Monte Carlo-based treatment planning (MCTP) for ion beam therapy

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MC for hadron therapy (HT) treatment planning

Some features of MC

- **Potentially the most accurate dose predictions (`golden standard')**
  - **Accurate predictions for heterogeneous regions**
  - **Does not use the water-equivalent approach**
  - **But takes into account details of material composition**
- **High flexibility**
- **Computation time**

Examples of usage at clinical facilities (CNAO, HIT)

- **TPS basic physics data generation**
- **Support in commissioning phase**
- **PET in-vivo treatment verification**
- **Re-calculation of treatment plans**

Full MCTP ... what for?

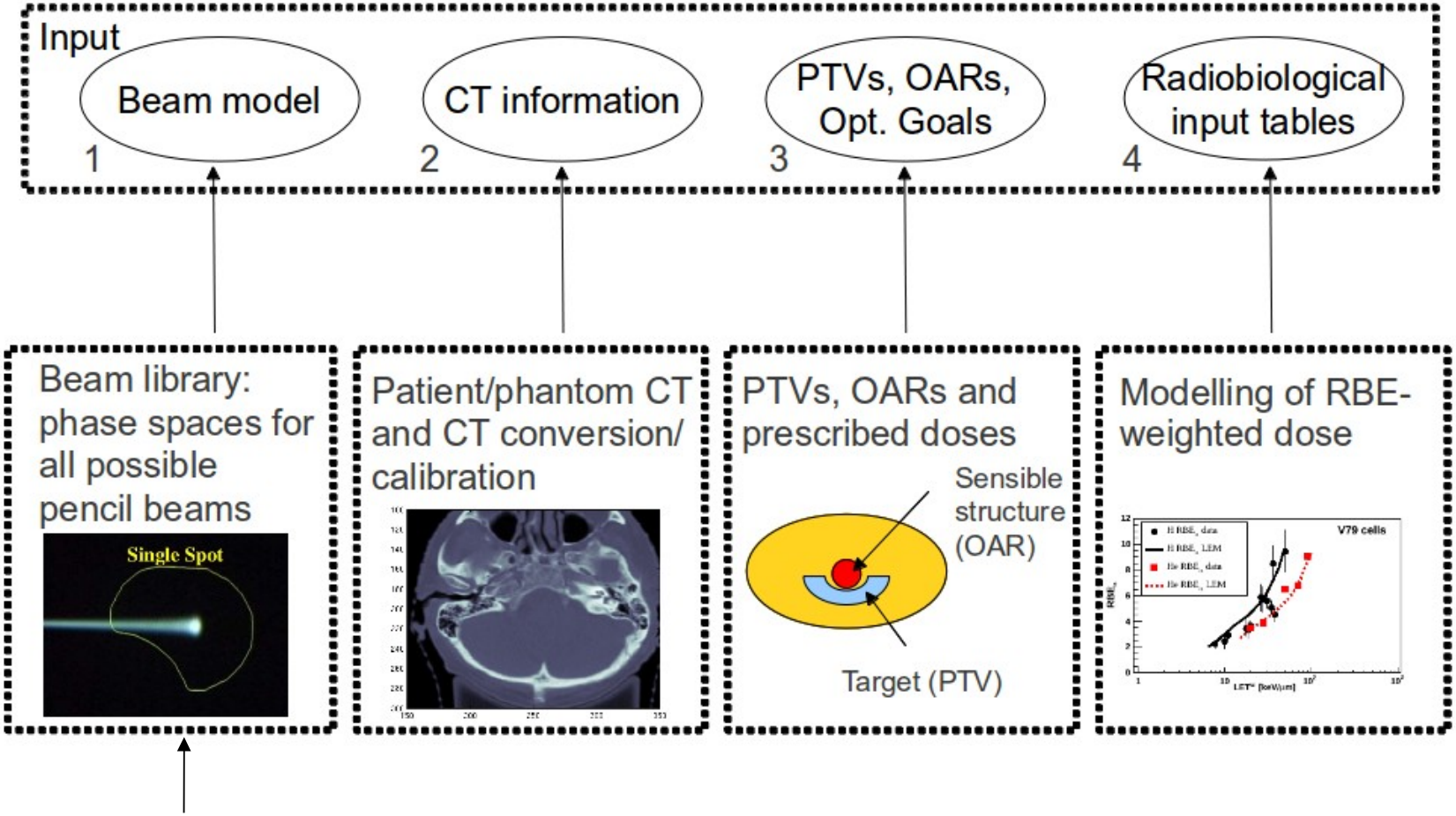
Work aimed at exploring at R&D-level the possibility of a Monte Carlo-based treatment planning (MCTP) for protons and ions!

- **MC re-calculation vs. full MCTP**
  → Not only "re-check" a given plan but also suggest a better solution!

- **Research applications:**
  - **New ions** (Z=1 – 8) and **combined ion fields**
  - Testing **new radiobiol. models** and **optim. algorithms/approaches**
  - **Secondary fluxes for: PET and prompt gamma**

- **Two modes:**
  - **Stand-alone** (no dependences on certified/commercial TPS)
  - **MC re-optimization of TPS calculated plans** (e.g. at CNAO/HIT)
    → increased flexibility for research!

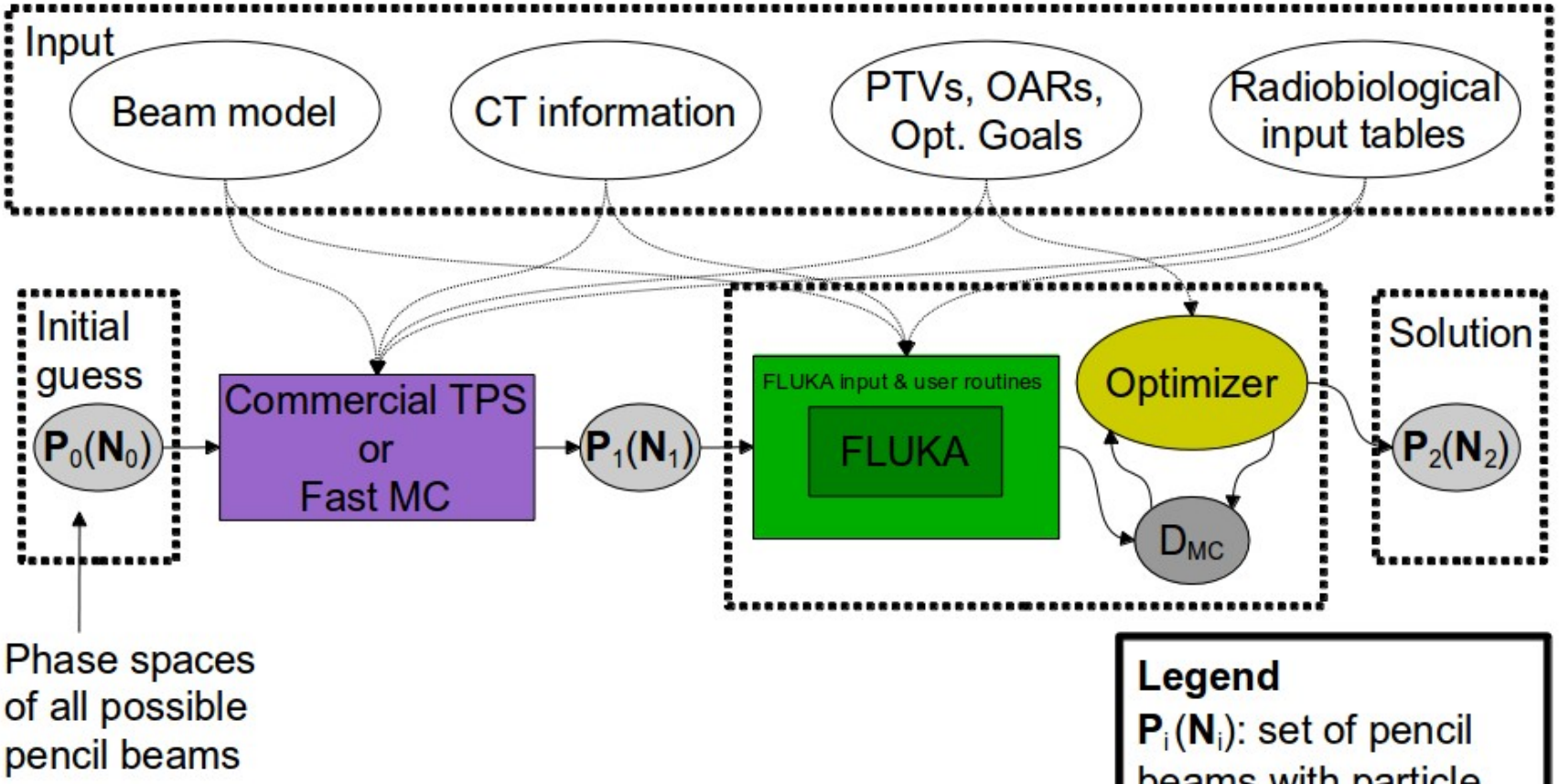
Treatment- and facility-specific input for the MCTP tool



Beam delivery: Scanning with active energy variation

Components and workflow

Multi-step procedure for dose calculation and optimization



Legend
$P_i(N_i)$: set of pencil beams with particle numbers N_i
D_{MC}: MC dose kernel

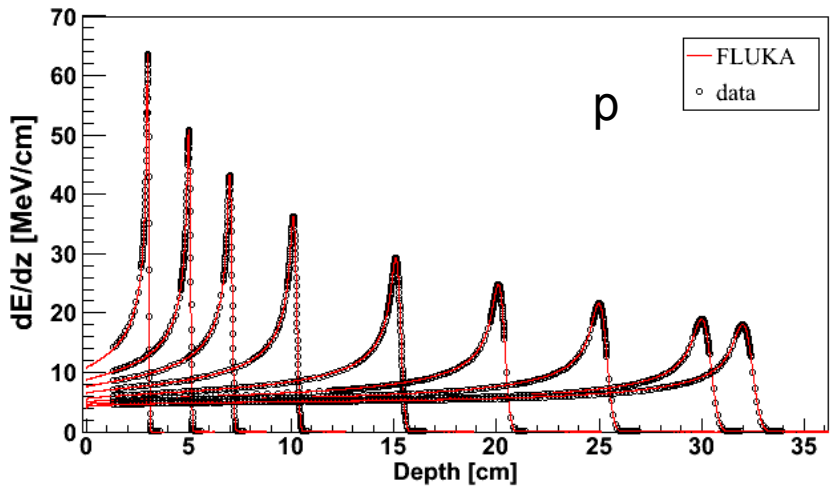
Optimization:
- different, mostly gradient-based, algorithms
- absorbed and RBE-weighted dose
- single- and simultaneous multi-field optimization (IMPT)

FLUKA and physical data base (CNAO)

Starting from a tool already validated and tuned for treatment conditions at CNAO (Pavia, Italy) and HIT (Heidelberg, Germany)

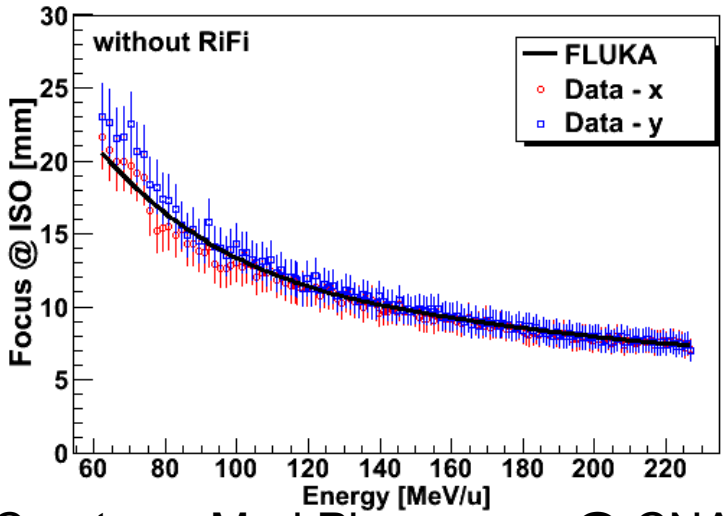
Example: CNAO beam library

FLUKA-calculated depth-dose distribution in water



Courtesy: Med Phys group @ CNAO

147 Energy steps (30-320 mm)
1 Focus size @ ISO



Courtesy: Med Phys group @ CNAO

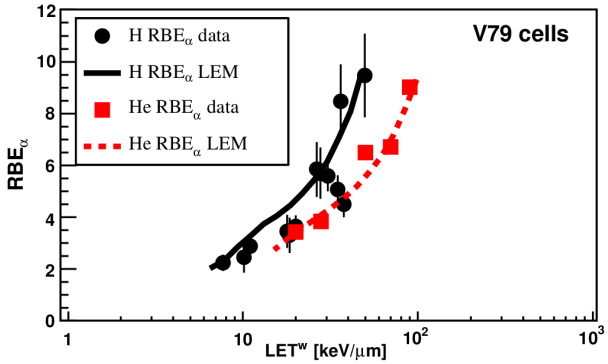
For HIT see: Parodi et al, PMB 57 (2012)

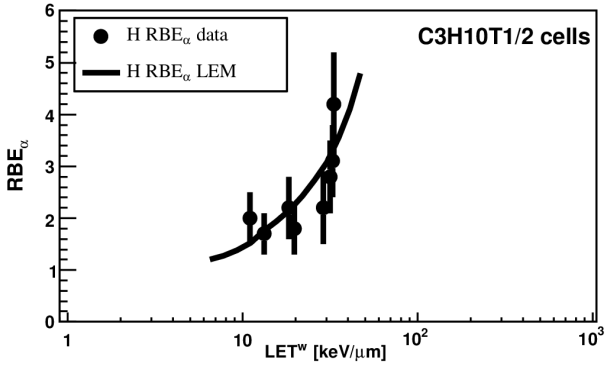
Radiobiol. input (tables)

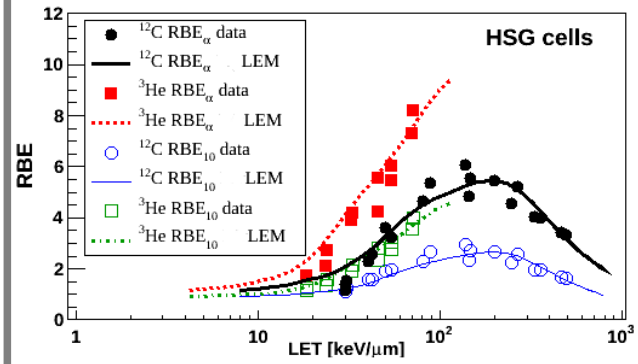
Some current options

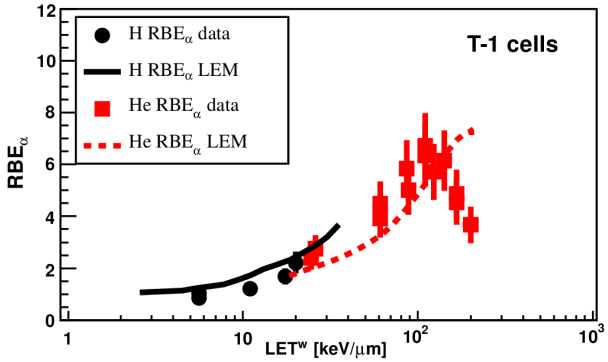
- LEM calculated Relative Biological Effectiveness (RBE)
  - LEM-I
  - HIT re-implementation of LEM-IV version published in Elsässer et al. IJROBP 2010
- Using standard constant RBE of 1.1 for protons

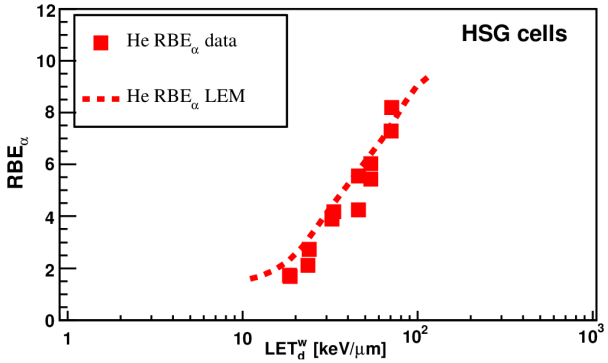
Benchmarks of HIT re-implementation of LEM-IV (Mairani et al.)







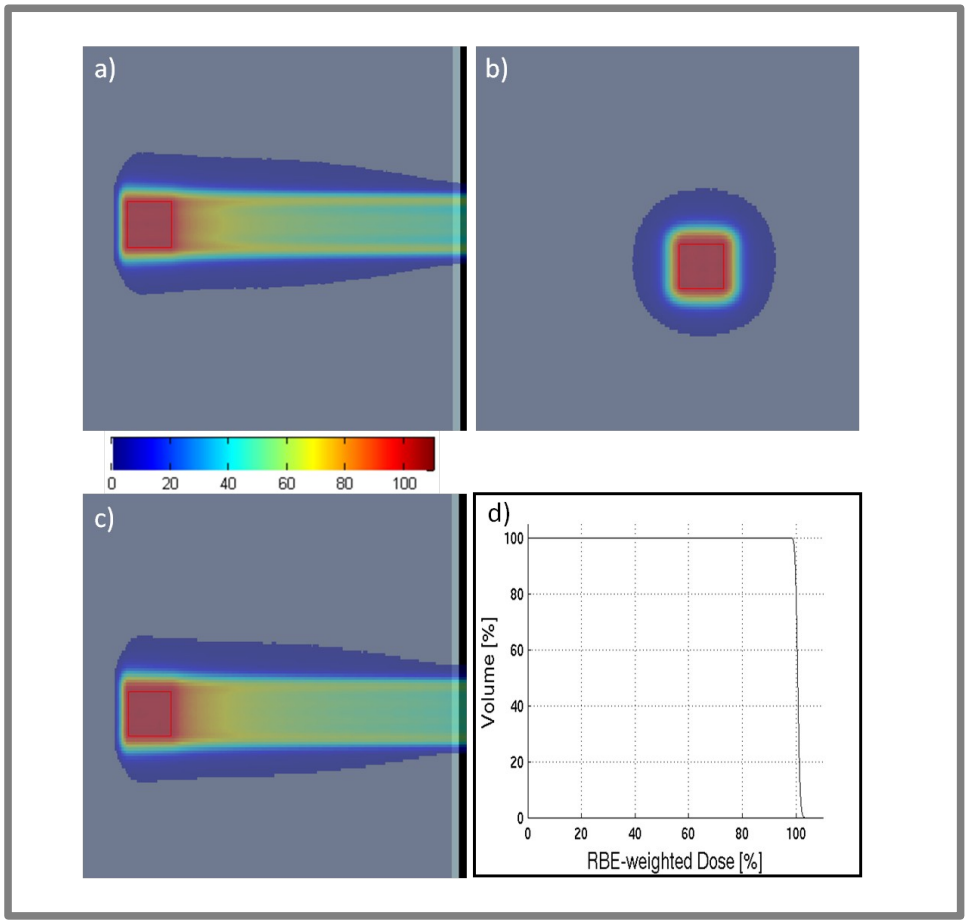




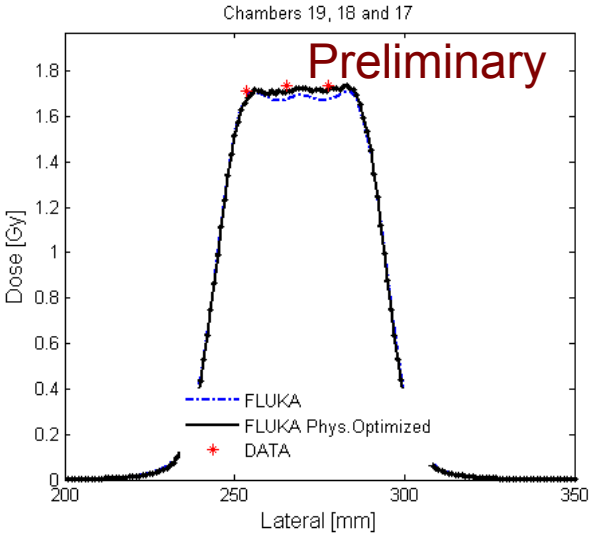
Spread-Out Bragg Peak (SOBP) in water with RBE= 1.1 – Optimized

Bio Dose distribution for a cubic shaped tumour (side = 3 cm) located between 19.5 and 22.5 cm depths in water using fixed RBE = 1.1 with 3438 pencil beams.
MC calculation of dose/RBE-weighted dose matrixes (50 k MC histories per pencil) = 7 hours and 10 min (24 CPUs)
Optimization time = 50 min (1 CPU)

8 hours



Dosimetric verification in progress at CNAO

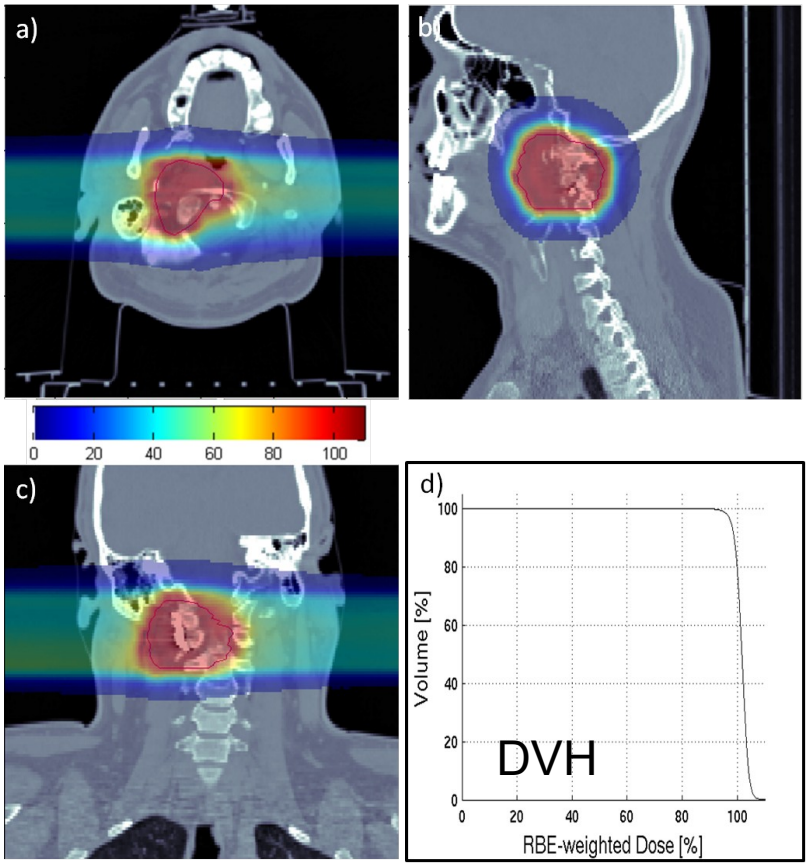


Courtesy of T. Tessonnier

Example plan: Chordoma protons (CNAO)

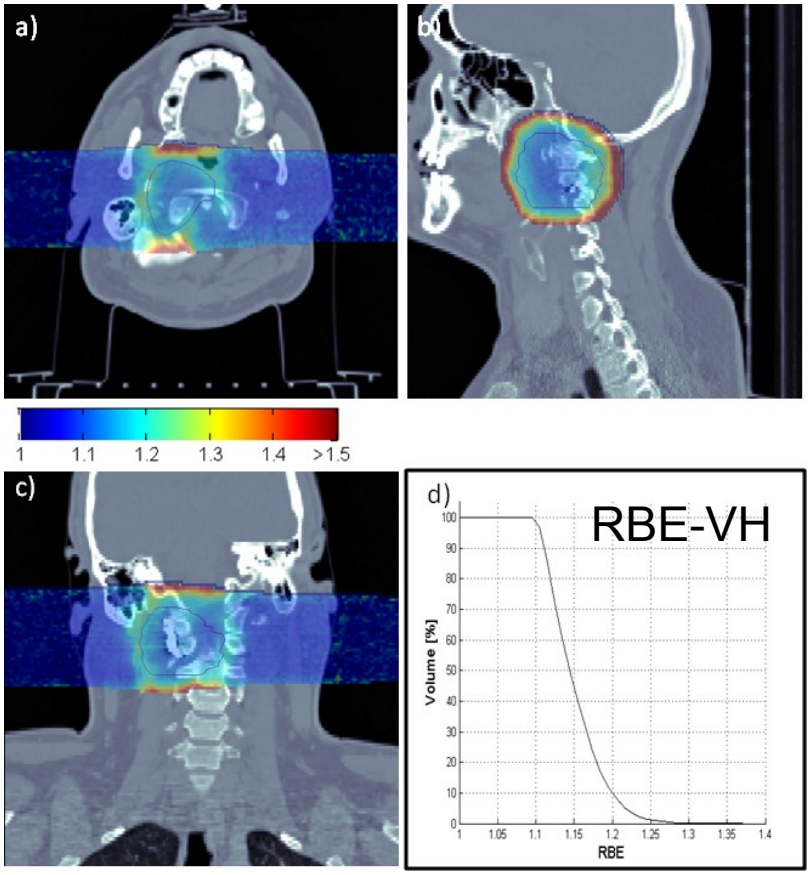
2 field IMPT using constant RBE = 1.1

2.0 GyE



Re-plotting using a variable RBE

LEM*-computed RBE for
same particle fluences

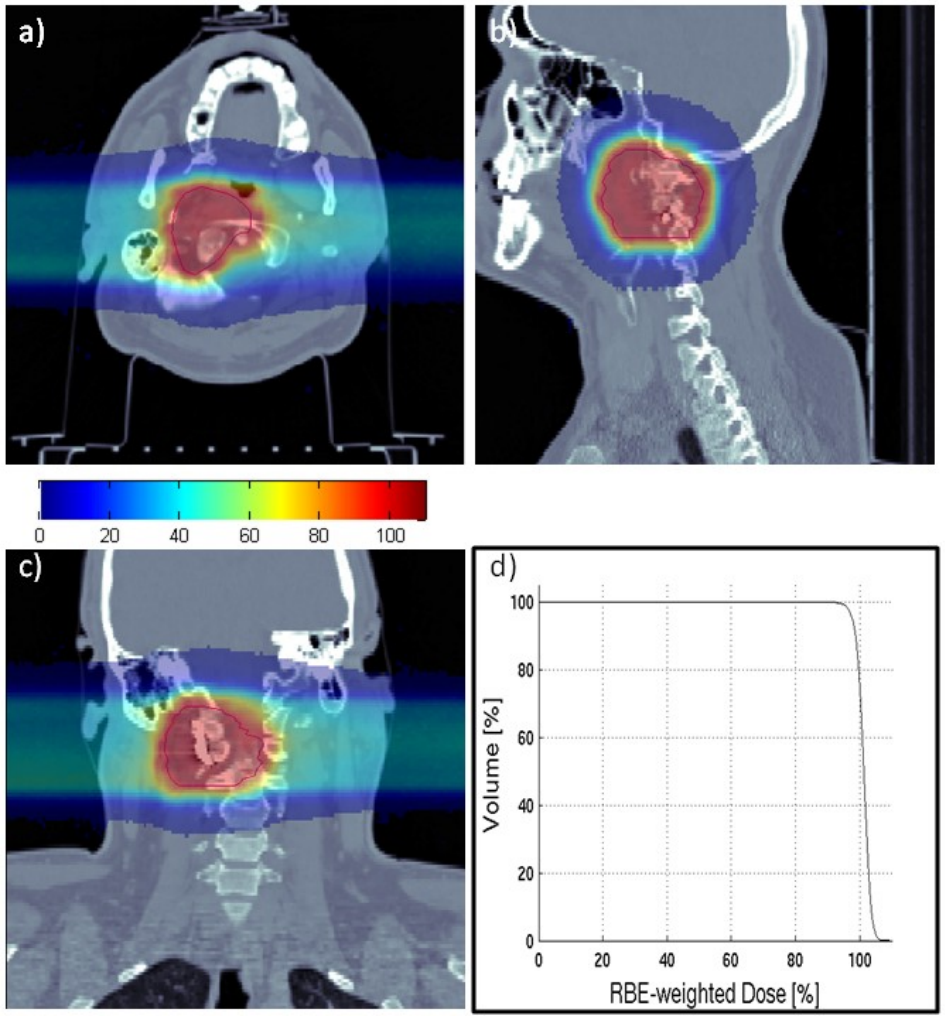


10.5ms per primary = on a **cluster with 24 CPUs of about 22 hours**
(10 000 primary protons per pencil beam, 13000 pencil beams)

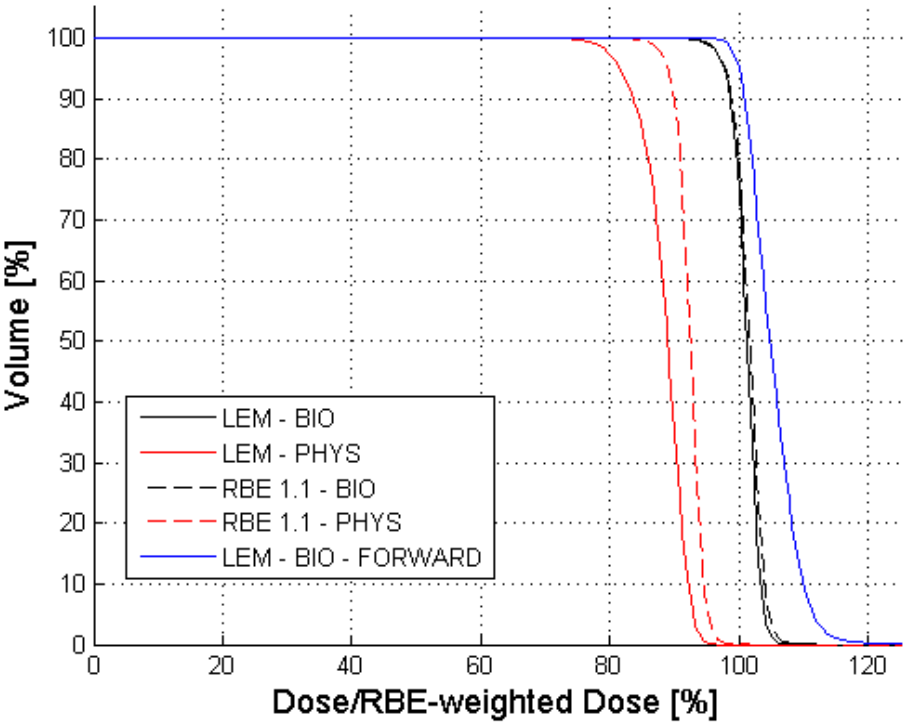
RBE for V79
→ no direct clinical interpretation!

Example plan: Chordoma protons (CNAO)

2 field IMPT using RBE computed with LEM*



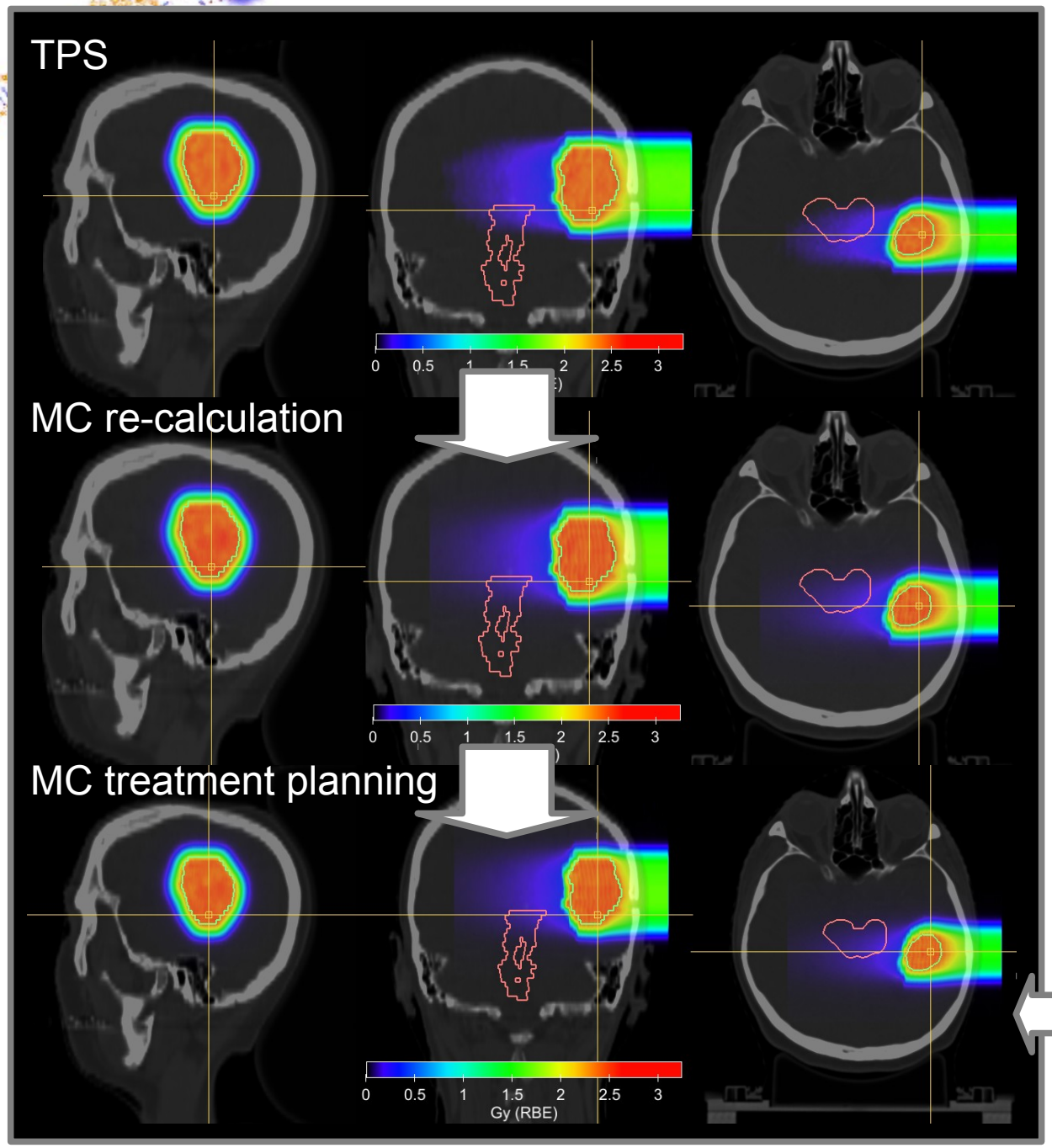
Differences in DVHs for the two RBE schemes:
variable (LEM*) vs constant

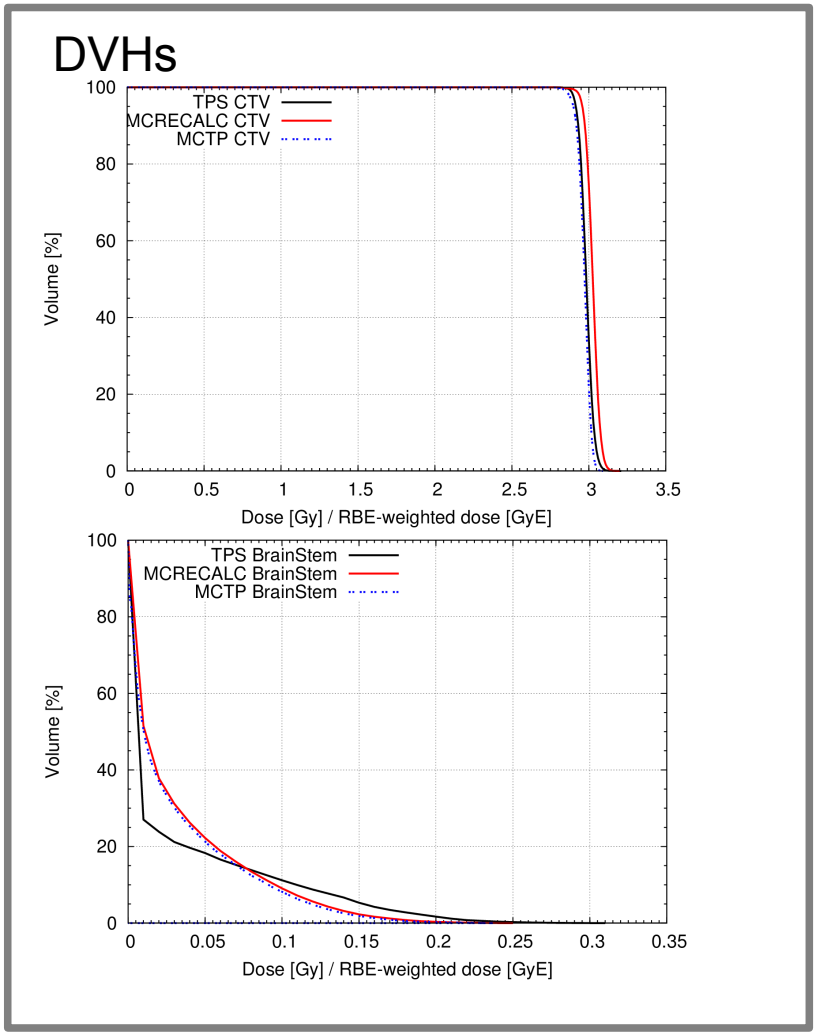


Constant RBE=1.1 results in 12% higher number of primary proton.

RBE for V79 → no direct clinical interpretation!

Example plan: Brain tumour carbon ions (HIT)



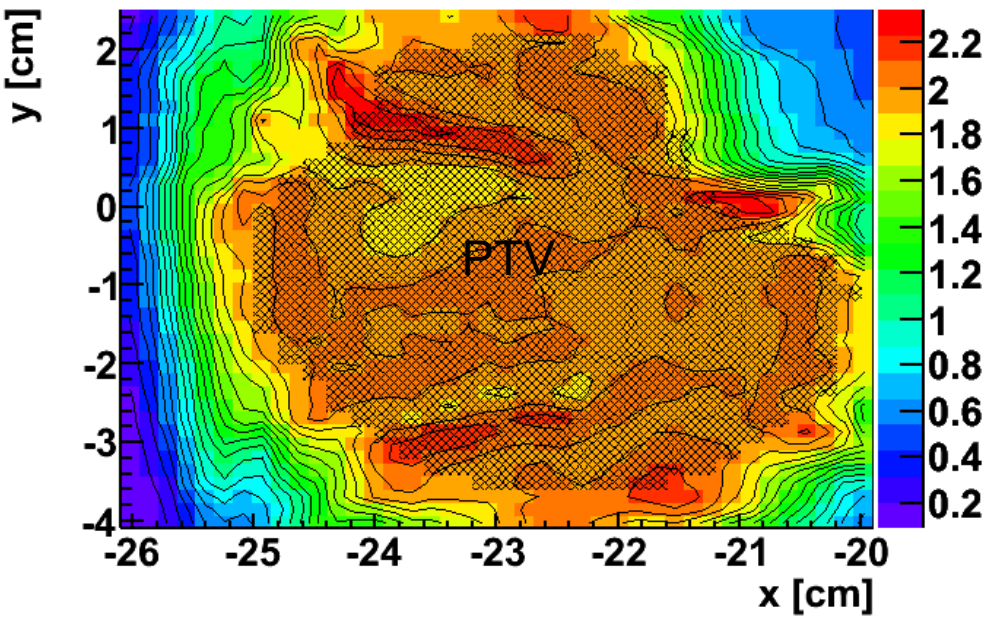


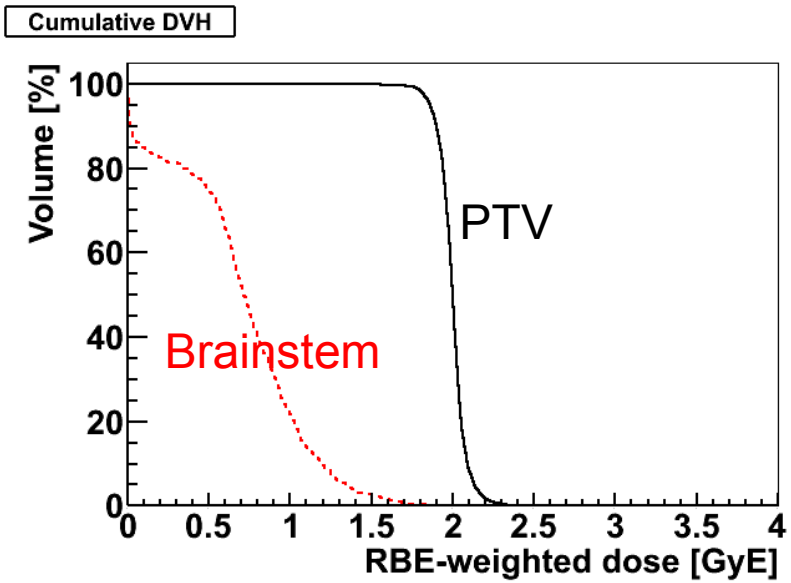
Framework used for HIT MC patient re-calculation (`FICTION') was also developed in the frame of a PARTNER project by Florian (Sommerer et al. 2012, Med Phys submitted)

Example plan: Brain tumour (CNAO)

2 field IMPT using RBE computed with LEM*

Preliminary results: Low statistics & test optimization

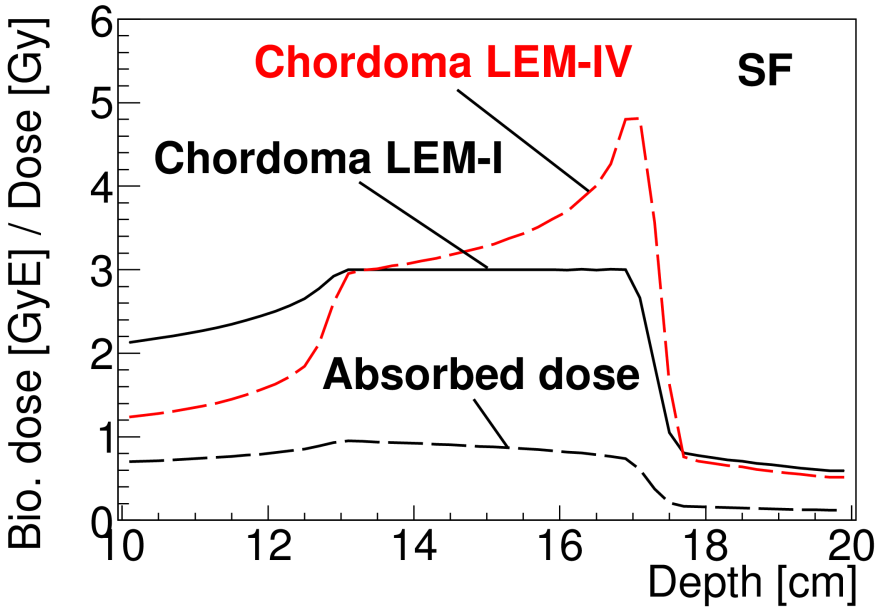




HSG

Biol. robustness of treatment plans: Systematics in RBE prediction

Evolution of LEM (version I → IV) revealed some systematics (Elsässer et al. 2008, 2010)



Also in future investigations might reveal systematics in estimations of biological doses ...

How does the optimization strategy influence biological robustness?

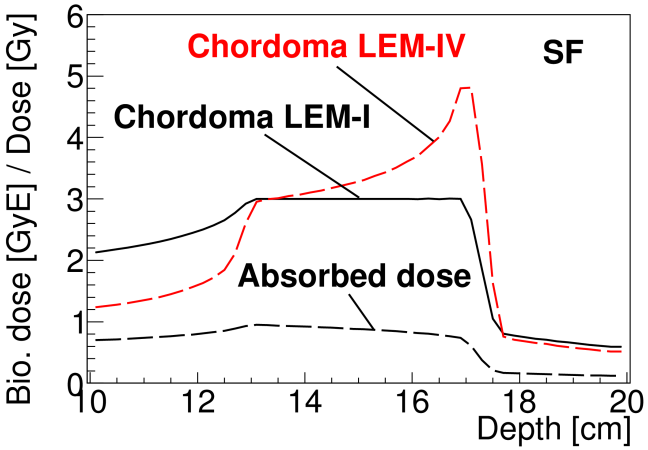
Opposed fields

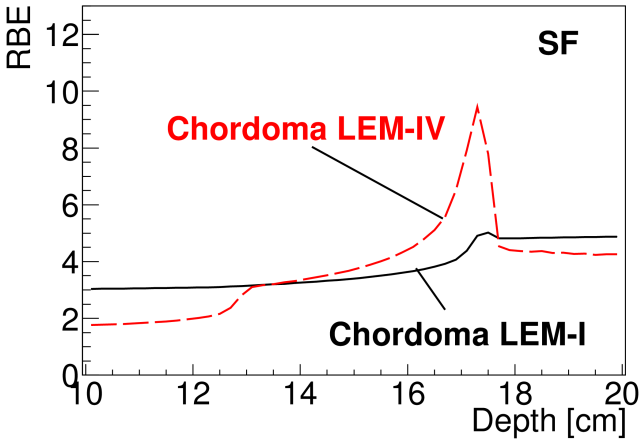
LEM-I → LEM-IV ...

Biol. dose

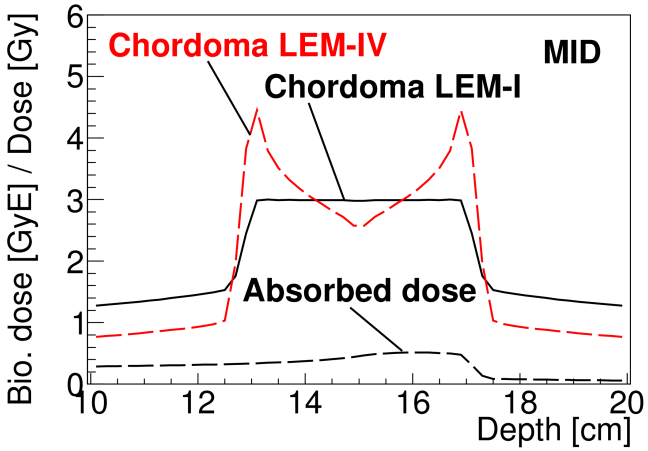
RBE

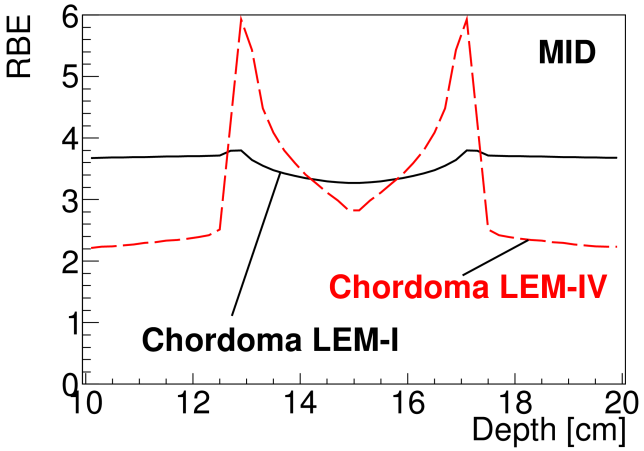
Single field





Opposed fields w. Minimum integral dose





Opposed fields

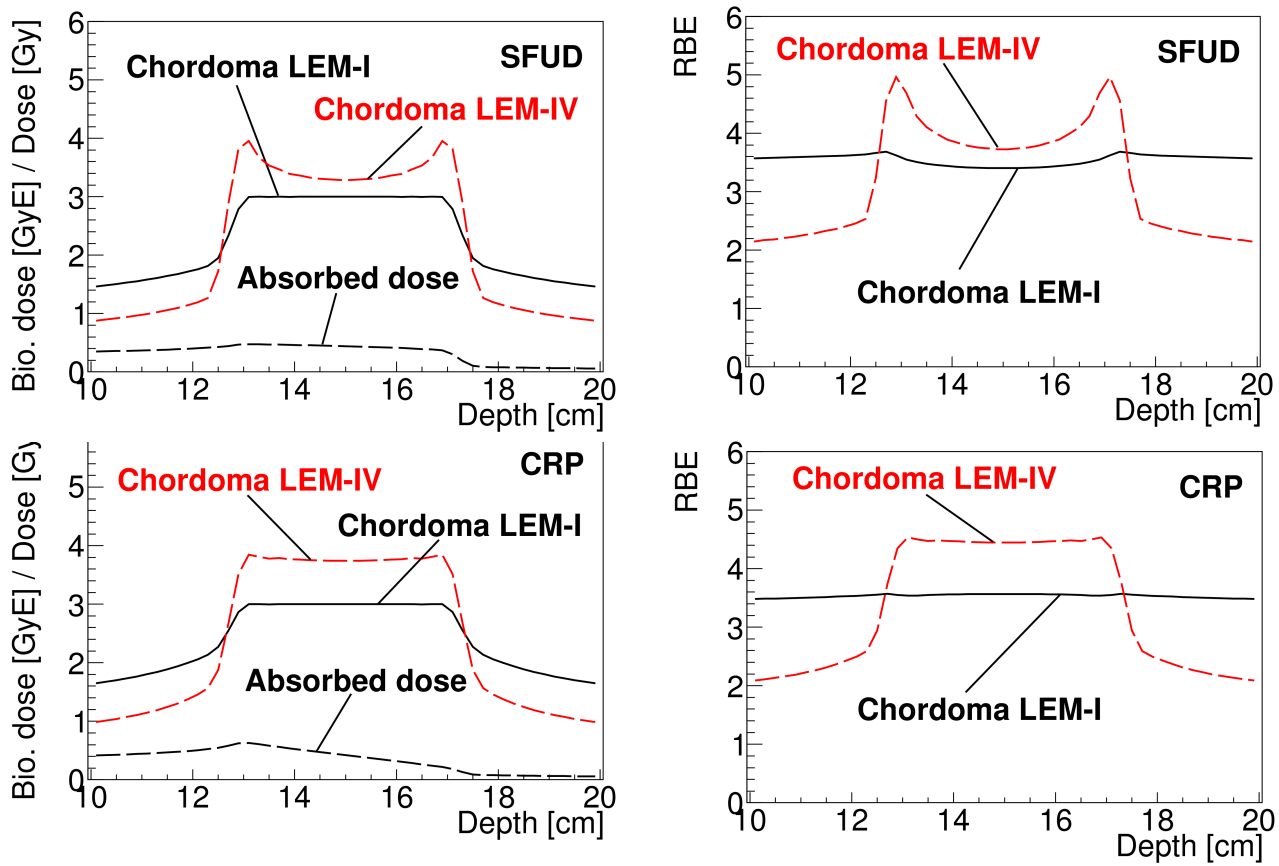
LEM-I → LEM-IV ...

Opposed fields w. Single-field uniform dose

Opposed fields w. Constant RBE in PTV

Biol. dose

RBE



… **reduced gradients** due to more uniform radiation quality!

Conclusions and Perspective

- Prototype of a **MC-based TP tool** established for **protons** and extended to **ions**
- **Physical and biological calculations/optimization** can be performed for **realistic patient treatment conditions with acceptable CPU time** (for research)
- Phantom-based simulations can be achieved for **dosimetric applications**
- **Large flexibility for research applications**
- Procedure to be revised: **simplified workflow** and **optimized regarding speed**

Many thanks to ...

fondazione CNAO

HIT Heidelberger Ionenstrahl-Therapiezentrum

… the Medical Physicist groups at CNAO and HIT ...

PARTNER Particle Training Network for European Radiotherapy

ENVISION

… PARTNER and ENVISION ...

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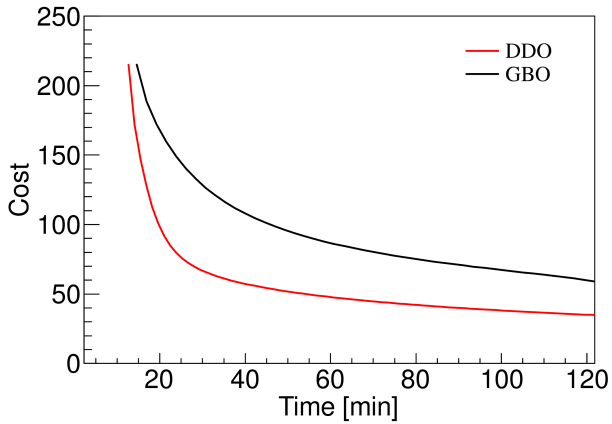
… and you!

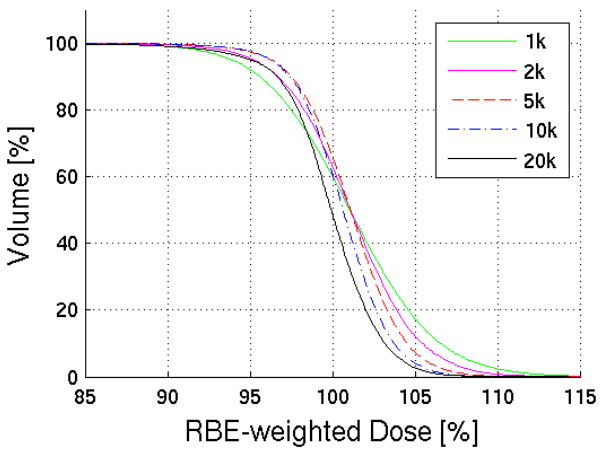
Add. slides

Example plan: Chordoma protons (CNAO)

Statistical study



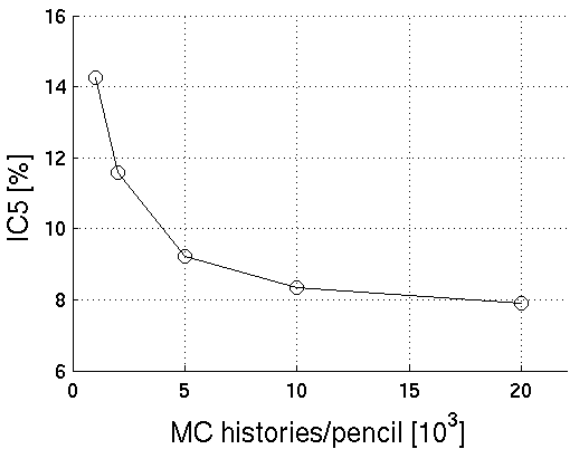
Small voxel size



DVH as function of the simulated MC histories per pencil beam.

Voxel sizes:
1x1x2mm3 (small, CT resolution)
2x2x2mm3 (large, as used by TPS)

Total number of pencil beams: 13920

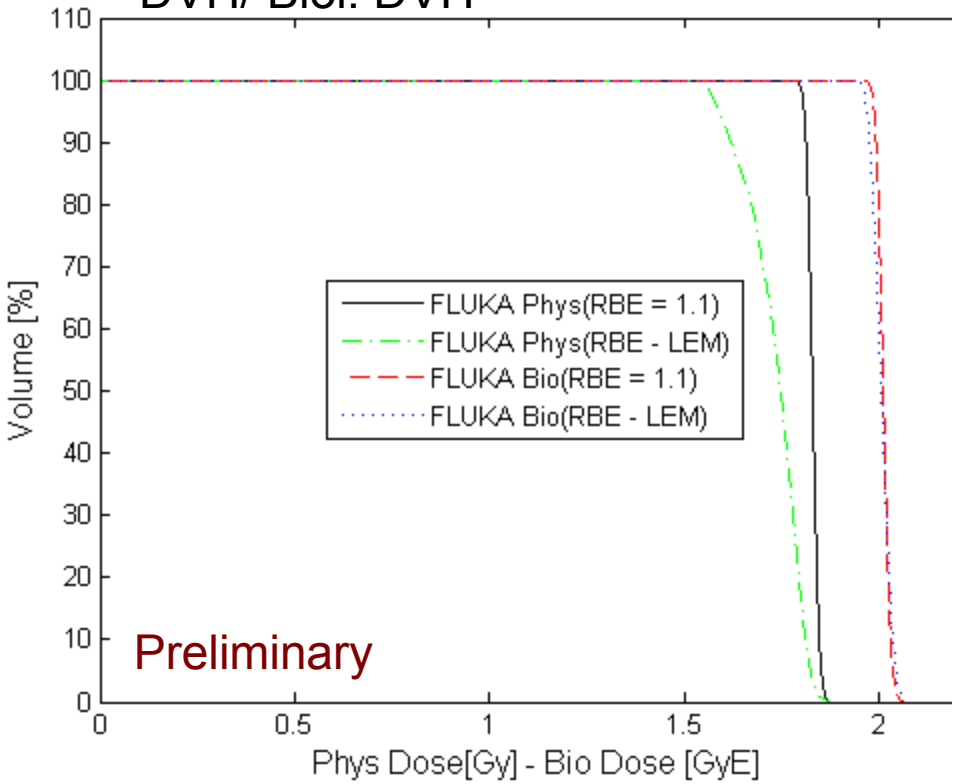


IC5 as a function of the simulated MC histories per pencil beam.

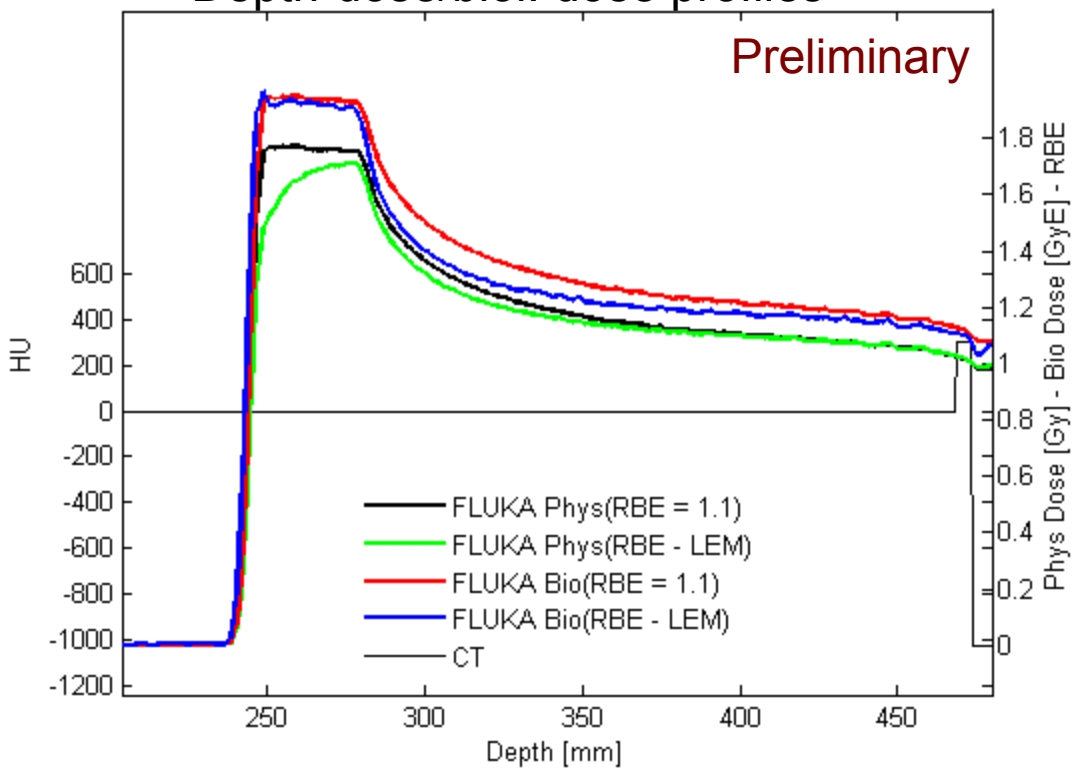
Range differences: constant vs. variable RBE

SOBP: RBE=1.1 vs RBE-LEM for V79

DVH/ Biol. DVH



Depth-dose/biol. dose profiles



Range comparison at 80% planned dose (2GyE)

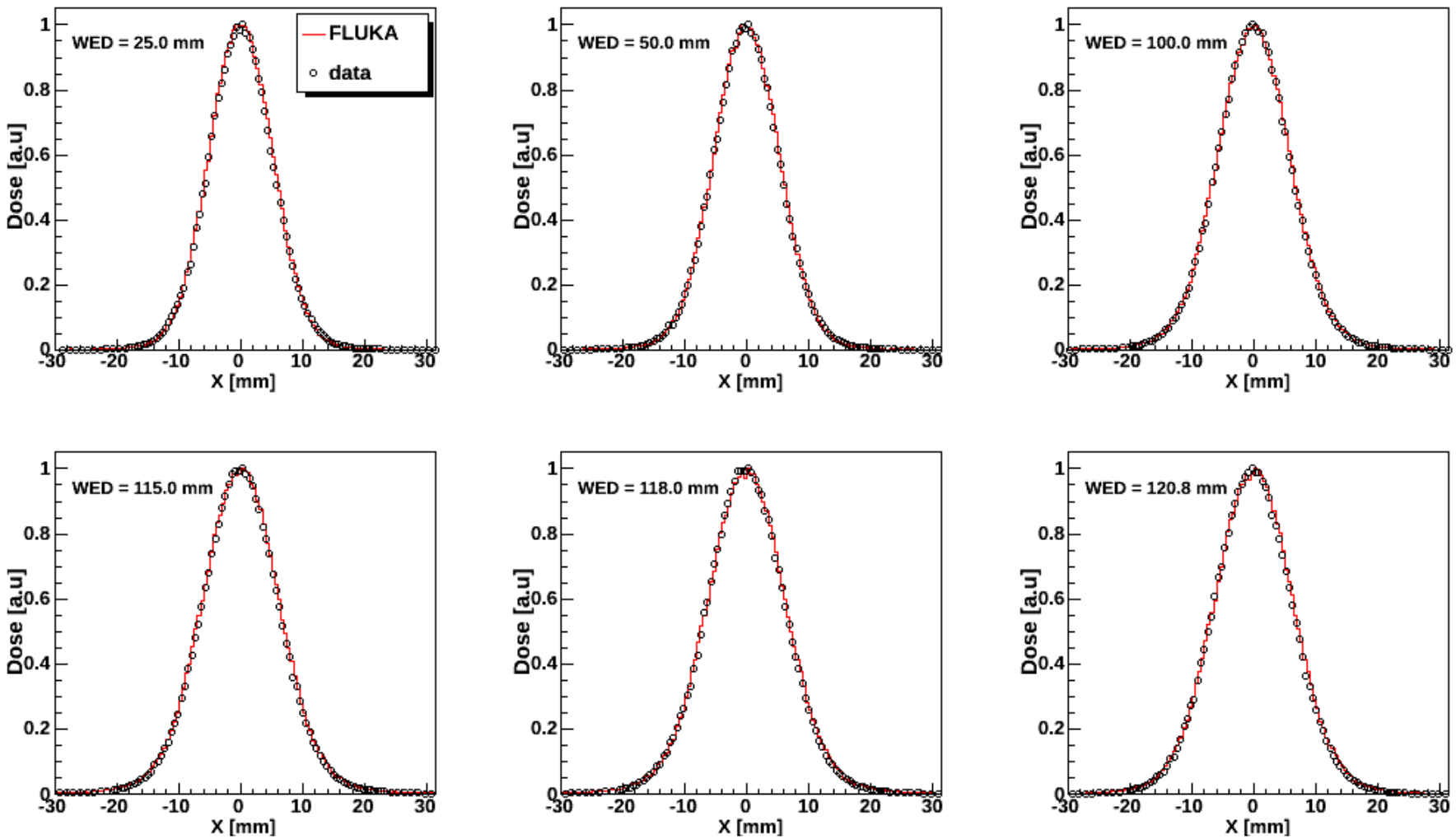
$$R_{80}^{RBE=1.1} - R_{80}^{RBE-LEM-forward} = -1.70mm$$

$$R_{80}^{RBE=1.1} - R_{80}^{RBE-LEM-optimized} = -0.94mm$$

see also Paganetti 2012, PMB

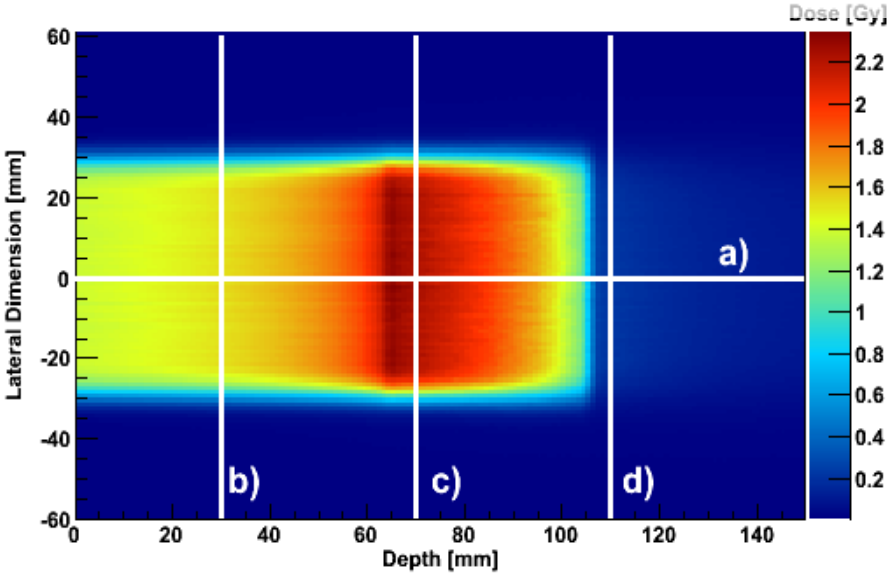
Physical Database II (CNAO)

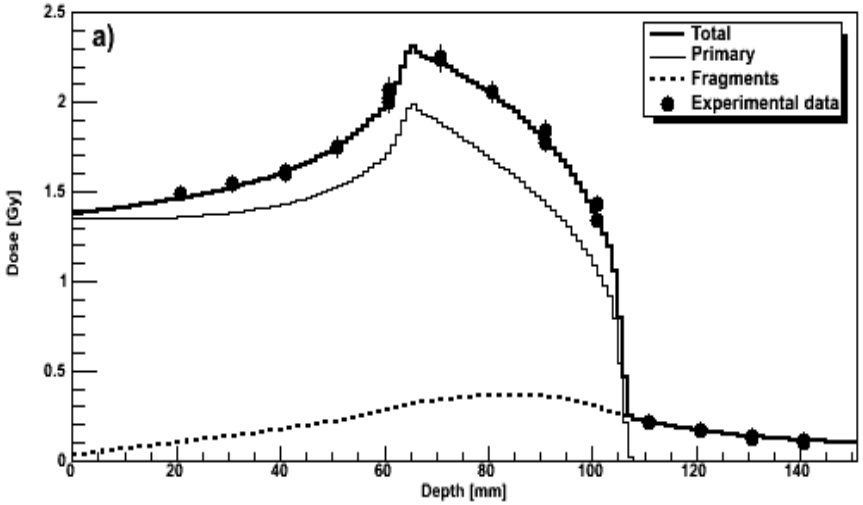
FLUKA-calculated lateral dose profiles at different Water Equivalent Depths (WED) for 130.57 MeV/u protons

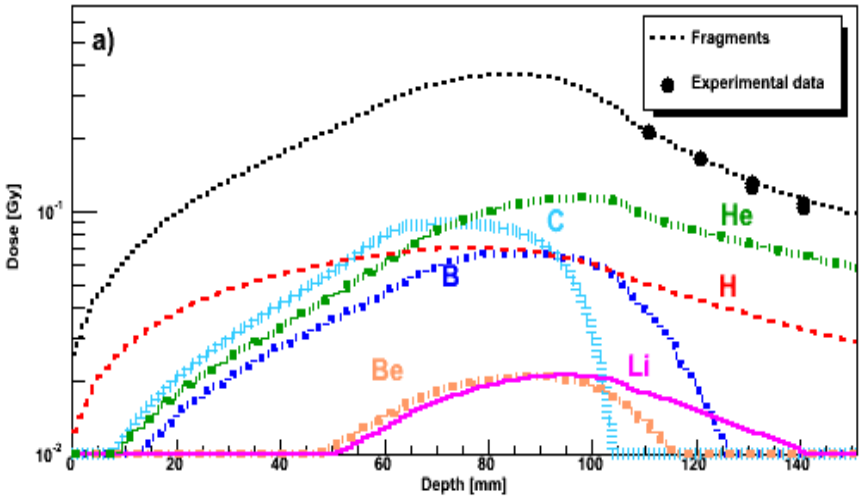


Both the experimental data and the MC results are renormalized to the maximum at each depth.

Characterizing a ^{12}C SOBP in water @ HIT I







- Max % difference MC(FLUKA)–DATA =1.5%
- At the depths of 3 cm and 7 cm the fragments contribution is 7% and 15% of the total dose.

Mairani et al, submitted to Med. Phys.

Coupling FLUKA with biological databases

Given a biological model as a input of the simulation (in terms of particle type, energy or LET)

Whenever an energy E is deposited in a target voxel by a certain radiation type, the biological response is evaluated on-line taking into account the biological database

According to the typical linear-quadratic dependence ($\varepsilon(D) = \alpha D + \beta D^2$) and the TDRA (Theory of Dual Radiation Action) the number of lesions in a Mixed Radiation Field can be expressed as

$$\epsilon(D_1, D_2, ..., D_n) = \sum_{i=1}^{n} \alpha_i D_i + (\sum_{i=1}^{n} \sqrt{\beta_i} D_i)^2$$

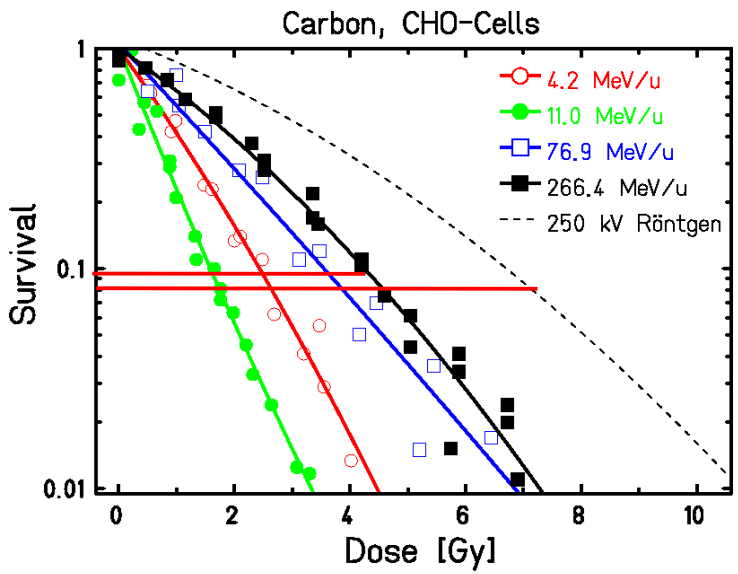
In FLUKA ("extended") the sums of D_i, $\alpha_i D_i$ and $\beta_i^{1/2} D_i$ can be scored during runtime in different arrays to allow final determination of the average parameters for a mixed field:

$$\overline{\alpha} = \frac{\sum_{i=1}^{n} \alpha_i D_i}{\sum_{i=1}^{n} D_i} ,$$

$$\overline{\beta} = (\frac{\sum_{i=1}^{n} \sqrt{\beta_i} D_i}{\sum_{i=1}^{n} D_i})^2 .$$

From K. Parodi

Relative Biological Effectiveness (RBE)

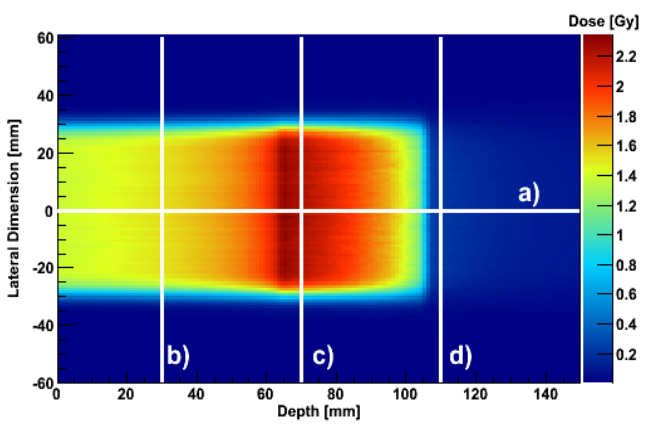


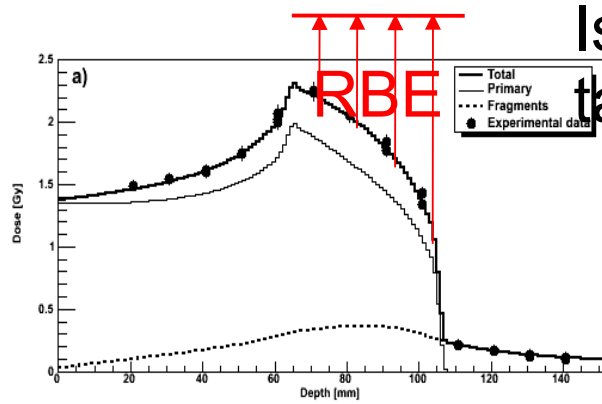
W. Kraft-Weyrather et al. Int. J. Radiat. Biol. 1999

Linear-Quadratic-Linear (LQL) model

$$S(D) = \begin{cases} \exp\left(-\alpha D - \beta D^2\right) & \text{for } D \le D_t \\ \exp\left(-\alpha D_t - \beta D_t^2 - (D - D_t) s_{max}\right) & \text{for } D > D_t \end{cases}$$

$$s_{max} = \alpha + 2\beta D_t.$$





Iso-effective dose (GyE) in target volume

= RBE x Dose

$$RBE^{IE} = \frac{D_{\gamma}^{IE}}{D_{ion}^{IE}}$$

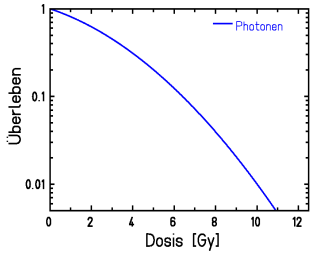
IE: isoeffect

RBE modelling

Local effect model (LEM)

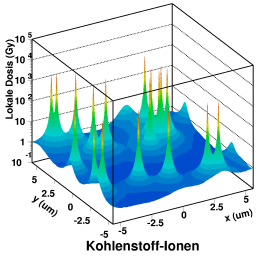
Basic assumption of LEM

Local Effect (Photons) = Local Effect (Ions)



M. Scholz et al. (GSI)

+



(for scanned carbon ions)

➡ RBE !

Large complexity:

Response dependencies physics:

- Dose
- Microscopic energy deposition patterns (LET)

Response dependencies biology:

- Tumour/tissue type
- Mutations
- Oxygenation / nutrition conditions
- Cell cycle effects
- …

The uncertainty of iso-effective dose for carbon ion treatments is estimated to be in the range of 20% (Krager and Jäkel 2007).

A HIT re-implementation of LEM-IV

Original LEM: M. Scholz and co-workers

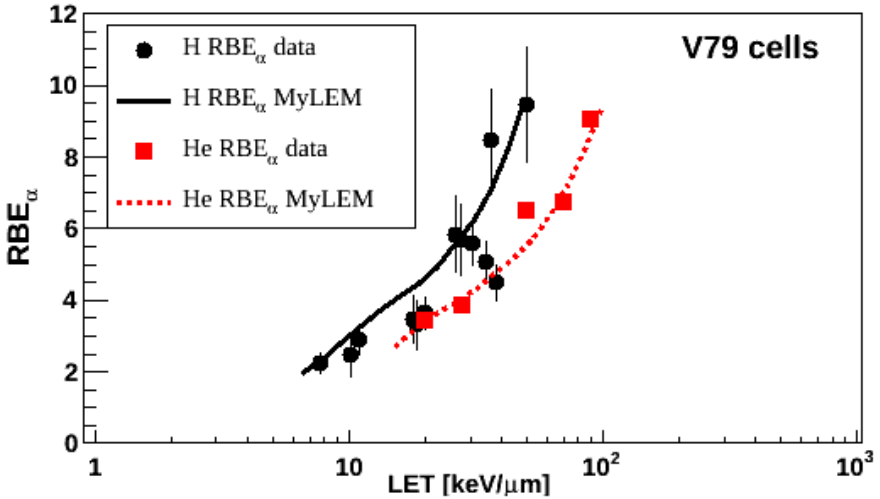
LEM-I: Scholz et al., Rad. Env. Biophys. 1997

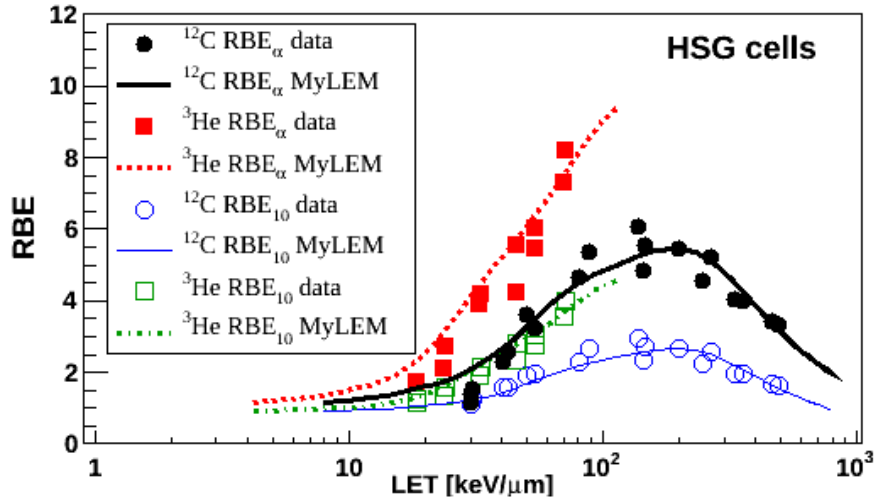
LEM-II (SSB + SSB -> DSB): Elsässer et al., Rad. Res. 2007

LEM-III (Improved Track Structure): Elsässer et al., IJROBP. 2008

LEM-IV (Effect derived from DSB(*x,y,z*): DSB + DSB -> complex DSB): Elsässer et al., IJROBP 2010

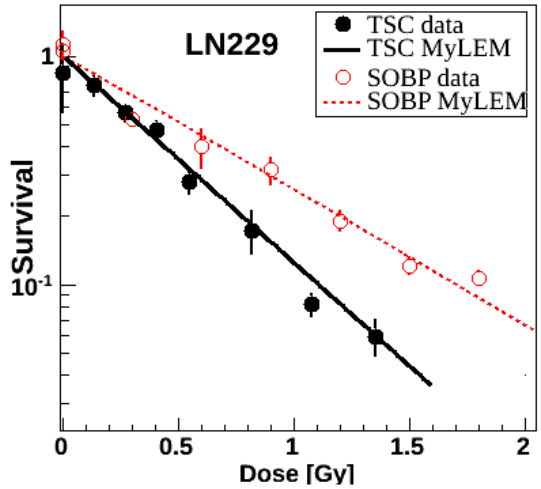
Example of benchmark of the re-implementation (Mairani et al.)

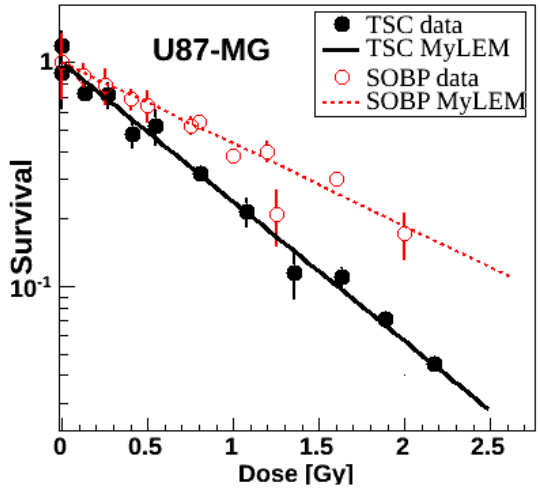




Exp Data: Belli et al.
Furusawa et al., Rad. Res. 2000

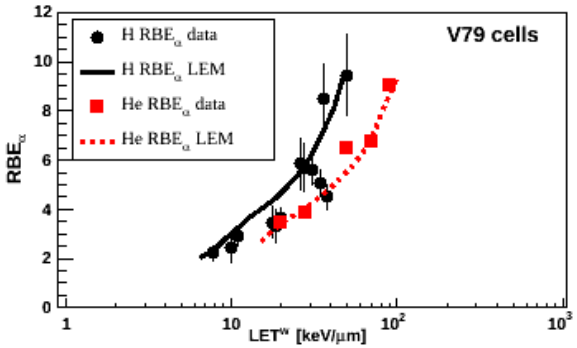
A HIT re-implementation of LEM-IV

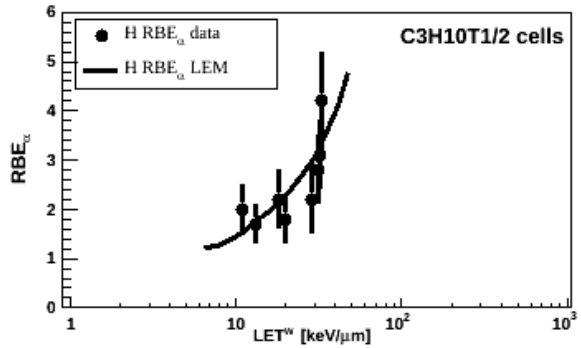




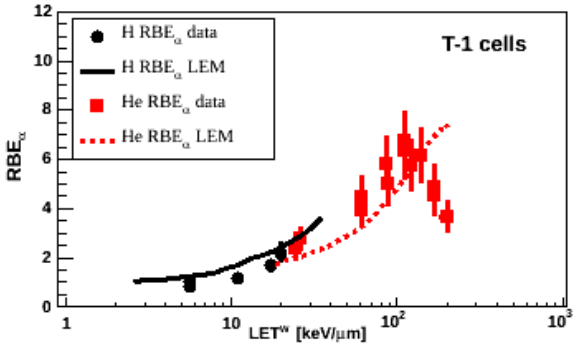
S.E. Combs et al. Int. Jour. Rad. Biol. 2009

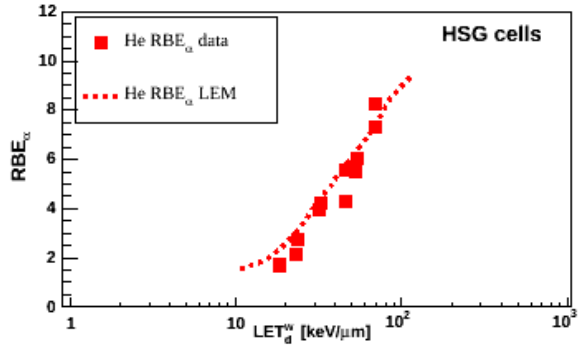
Glioblastoma cell lines, C-ions LET 103keV/μm, 172keV/μm (and X-ray)





Light ions

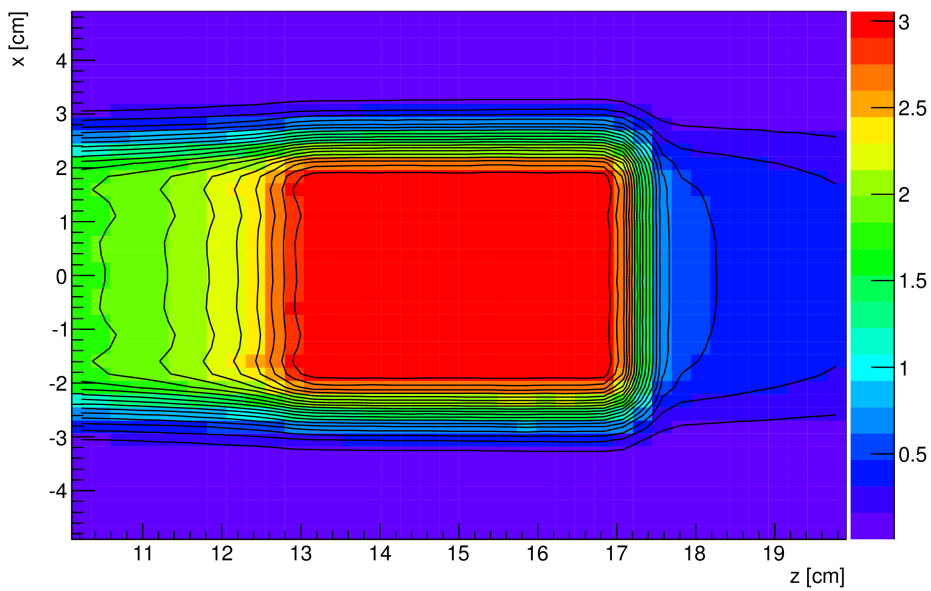


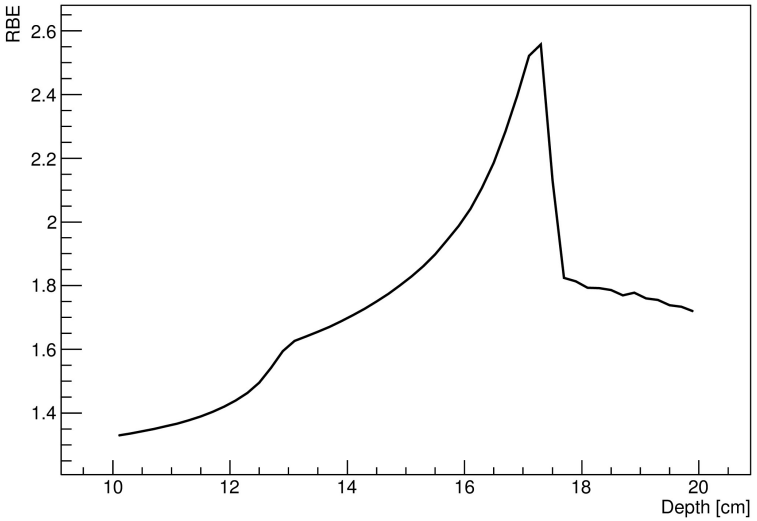


V79: Belli et al 1998, Folkard et al 1996 and Cox et al 1977; C3H10T1/2: Bettega et al 1998; T-1: Barendsen et al 1963 and Barendsen 1964; HSG: Furusawa et al 2000

Impact on treatment fields

Carbon ion treatment field in water optimized for nominal HSG parameters



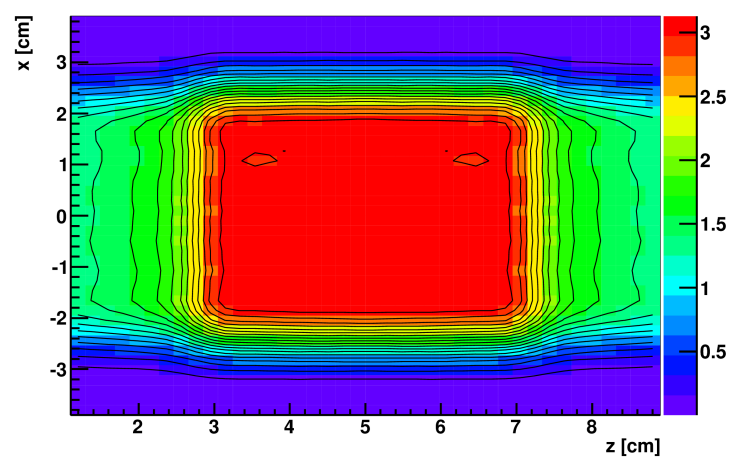


Single field, HSG, 3GyE, 64ml and 15cm depth

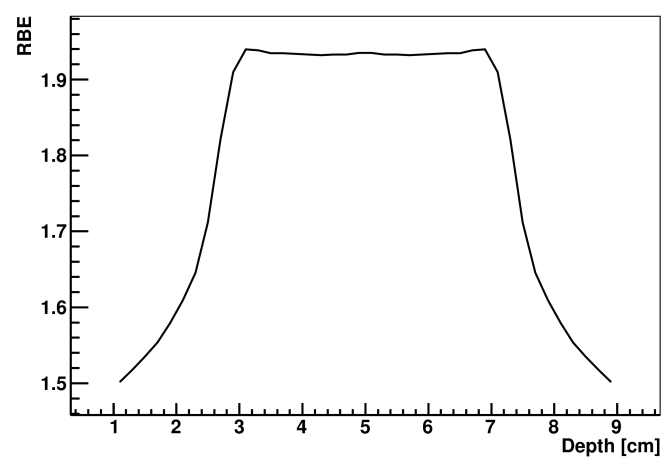
Treatment plans

Opposed beam geometry ...

Biol. dose

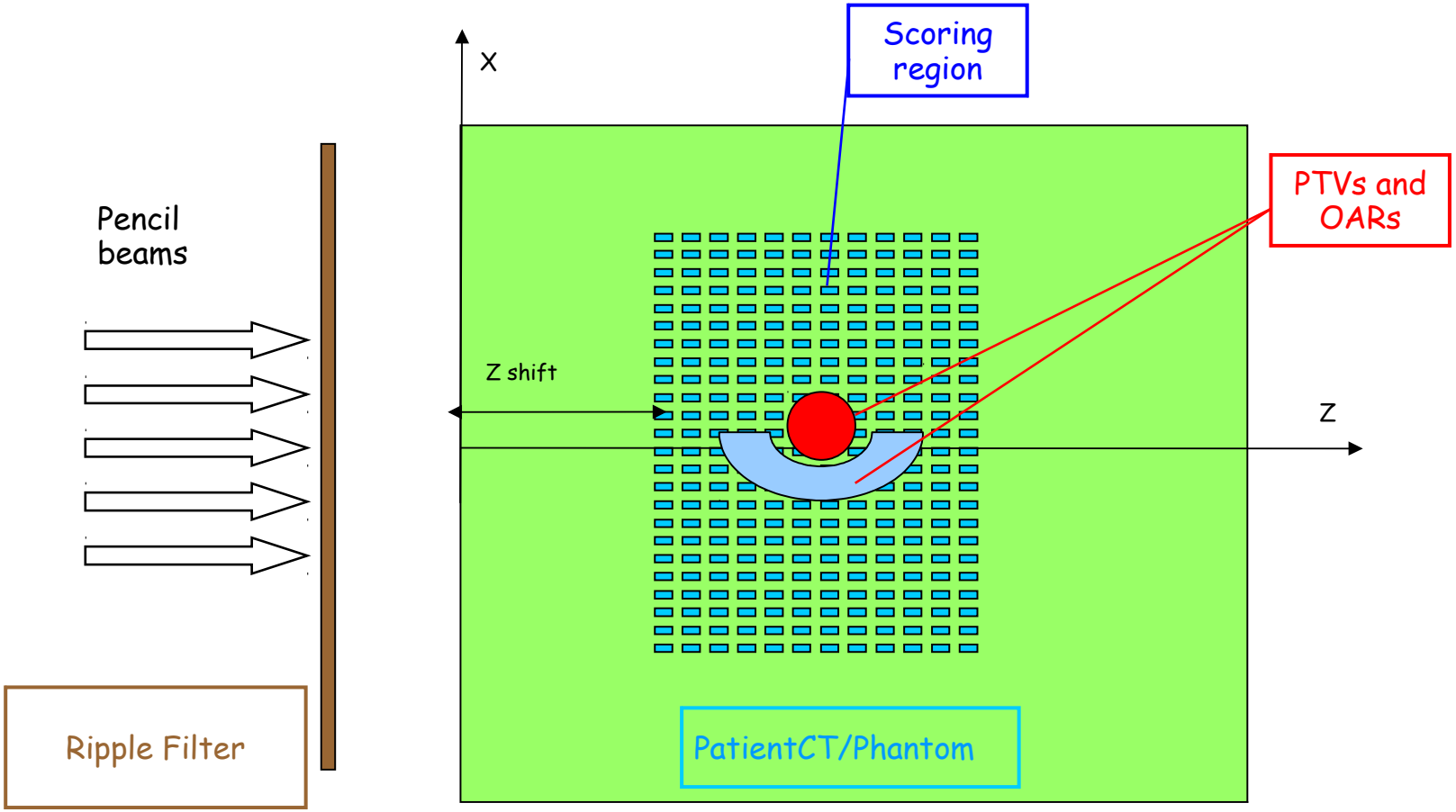


RBE



… using dual-criteria optimization:
Biol. dose **+ const. RBE in PTV**

MCTP simulation set-up



Typical dimensions:

Voxels = 2 x 2 x 2 mm^3

Scoring grid = 10x10x10 cm^3

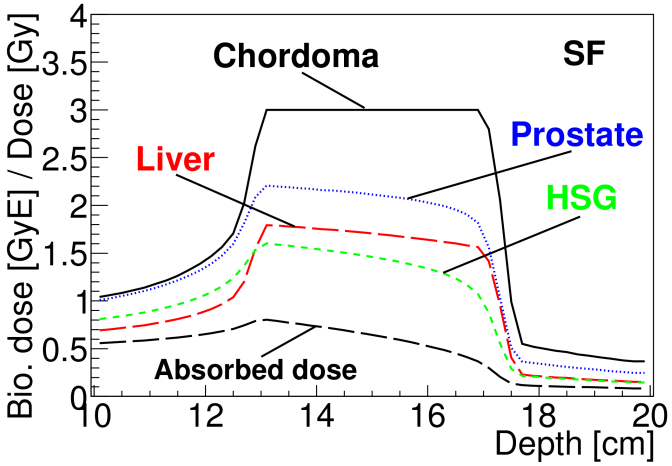
Opposed fields

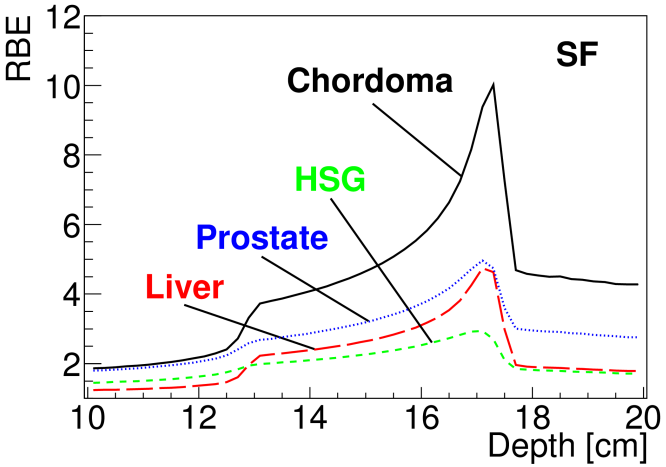
Chordoma → various tumours ...

Biol. dose

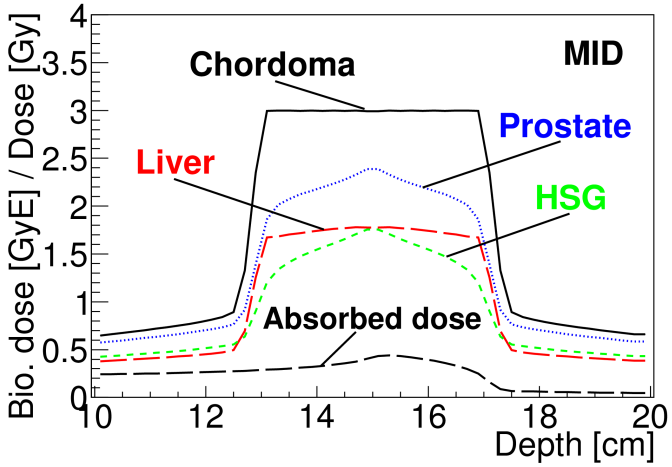
RBE

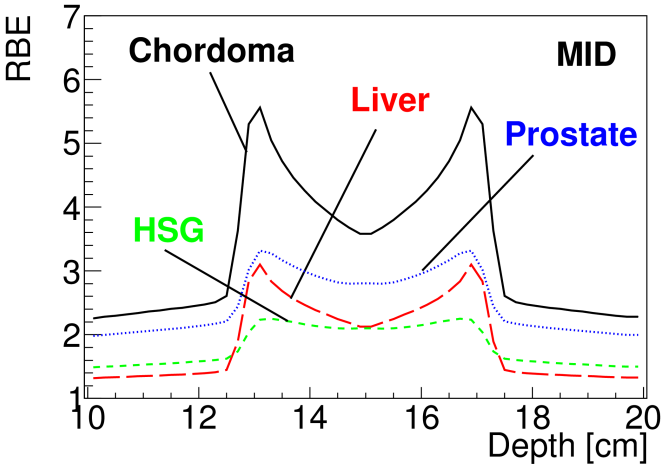
Single field





Opposed fields w. Minimum integral dose





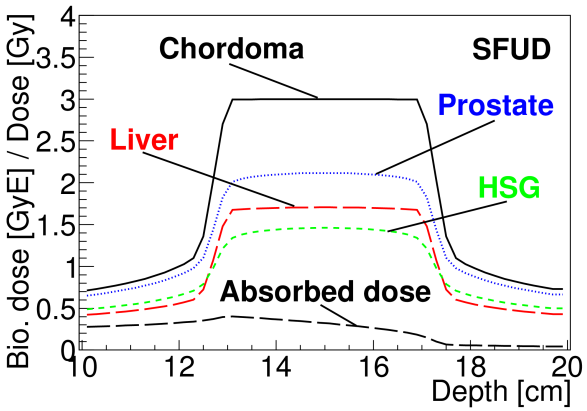
Opposed fields

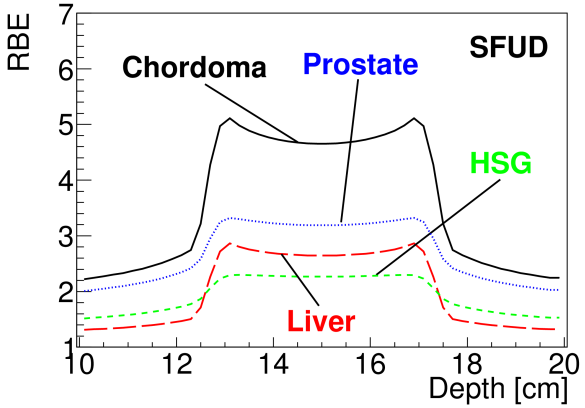
Chordoma → various tumours ...

Biol. dose

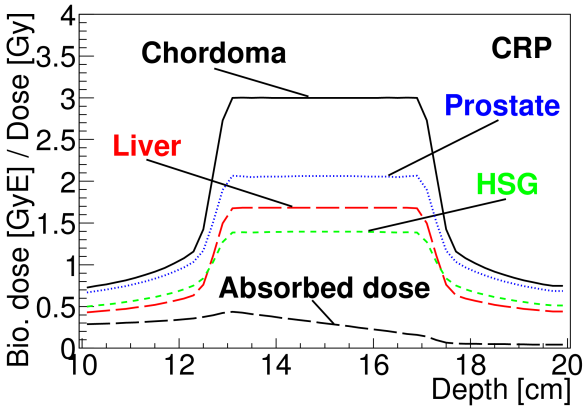
RBE

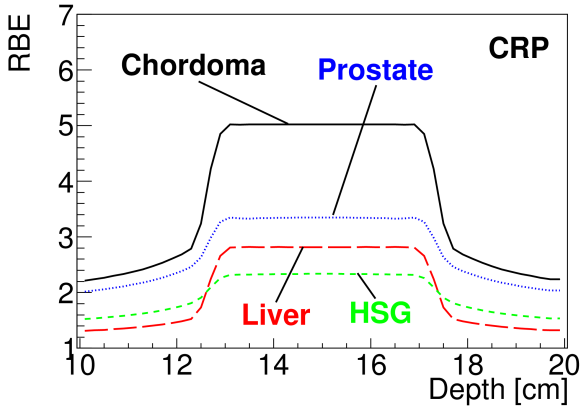
Opposed fields w. Single-field uniform dose





Opposed fields w. Constant RBE in PTV

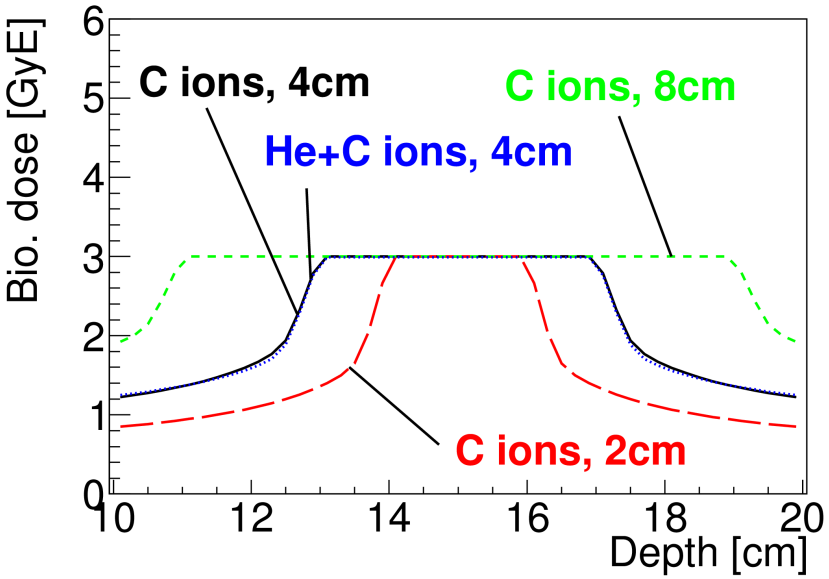


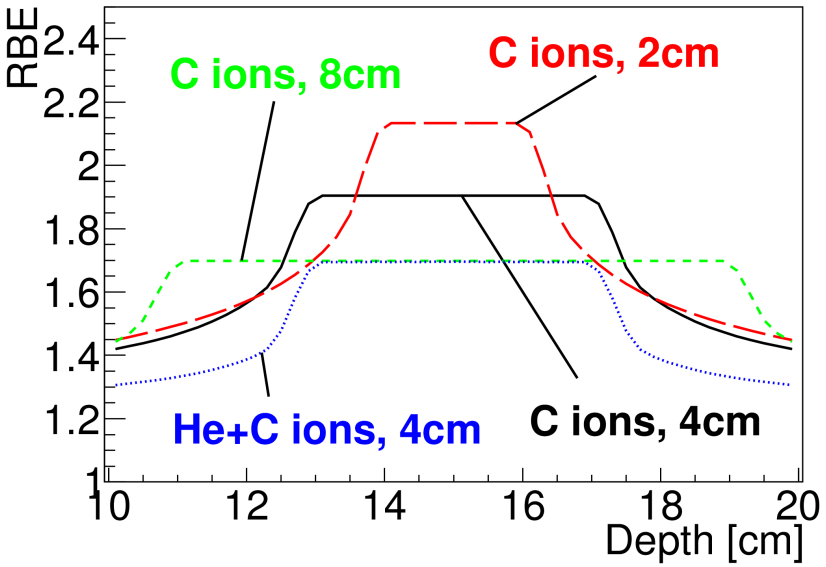


… **reduced gradients** due to more uniform radiation quality!

Dual ion fields

Example: He+C fields with const. RBE in PTV to have a constant radiation quality as a function of field size

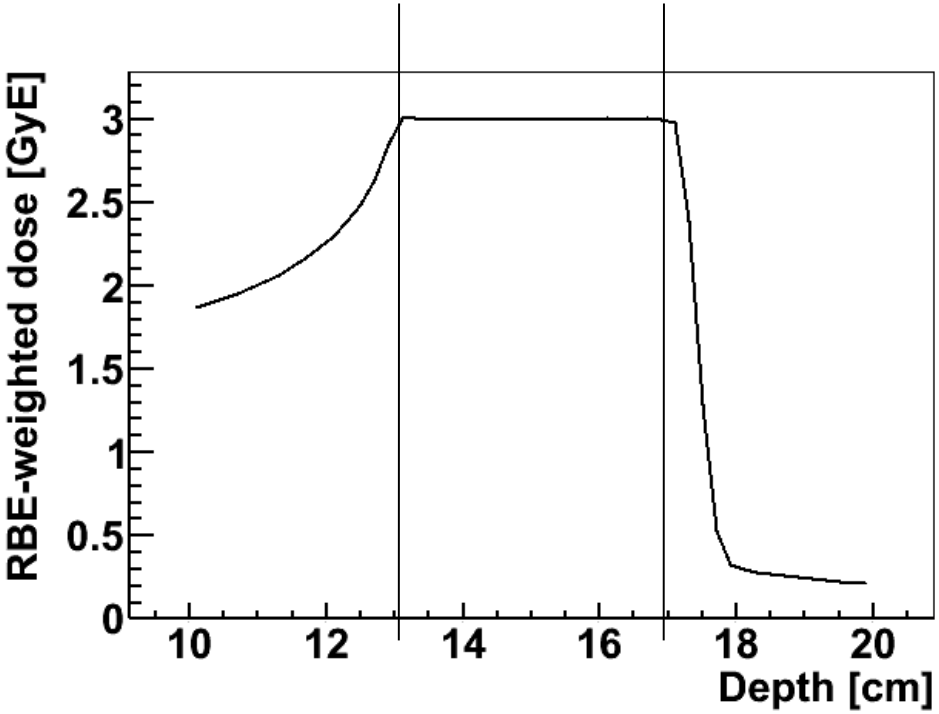


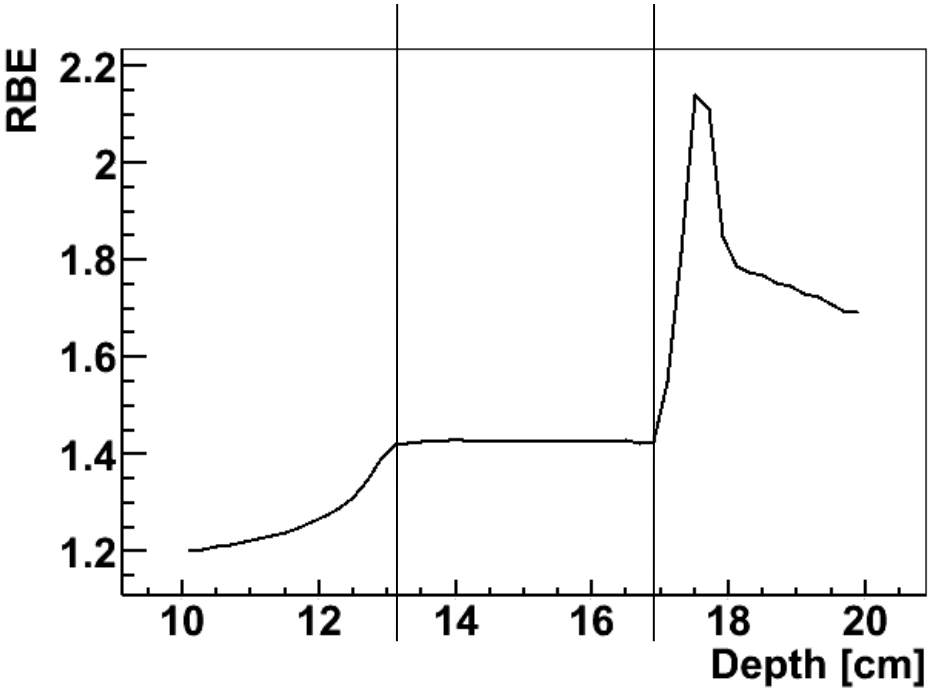


+ Reduces risk for possible relative misestimations as a function of field size (and also field depth)
– Dilutes (the probably advantageous) high-LET component of C ions.
+ However for treatments with higher-LET ions, such as oxygen, the mixture with lower-Z ions could additionally help to reduce the fragmentation tail.

Dual ion fields

Example: monodirectional H+C fields with const. RBE in PTV (HSG)





- Allows to optimize for **wanted radiation quality** (based on RBE, LET, lineal energy, …?)
  - Independently of field size and depth
- Also usable for orthogonal and patched field geometries
- **Similarity to** "**LET painting**"-approach → region with uniform rad. quality