Monte Carlo Dose Calculations

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HITRI plus
Heavy Ion Therapy Research Integration

NCT
NATIONAL CENTER
FOR TUMOR DISEASES
HEIDELBERG

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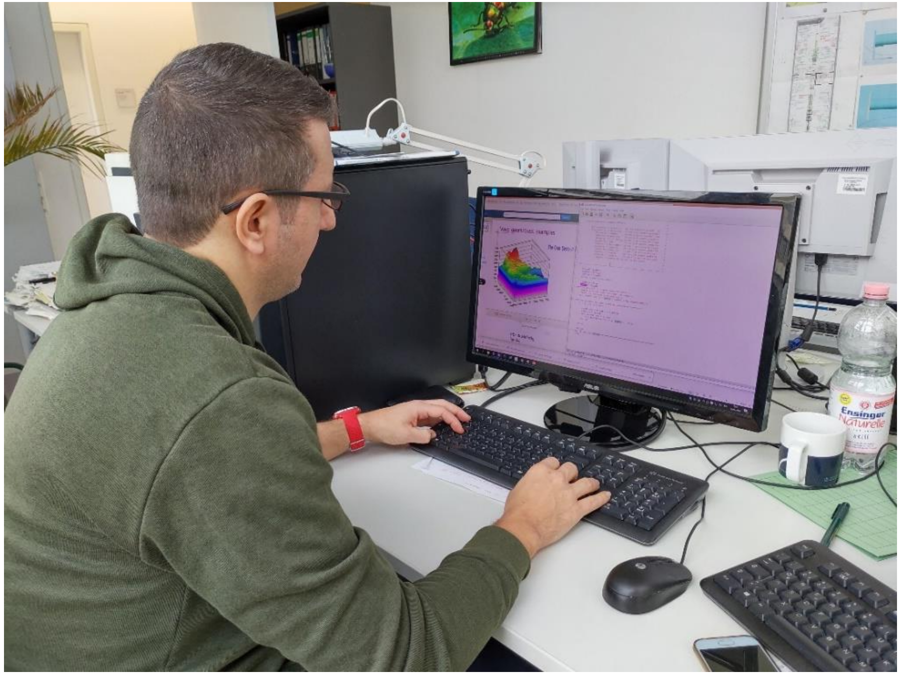
German Cancer Research Center (DKFZ)
Heidelberg University Medical Center
Hospital for Thoracic Diseases
German Cancer Aid

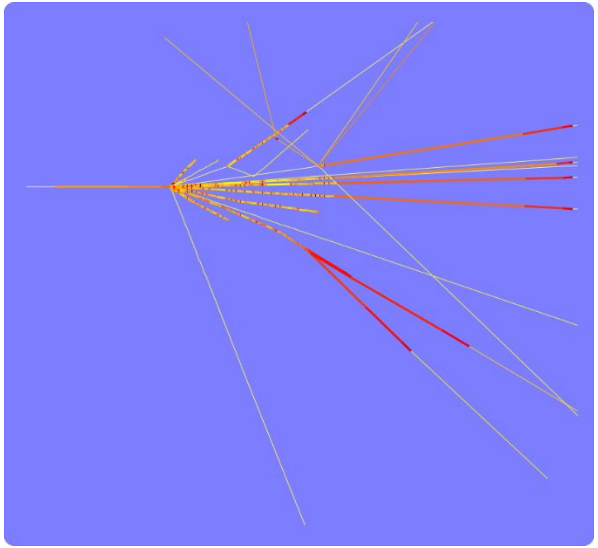
The Common Perception of Monte Carlo

The Concept of Monte Carlo for Me and



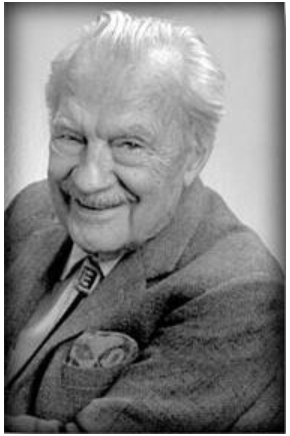
Maybe You After This Talk….

200 MeV/u ^{12}C ions shower



The Monte Carlo 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

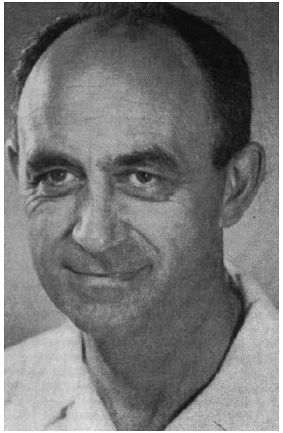
N. Metropolis

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

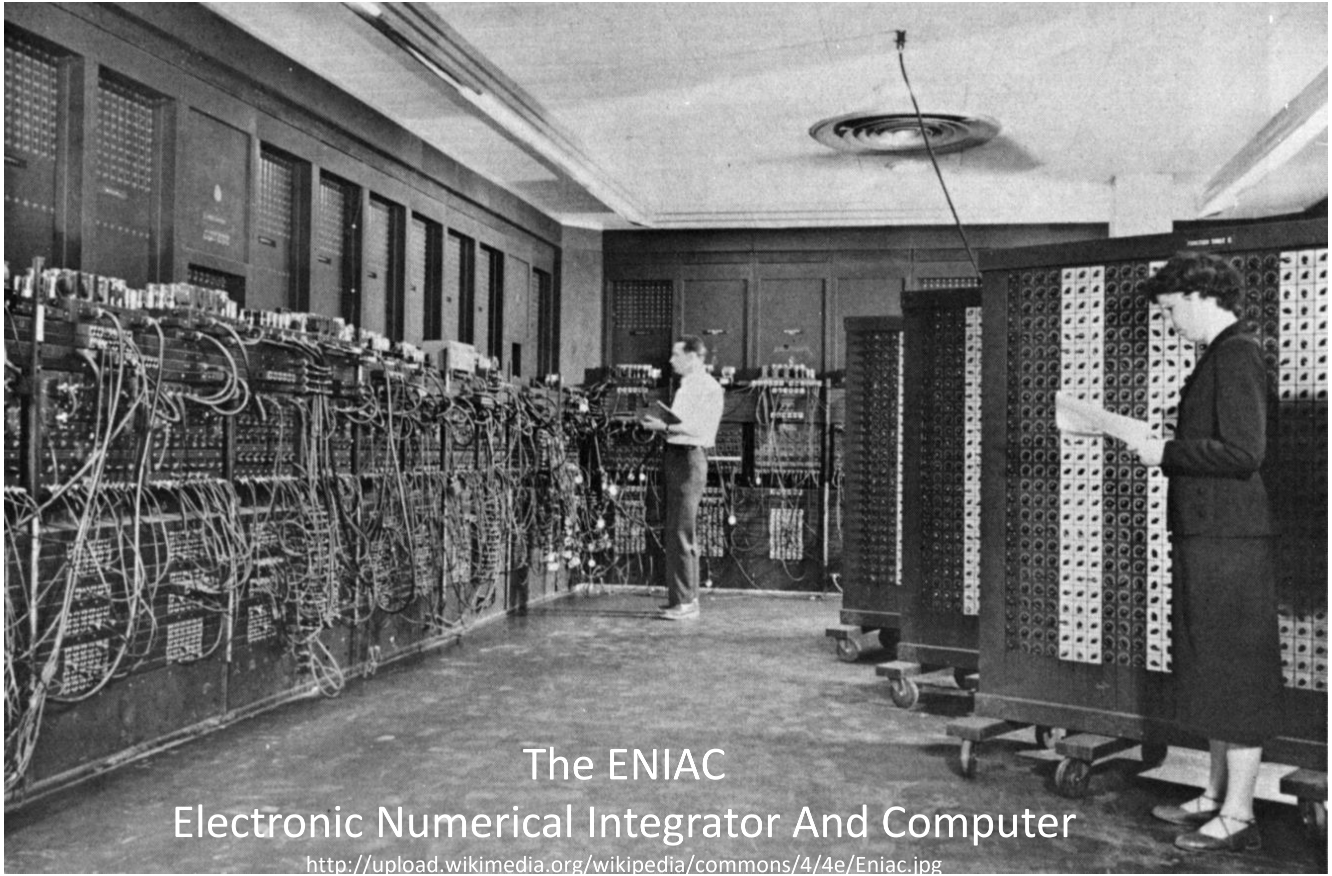
J. von Neumann



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

E. Fermi

Not your laptop size….



The ENIAC

Electronic Numerical Integrator And Computer

http://upload.wikimedia.org/wikipedia/commons/4/4e/Eniac.jpg

Integration? or Simulation ?

Why, then, is MC often considered a simulation technique?

Originally, the Monte Carlo method was not a simulation method, but a device to solve a multidimensional integro-differential equation by building a stochastic process such that some parameters of the resulting distributions would satisfy that equation

The equation itself did not necessarily refer to a physical process, and if it did, that process was not necessarily stochastic

Simulation: in special cases

- It was soon realized, however, that when the method was applied to an equation describing a physical stochastic process, such as neutron diffusion, the model (in this case a random walk) could be identified with the process itself
- In these cases the method (analog Monte Carlo) has become known as a simulation technique, since every step of the model corresponds to an identical step in the simulated process

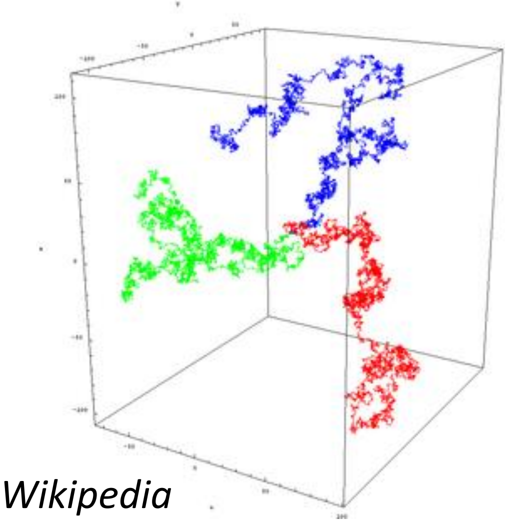


Image from Wikipedia

Particle Transport

- Particle transport is a typical physical process described by probabilities (cross sections = interaction probabilities per unit distance)

- Therefore it lends itself naturally to be simulated by Monte Carlo

- Many applications, especially in high energy physics and medicine, are *based on simulations* where the history of each particle (trajectory, interactions) is reproduced in detail

- However in other types of application, typically shielding design, the user is interested only in the expectation values of some quantities (fluence and dose) at some space point or region, which are *calculated as solutions of a mathematical equation*

- This equation (the Boltzmann equation), describes the statistical distribution of particles in phase space and therefore does indeed represent a physical stochastic process

- But in order to estimate the desired expectation values it is not necessary that the Monte Carlo process be identical to it

Integration Without Simulation

- In many cases, it is more efficient to replace the actual process by a different one resulting in the same average values but built by sampling from modified distributions

- Such a *biased process*, if based on mathematically correct variance reduction techniques, converges to the same expectation values as the unbiased one

- But it cannot provide information about the higher moments of statistical distributions (fluctuations and correlations)

- In addition, the faster convergence in some user-privileged regions of phase space is compensated by a slower convergence elsewhere

Particle Transport Monte Carlo

Application of Monte Carlo to particle transport and interaction:

- Each particle is followed on its path through matter
- At each step the occurrence and outcome of interactions are decided by random selection from the appropriate probability distributions
- All the secondaries issued from the same primary are stored in a “stack” or “bank” and are transported before a new history is started
- The accuracy and reliability of a Monte Carlo depend on the models or data on which the probability distribution functions are based
- Statistical precision of results depends on the number of “histories“
- Statistical convergence can be accelerated by “biasing" techniques

Assumptions made by most Monte Carlo codes

- Static, homogeneous, isotropic, amorphous media and geometry *<u>Problems</u>: e.g. moving targets*, atmosphere must be represented by discrete layers of uniform density, radioactive decay may take place in a geometry different from that in which the radionuclides were produced*.*

  **These restrictions have been overcome in few Monte Carlo codes*

- Markovian process: the fate of a particle depends only on its actual present properties, not on previous events or histories

- Particles do not interact with each other

  <u>Problem</u>: e.g. the Chudakov effect (charges cancelling in e^+e^- pairs)

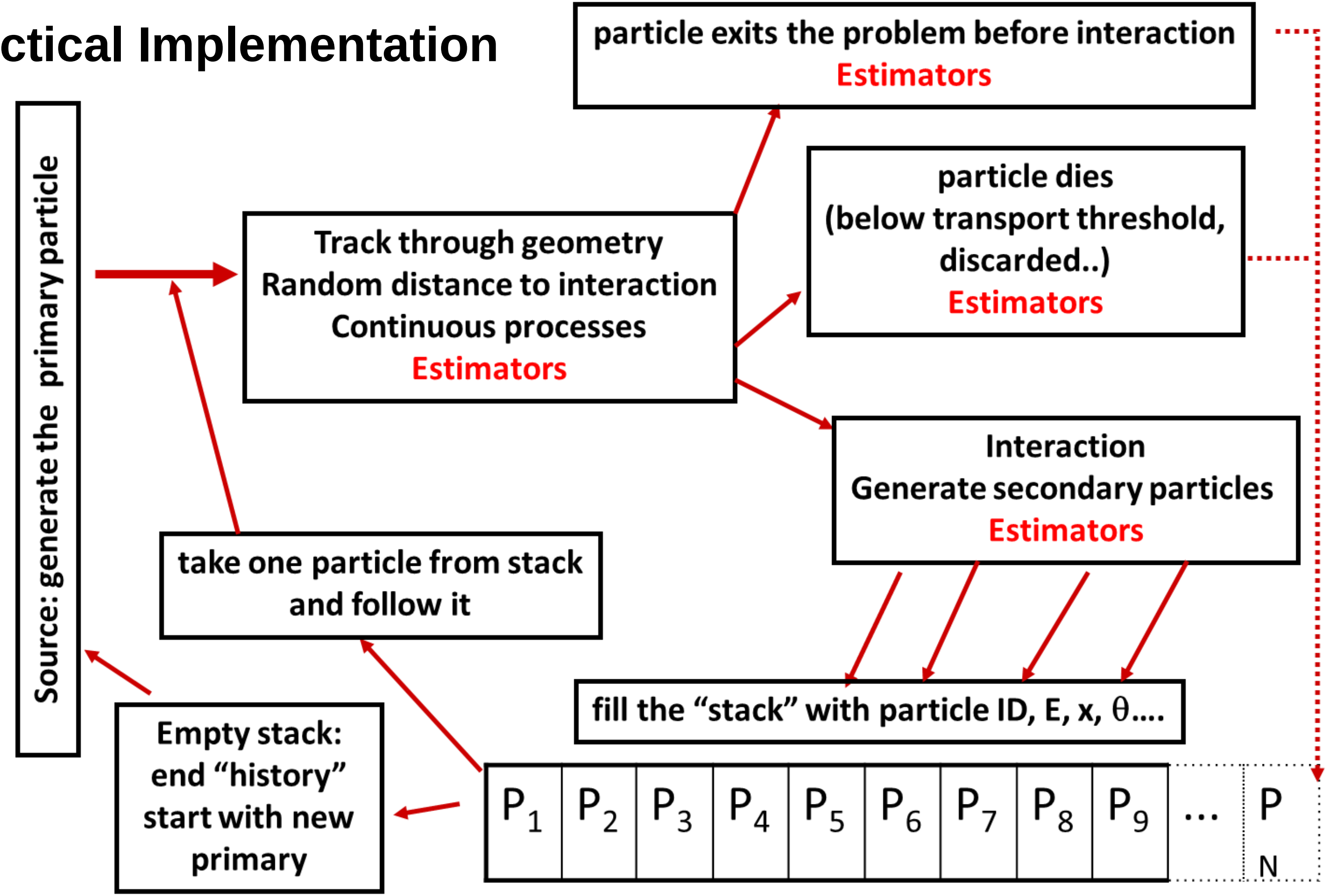
- Particles interact with individual electrons / atoms / nuclei / molecules

  <u>Problem</u>: invalid at low energies (X-ray mirrors)

- Material properties are not affected by particle reactions

  <u>Problem</u>: e.g. burnup

Practical Implementation



Source: generate the primary particle

Track through geometry
Random distance to interaction
Continuous processes
Estimators

particle exits the problem before interaction
Estimators

particle dies
(below transport threshold,
discarded..)
Estimators

Interaction
Generate secondary particles
Estimators

fill the "stack" with particle ID, E, x, θ....

P_1	P_2	P_3	P_4	P_5	P_6	P_7	P_8	P_9	…	P_N

take one particle from stack
and follow it

Empty stack:
end "history"
start with new
primary

Statistical errors, systematic errors, and...mistakes

Systematic errors, due to code weaknesses

- Apart from the statistical error, which other factors affect the accuracy of MC results?
  - ❑ **physics**: different codes are based on different physics models. Some models are better than others. Some models are better in a certain energy range. Model quality is best shown by benchmarks at the microscopic level (e.g. thin targets)

  - ❑ **artifacts**: due to imperfect algorithms, e.g., energy deposited in the middle of a step, inaccurate path length correction for multiple scattering, missing correction for cross section and *dE/dx* change over a step, etc. Algorithm quality is best shown by benchmarks at the macroscopic level (thick targets, complex geometries)

  - ❑ **data uncertainty**: an error of 10% in the absorption cross section can lead to an error of a factor 2.8 in the effectiveness of a thick shielding wall (10 attenuation lengths). Results can never be better than allowed by available experimental data!

Statistical errors, systematic errors, and...mistakes

Systematic errors, due to user ignorance

- Missing information:
  - material composition not always well known. In particular concrete/soil composition (how much water content? Can be critical)
  - beam losses: most of the time these can only be guessed. Close interaction with engineers and designers is needed
  - presence of additional material, not well defined (cables, supports...)
  - Is it worth to do a very detailed simulation when some parameters are unknown or badly known?

Systematic errors, due to simplification

- Geometries that cannot be reproduced exactly (or would require too much effort)
- Air contains humidity and pollutants, has a density variable with pressure

Statistical errors, systematic errors, and...mistakes

Code mistakes (“bugs”)

- MC codes can contain bugs:
  - Physics bugs
  - Programming bugs

User mistakes

- mis-typing the input
- error in user code: use the built-in features as much as possible!
- wrong units
- wrong normalization: quite common
- unfair biasing: energy/space cuts cannot be avoided, but must be done with much care

Monte Carlo Codes for Dose Calculation

- **General purposes (GPMC)**:

  FLUKA, GEANT4, MCNP, TOPAS, PHITS, ….

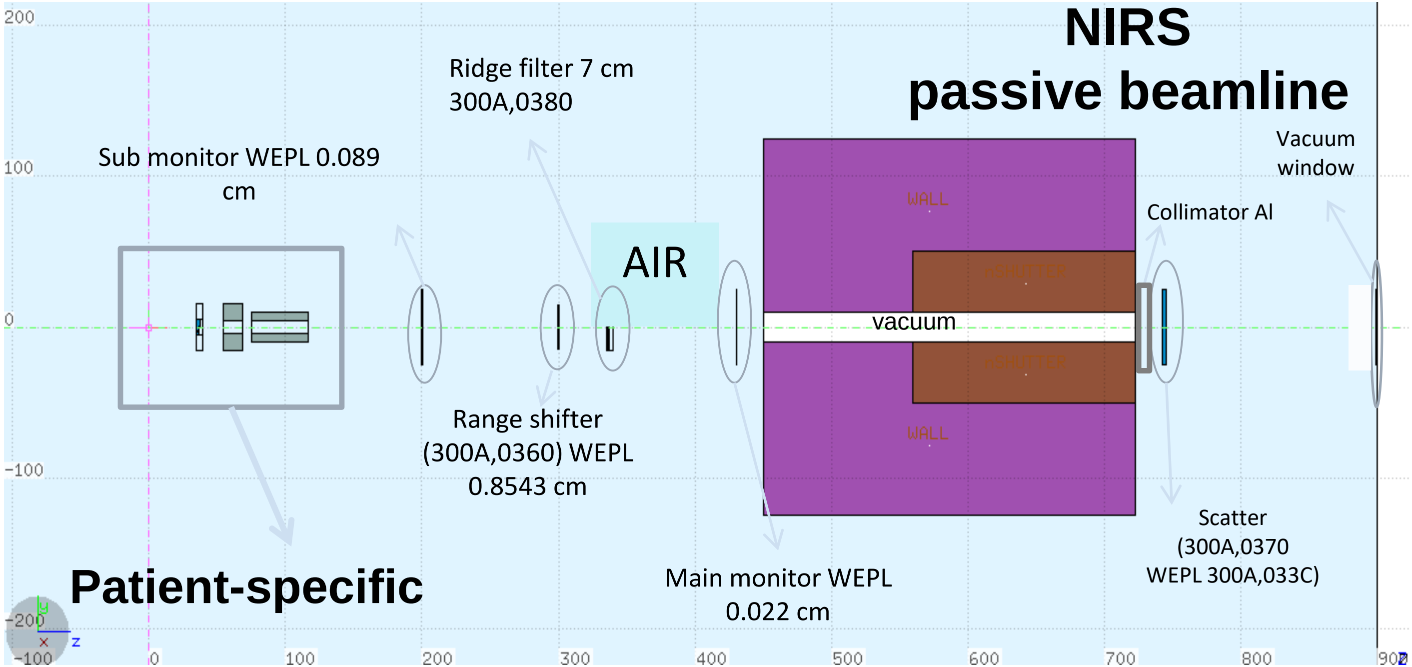
- **Tailored for medical applications:**

  RayStation MC, gPMC, FRED, MonteRay, …

- **Why Monte Carlo for this task?**
  1. Better description of the physical processes
  2. Flexibility
  3. -> Gold Standard (GPMC) where data are not available

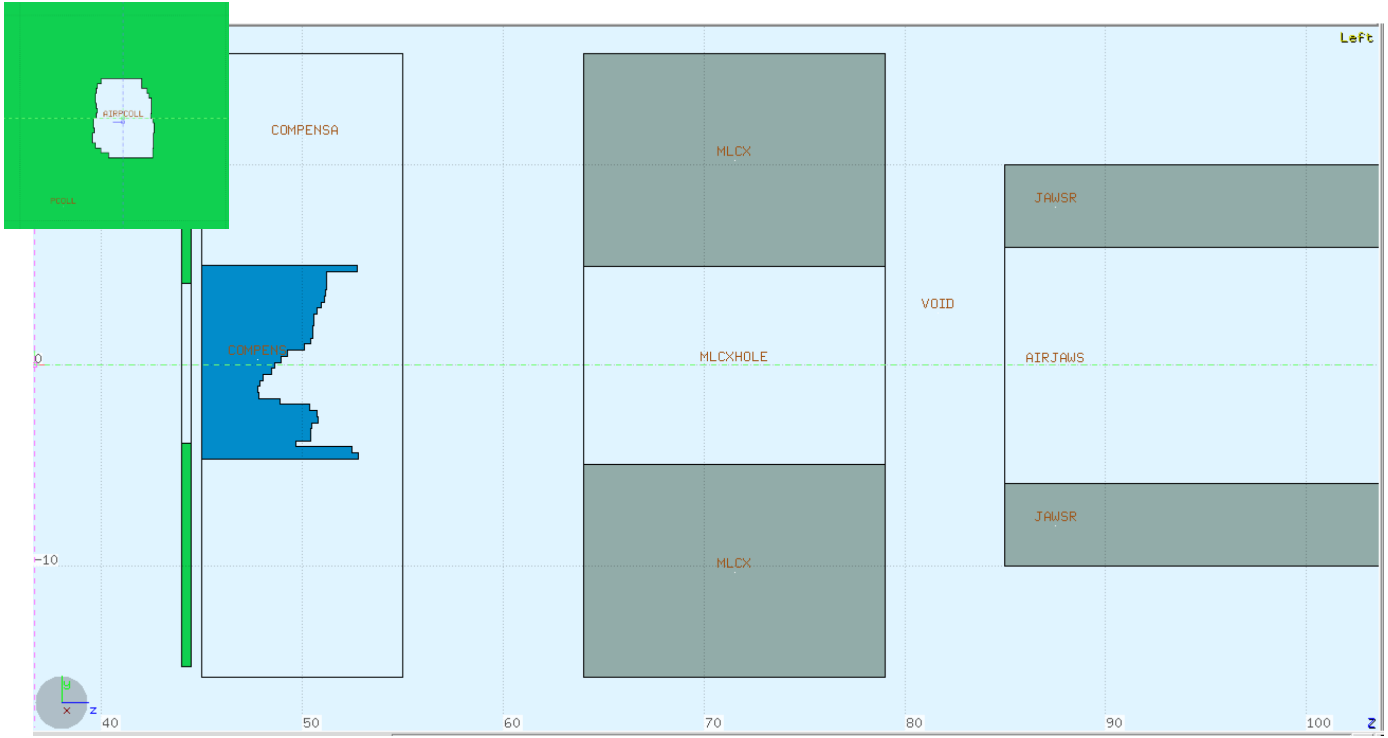
Geometry

- **Beamline: full geometry or phase space ?**



Geometry

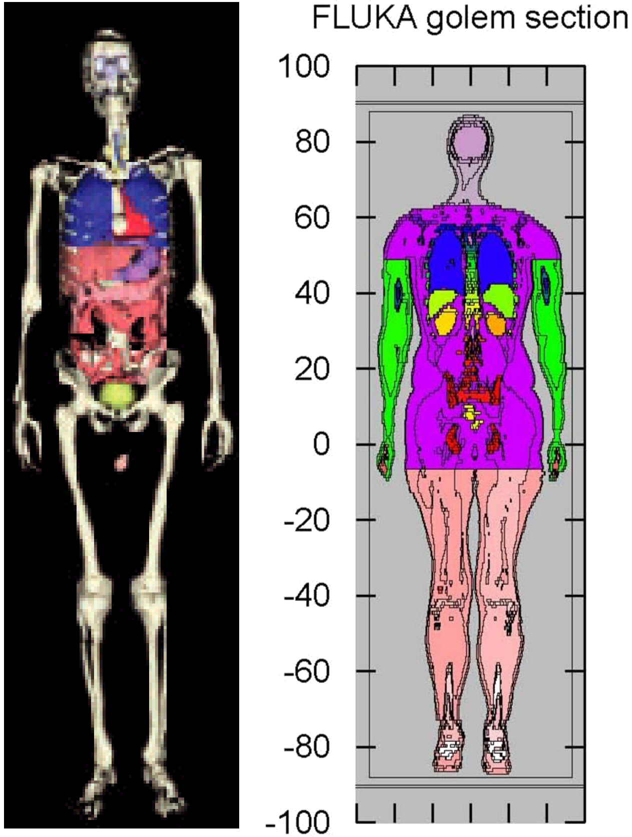
- **Patient-specific components**



Geometry

- **Patient CT/ Phantom**

Petoussi-Henss et al, 2002



Materials for the Monte Carlo physical processes

General problems for MC calculations on CT scans

- How to assign realistic human tissue parameters (= materials) for MC Calculation ?

- How to find a good compromise between the number of different HU values (~ 3000-5000) and the materials to be considered in the MC ?

  (issues on memory and computation speed when attempting to treat each HU number as a different material !!!)

- How to preserve continuous, HU-dependent information when segmenting the HU numbers into intervals sharing the same “tissue” material ?

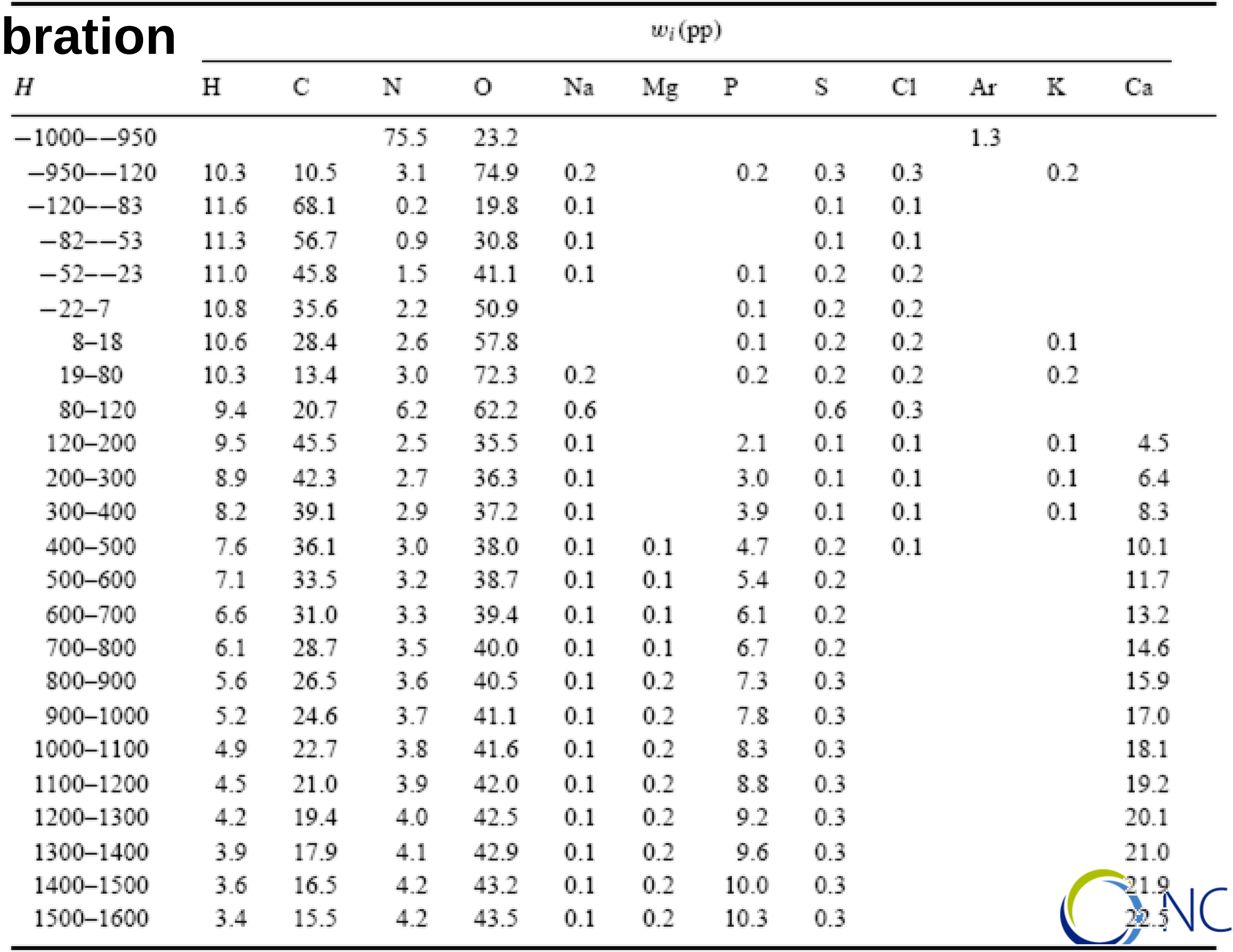
  (critical for ion range calculation in charged hadron therapy !!!)

CT stoichiometric calibration

Air, Lung, Adipose tissue

Soft tissue

Skeletal tissue

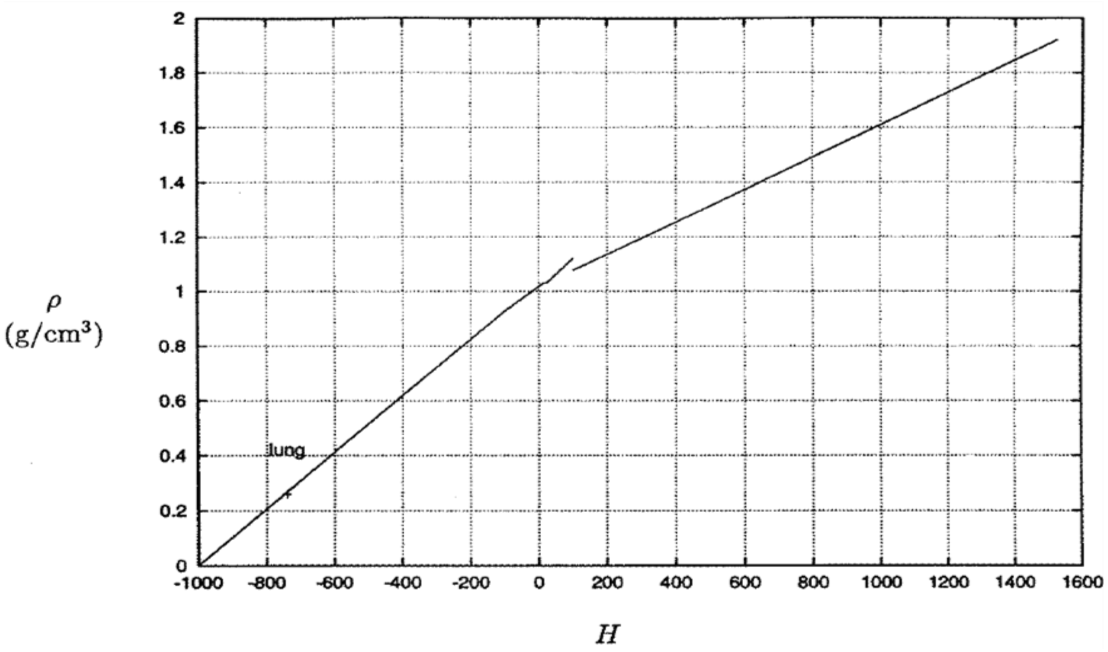


	w_i (pp)											
H	H	C	N	O	Na	Mg	P	S	Cl	Ar	K	Ca
−1000–−950			75.5	23.2						1.3		
−950–−120	10.3	10.5	3.1	74.9	0.2		0.2	0.3	0.3		0.2	
−120–−83	11.6	68.1	0.2	19.8	0.1			0.1	0.1			
−82–−53	11.3	56.7	0.9	30.8	0.1			0.1	0.1			
−52–−23	11.0	45.8	1.5	41.1	0.1		0.1	0.2	0.2			
−22–7	10.8	35.6	2.2	50.9			0.1	0.2	0.2			
8–18	10.6	28.4	2.6	57.8			0.1	0.2	0.2		0.1	
19–80	10.3	13.4	3.0	72.3	0.2		0.2	0.2	0.2		0.2	
80–120	9.4	20.7	6.2	62.2	0.6			0.6	0.3			
120–200	9.5	45.5	2.5	35.5	0.1		2.1	0.1	0.1		0.1	4.5
200–300	8.9	42.3	2.7	36.3	0.1		3.0	0.1	0.1		0.1	6.4
300–400	8.2	39.1	2.9	37.2	0.1		3.9	0.1	0.1		0.1	8.3
400–500	7.6	36.1	3.0	38.0	0.1	0.1	4.7	0.2	0.1			10.1
500–600	7.1	33.5	3.2	38.7	0.1	0.1	5.4	0.2				11.7
600–700	6.6	31.0	3.3	39.4	0.1	0.1	6.1	0.2				13.2
700–800	6.1	28.7	3.5	40.0	0.1	0.1	6.7	0.2				14.6
800–900	5.6	26.5	3.6	40.5	0.1	0.2	7.3	0.3				15.9
900–1000	5.2	24.6	3.7	41.1	0.1	0.2	7.8	0.3				17.0
1000–1100	4.9	22.7	3.8	41.6	0.1	0.2	8.3	0.3				18.1
1100–1200	4.5	21.0	3.9	42.0	0.1	0.2	8.8	0.3				19.2
1200–1300	4.2	19.4	4.0	42.5	0.1	0.2	9.2	0.3				20.1
1300–1400	3.9	17.9	4.1	42.9	0.1	0.2	9.6	0.3				21.0
1400–1500	3.6	16.5	4.2	43.2	0.1	0.2	10.0	0.3				21.9
1500–1600	3.4	15.5	4.2	43.5	0.1	0.2	10.3	0.3				22.5

Schneider et al PMB 45, 2000

CT stoichiometric calibration

Assign to each material a "nominal mean density", e.g. using the density at the center of each HU interval **(Jiang et al, MP 2004)**

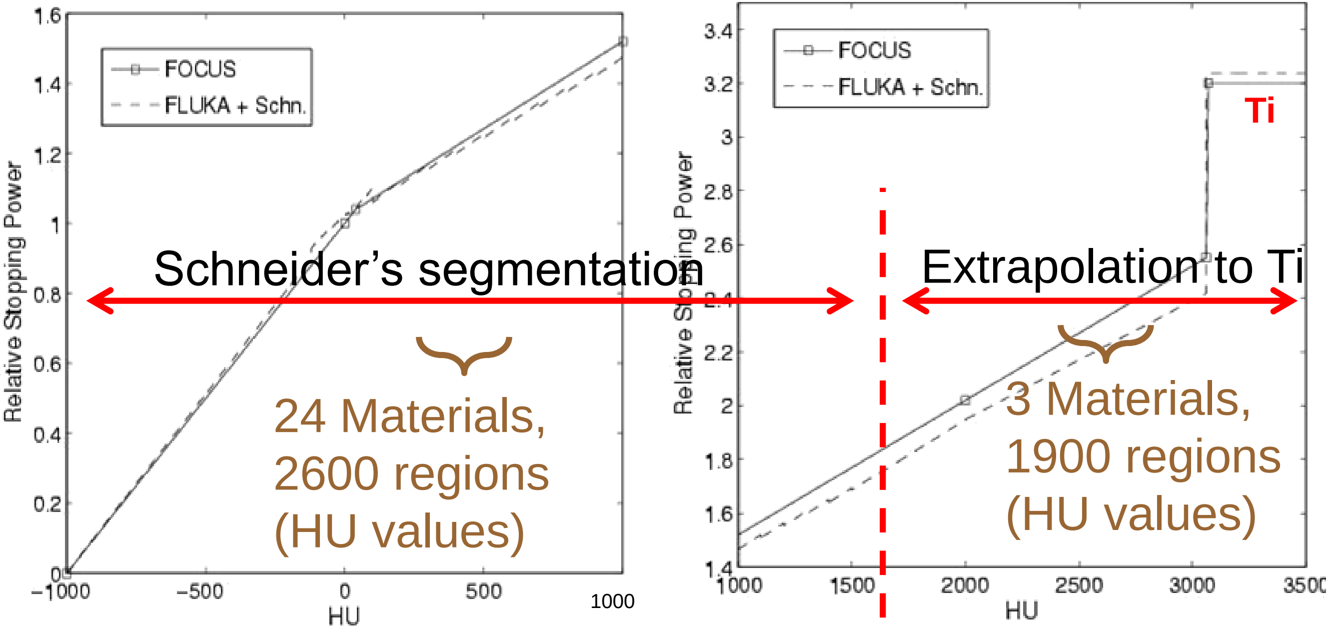


But "real density" (and related physical quantities) varies continuously with HU value !!!

Schneider et al PMB 45, 2000

Forcing MC to follow the same range calibration curve as TPS for p

The CORRFACT ionization scaling factors were obtained from the dEdx ratio between TPS and FLUKA (+ Schneider “mass density”)



Schneider’s segmentation

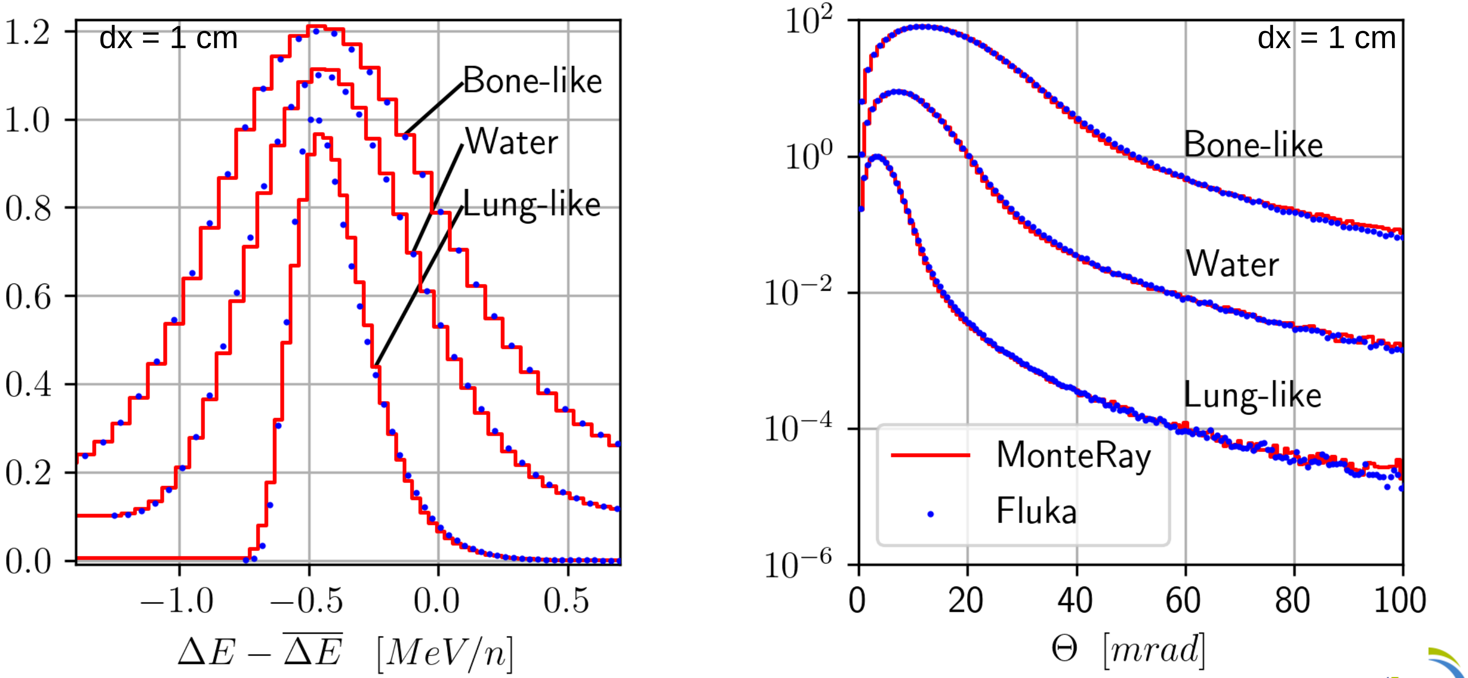
Extrapolation to Ti

24 Materials, 2600 regions (HU values)

3 Materials, 1900 regions (HU values)

Parodi et al MP 34, 2007, Parodi et PMB 52, 2007

EM interactions for 150 MeV proton: picking energy loss and scattering angle

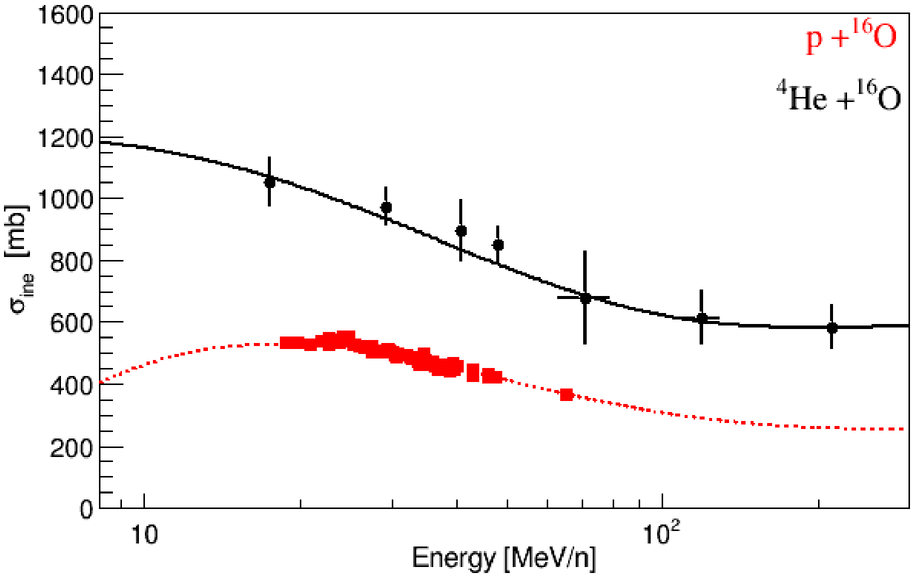


Energy Loss

Scattering

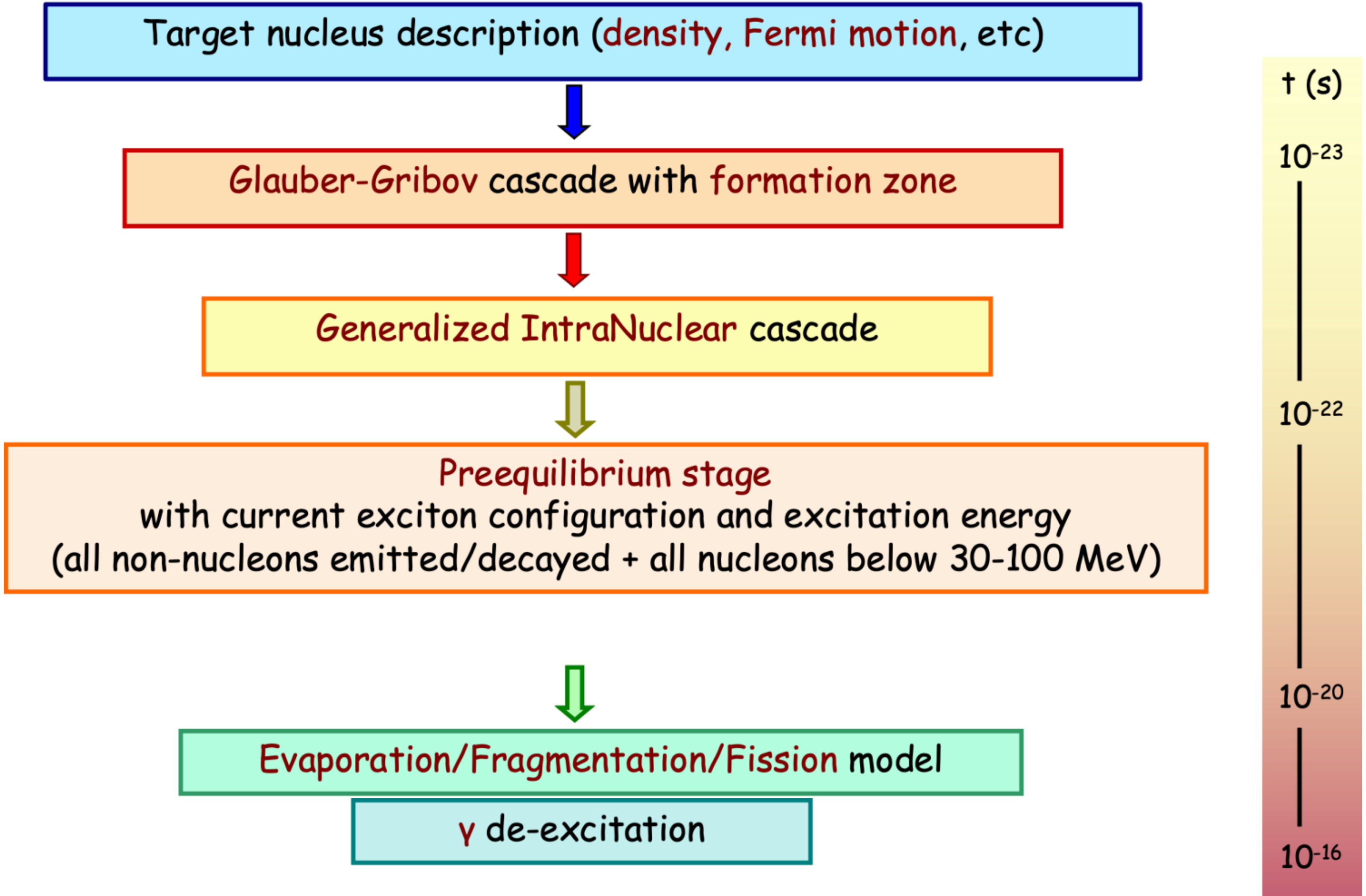
Left: energy loss distributions shifted along the x-axis by the mean energy. Right: angular distributions.

Inelastic Cross Section



Inelastic p+^{16}O and ^{4}He+^{16}O cross sections as function of the beam energy per nucleon: points and lines represent experimental data and model predictions, respectively.

Simplified Scheme of Nuclear Interactions



Target nucleus description (density, Fermi motion, etc)

Glauber-Gribov cascade with formation zone

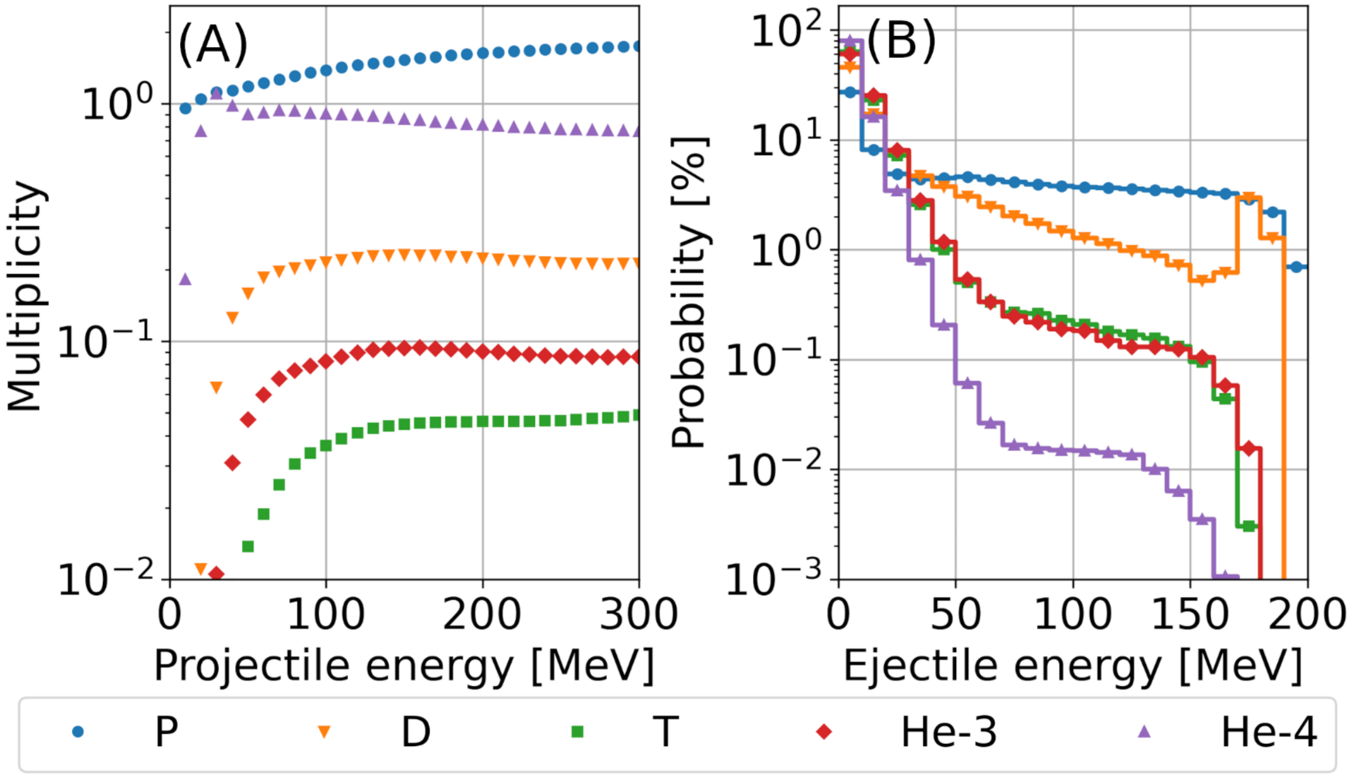
Generalized IntraNuclear cascade

Preequilibrium stage
with current exciton configuration and excitation energy
(all non-nucleons emitted/decayed + all nucleons below 30-100 MeV)

Evaporation/Fragmentation/Fission model

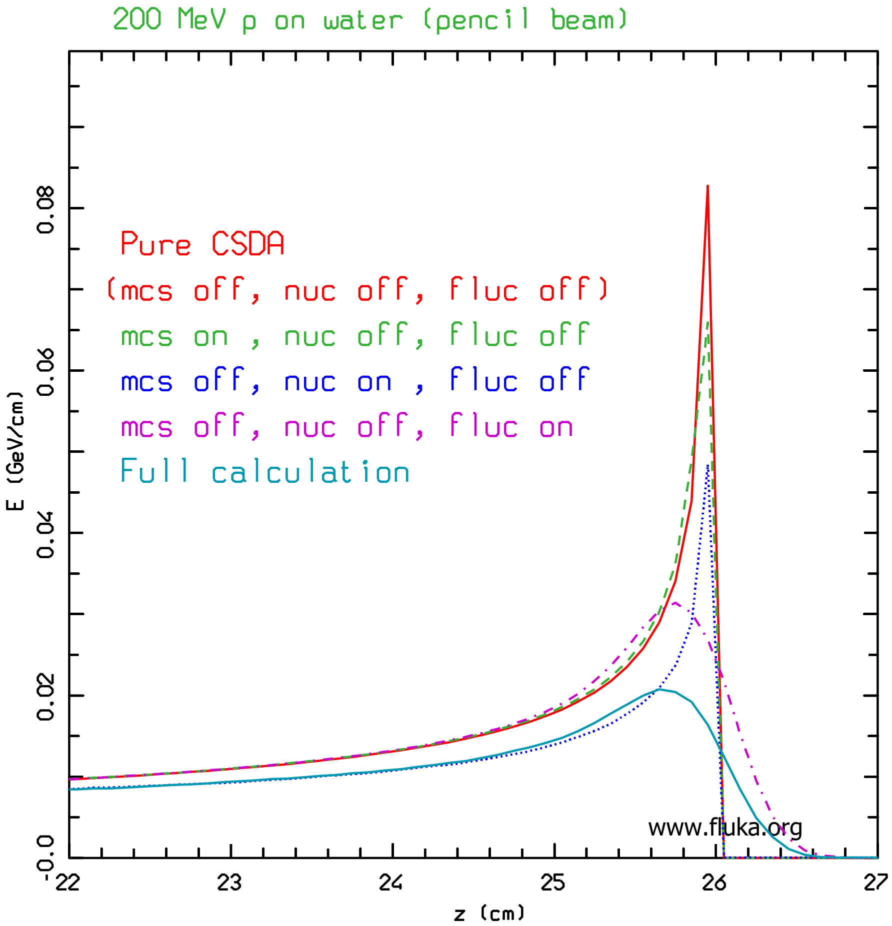
γ de-excitation

Secondaries produced in nuclear interactions

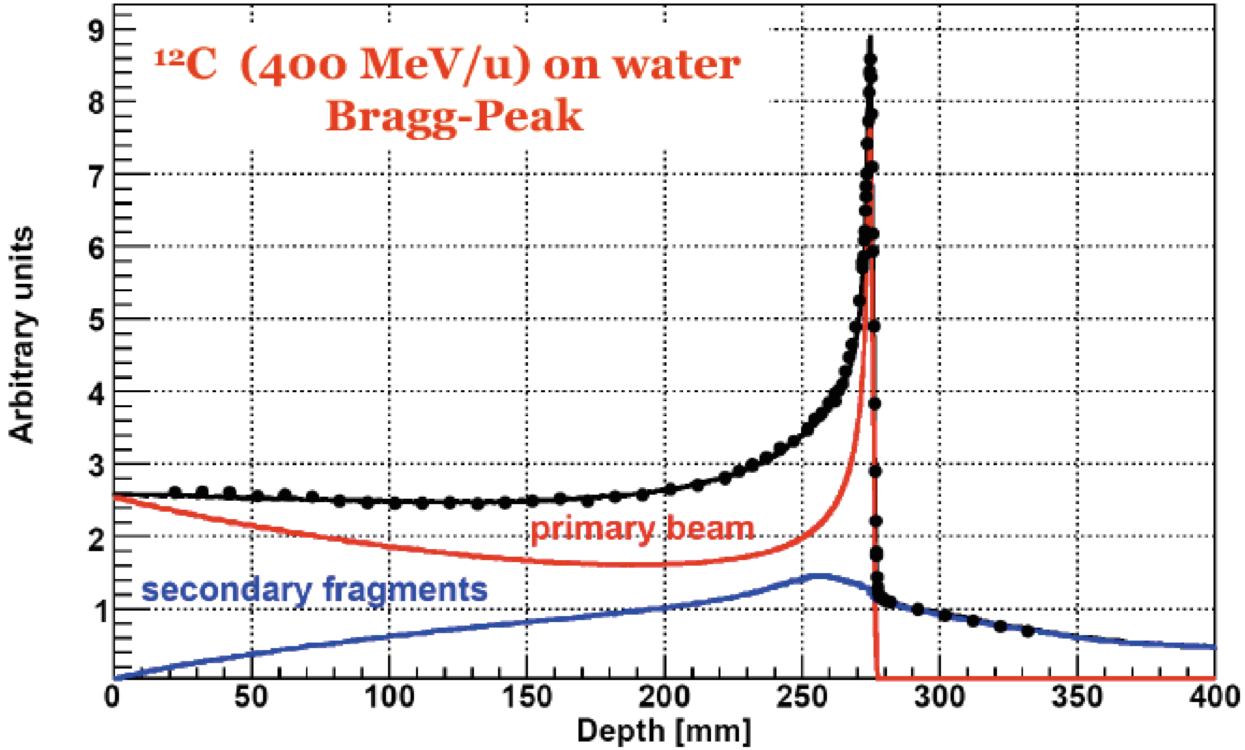


(A) Average number of particles produced per p+^{16}O collision as a function of proton beam energy. (B) For 200 MeV p+^{16}O collisions, the angularly integrated probability of a product particle being produced in a certain energy bin (bin size: 10 MeV) is shown.

The Effect of Physical Processes on Bragg Peak



Carbon Ions: Large Contributions of Secondaries

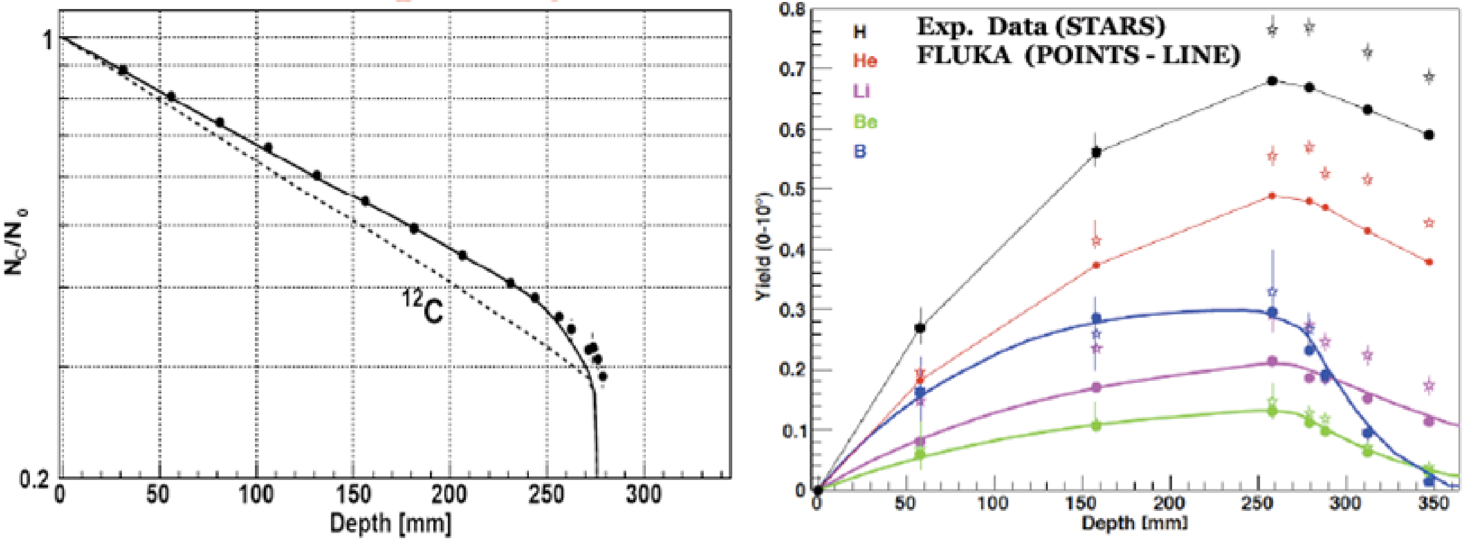


Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006

Simulation: A. Mairani PhD Thesis, 2007, Nuovo Cimento C, 31, 2008

Carbon Ions: Large Contributions of Secondaries

^{12}C (400 MeV/u) on water

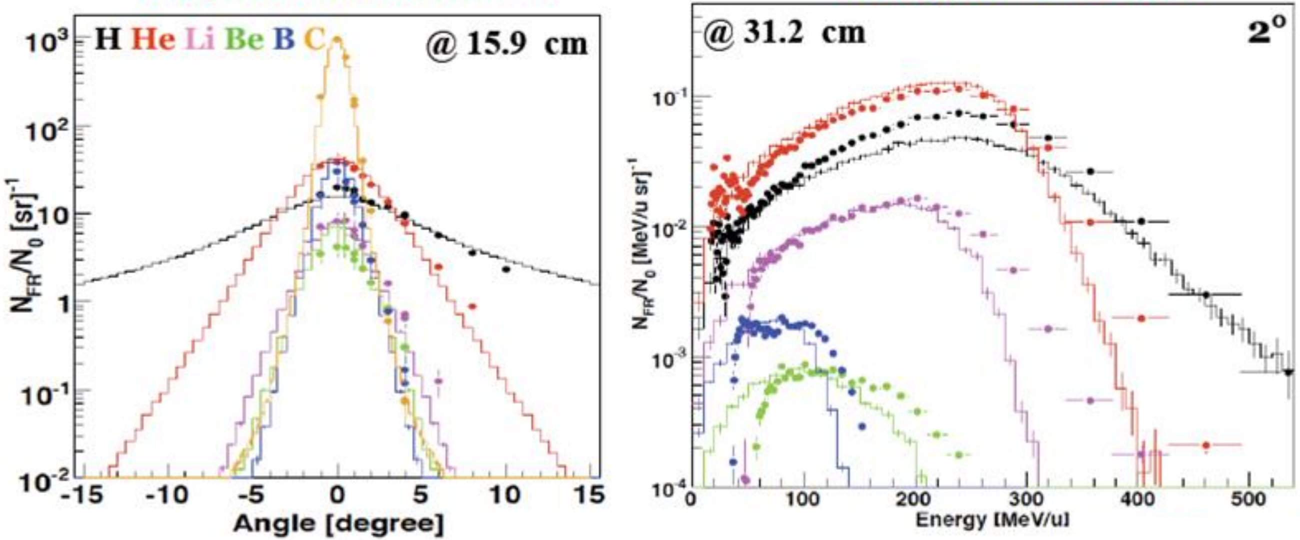

Attenuation of primary beam

Build-up of secondary fragments

Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006
Simulation: A. Mairani PhD Thesis, 2007,

Böhlen, Cerutti, Dosanjh, A Ferrari, Gudowska, Mairani and Quesada PMB 55 2010

Carbon Ions: Large Contributions of Secondaries



^{12}C (400 MeV/u) on water

Angular distribution

Energy distribution

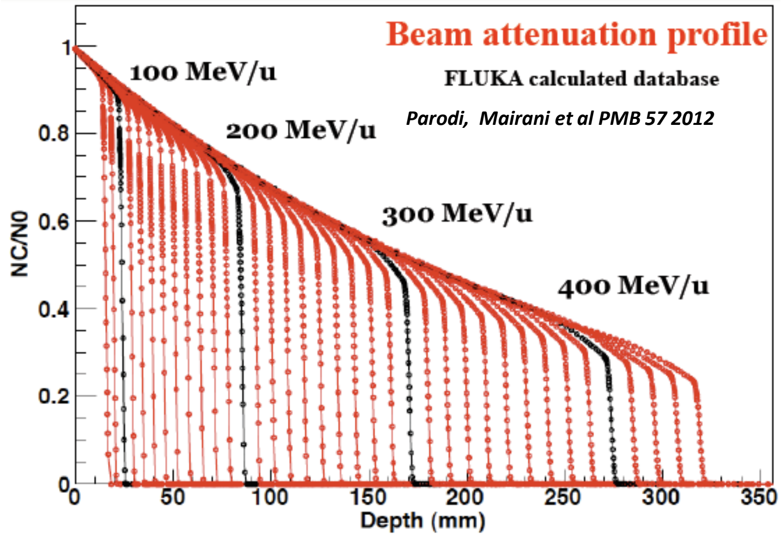
Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006

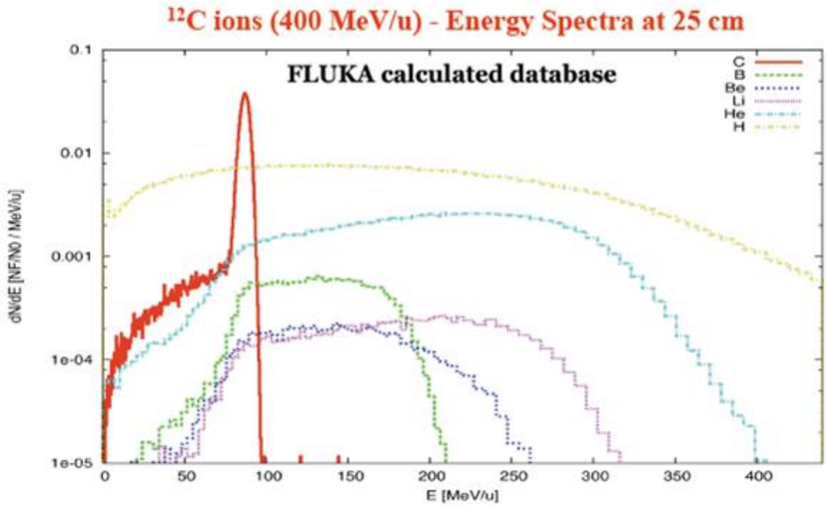
Simulation: A. Mairani PhD Thesis, 2007

Böhlen, Cerutti, Dosanjh, A Ferrari, Gudowska, Mairani and Quesada PMB 55 2010

Carbon Ions: Towards Biological Calculations

Monte Carlo calculation of fragment spectra in water for ^{12}C (80-440 MeV/u)





ARTEMIS – Adaptive RadioThErapie mit IonenStrahlen

GEFÖRDERT VOM
Bundesministerium
für Bildung
und Forschung

Vision: MR- Image-guided radiotherapy with ion beams

Task: Develop a fast Monte Carlo dose optimization and calculation engine to perform the following:

1. simulate Proton, Helium and Carbon beam transport and interaction with matter
2. Simulate changes in particle transport due to magnetic fields / charged particle interaction (deflection).
3. Accelerated computation, fast enough for daily adaptation.

MonteRay – Fast Dose Calculation Engine

Depth-dose distributions in water

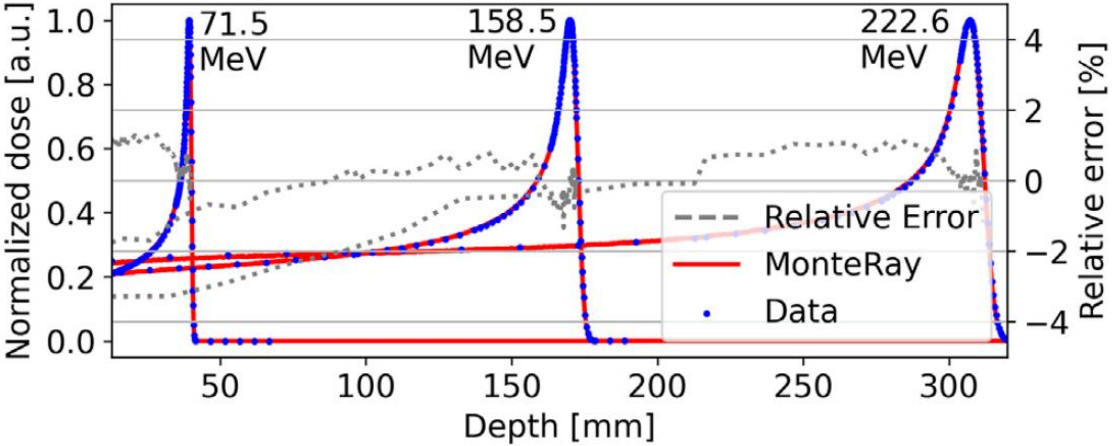


FIGURE 2 | Integrated depth-dose profiles of quasi-monoenergetic beams with energies of 71 MeV, 158.5, and 222.6 MeV are shown. Peakfinder measurements are indicated by blue points and MonteRay simulations as solid red lines. The relative error, after correcting for a lateral shift, between measurements and MonteRay simulations is shown with grey dotted lines after correcting for the lateral shift.

Lysakovski, …, Mairani (2021) Front. Phys. 9:741453. doi: 10.3389/fphy.2021.741453

MonteRay – Fast Dose Calculation Engine

Lateral dose distributions in water

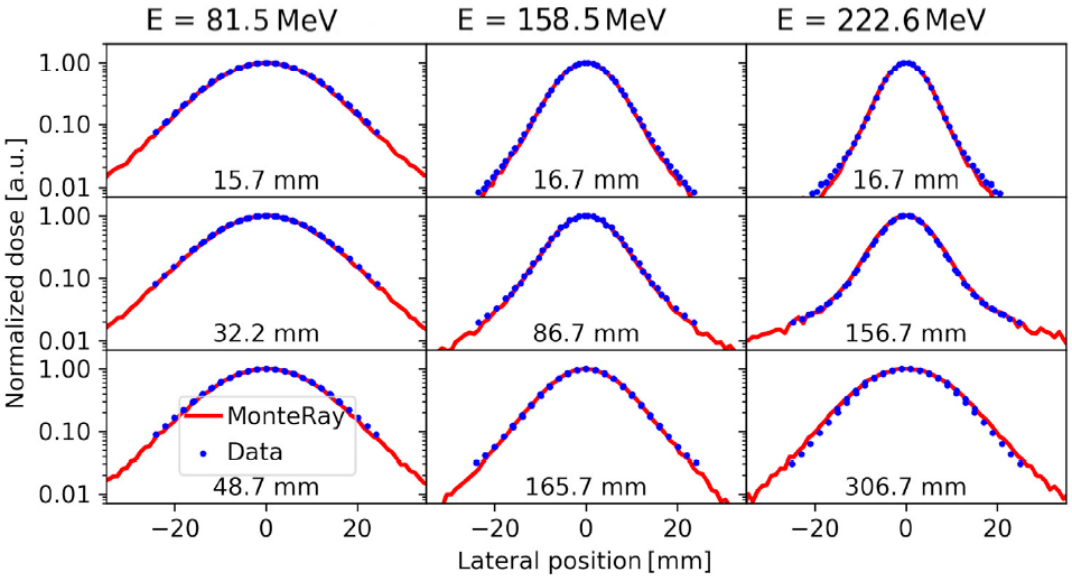
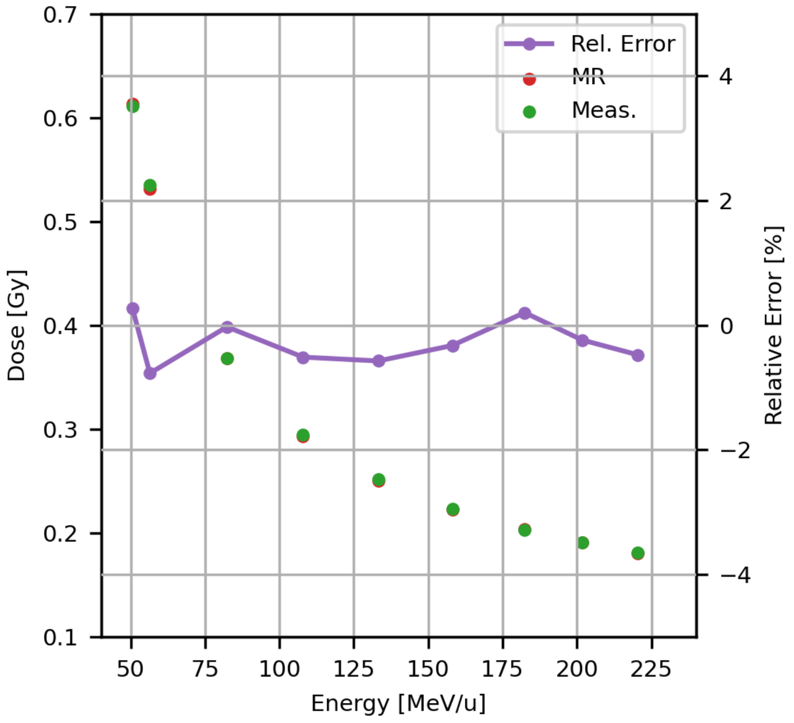


FIGURE 3 | Lateral dose profiles of vertically scanned proton lines at 81.5 MeV **(left column)**, 158.5 MeV (central column) and 222.6 MeV **(right column)** at different depths as reported in the panels. Measurements (blue points) are compared against MonteRay simulations (red lines).

Lysakovski, …, Mairani (2021) Front. Phys. 9:741453. doi: 10.3389/fphy.2021.741453

MonteRay – Fast Dose Calculation Engine

Absolute dose in water: monitor calibration



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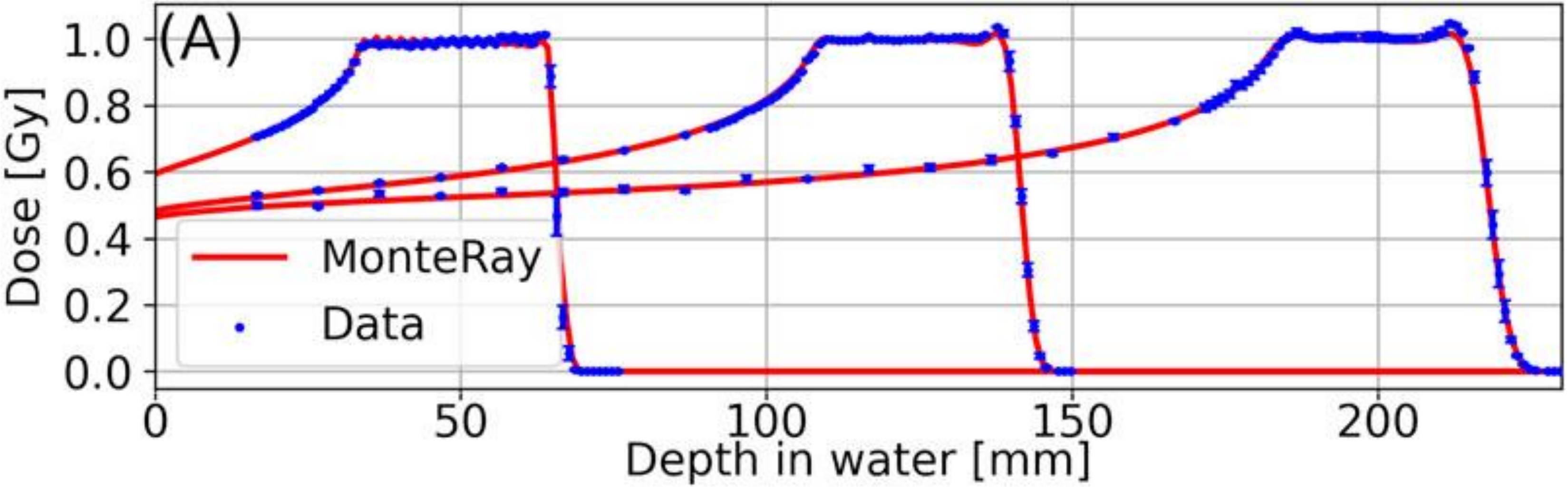
MonteRay – Fast Dose Calculation Engine

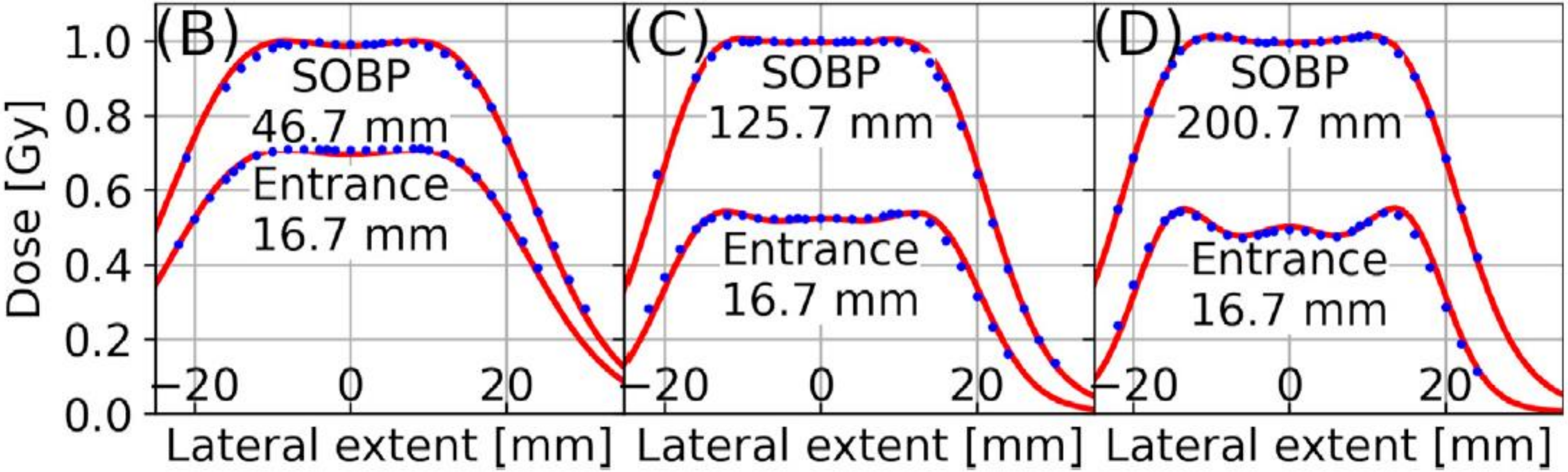
Spread-Out Bragg Peak: depth-dose distributions



Lysakovski, …, Mairani (2021) Front. Phys. 9:741453. doi: 10.3389/fphy.2021.741453

MonteRay – Fast Dose Calculation Engine

Spread-Out Bragg Peak: Lateral dose distributions



Lysakovski, …, Mairani (2021) Front. Phys. 9:741453. doi: 10.3389/fphy.2021.741453

MonteRay – Fast Dose Calculation Engine

Pencil beams in magnetic field

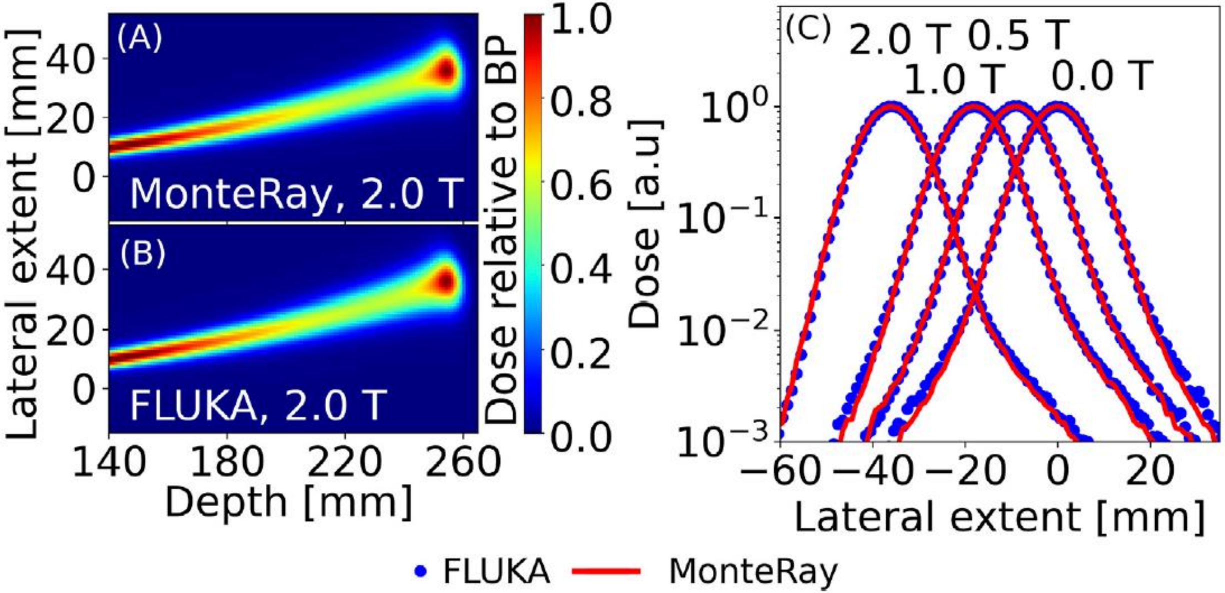


FIGURE 5 | For 200 MeV protons in water, 2D dose distributions calculated with MonteRay **(A)** and FLUKA **(B)** are shown in a plane perpendicular to the 2 T magnetic field. In **(C)**, Lateral profiles for 200 MeV protons in water and with magnetic field strengths of 0 T, 0.5 T, 1 T, and 2 T are displayed at the location of the BP. MonteRay's results are indicated by a red line while FLUKA's results are displayed as blue dots.

Lysakovski, …, Mairani (2021) Front. Phys. 9:741453. doi: 10.3389/fphy.2021.741453

MonteRay – Fast Dose Calculation Engine

Patient recalculation

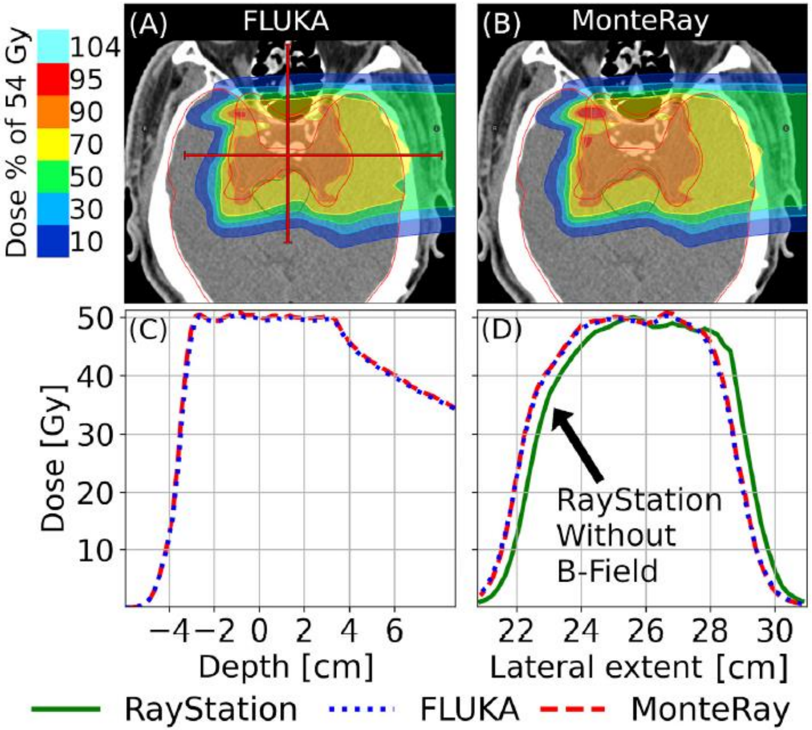


FIGURE 8 | Axial views of calculated doses for the plan described in Section 2.2.4 with an added perpendicular magnetic field of 1 T are shown for **(A)** FLUKA and **(B)** MonteRay. In panels **(C)** and **(D)**, longitudinal and lateral profiles are shown, respectively. Besides the lateral profiles obtained from FLUKA and MonteRay, we also show the lateral profile of the RayStation dose calculated without a magnetic field. The locations of the profiles relative to the 2D plots are indicated trough red lines in panel **(A)**. RayStation profiles are indicated by a solid green line, FLUKA profiles by a dotted blue line and MonteRay profiles by a dashed red line.

Lysakovski, …, Mairani (2021) Front. Phys. 9:741453. doi: 10.3389/fphy.2021.741453

MonteRay – Fast Dose Calculation Engine

Patient recalculation

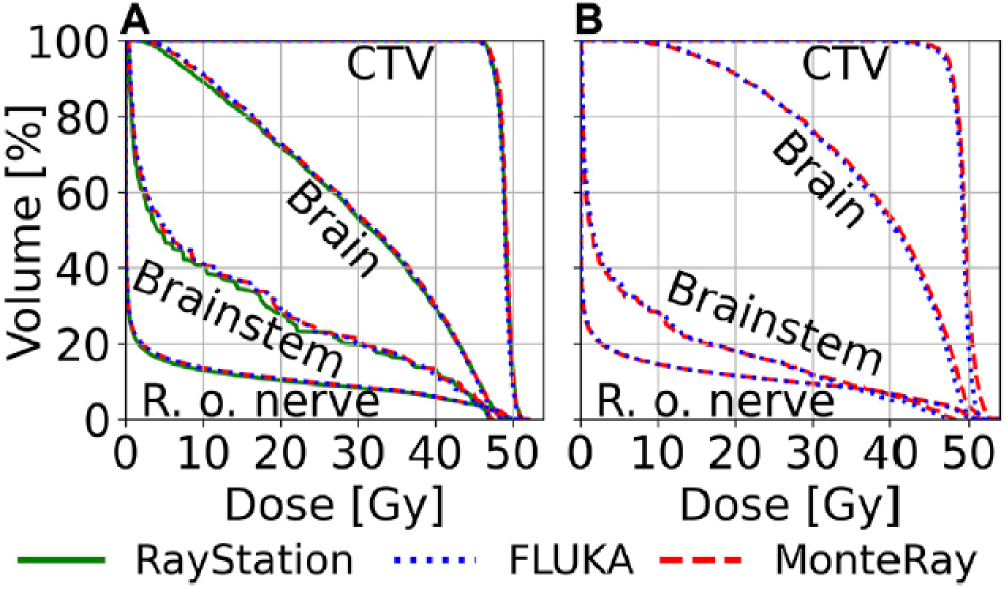
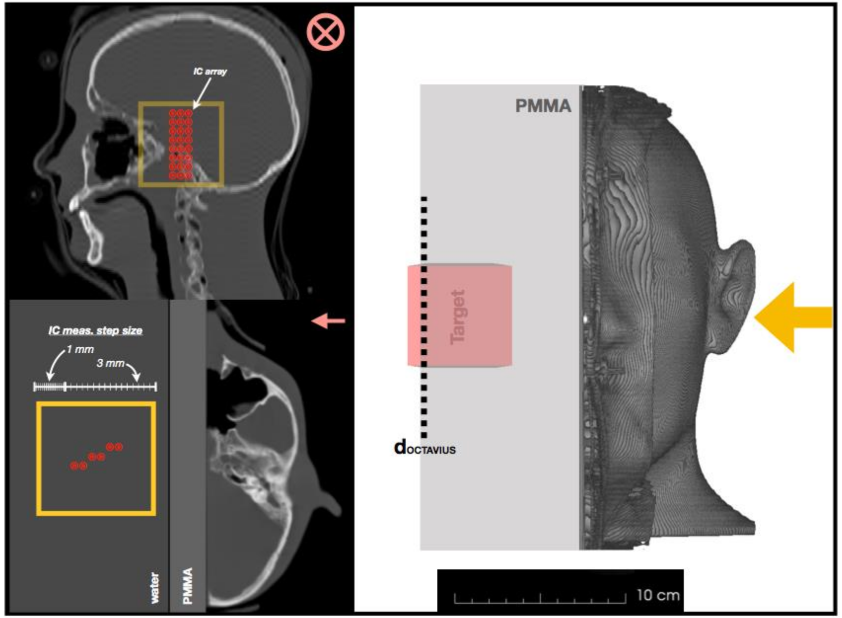


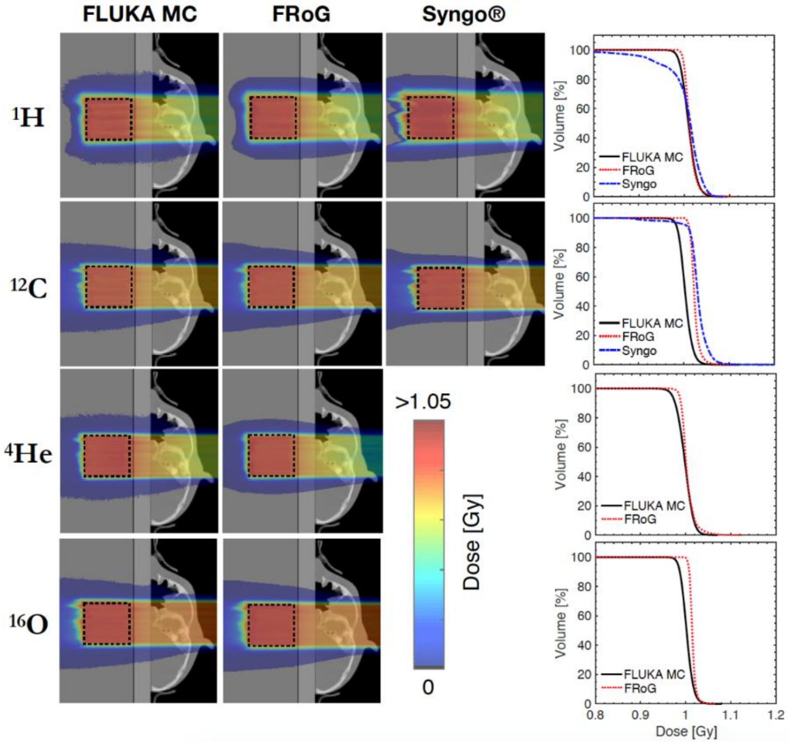
FIGURE 7 | Computed DVHs for the CTV, the brain, the brainstem and the right optical nerve (r. o. nerve) are shown. DVHs were computed for RayStation (green, solid line), FLUKA (blue, dotted line) and MonteRay (red, dashed line). In panel **(A)**, DVHs for the patient case without a magnetic field are shown while in panel **(B)** DVHs calculated for the case with an applied magnetic field are shown.

Lysakovski, …, Mairani (2021) Front. Phys. 9:741453. doi: 10.3389/fphy.2021.741453

Experimental Validation in complex scenario: TPS vs MC

experimental

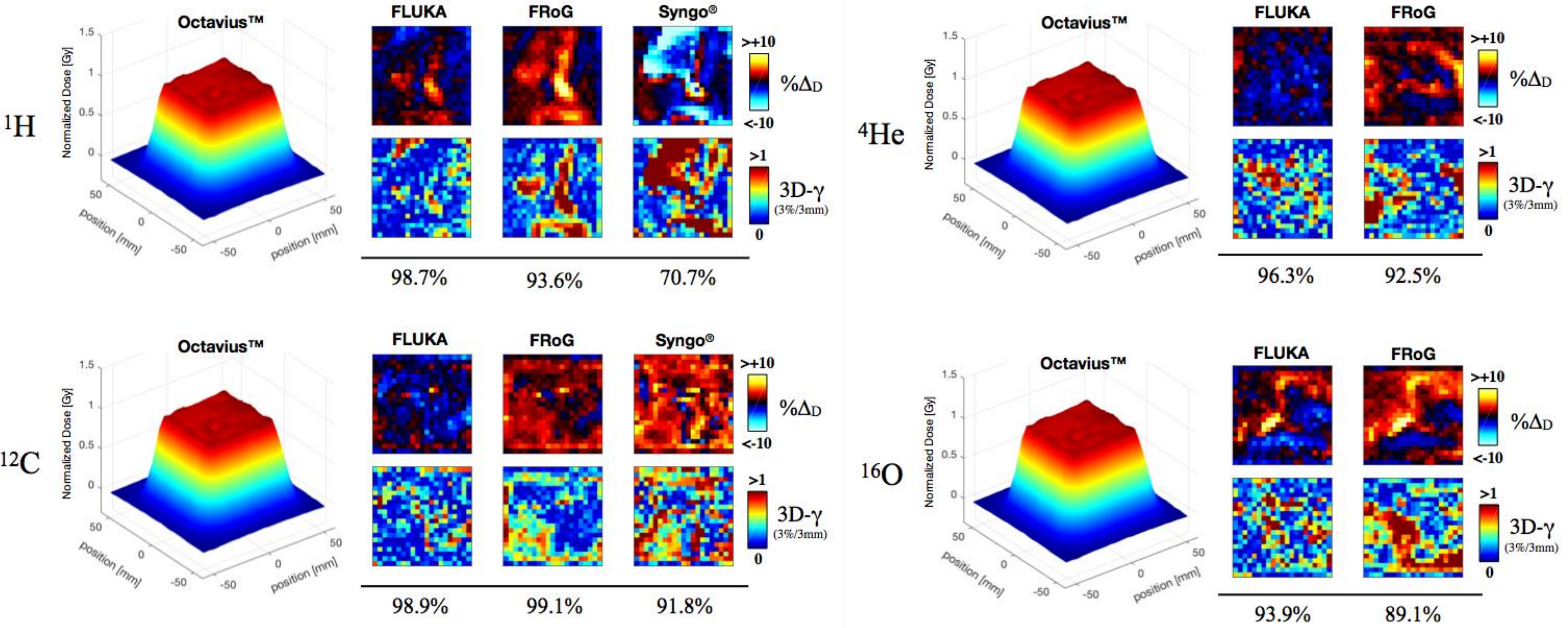




On average: FRoG matches FLUKAs D_{95}, D_{50}, D_5 within 2%. Measurements are ~2% difference.

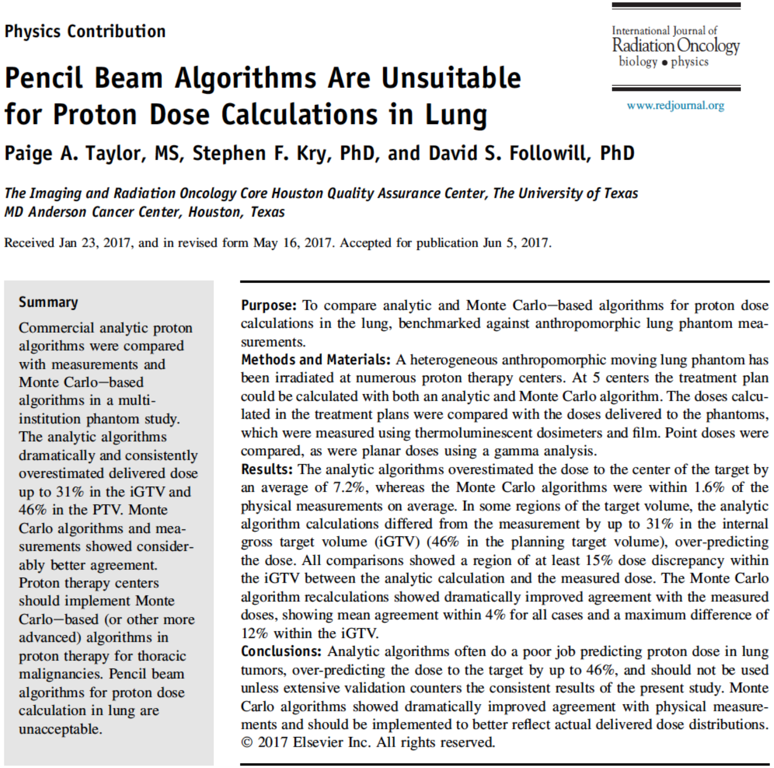
S. Mein et al 2019 Phys. Med.

Experimental Validation in complex scenario: TPS vs MC



S. Mein et al 2019 Phys. Med.

Accuracy: MC vs. FRoG vs. clinical TPS (MC)



Physics Contribution

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Pencil Beam Algorithms Are Unsuitable for Proton Dose Calculations in Lung

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Summary

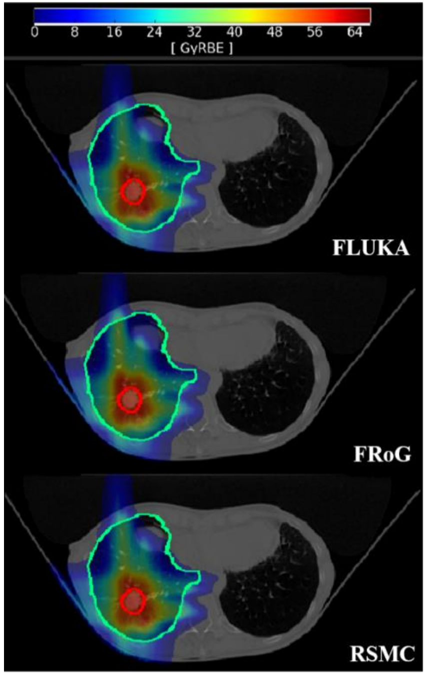
Commercial analytic proton algorithms were compared with measurements and Monte Carlo–based algorithms in a multi-institution phantom study. The analytic algorithms dramatically and consistently overestimated delivered dose up to 31% in the iGTV and 46% in the PTV. Monte Carlo algorithms and measurements showed considerably better agreement. Proton therapy centers should implement Monte Carlo–based (or other more advanced) algorithms in proton therapy for thoracic malignancies. Pencil beam algorithms for proton dose calculation in lung are unacceptable.

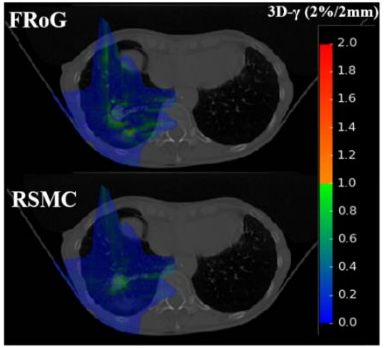
Purpose: To compare analytic and Monte Carlo–based algorithms for proton dose calculations in the lung, benchmarked against anthropomorphic lung phantom measurements.

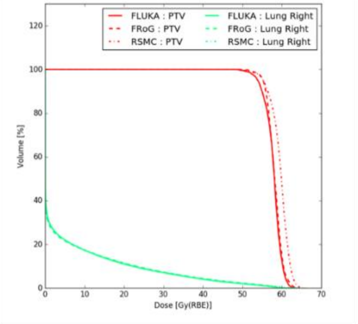
Methods and Materials: A heterogeneous anthropomorphic moving lung phantom has been irradiated at numerous proton therapy centers. At 5 centers the treatment plan could be calculated with both an analytic and Monte Carlo algorithm. The doses calculated in the treatment plans were compared with the doses delivered to the phantoms, which were measured using thermoluminescent dosimeters and film. Point doses were compared, as were planar doses using a gamma analysis.

Results: The analytic algorithms overestimated the dose to the center of the target by an average of 7.2%, whereas the Monte Carlo algorithms were within 1.6% of the physical measurements on average. In some regions of the target volume, the analytic algorithm calculations differed from the measurement by up to 31% in the internal gross target volume (iGTV) (46% in the planning target volume), over-predicting the dose. All comparisons showed a region of at least 15% dose discrepancy within the iGTV between the analytic calculation and the measured dose. The Monte Carlo algorithm recalculations showed dramatically improved agreement with the measured doses, showing mean agreement within 4% for all cases and a maximum difference of 12% within the iGTV.

Conclusions: Analytic algorithms often do a poor job predicting proton dose in lung tumors, over-predicting the dose to the target by up to 46%, and should not be used unless extensive validation counters the consistent results of the present study. Monte Carlo algorithms showed dramatically improved agreement with physical measurements and should be implemented to better reflect actual delivered dose distributions.





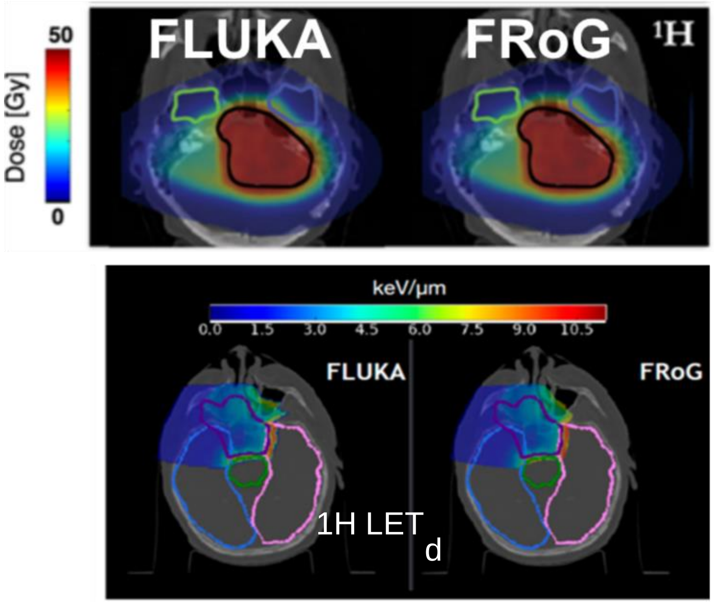


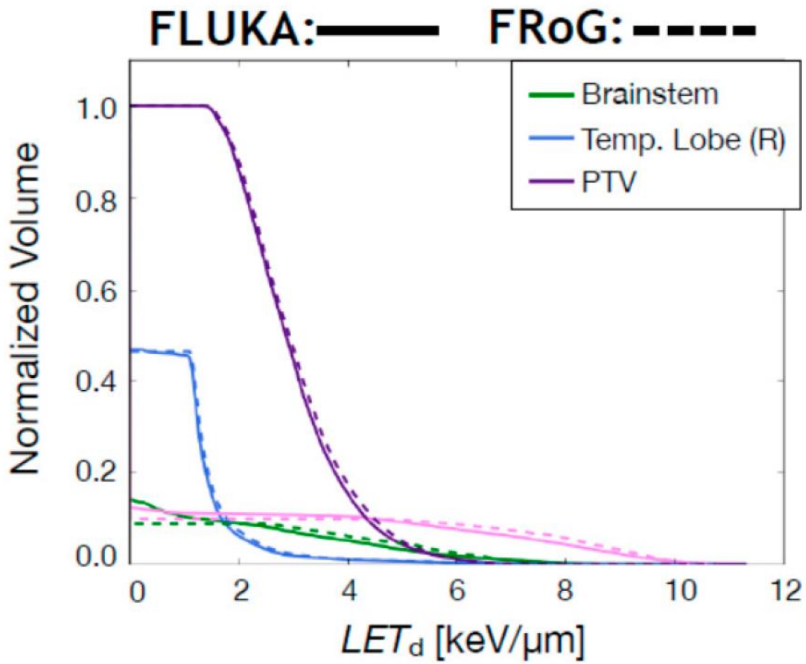
3D-γ passing rate (2mm/2%): RS-MC = 98%, FRoG = 94%

G. Magro,…,Mairani, 86, 2021 Physica Medica

LETd distributions in proton therapy

in silico





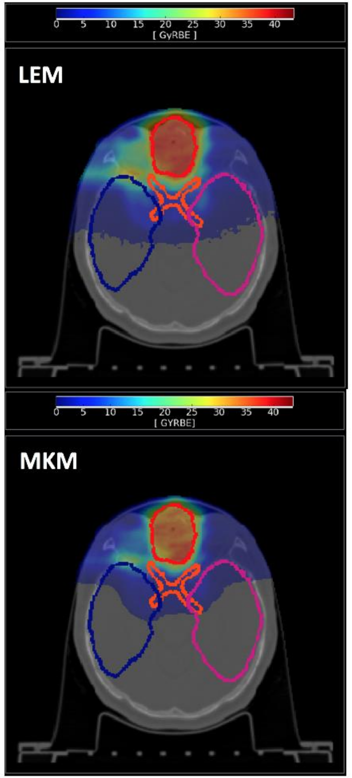
LET$_d$ values match within 0.3 keV/μm

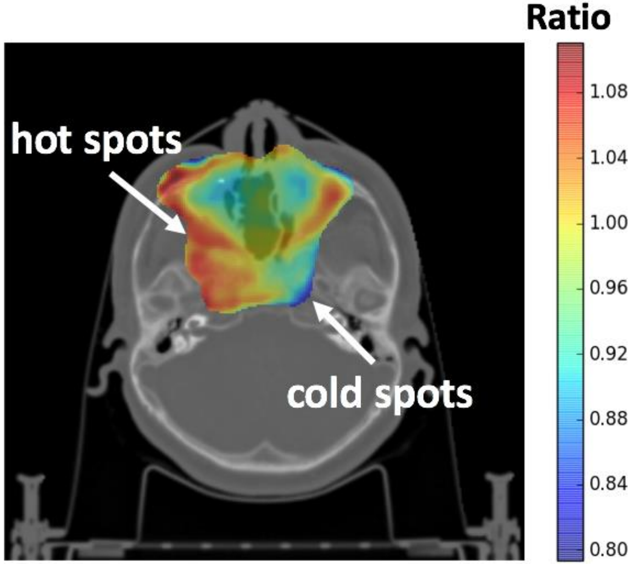
S. Mein et al. 2018 Sci Rep.; K. Choi et al. 2018 Cancers 10, 395

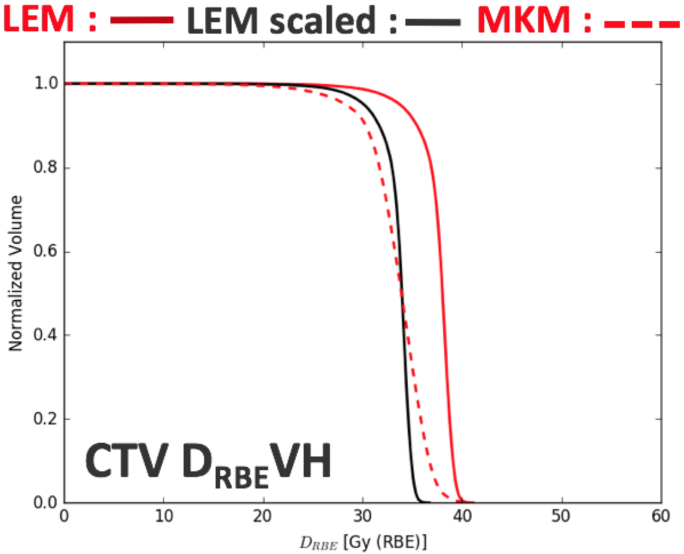
Biological calculations for ^{12}C ions

RBE model comparison: LEM vs. MKM

K. Choi,...,A. Mairani Cancers, 2018, 10, 395

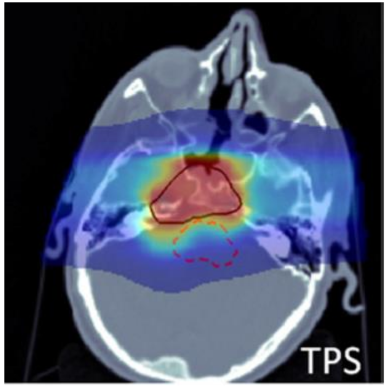


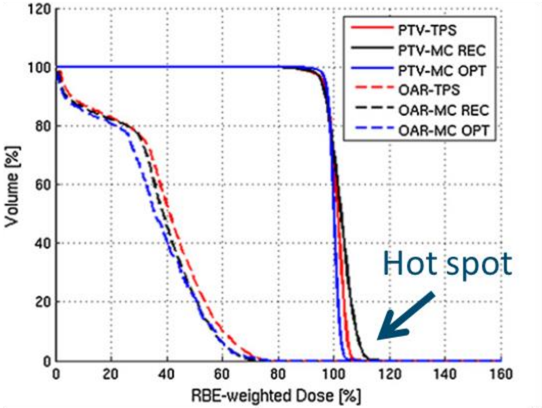




NCT

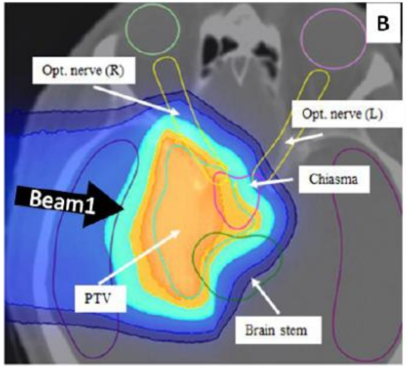
First Monte Carlo-based TPS for p, ^{4}He, ^{12}C



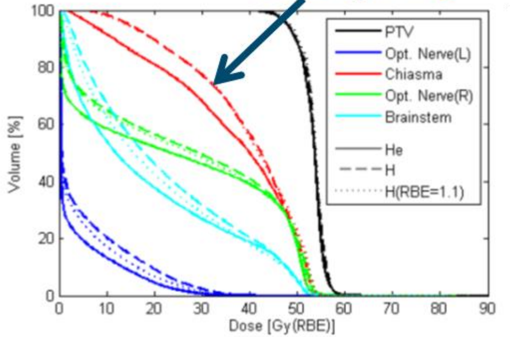


Hot spot

Proton Patient Plan:
TPS
vs
MC re-calculation
vs
MC optimization



Dose sparing



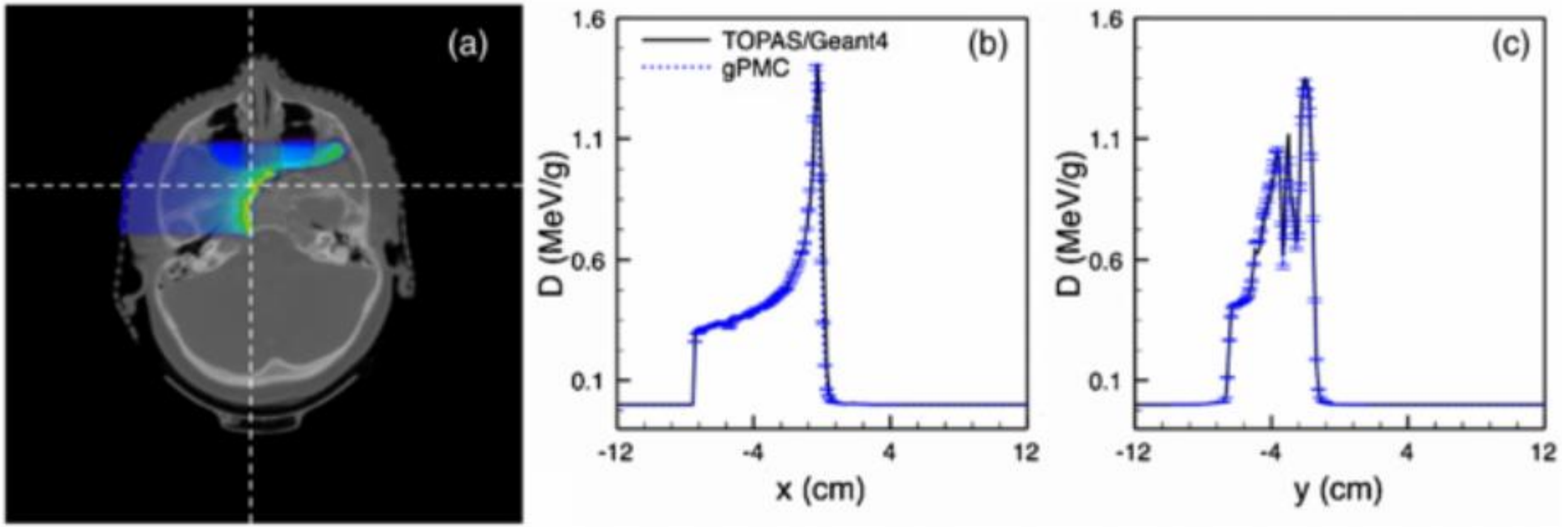
Proton
vs
^{4}He
Patient Plan:
normal tissue sparing
with ^{4}He ion

A. Mairani, et al Physics in Medicine Biology, 2013, 58, 2471
T. Tessonnier, A. Mairani, et al. Radiation Oncology, 2018, 13,1

The common application of a Graphics Processing Unit (GPU)

Fast Monte Carlo on GPU: an example

GPU-based fast MC (gPMC) vs. general purpose MC (TOPAS), 3Dγ (2%/2mm) 99%
Calculation Time: **seconds vs. hours**



Jia et al 2012 PMB

Conclusions

- Monte Carlo Methods became a standard for dose computation in radiation therapy
- Fast CPU and GPU Monte Carlo codes are available
- General purposes Monte Carlo codes remain the gold standard in case where experimental data are not available
- None MC is perfect, it is important to understand the limitations and perform experimental validations!

Thank you for your attention!

BioPT + PartRadBio hike 2021