Part 2: Modeling Ion-Beam Cancer Therapy on macro and micro scales

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FIAS Frankfurt Institute for Advanced Studies

HIC for FAIR Helmholtz International Center

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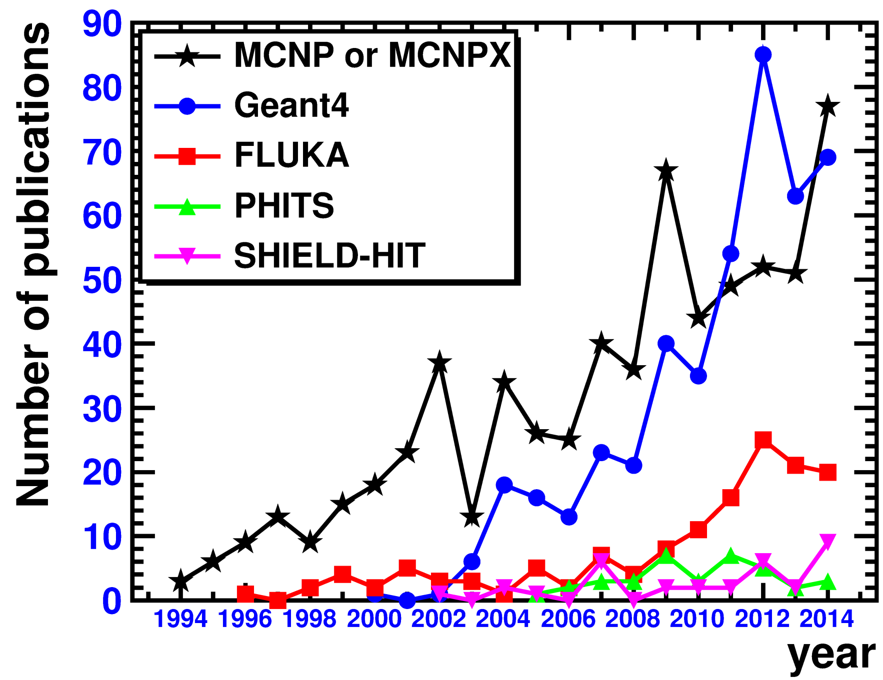
1. Introduction

Monte Carlo modeling of hadron therapy

A set of various models is needed to simulate propagation and interaction of therapeutic ion beams in tissue-like media.

Now several general-purpose Monte Carlo particle transport codes (FLUKA, Geant4, MCNP, PHITS and SHIELD-HIT) are used for simulations in the field of hadron therapy.

For our study we decided to use models from open-access toolkit Geant4

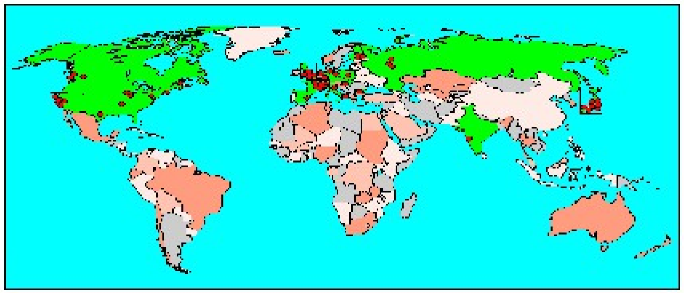


Annual number of publications in the field of hadron therapy, where respective Monte Carlo codes/tools were used.

Estimated from the Web of Science (Thomson Reuters) database 2015.

Geant4 is a rapidly developing toolkit for nuclear, particle, space and medical physics

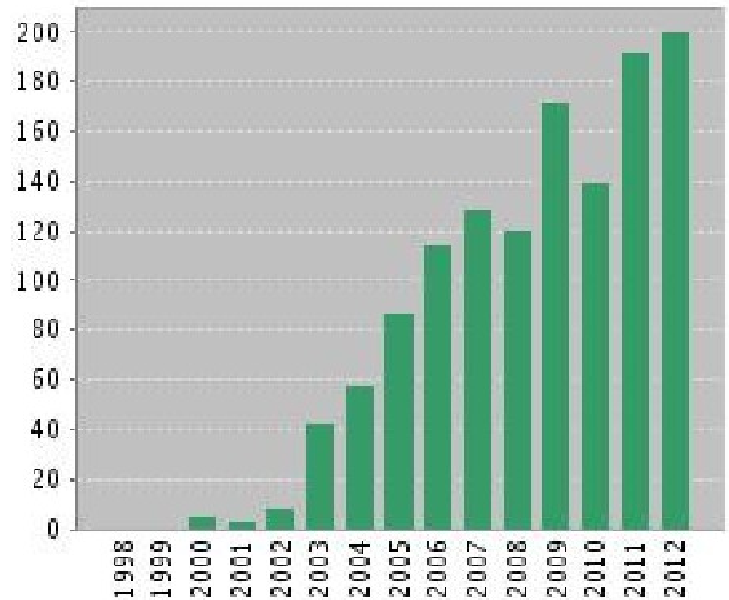
Geant4 collaboration

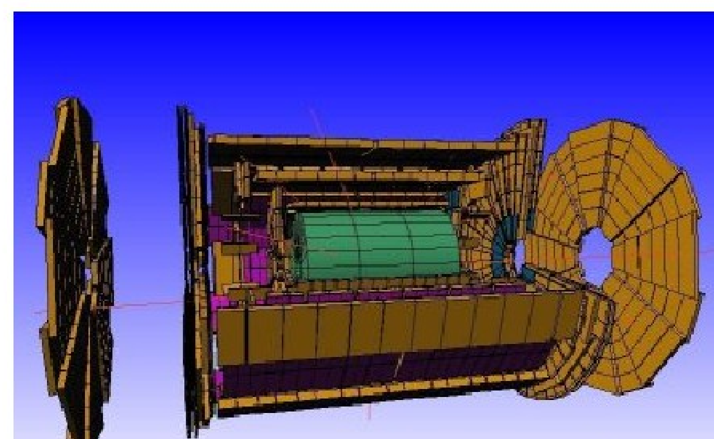


Collaborators also from non-member institutions, including
Budker Inst. of Physics
IHEP Protvino
MEPHI Moscow
Pittsburg University

http://geant4.cern.ch/geant4/

Papers based on Geant4 published each year (ISI, 10.10.12)





Geant4: ATLAS @LHC

Geant4 toolkit

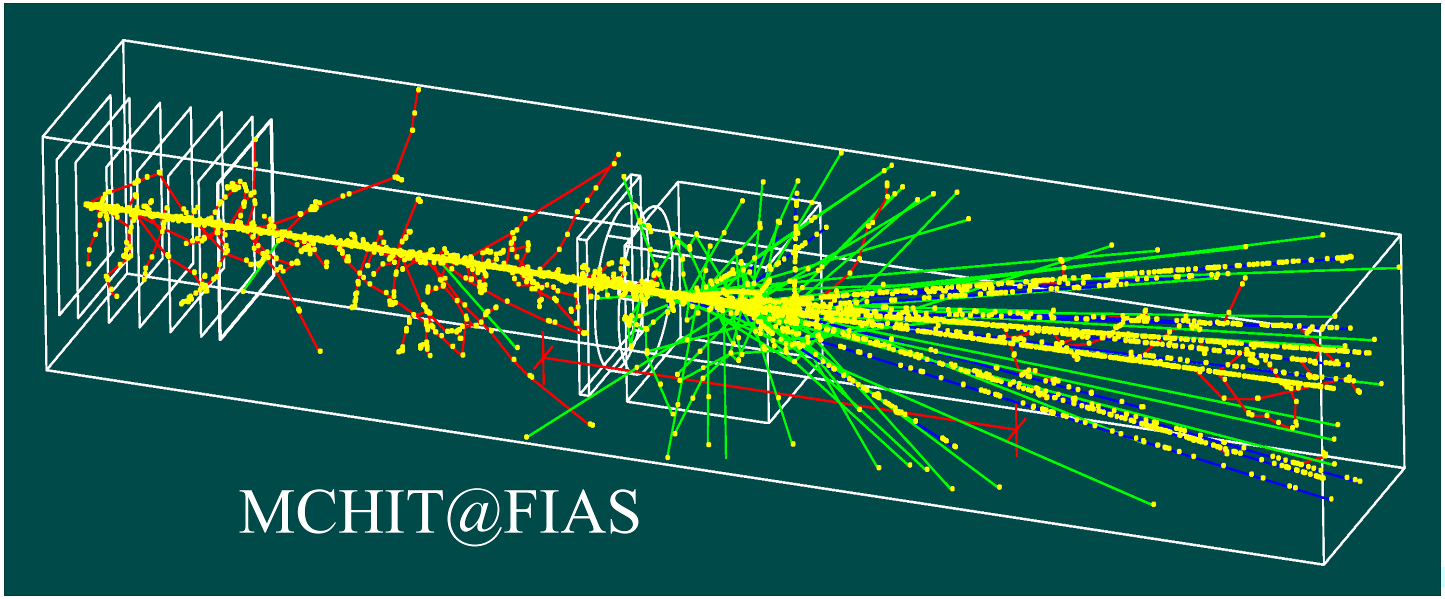
- **Geant4 (for GEometry ANd Tracking) is a platform for the simulation of the propagation and interactions of particles in the matter.**
- **Developed and maintained by the international Geant4 Collaboration with headquarters at CERN (Geneva).**
- **The source code (in C++) is freely available.**
- **It provides an abundant set of physical models to handle diverse interactions of particles with matter over a wide energy range.**
- **It includes a complete set of tools for handling geometry, tracking, detector response, visualization and user interface.**
- **The user should build his own application using the relevant components of the toolkit.**

Agostinelli S et al. 2003 GEANT4—a simulation toolkit, Nucl. Instrum. Methods A 506 (2003) 250–303; has more than 7000 citations in Google database!

#

Monte Carlo for Heavy Ion Therapy (MCHIT) GEANT4-based application created at FIAS

- Uses FIAS expertise in heavy-ion physics (QMD and SMM);
- GEANT4 toolkit accumulates rich experience of international nuclear community over decades;
- GEANT4-based models are used now for modeling a rich verity of physical processes relevant to ion-beam therapy;
- Works with simple phantoms and beam-line elements;
- Simulations are done on event-by-event basis.

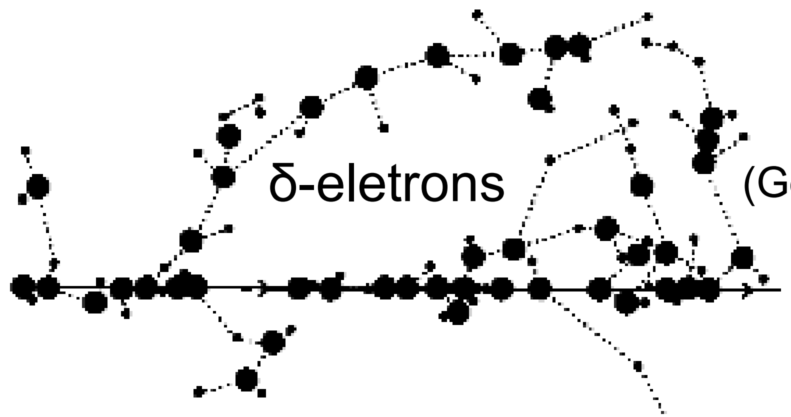


The MCHIT model

2. Models included in MCHIT

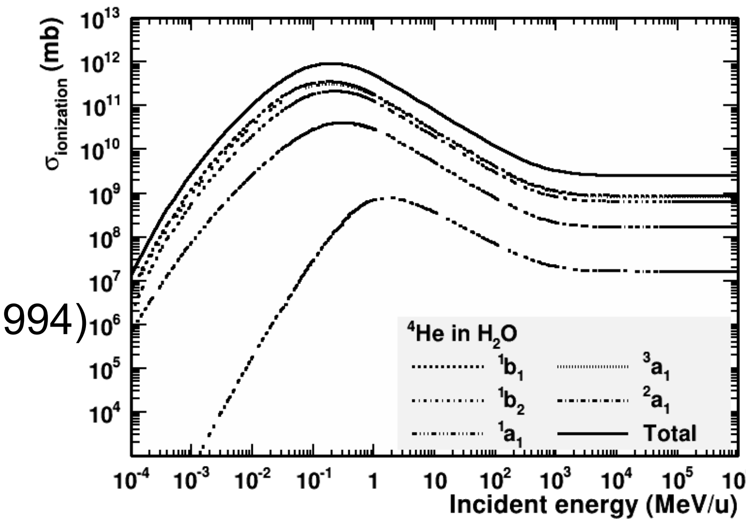
Relevant physical interactions in ion-beam cancer therapy

1. Coulomb scattering and ionizations arethe most frequent interaction processes for ions along their way to the tumour. described bv Bethe-Bloch formula

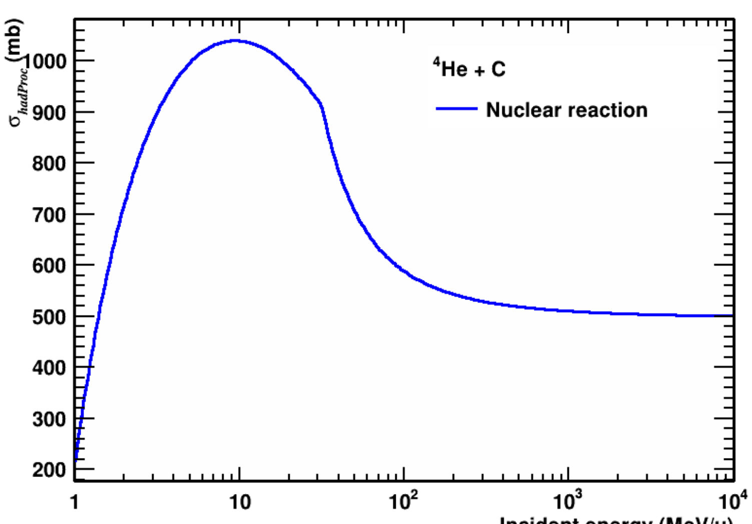


(Goodhead 1994)

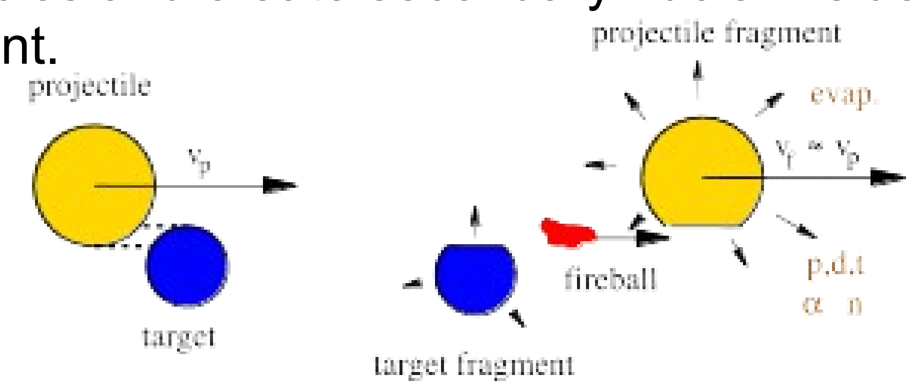
Ionization cross section



Nuclear reaction cross section

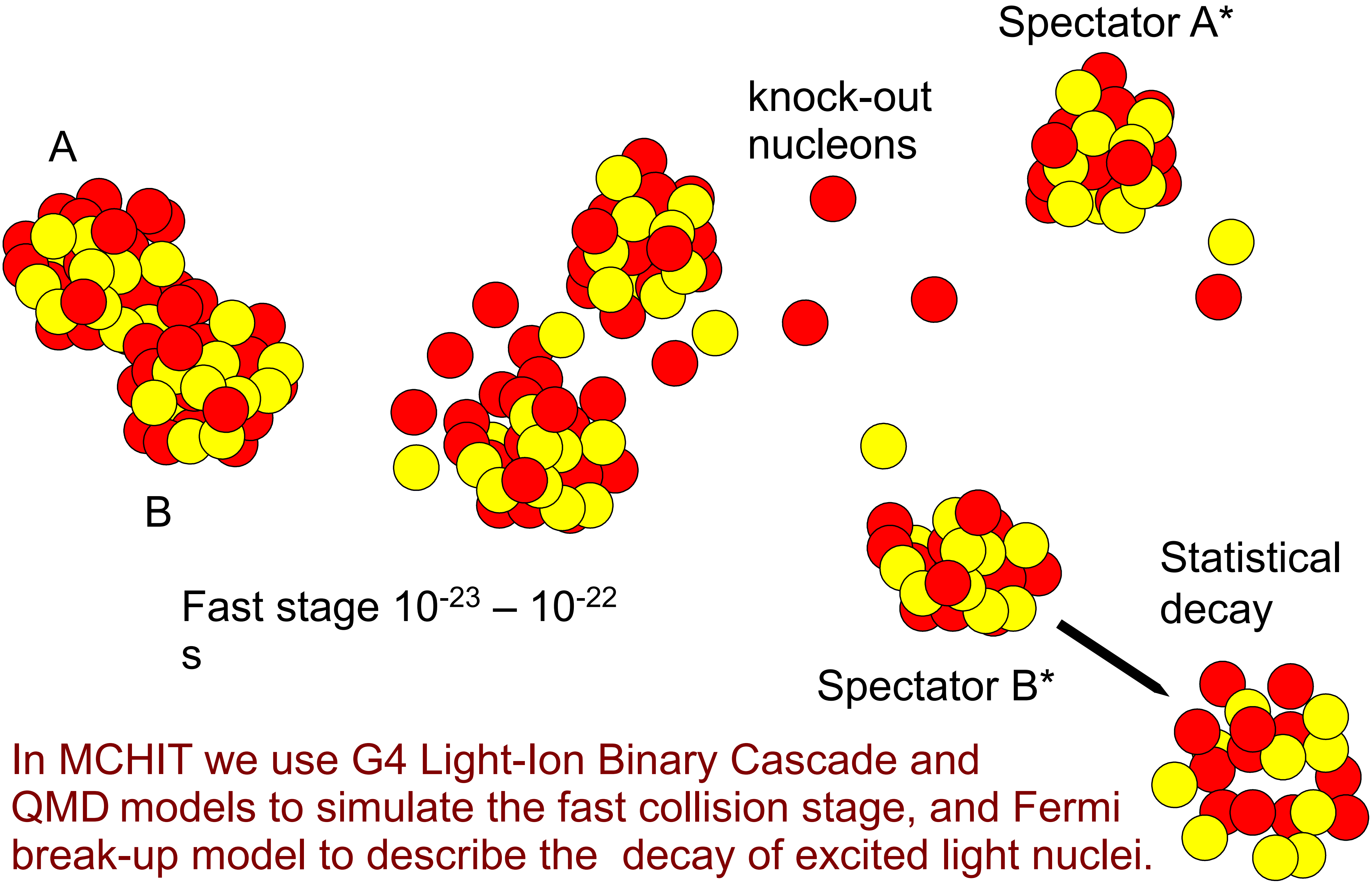


2. Nuclear collisions attenuate the beam particles and create secondary nuclei inside the patient.



(D. Schardt et al 2010)

Artist's view of a nucleus-nucleus collision



In MCHIT we use G4 Light-Ion Binary Cascade and QMD models to simulate the fast collision stage, and Fermi break-up model to describe the decay of excited light nuclei.

Our simulations are mostly done with:

•**Intra-Nuclear Cascade (INC liege) model:**

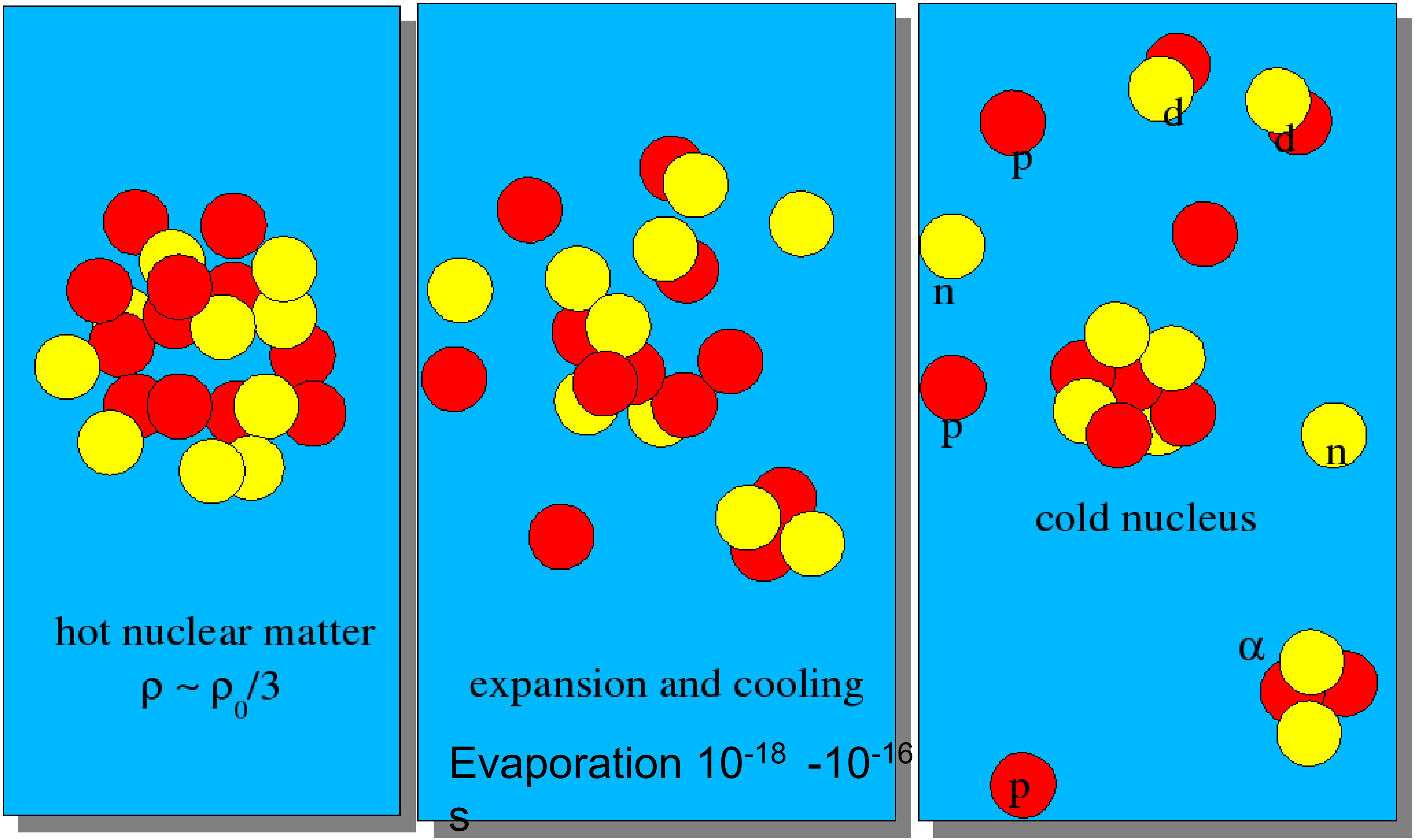
- considers nucleus-nucleus collisions as a set of individual nucleon-nucleon collisions in the participant zone
- estimates the excitation energy of residual nuclei as the sum of energies of holes (knocked-out nucleons) and particles (trapped nucleons)
- Pauli-blocking is applied to NN collisions leading to occupied levels
- local density approximation and scalar potentials for nucleons

•**Quantum Molecular Dynamics (QMD) model:**

- each nucleon is represented as a Gaussian wave packet.
- propagation with scattering term which takes into account Pauli principle
- self-consistent potentials

Both models are combined to de-excitation codes of Geant4 to simulate further decays of hot (pre)fragments

Decay of residual nuclei: sequential evaporation vs simultaneous break-up?



De-excitation of residual nuclei

The **mass, charge and excitation energy** of excited residual nuclei are determined from the dynamical stage event-by-event.

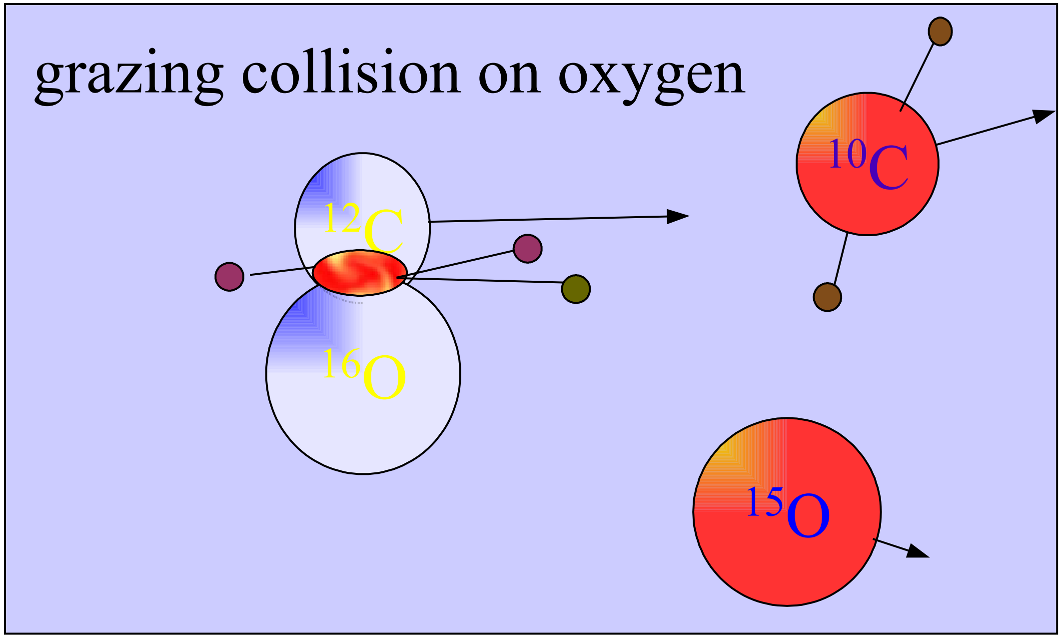
Decay channels for heavy residual nuclei are generated by Monte Carlo method, according to the **Evaporation Model** or **Statistical Multifragmentation Model (SMM)**.

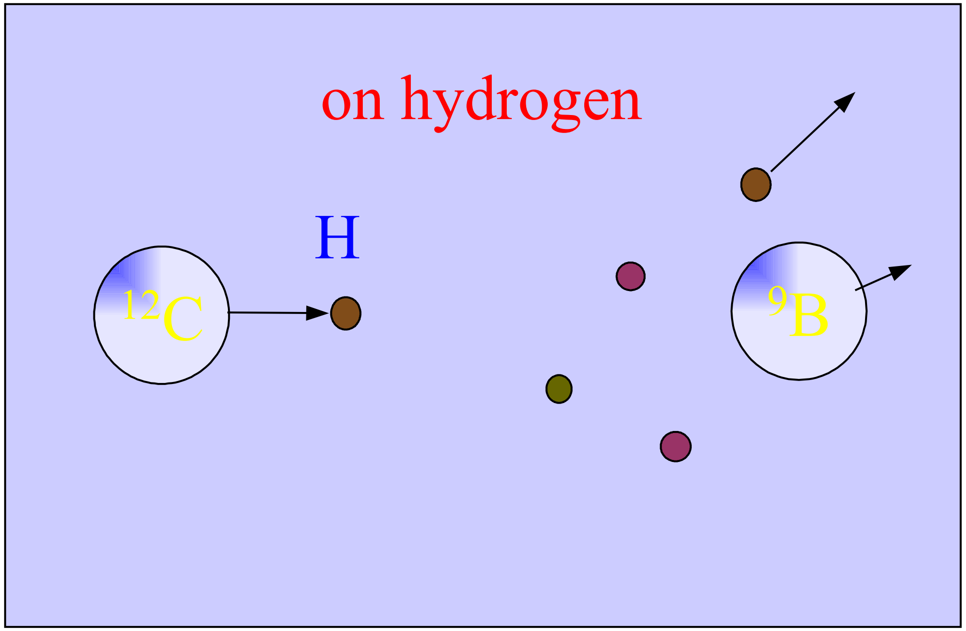
Fermi break-up model is used to simulate decays of highly excited ligh nuclei up to ^{16}O, all fragmentation channels are included
(this model works stable and has been validated before)

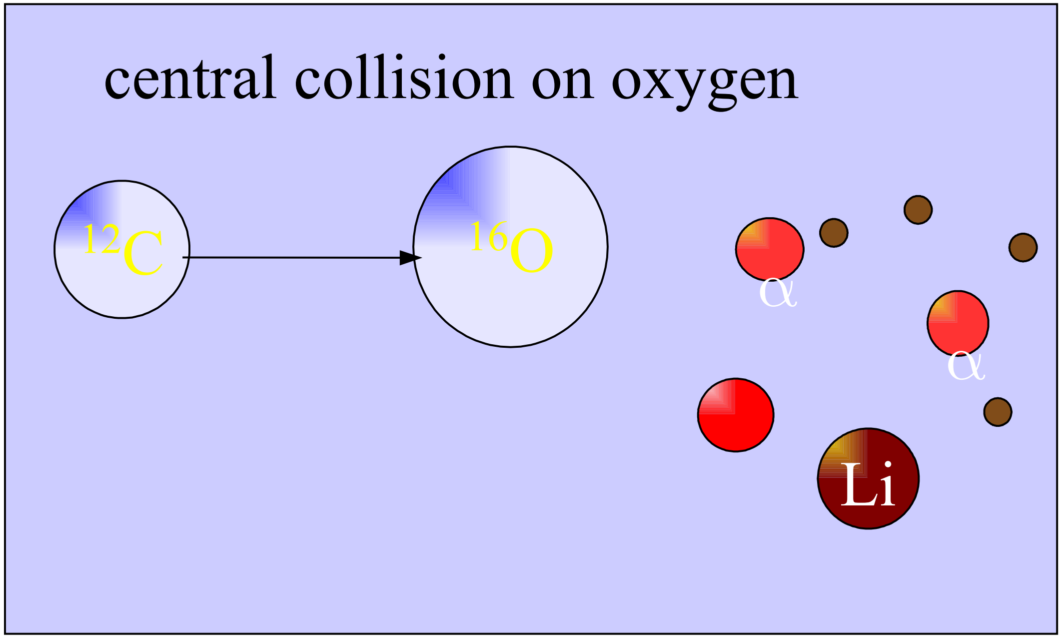
These models are verified by numerous experiments. They are used in nuclear physics community for decades

3. MCHIT-based simulations of ion-beam therapy

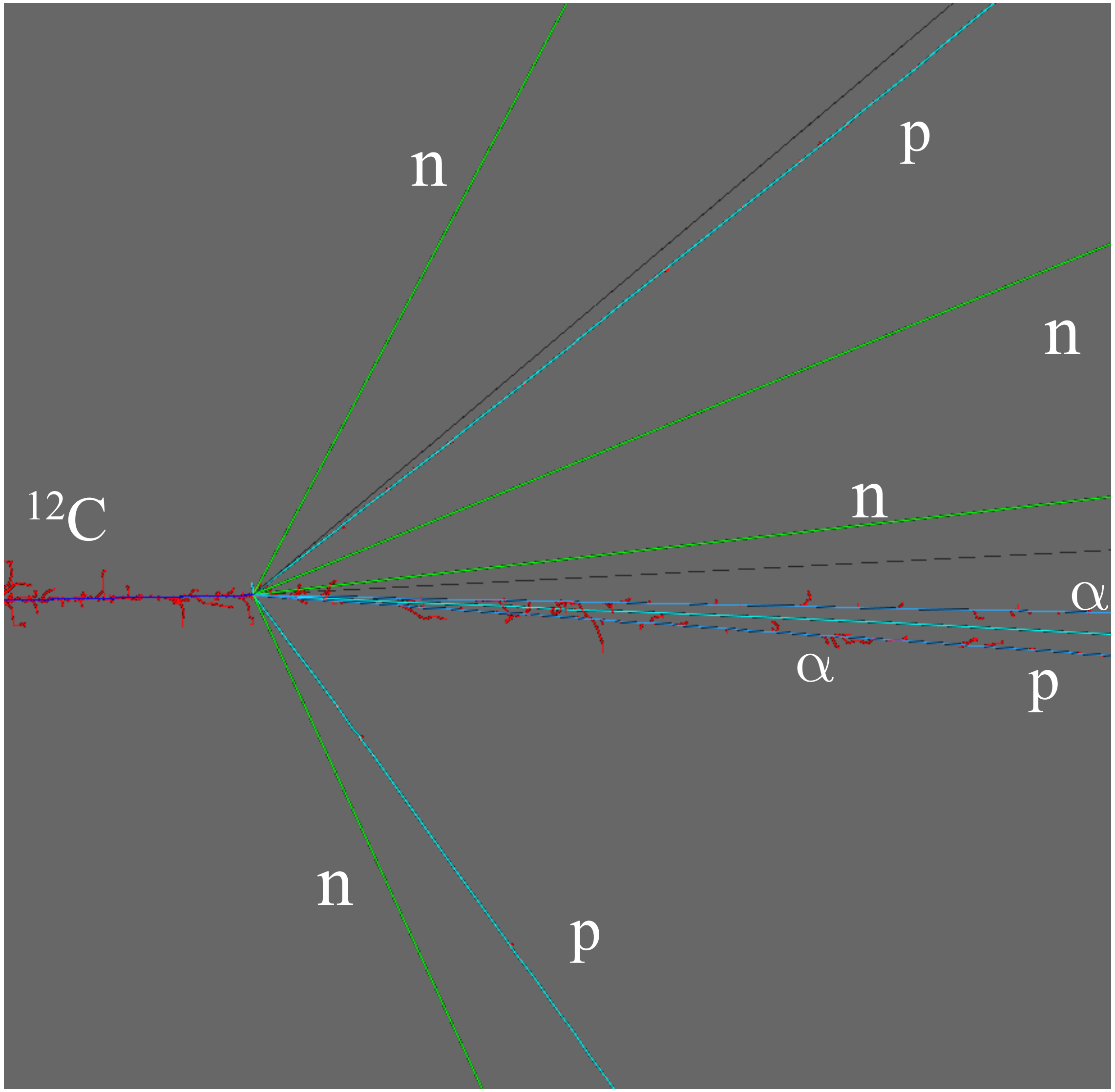
^{12}C break-up processes in water simulated with MCHIT





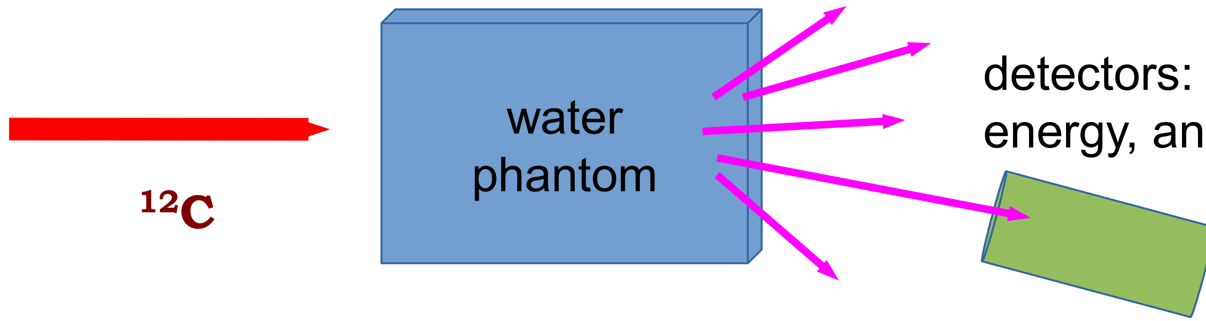


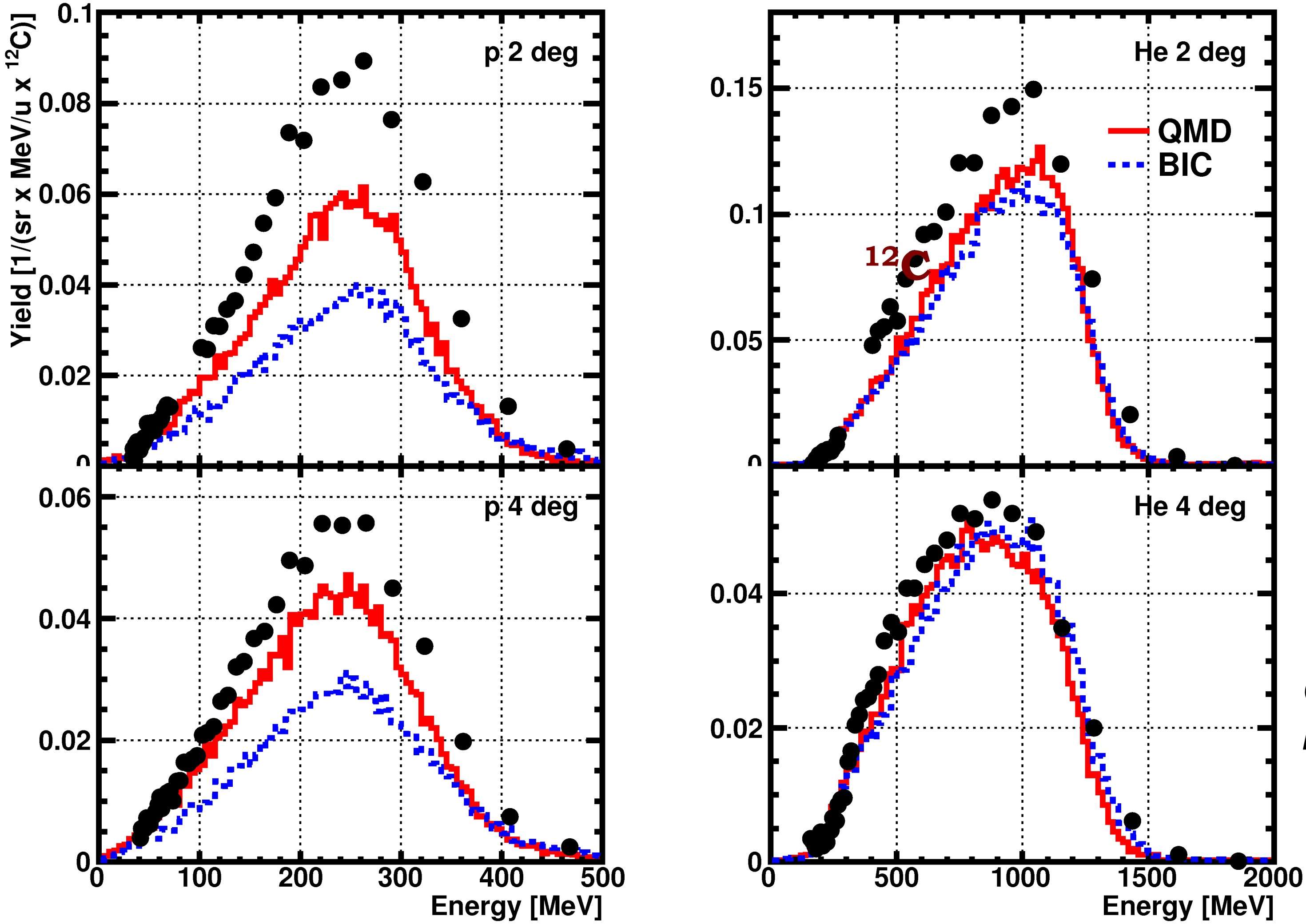
One ^{12}C break-up event simulated with MCHIT on macro scale



Models at work, BIC vs QMD: energy spectra

GSI experiment:



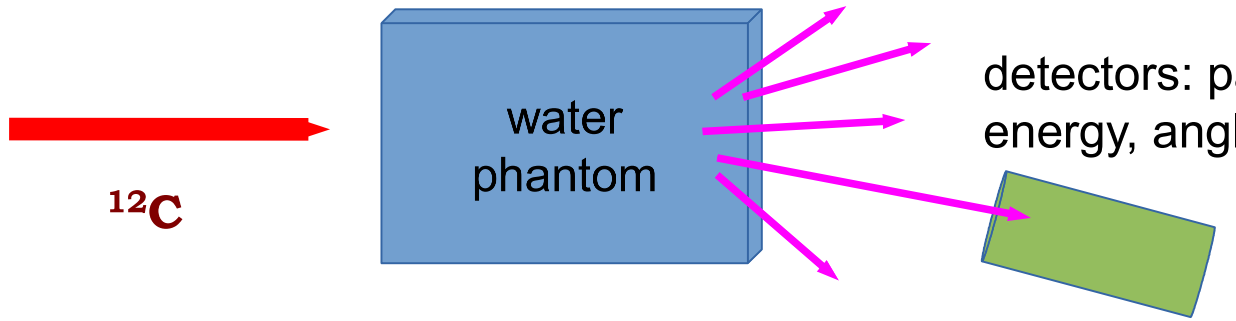


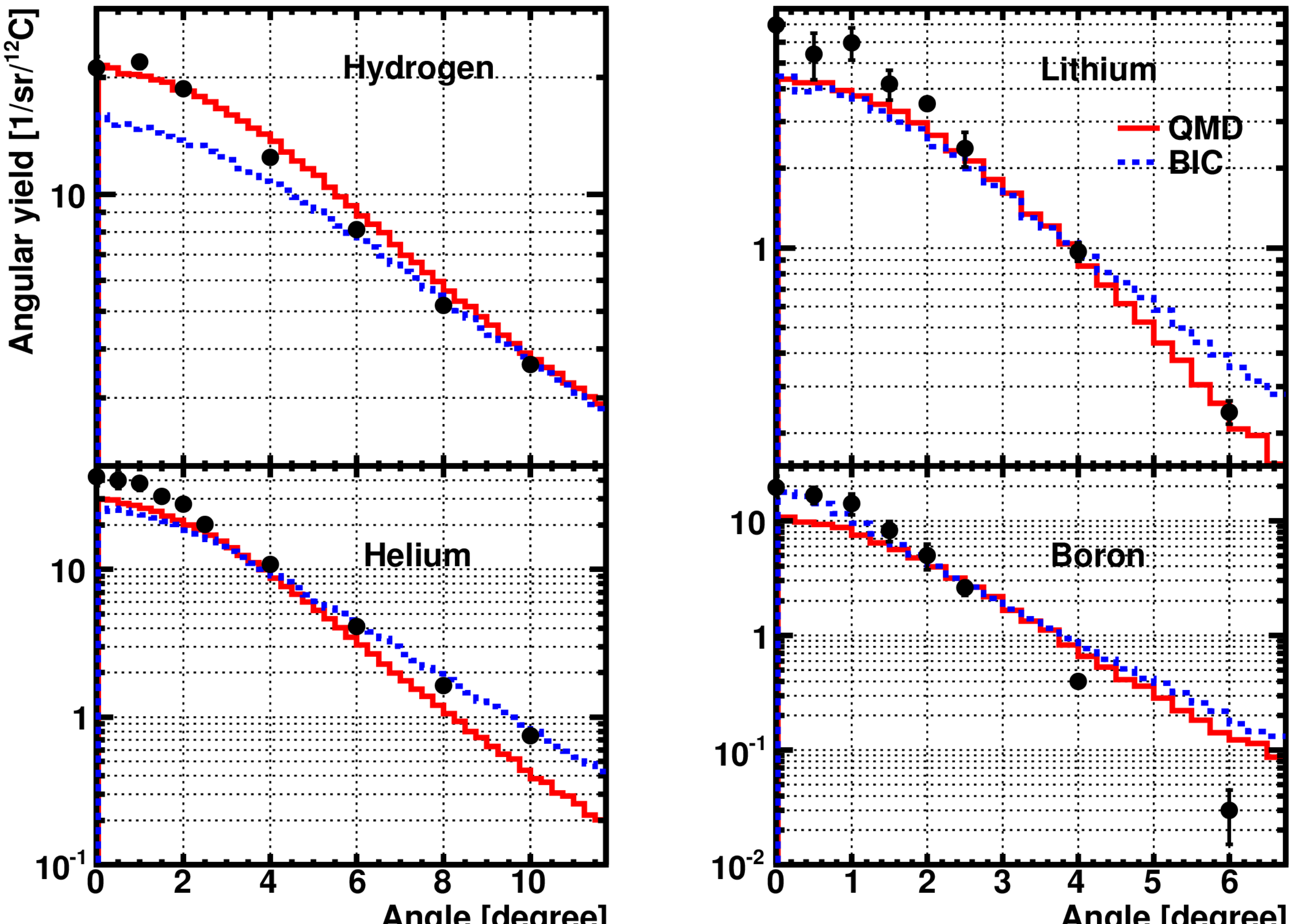
QMD is closer to data, but still not perfect
Max. deviations on level of 30%

GSI Data: E. Haetner et al., PMB 58, 8265 (2013)

Models at work, BIC vs QMD: angular distributions

GSI experiment:





QMD is better compared to BIC

GSI data: E. Haetner et al., PMB 58, 8265 (2013)

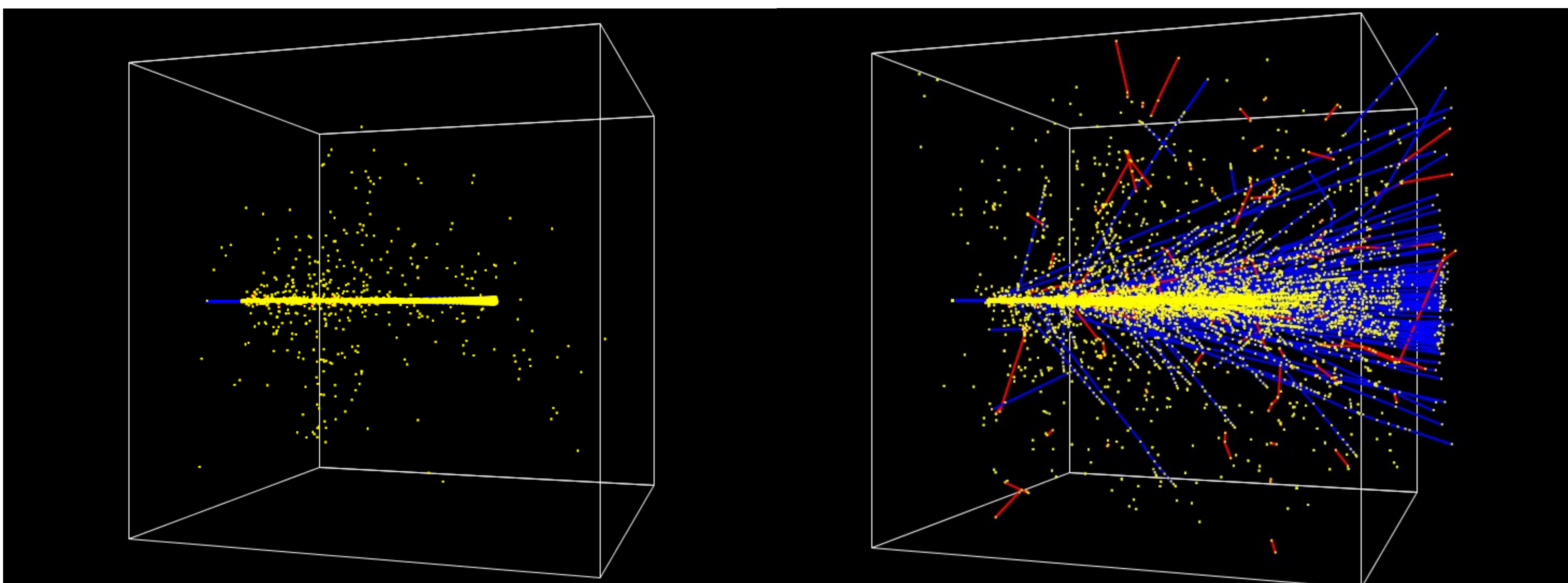
Importance of nuclear fragmentation reactions in carbon therapy

100 events of ^{12}C @ 330 AMeV in water cube $(30\ cm)^3$

fragments and protons in blue, electrons in red, yellow dots are interaction points

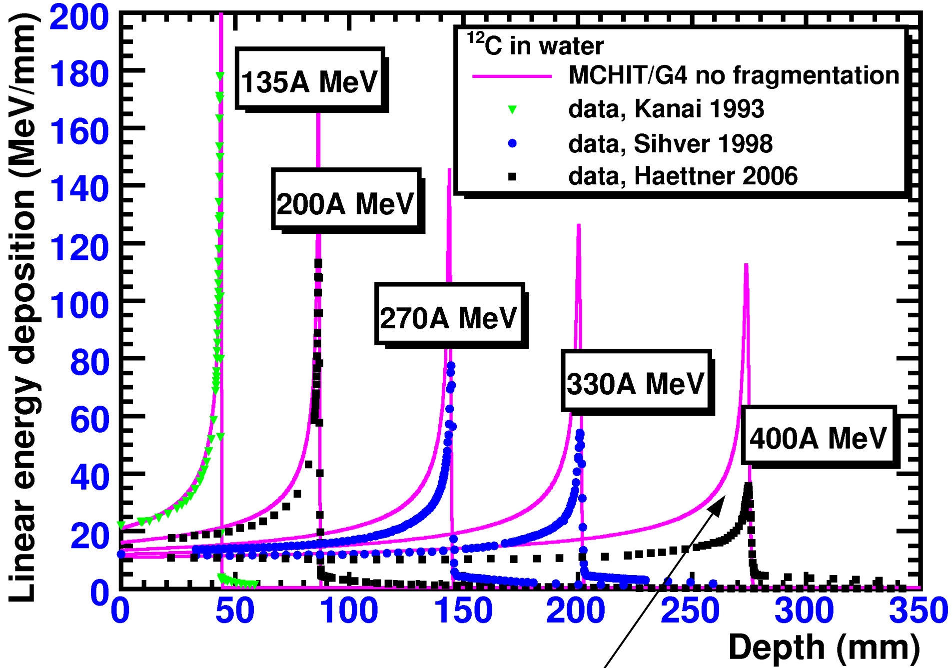
Electromagnetic interactions only

EM interactions + hadronic elastic scattering and fragmentation reactions



Precise dose calculations have to account for fragmentation reactions, otherwise...

without nuclear fragmentation

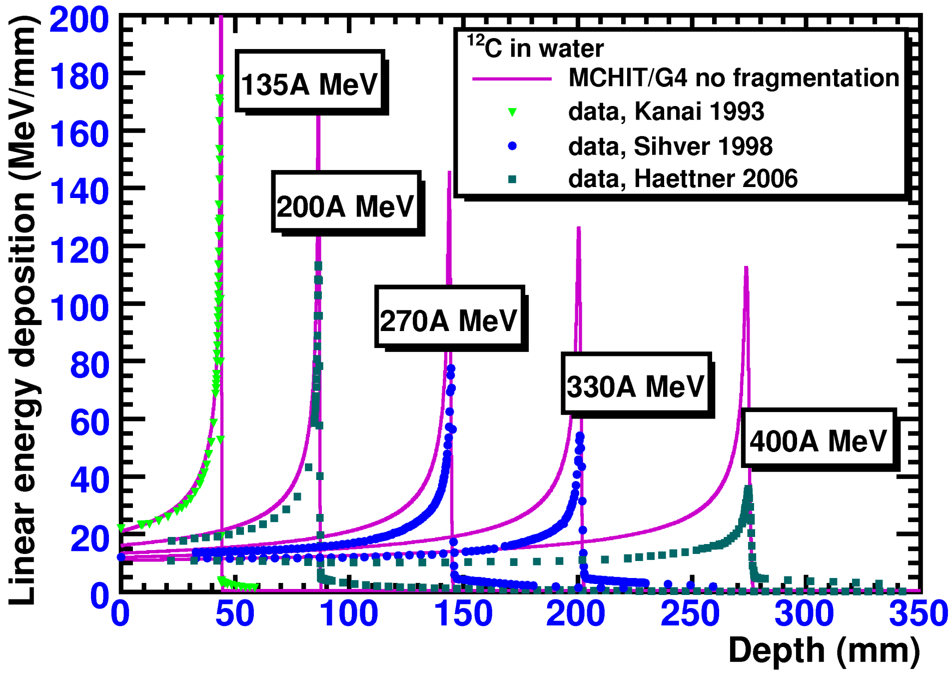


the dose would be largely overestimated at deep penetrations. The fragmentation of nuclei leads to the reduction of energy deposition on the way to the Bragg peak

$$Z^2=(Z_1+Z_2+...)^2>Z_1^2+Z_2^2+...$$

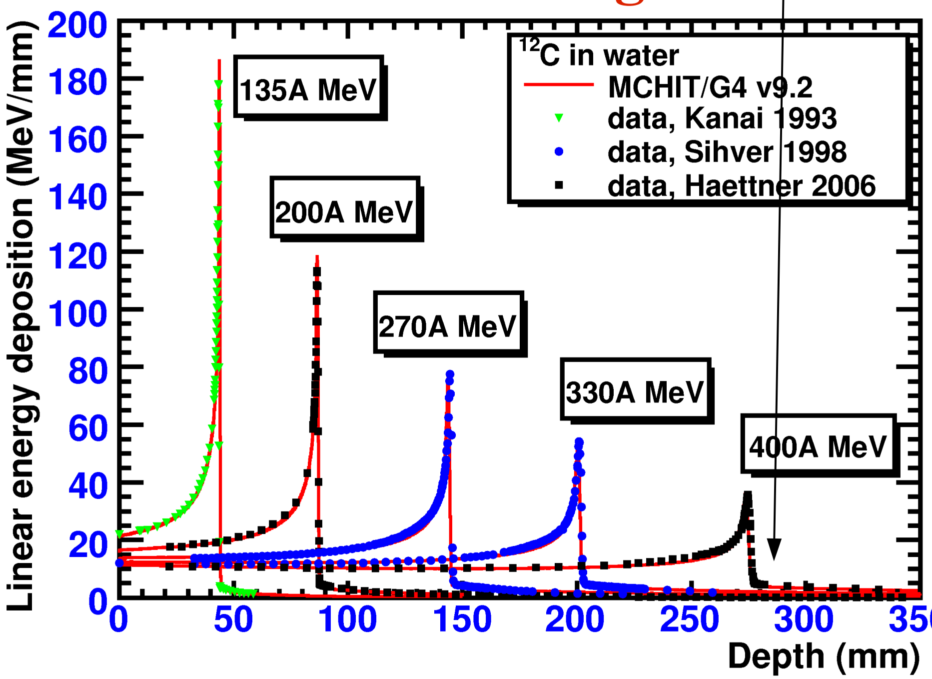
Precise dose calculations must account for fragmentation reactions!

without nuclear fragmentation



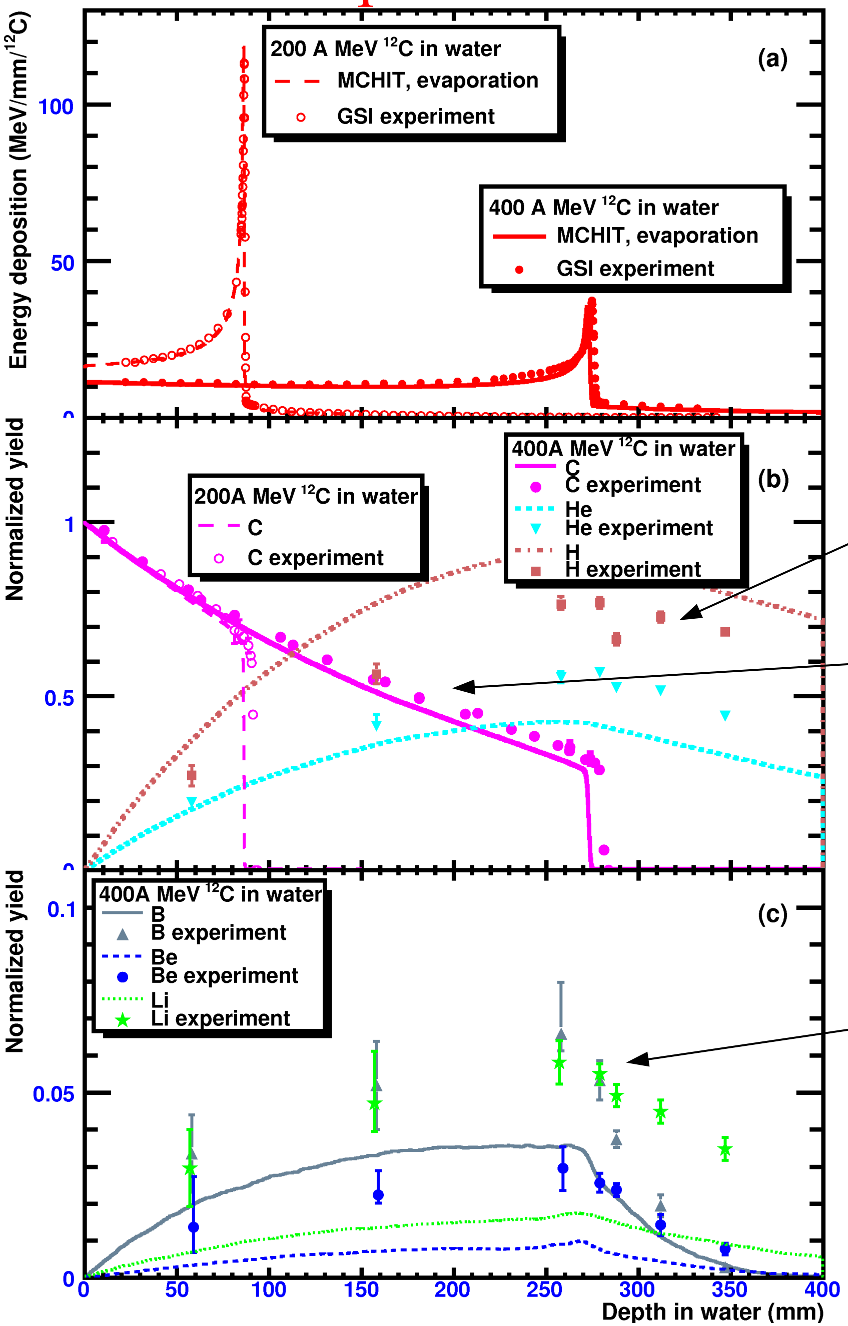
Dose tails beyond the Bragg peak, produced by the light secondary fragments (n, p, He,...), should be accurately accounted for in the treatment planning (~10% effect!).

with nuclear fragmentation



Secondary fragments: models at work

Evaporation



Calculations with the Wilson abrasion model: Bragg peaks well reproduced

Yields of protons are overestimated

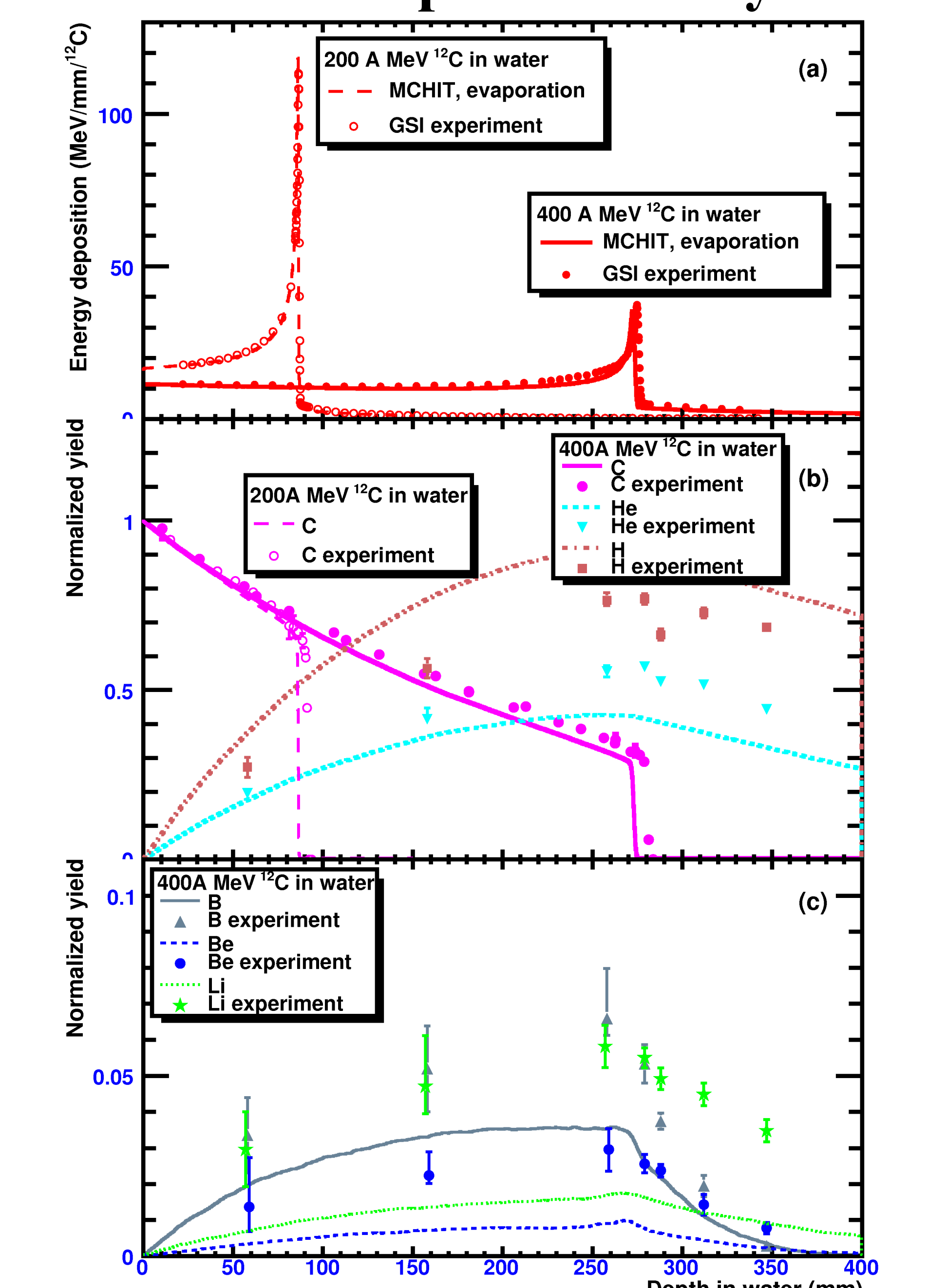
30 to 70% of beam ions are destroyed in nuclear fragmentation reactions

Yields of Li, Be and B are too low

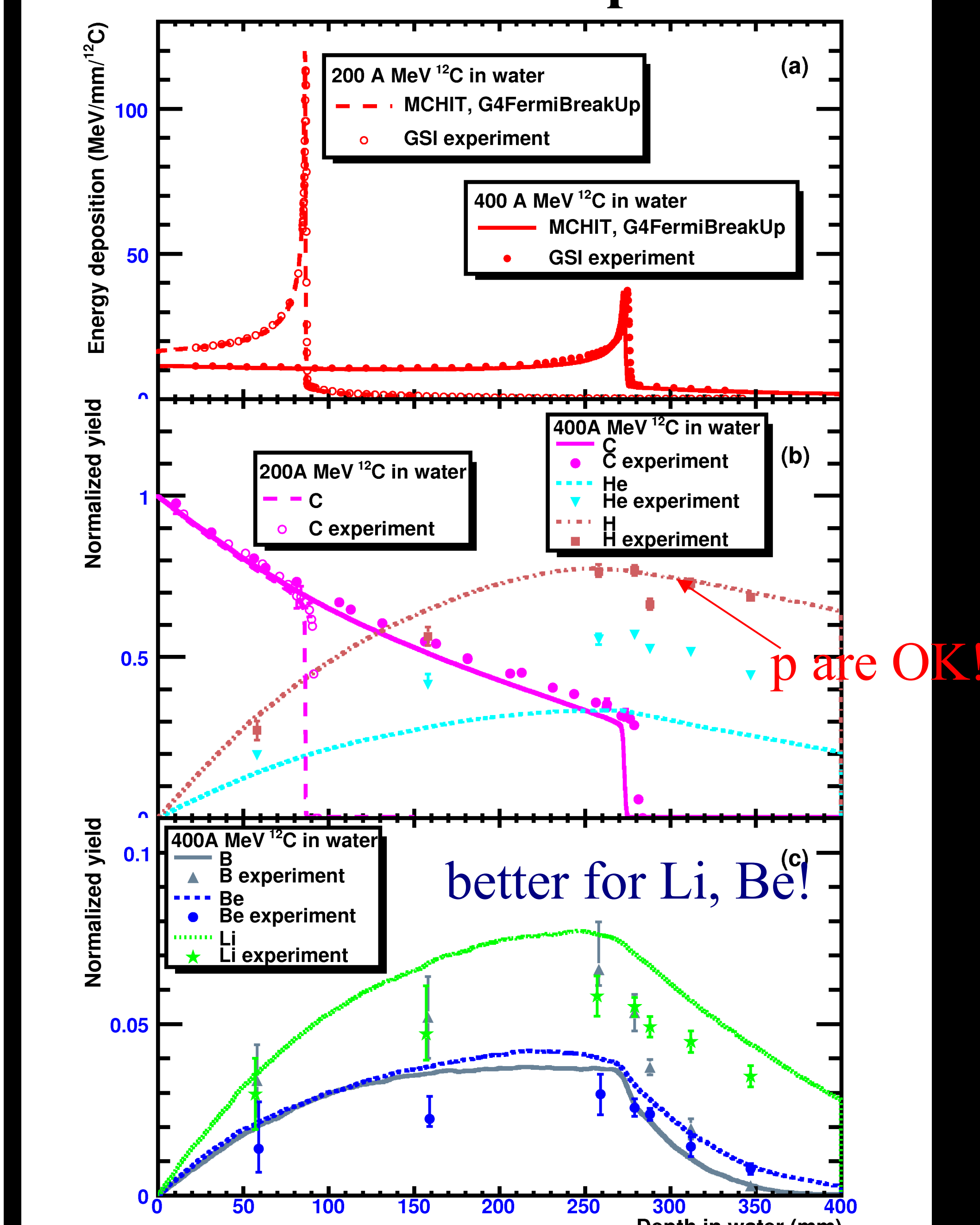
data: ***E. Haettner et al., Rad. Prot. Dosim. 122 (2006)48*****, within θ<10º acceptance**

Secondary fragments: models at work

Evaporation only



Fermi break-up added

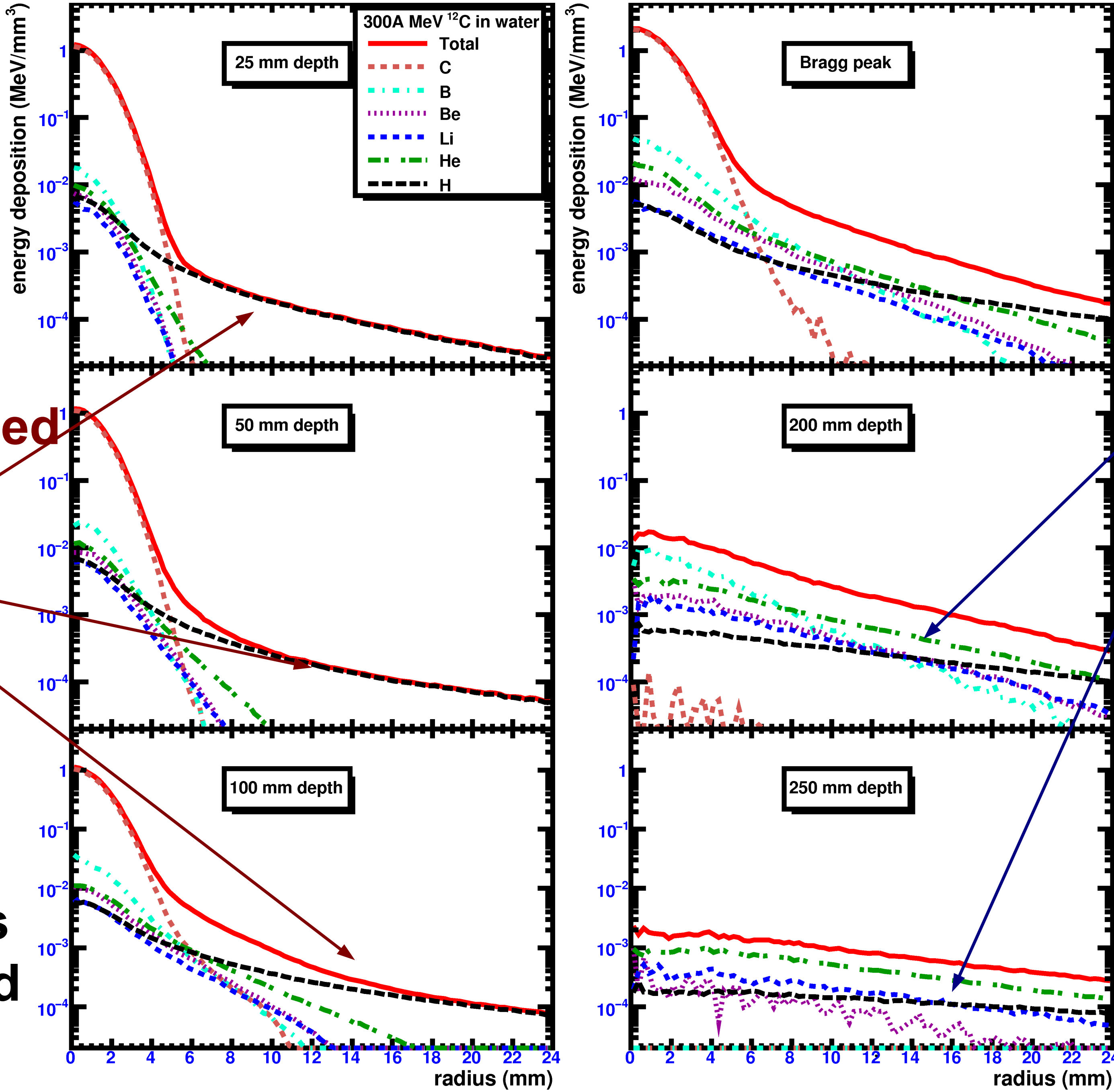


et al., Rad. Prot. Dosim. 122 (2006)48, within θ<10° acceptance

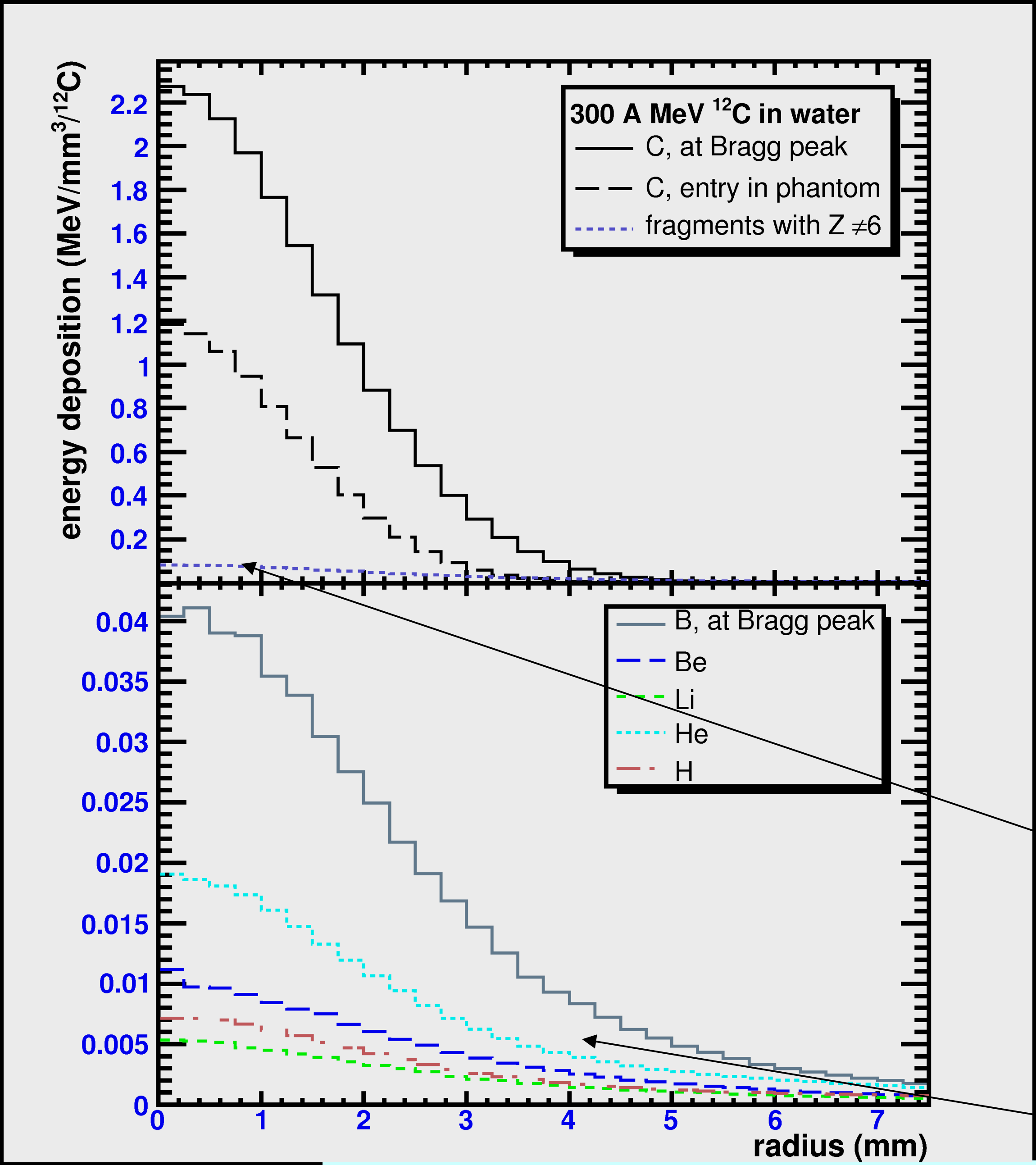
Radial distributions of dose for different depths

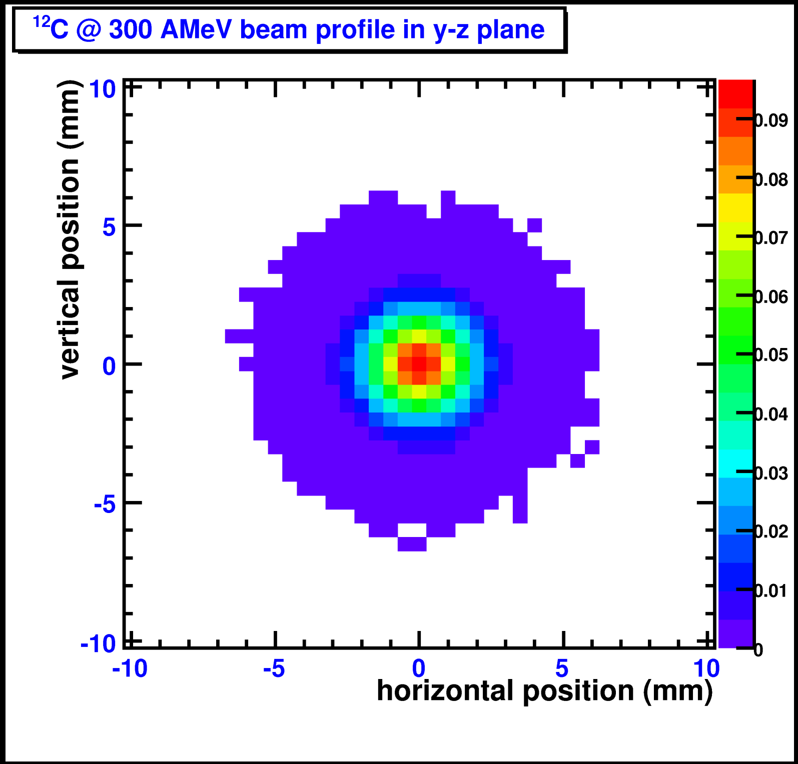
^{12}C beam is surrounded by protons

Recoil protons created in neutron interactions are included



Mostly He fragments after the peak


300 A MeV ¹²C in water
C, at Bragg peak
C, entry in phantom
fragments with Z ≠6
B, at Bragg peak
Be
Li
He
H
energy deposition (MeV/mm³/¹²C)
radius (mm)


¹²C @ 300 AMeV beam profile in y-z plane
vertical position (mm)
horizontal position (mm)

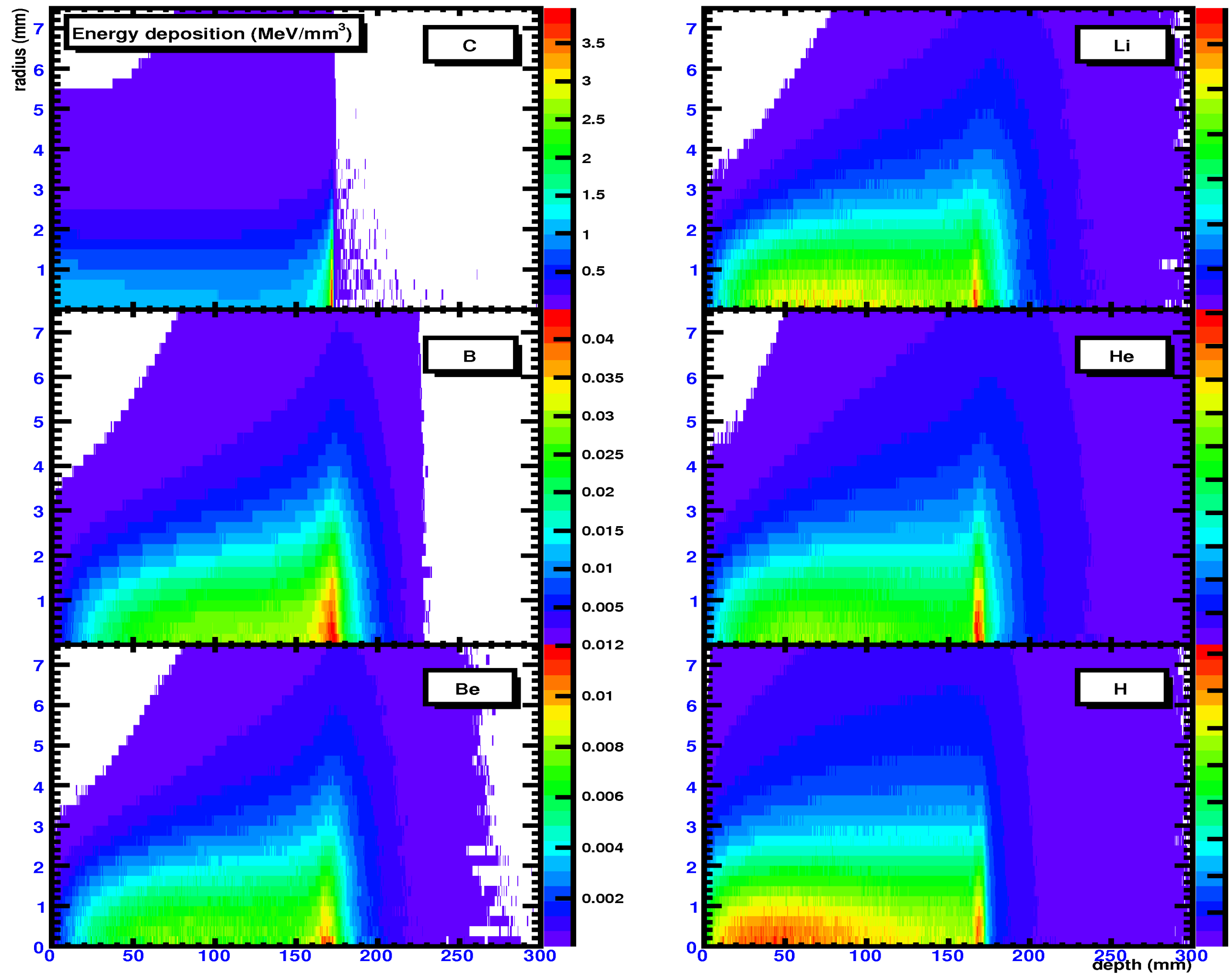
MCHIT can be used for calculating 3D dose distributions for specific fragments

beam of 3 mm FWHM

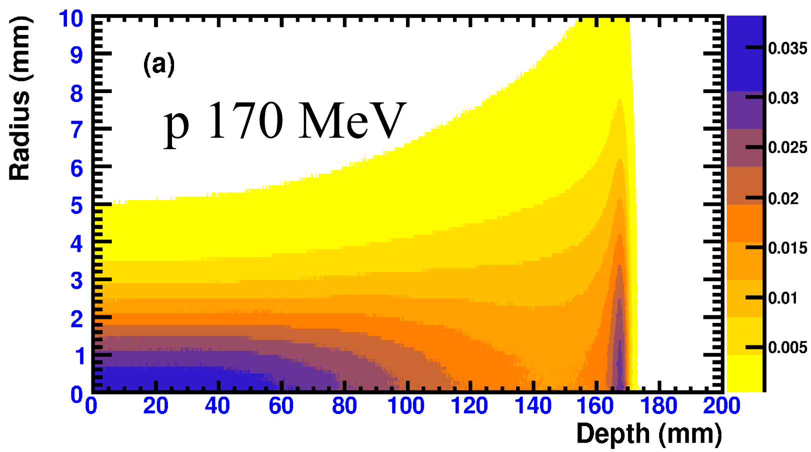
MCHIT results for volume energy deposition (in MeV/mm^3) per beam particle

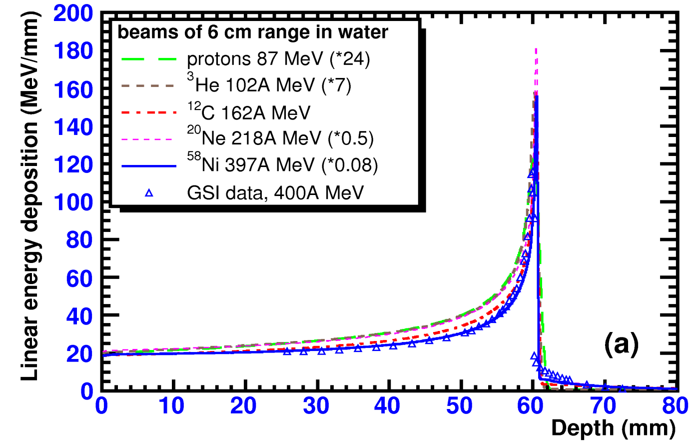
Note different dose scales for each fragment

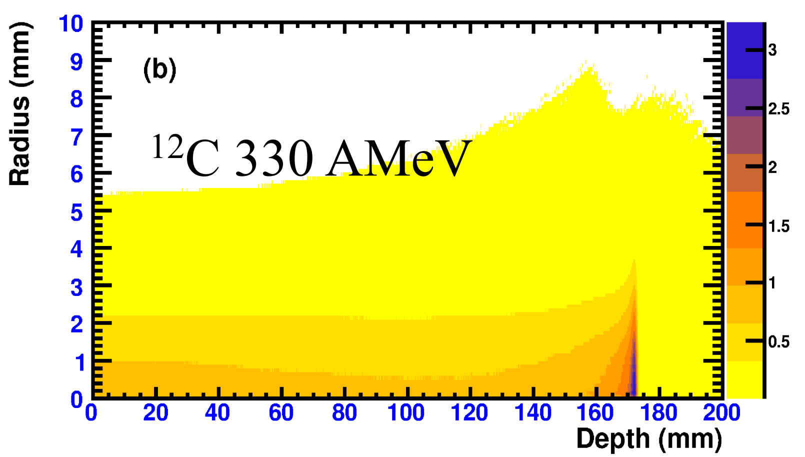
300 A MeV ^{12}C in water

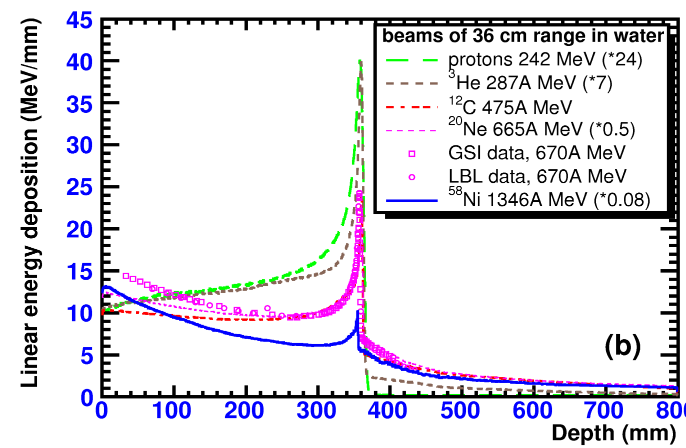


Dose distributions for different beams: p, ^{3}He, C, Ne. Ni









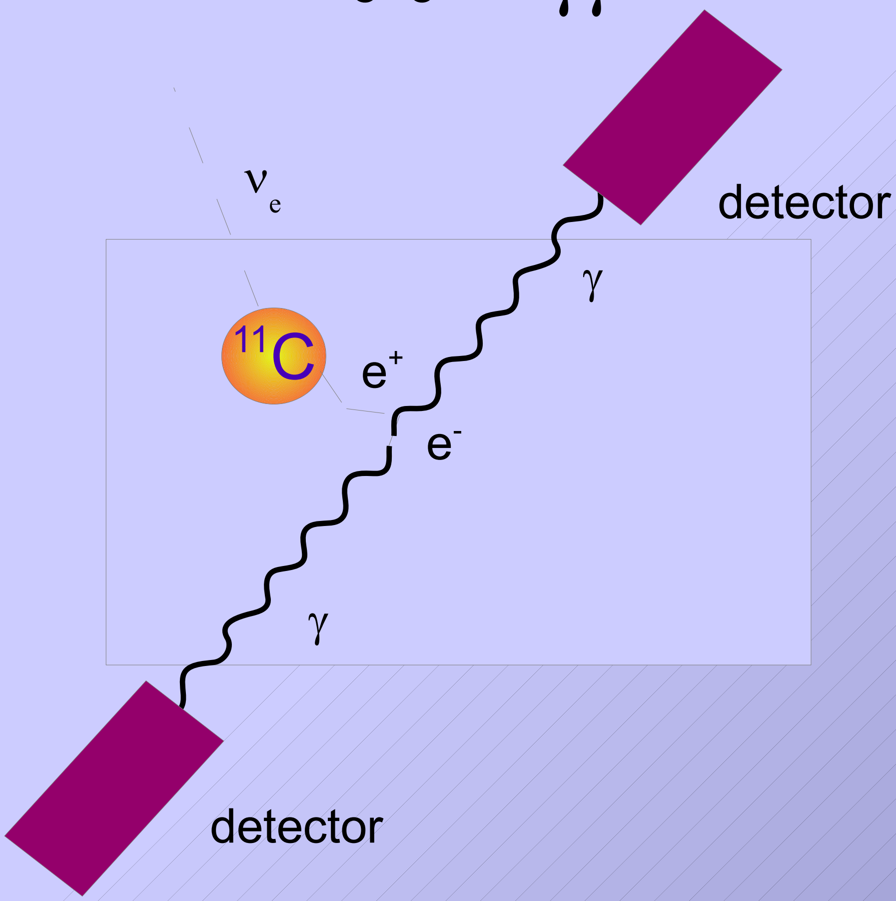
Ions heavier than Ne are not suitable for irradiation of deeply-sitting tumors, they are destroyed on the way!

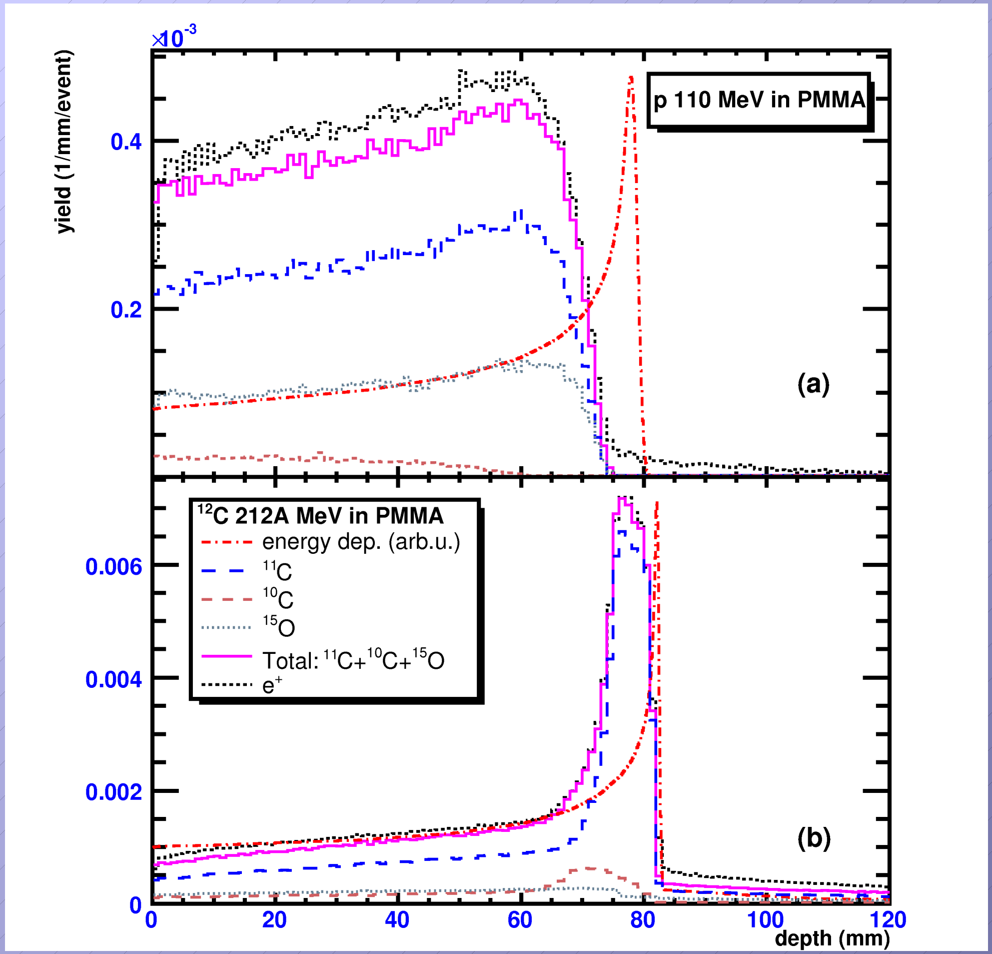
I. Pshenichnov, I. Mishustin, W. Greiner, *Compartive study of depth-dose distributions for beams of light and heavy nuclei in tissue-like media,* Nucl. Inst. Meth. B **266** (2008) 1094

Dose distribution monitoring with Positron-Emision Tomography (PET)

Positron-emitting nuclei ^{10}C, ^{11}C are produced in ^{12}C fragmentation reactions. Than positrons annihilate on nearby electrons:

$e^+e^- \rightarrow \gamma\gamma$





I. Pshenichnov, A. Larionov, I. Mishustin, W. Greiner, Phys. Med. Biol. **52** (2007) 7295

I. Pshenichnov, I. Mishustin, W. Greiner, Phys. Med. Biol. **51** (2006) 6099

PET monitoring of delivered dose


GSI, Darmstadt

in situ →

- Dose delivered to patient
- Measured distribution of positron-emitting nuclei

in silico →

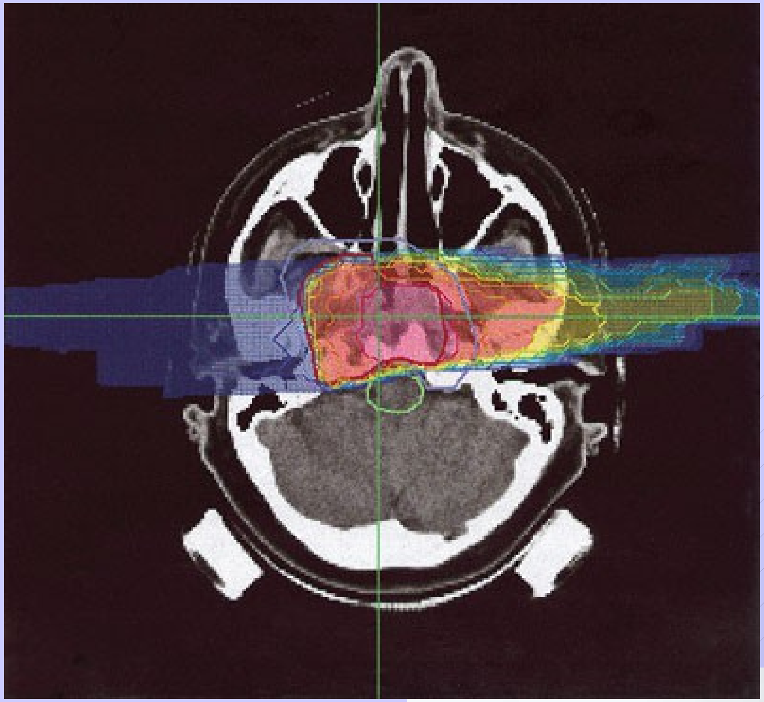
- Calculated dose for this patient

Calculated distribution of positron-emitting nuclei

Comparison

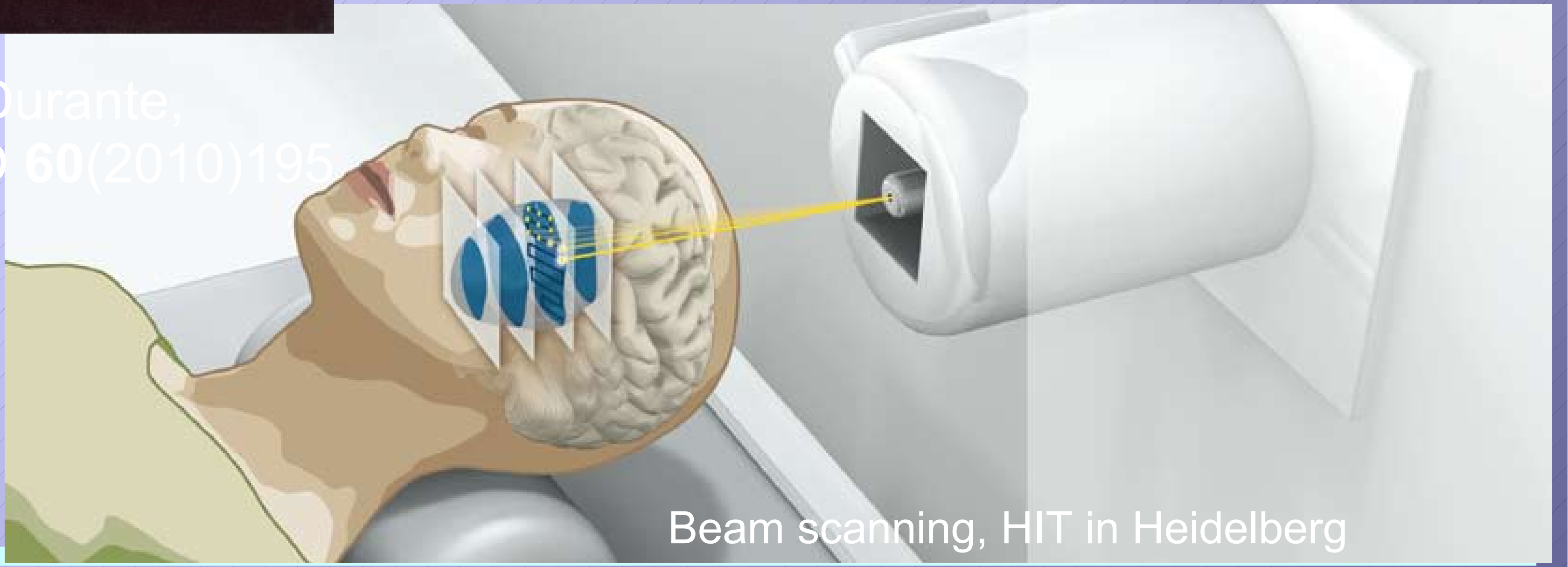
Conclusion on delivered dose

Thorough treatment planning and precise dose delivery are crucial for success



- Full 3D and 4D (with accounting for organ movement during irradiation) treatment planning;
- Thin (pencil-like, ~ 3 mm FWHM) beams applied from different directions;
- Active beam scanning technique: fast variation of beam energy and direction;
- Optimization of biological dose in tumor.

M.Krämer, M.Durante, Eur. Phys. J. D **60**(2010)195



Beam scanning, HIT in Heidelberg

Conclusions

- MCHIT can be used as a complementary software for simulations beyond the capabilities of traditional treatment planning systems to deal with:
  - – broad spectrum of incident particles and their energies;
  - – not only mean characteristics, but also their statistical fluctuations;
  - --various targets from single cells to tissue samples and realistic phantoms;
  - --benchmarking Monte Carlo simulations against of treatment planning software based on other methods (e.g. tabulated exp. data);

- Existing physical models allow quantitative description of energy deposition in tissue-like media;

- The important next step is to extend calculations on the micro-meter scales to evaluate the biological dose.

Main conclusion:

Further progress in the field of particle therapy is only possible via cooperation of physicists, biologists and medical doctors!

Thank you for the attention!