the high dose region
- Small differences in the tail
- Average dose-weighted dose-difference **from 0.4 to 2.5%**
  - → **Good results** of the **FLUKA models**
  - → Room for **improvements (production of secondaries ?)**

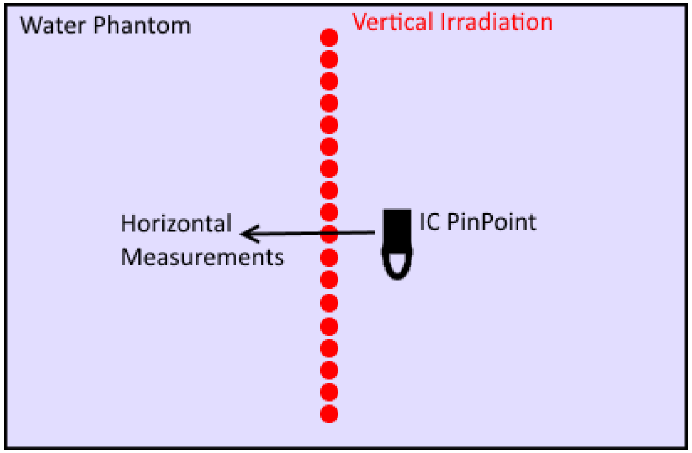
MC - Beam Modelling

Lateral Dose Distributions

Measurements

- **3 energies**
- After Vacuum Gaussian size assessment …





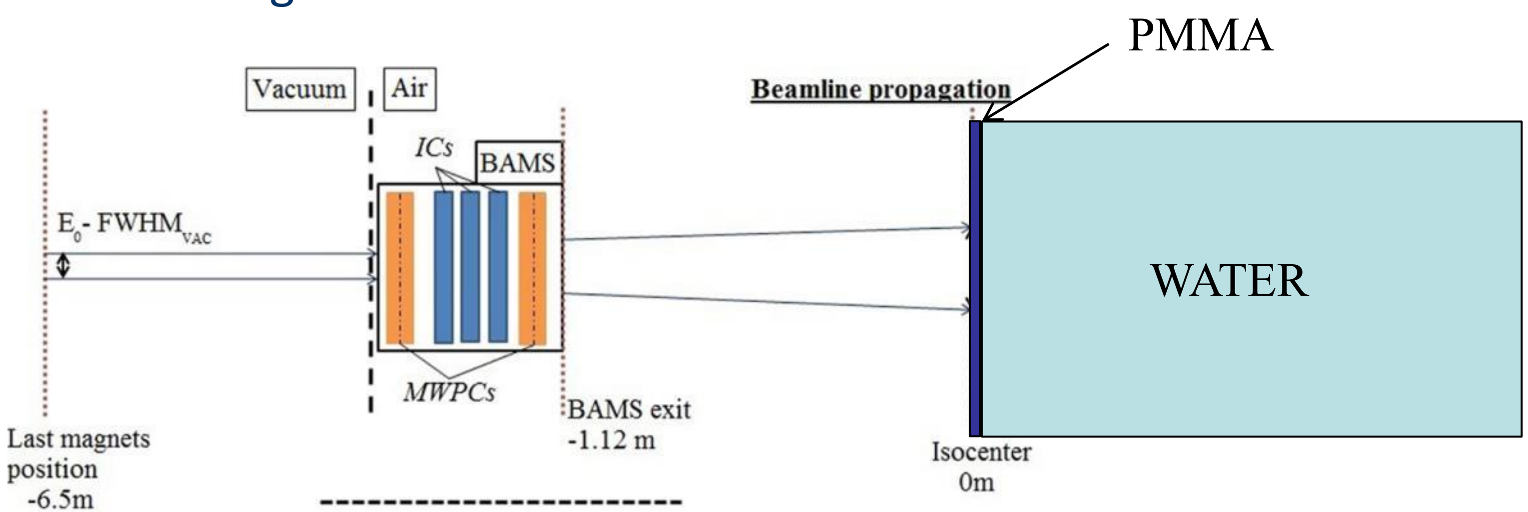
Measurements of verticaly scanned line

MC - Beam Modelling

Lateral Dose Distributions

Simulations

- **Detailed model** of the **HIT beamline** and **water**
- Binning 1x1x1mm^3
- 200x10^6 primary histories
- ICs sensitive volume



Analysis

- Simple Gaussian parametrization along depth
- Triple Gaussian parametrization along depth

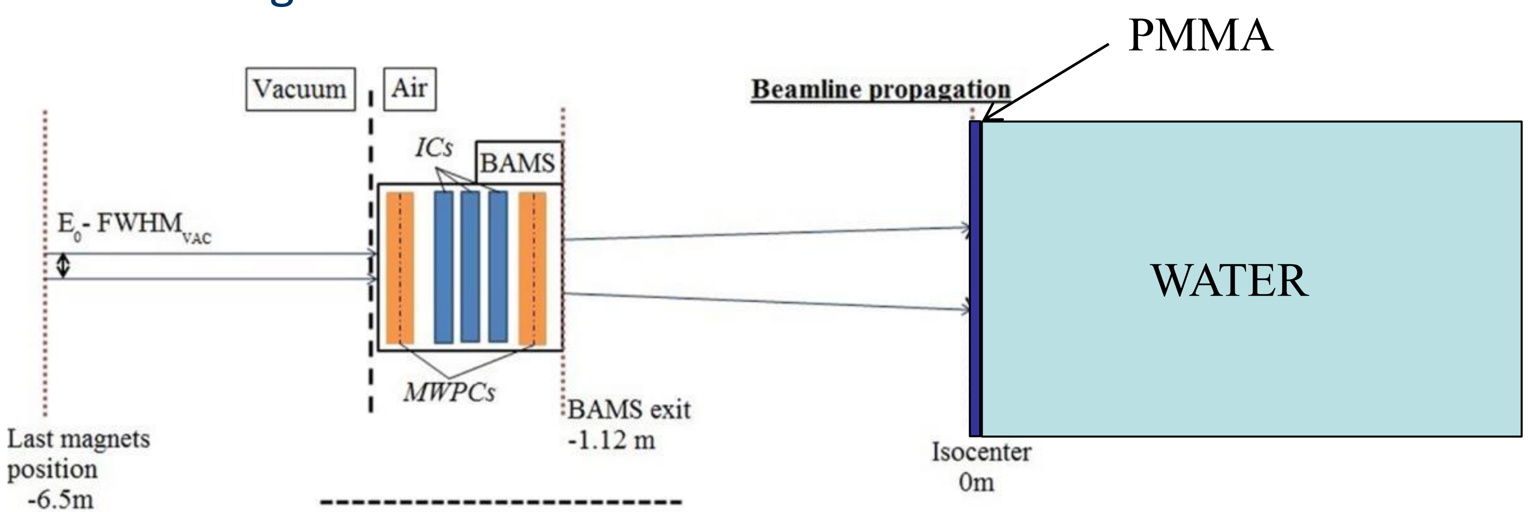
(ROOT – Minuit Package)

MC - Beam Modelling

Lateral Dose Distributions

Simulations

- **Detailed model** of the **HIT beamline** and **water**
- Binning 1x1x1mm^3
- 200x10^6 primary histories
- ICs sensitive volume



Analysis

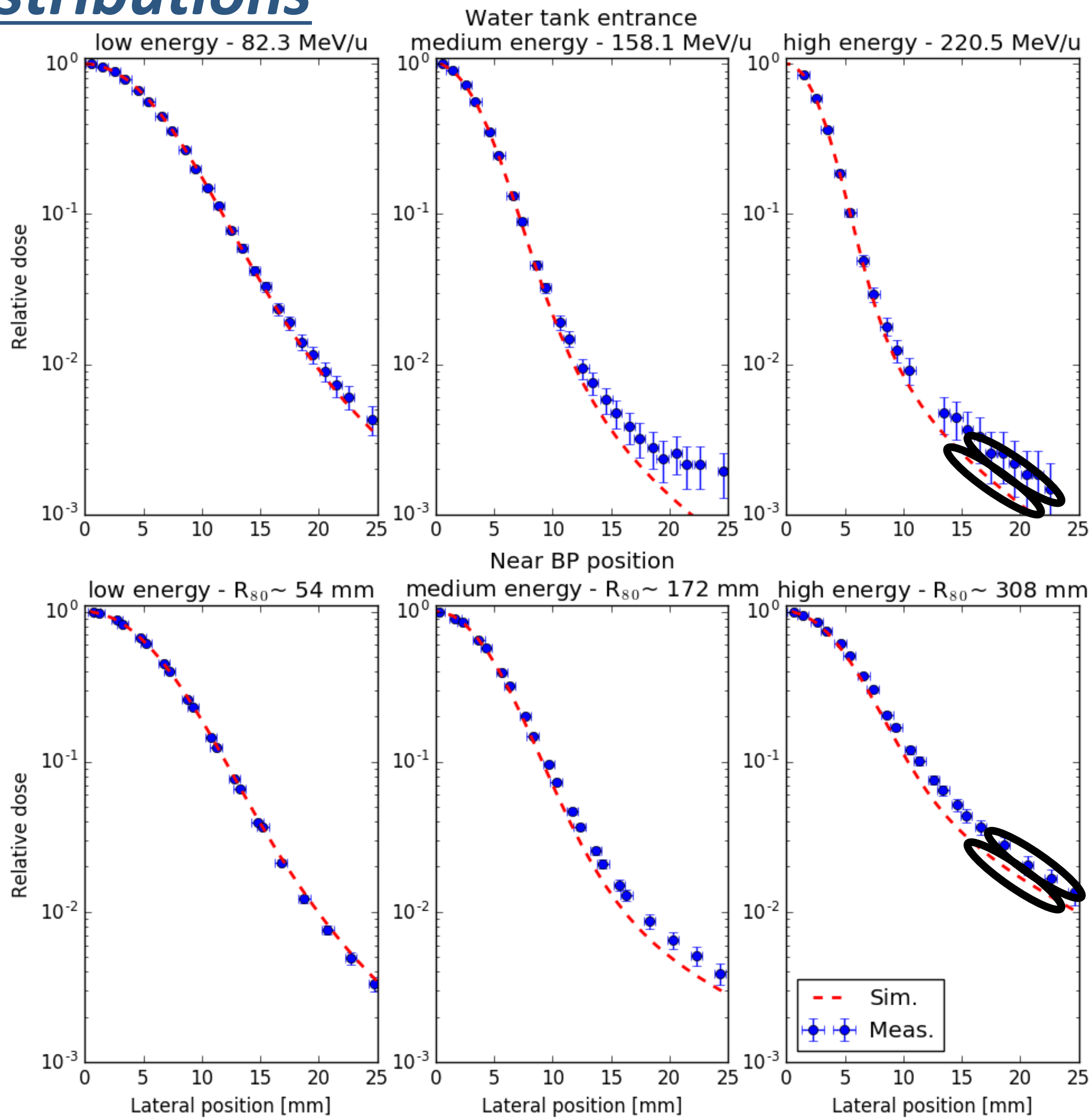
- Simple Gaussian parametrization along depth → FWHM evolution
- Triple Gaussian parametrization along depth → Dose contributions

(ROOT – Minuit Package)

MC - Beam Modelling

Lateral Dose Distributions

Results



→ **Good agreements**

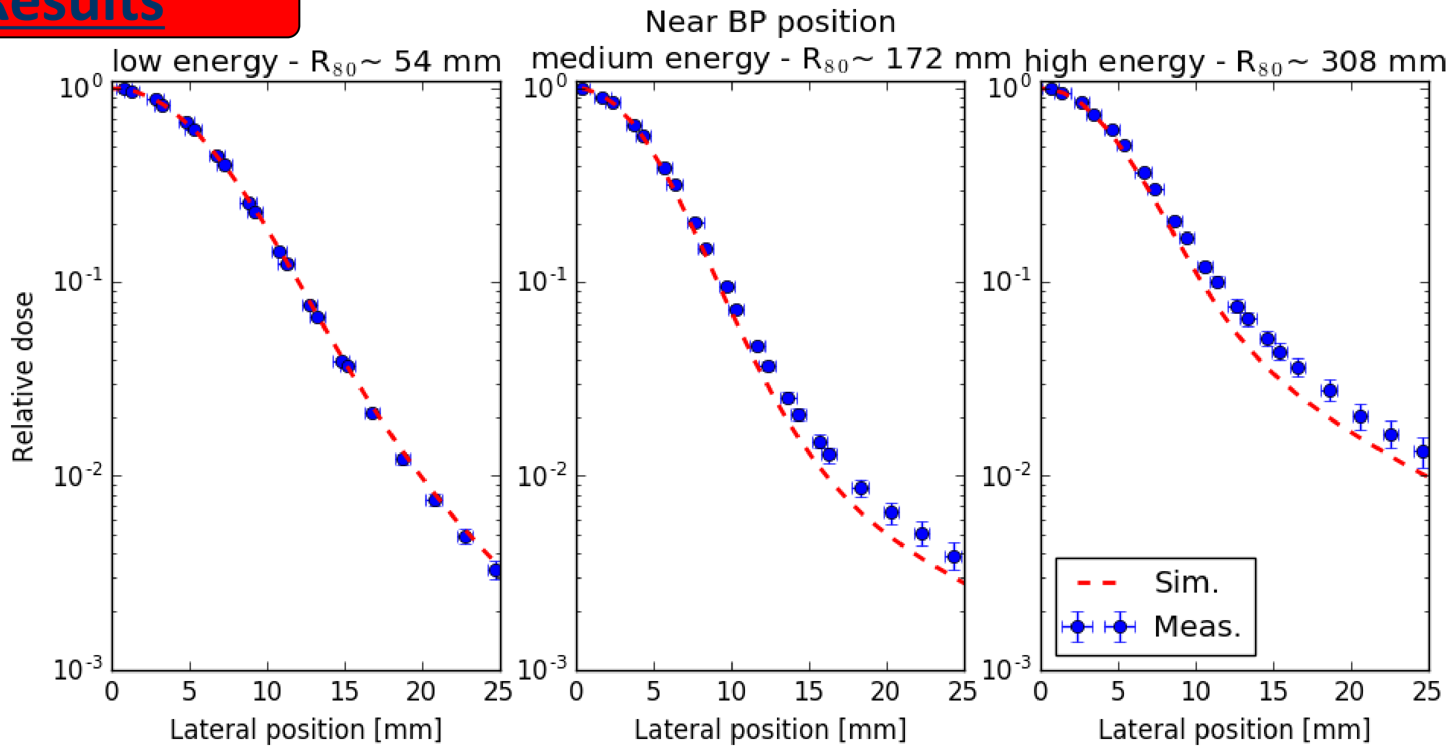
But differences for

- **High energies**
- **Large depth/Lat. position**

MC - Beam Modelling

Lateral Dose Distributions

Results



- FWHM differences **< 0.5 mm** at the entrance and near Bragg peak region
- **Differences in the halo** for high energies at large depth

→ **Good results** of the **FLUKA models**

→ **Underestimation of secondary particles ? Large angles ?**

MCTP Platform

Physical Validation

Simulations

- **Optimization** with FLUKA–MCTP[11]
- SOBP **size**: **3x3x3** and **6x6x6** cm^3
- **Position** (center) of SOBPs: **5, 12.5 and 20 cm**
- **Dose** planned : 1Gy (physical optimization)
- **Re-calculation** with : $1x1x1mm^3$ bins / $150x10^6$primaries

Measurements

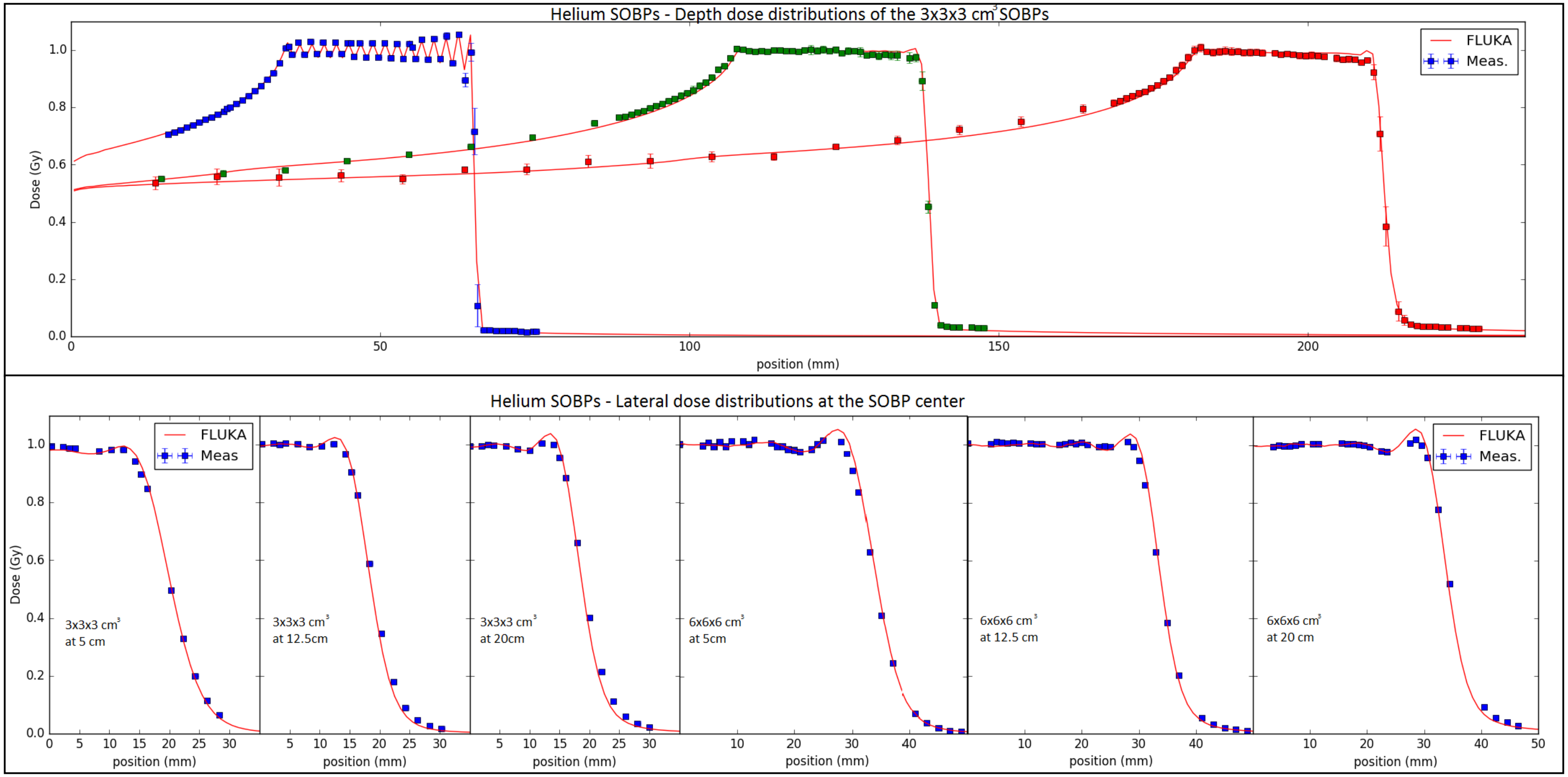
- **Measurements** in the water tank
- Acquisition of **depth-dose** distributions (step size 1 mm)
- Acquisition of **lateral dose** distributions (step size 2 mm)

Tessonnier,…,Mairani et al PMB (2017); 62(16):6579-6594

Tessonnier,…,Mairani et al PMB (2017); 62(16):6579-6594

MCTP Platform: He

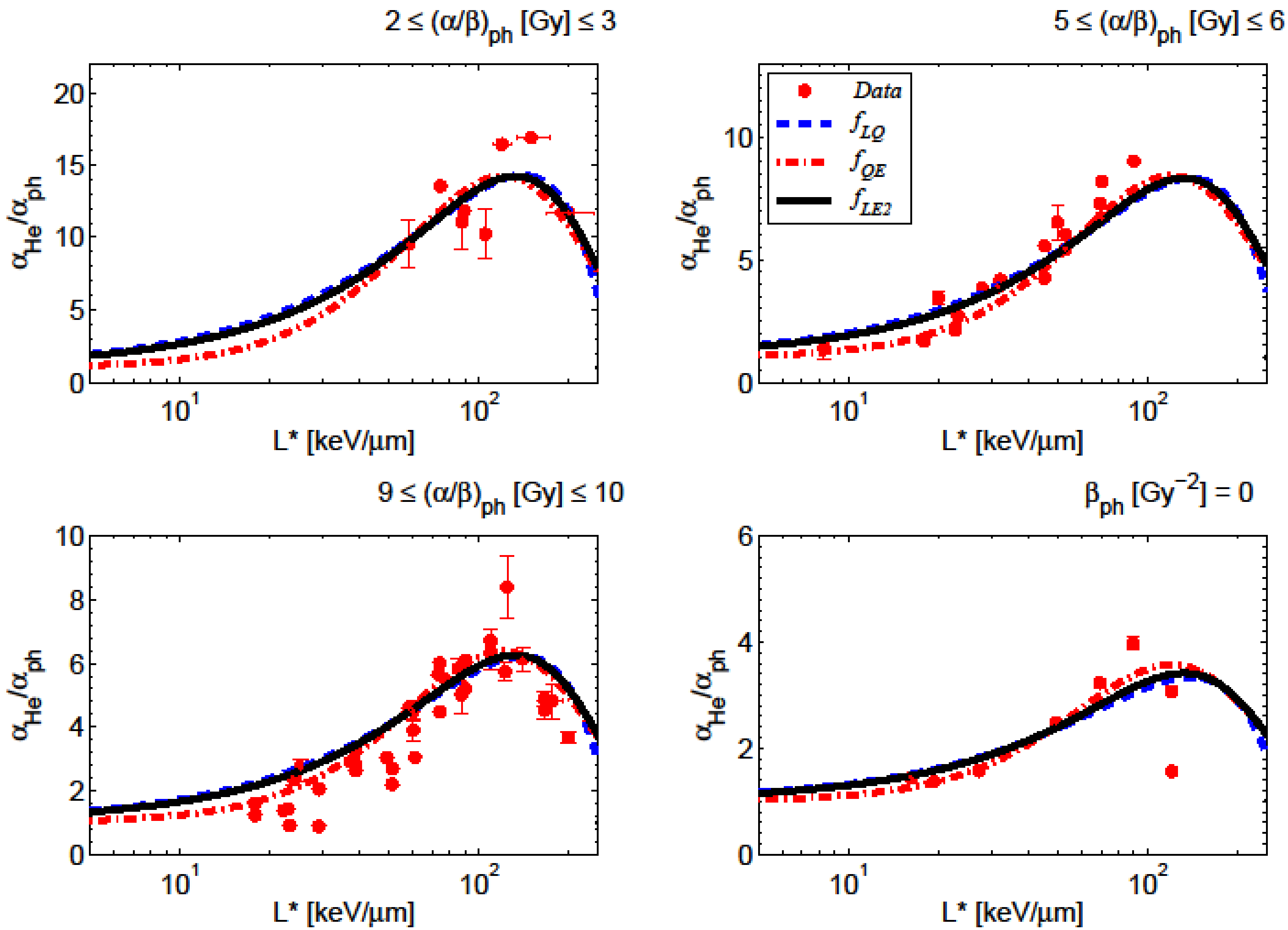
Results



- **Overall good agreement**
- Range difference **< 0.5 mm**
- **Global** dose deviation **< 2.5 %**
- Mean dose deviation in SOBP region **< 1%**
- **Consistent** results

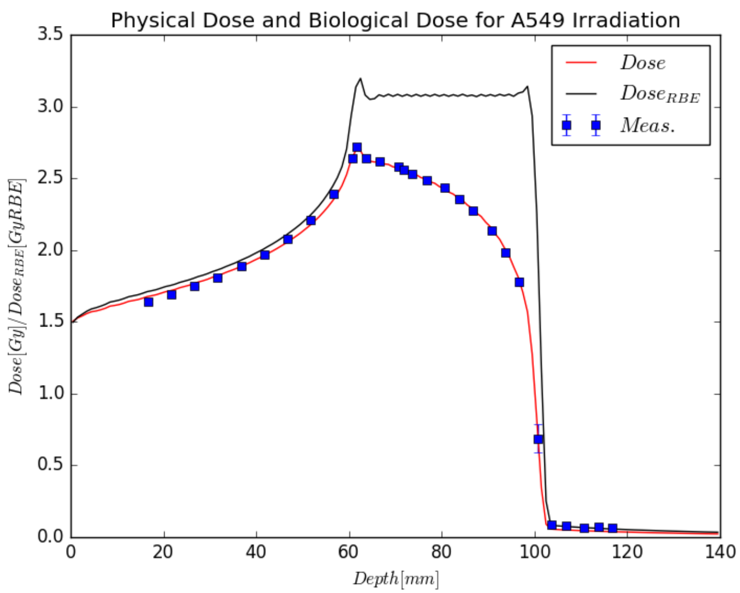
→ **Satisfying results** from **MC models**, the **optimizer** and **beam monitor calibration**

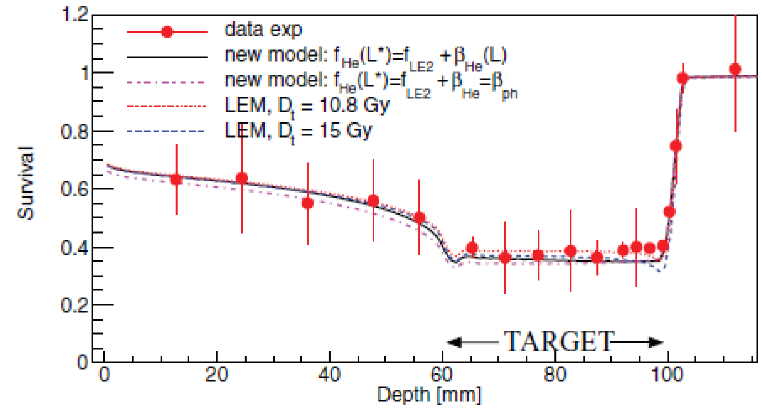
He RBE model development

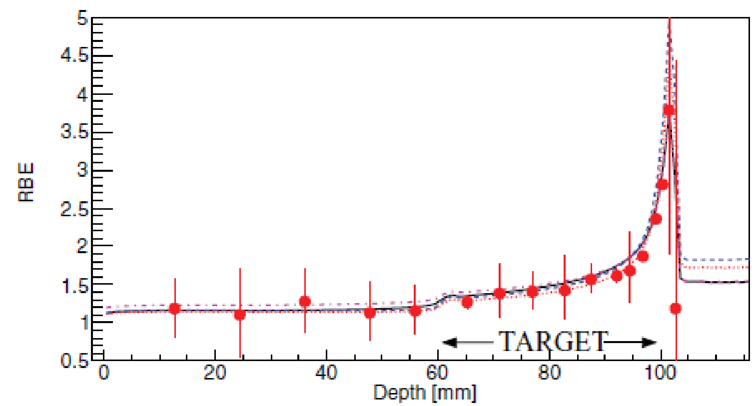


Mairani et al 2016 PMB 61 888, Mairani et al 2016 *PMB 61 4283*

RBE model validation







1 – Bio. Optimized SOBP
2 – Measurements verifications
3 – Cell Survival (A549) + RBE

→ **Validated in-house model for He (5%) and H (2%)**

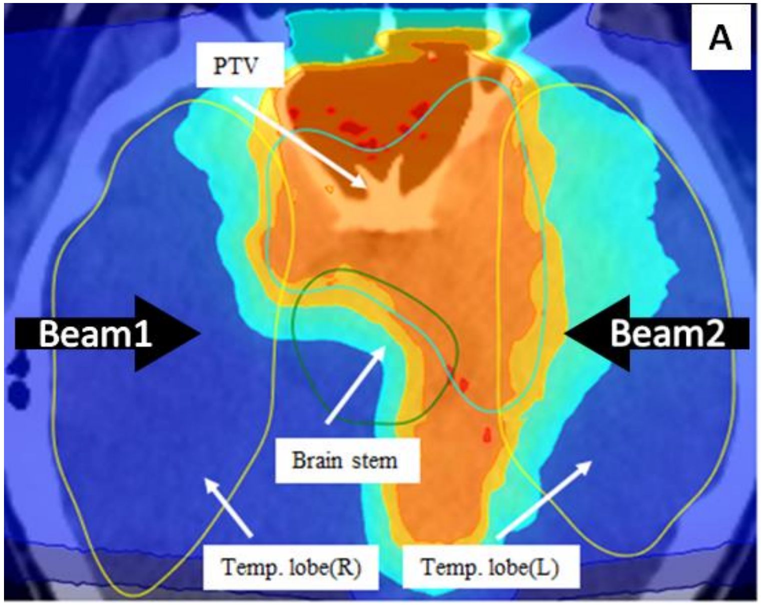
Mairani et al 2016 PMB 61 4283

Plan Comparisons

Methods

- Meningiomas treated with proton (4 patients)
- **Re-optimization** with **FLUKA–MCTP** for **helium** ions **AND protons**
- **Dose** in PTV 1.8 GyRBE

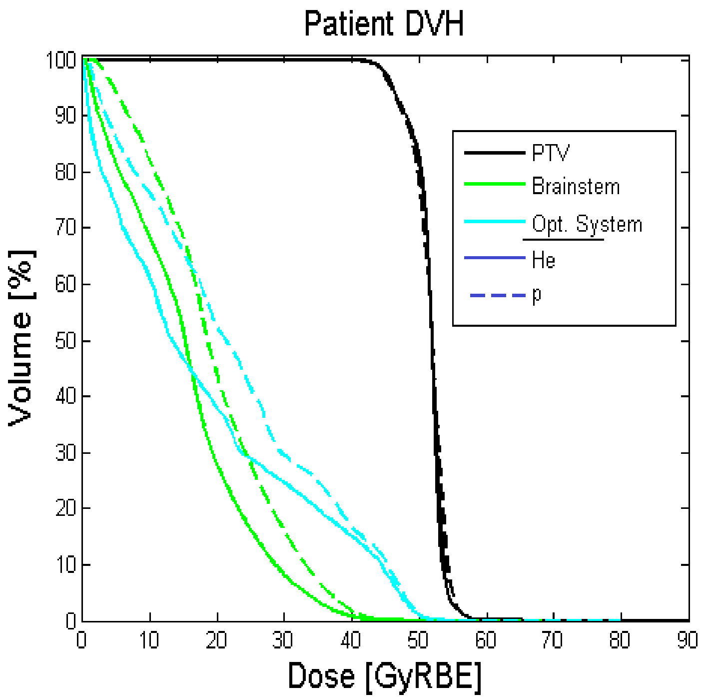
- Tissue types CNS α/β = 2 Gy , PTV α/β = 3.7 Gy
- **Protons** without RiFi, **variable RBE** (calculated "online")
- **Helium** ions with RiFi, **variable RBE** (calculated "online")
- Comparisons : DVH for **PTV** and **OAR**

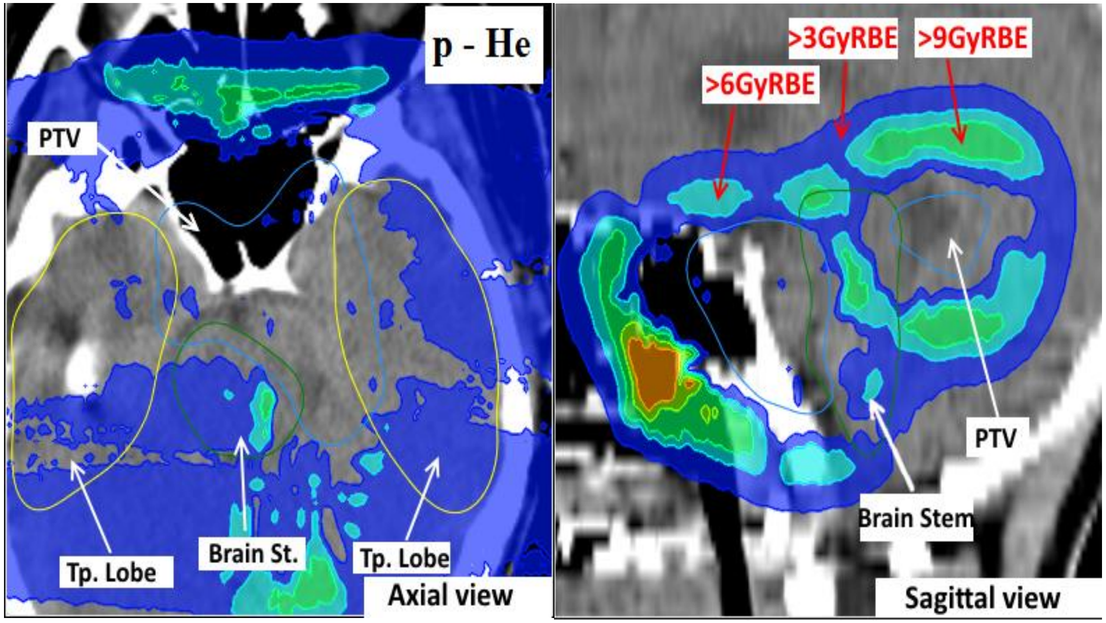


Tessonnier, Mairani et al 2018 Radiation Oncology 13(2)

Plan Comparisons

Results





Comparable **PTV coverage**

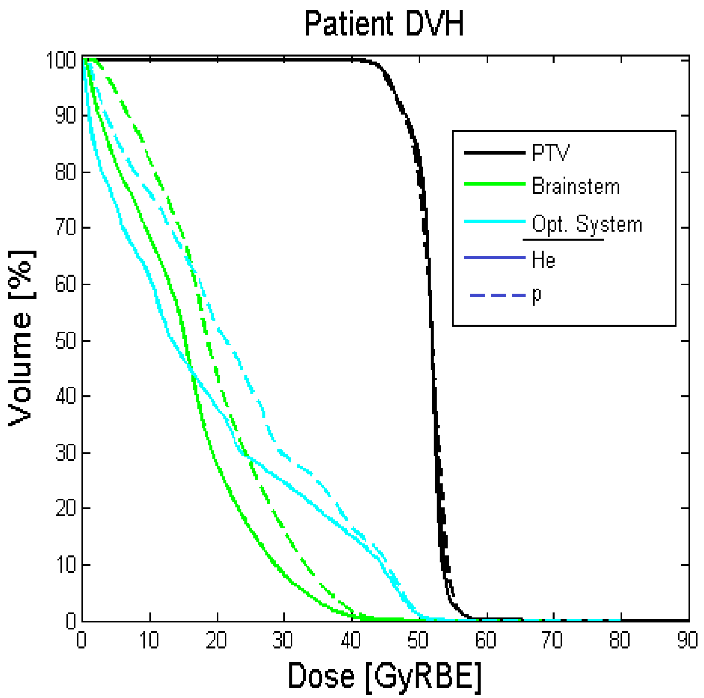
Better sparing of OAR with He

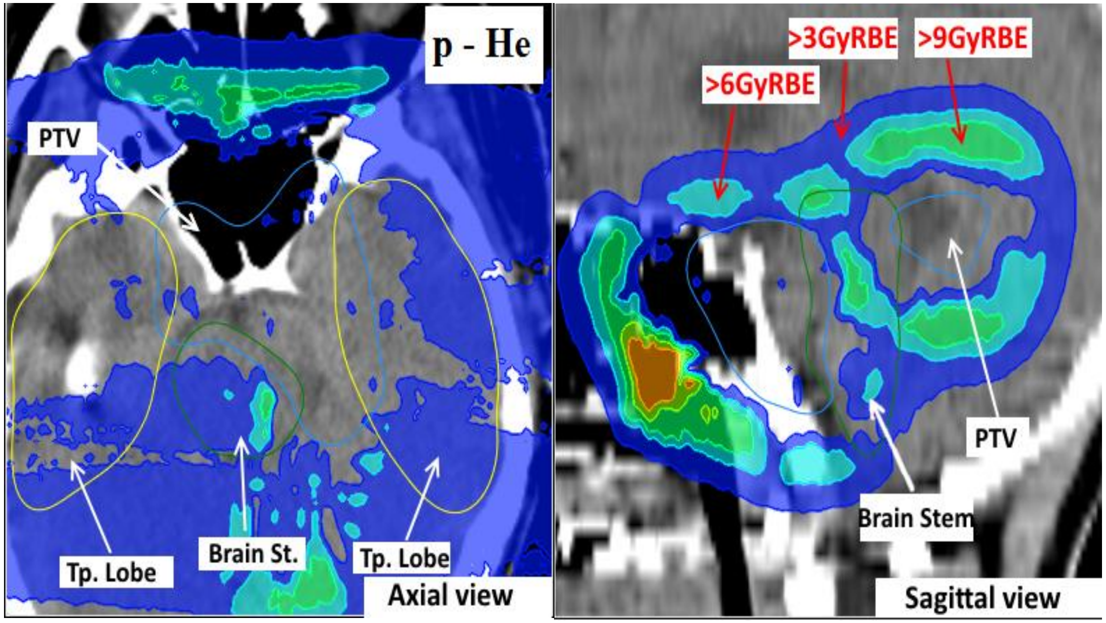
Less dose to normal tissues

Tessonnier, Mairani et al 2018 Radiation Oncology 13(2)

Plan Comparisons

Results





Higher benefits for large depth (lateral/distal fall-off)

→ **Promising results** from **plan comparison between He and protons**

Tessonnier, Mairani et al 2017 Radiation Oncology 13(2)

Thank you
for
Your Attention!