Il ruolo del Monte Carlo nell'Adroterapia

Alghero 1 Giugno 2009

G. Cuttone

INFN LNS

Hadrontherapy Motivitation

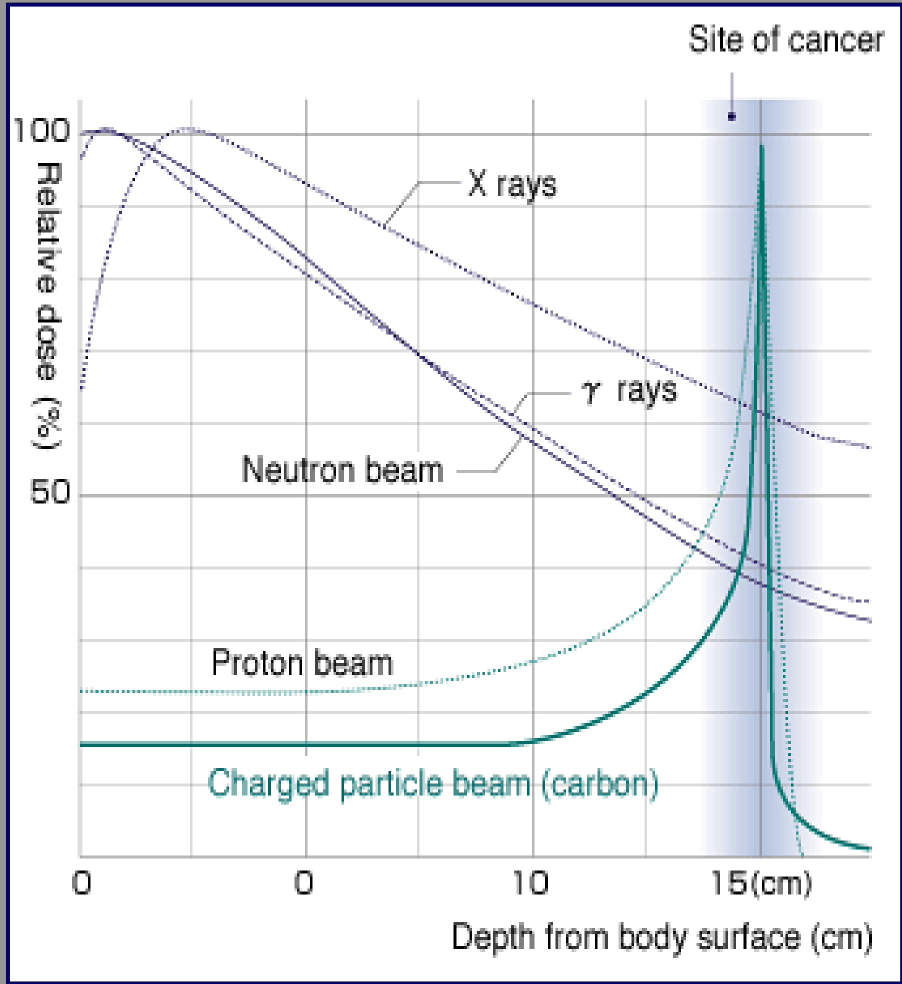
Light ions advantages in radiation treatments :

•Better Spatial selectivity in dose deposition: **Bragg Peak**

• Reduced lateral and longitudinal diffusion

• High Conformal dose deposition

• High Biological effectiveness



Treatment of highly radiation resistent tumours, sparing surrounding OAR

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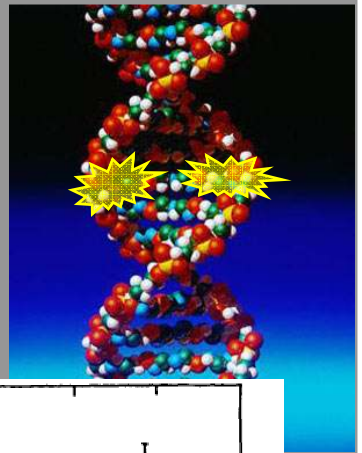
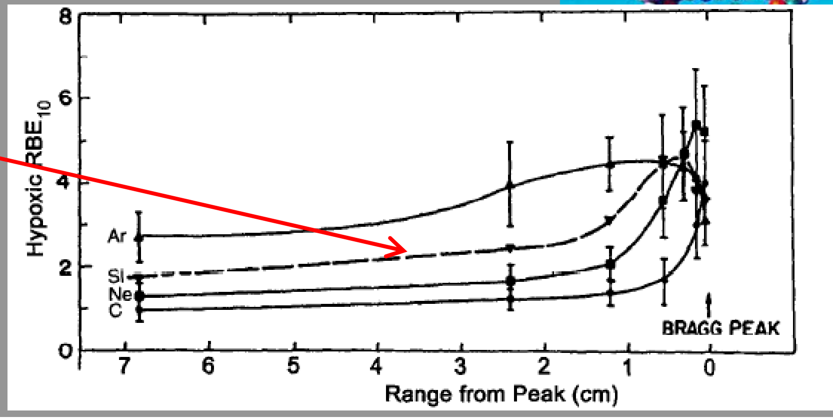
CARBON IONS ADVANTAGE



- Lower lateral and longitudinal diffusion vs. proton

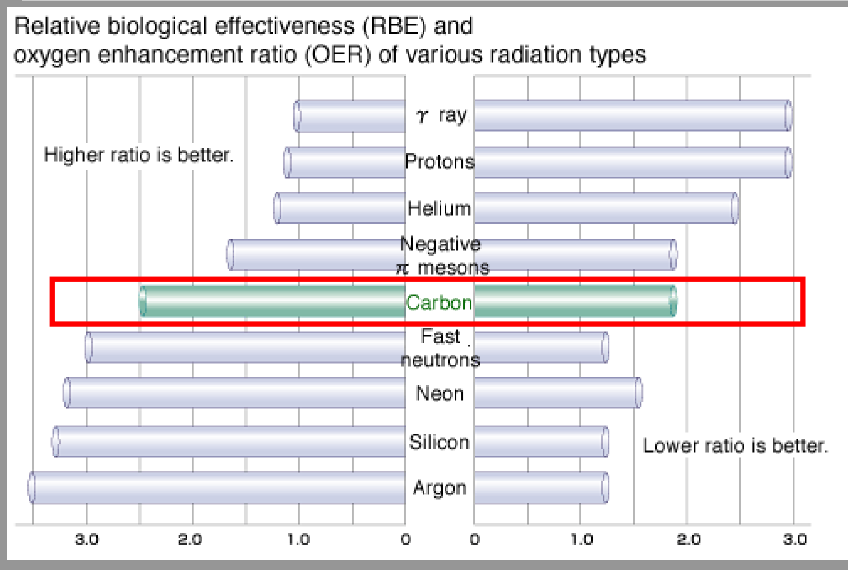
  ➡ More precise energy deposition

- Optimal RBE profile vs penetration depth position.



- Online PET for depth deposition monitoring

- Good Compromise between RBE and OER.



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DISADVANTAGE OF CARBON IONS

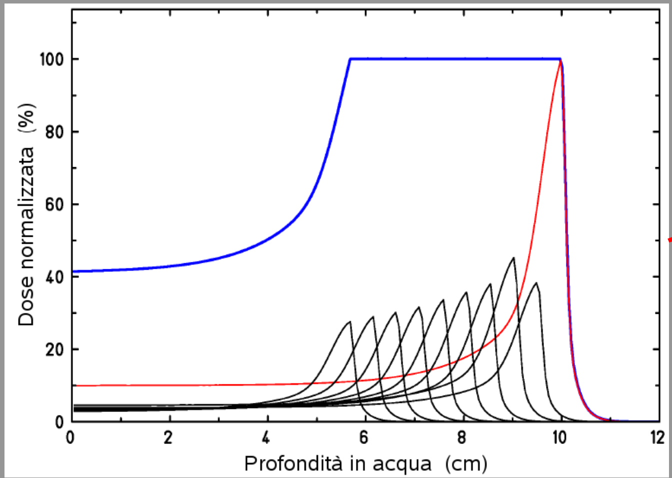
Nuclear Fragmentation of ^{12}C beam in the interaction processes with:

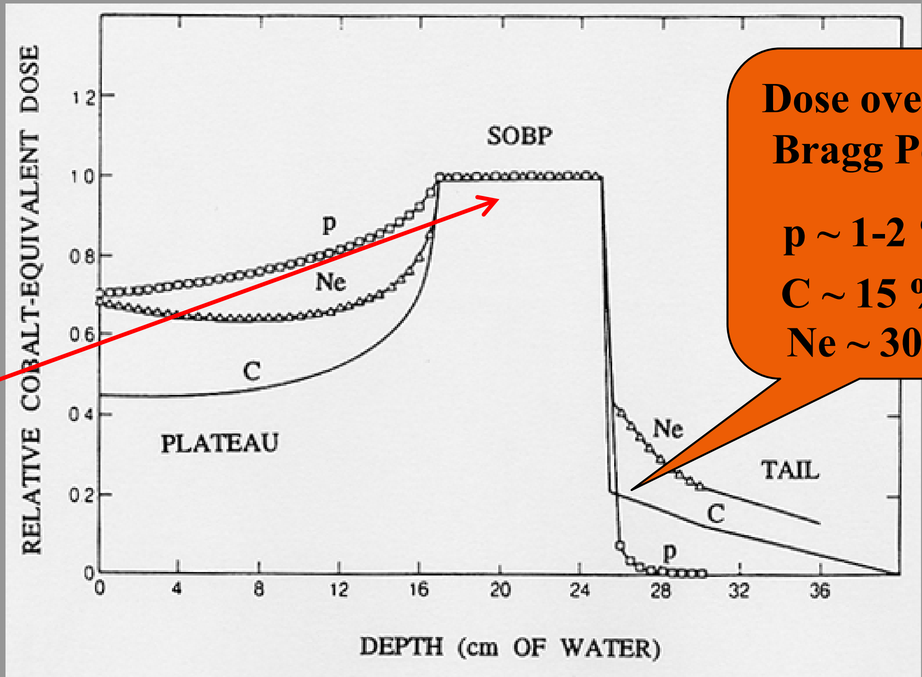
- *energy degraders,*
- *biological tissues*

Further problem ⟶ different biological effectiveness of the fragments

Mitigation and attenuation of the primary beam

Production of fragments with higher range vs primary ions





MAIN CHARACTERISTICS OF A MONTE CARLO APPLICATION FOR HADRONTHERAPY:

- Simple geometrical modules and possibility to switch between different configurations
- Calculation of physical quantities of interest as depth dose and lateral dose distributions, ranges and stopping powers in various materials;
- Commissioning of a Treatment Planning System (TPS) for clinical proton beams;
- Possibility to reconstruct physical dose and LET distributions in any material;
- Optimization of the physical dose distribution using a radiobiological model for RBE calculation;
- Simplicity in the activation of the physics models (both electromagnetic as well as hadronic ones);
- Optimization of setup for Radiobiological experiments.

... so we need to perform computer calculations with "reliable"particle and heavy ion transport codes

- 3-D Monte Carlo Codes
  - ➢ Geant4
    - ✓ The Geant Collaboration
  - ➢ HETC
    - ✓ NASA Transport Consortium
  - ➢ FLUKA
    - ✓ The Fluka Collaboration
  - ➢ Shield-HIT
    - ✓ Sobolevsky et al.
  - ➢ PHITS
    - ✓ RIST, JAEA, Chalmers and GSI
  - ➢ MCNPX
    - ➢ Los Alamos National Lab.

- 1-D deterministic codes
  - ➢ HZTREN
    - ✓ NASA Langley Research Center
  - ➢ HIBRAC
    - ✓ Chalmers
    - ….

BUT they have to be validated…

Then we have to know nuclear reaction models!!

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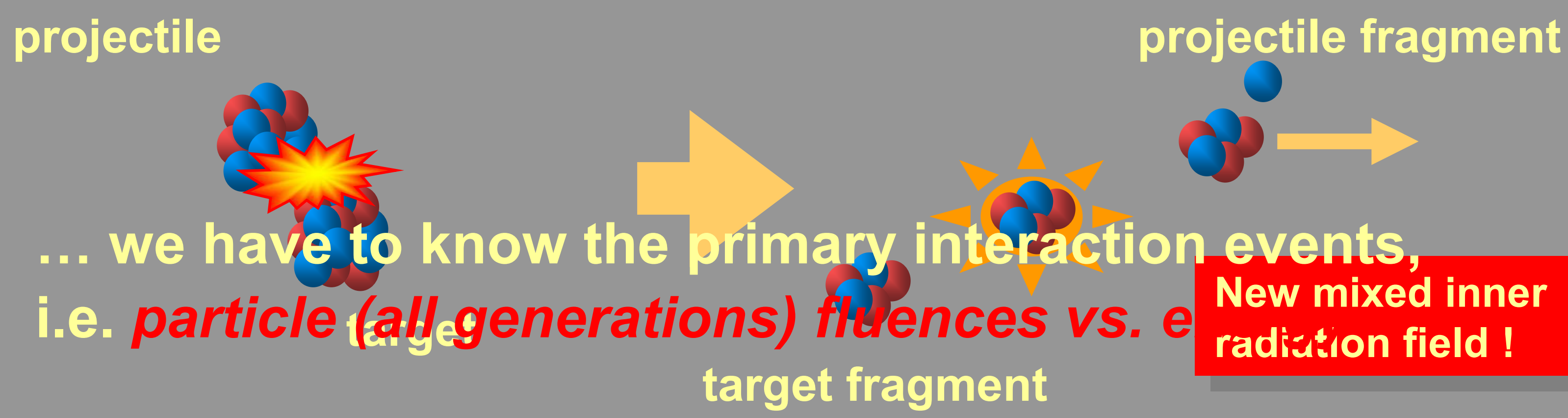
Nuclear fragmentation process

Outer radiation fields



… we have to know the primary interaction events,
i.e. *particle (all generations) fluences vs. e*

New mixed inner radiation field !

Interaction of the radiation with the spacecraft hulls, the body...

Target Fragments	*Projectile fragments*
… lower charge than target	… lower charge than primaries
… high LET	… mixed LET
… short ranges	… long ranges

First of all, we need to know the reaction and fragmentation cross sections and yields after shielding !!

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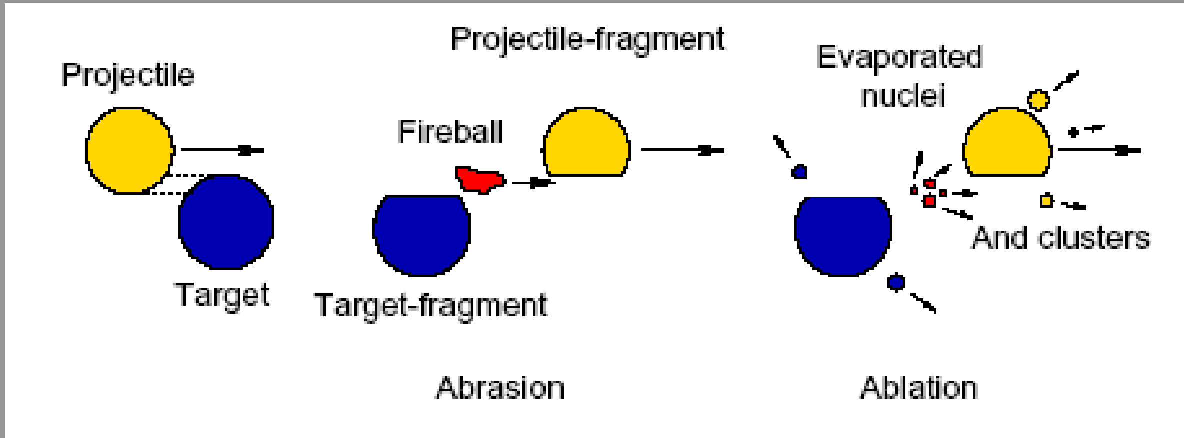
Heavy ion fragmentation



- The HZE particles of CGR produce secondary particles both in human body, and in needed shielding materials
- Carbon ions in radiation therapy undergo fragmentations inside the patient body

Change in the beam quality

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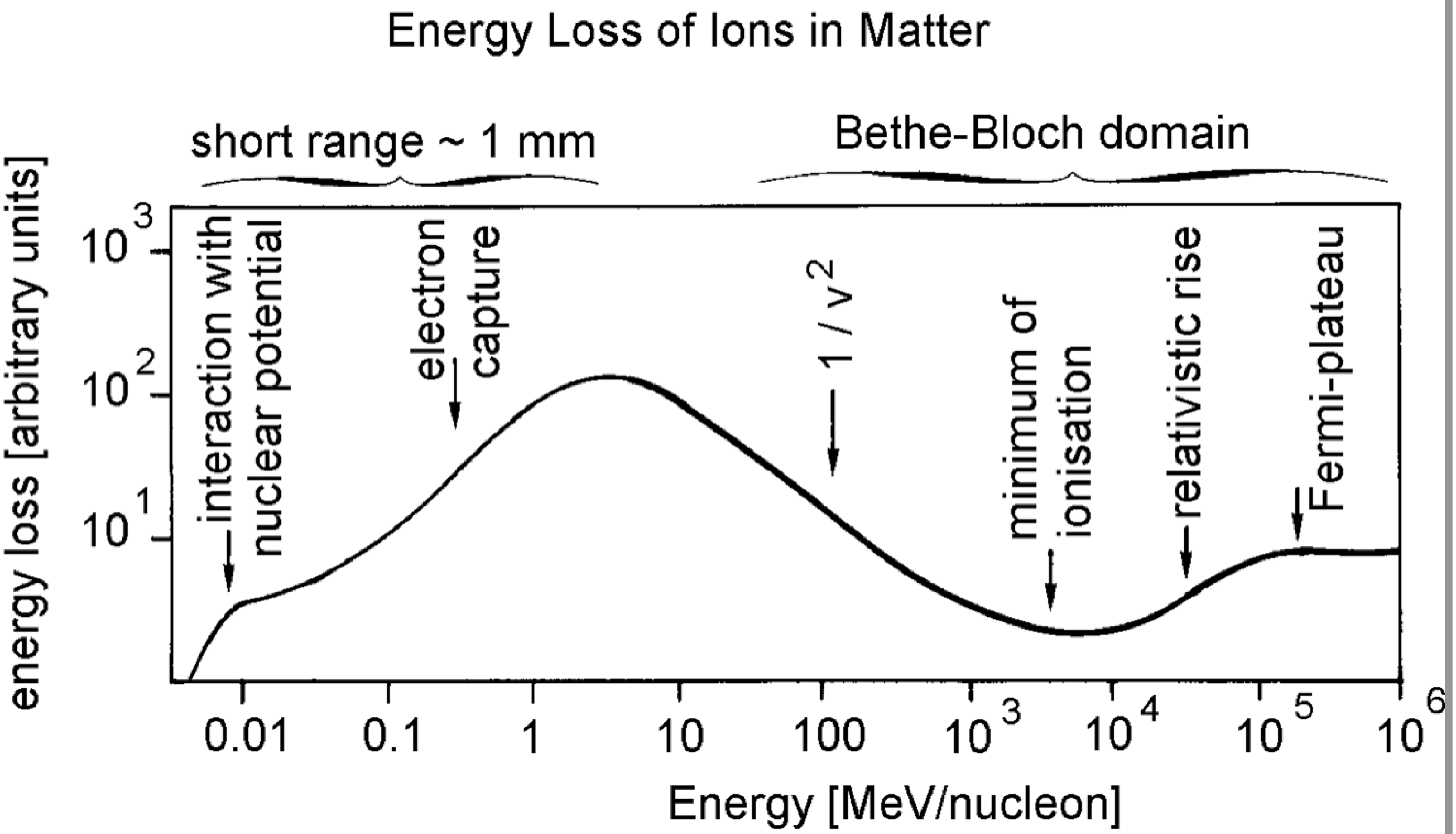
Energy loss of charged particles



Energy loss of ions in matter as a function of their energy

Cross Sections

P + T → F + X

- ## Total reaction

  - $\sigma_{tot} = \sigma_{reac} + \sigma_{el}$

- The probability, P(x), for a heavy ion to undergo a nuclear interaction in a thickness in a given target material T is given by

$P(x)=1-\exp(-N_A \sigma_{reac} x \rho_{target}/A_{target})$

σ_{reac} must be known with a great accuracy !!

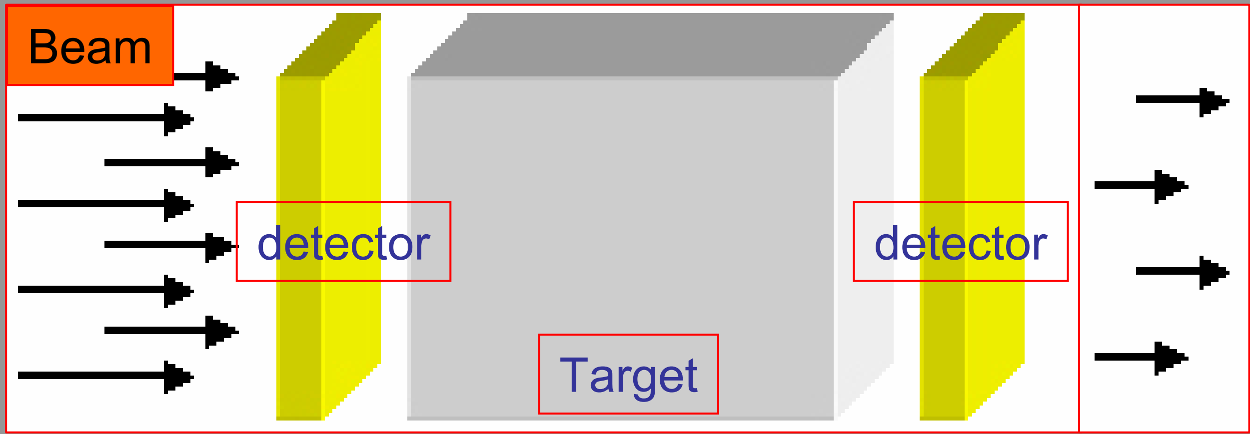
Cross Sections

P + T ⟶ F + X

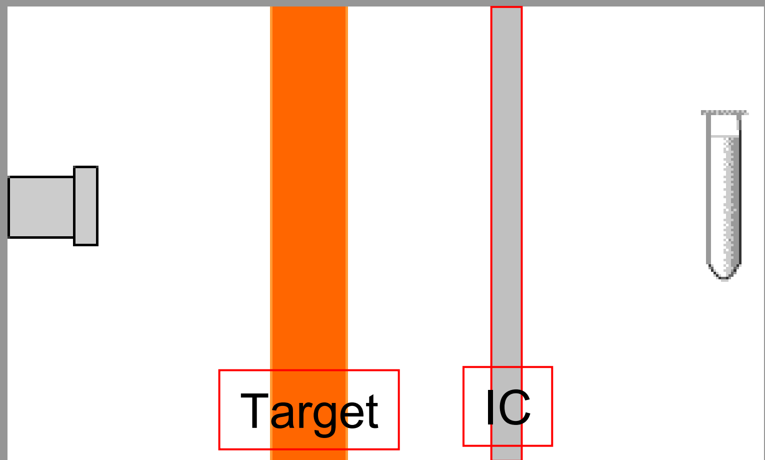
- **Inclusive**
  - $\sigma_{reac}=\sigma_{reac}(Z_{proj},A_{proj},E_{proj},Z_{targ},A_{targ})$
  - When no distinction is made as how the fragment "F" is produced, e.g. as to what comprises "X"
  - Includes all possible confgurations ("final states") of particles produced and/or emitted in the reactions
  - E.g. charge changing cross sections
- **Exclusive**
  - When there are distinctions made as how the fragment "F" is produced, e.g. as to what comprises "X"
- **Semi-inclusive**
  - When some but not all components ("final states") of "X" are measured

Experimental configuration for mixed radiation field studies and shielding optimization

Physics

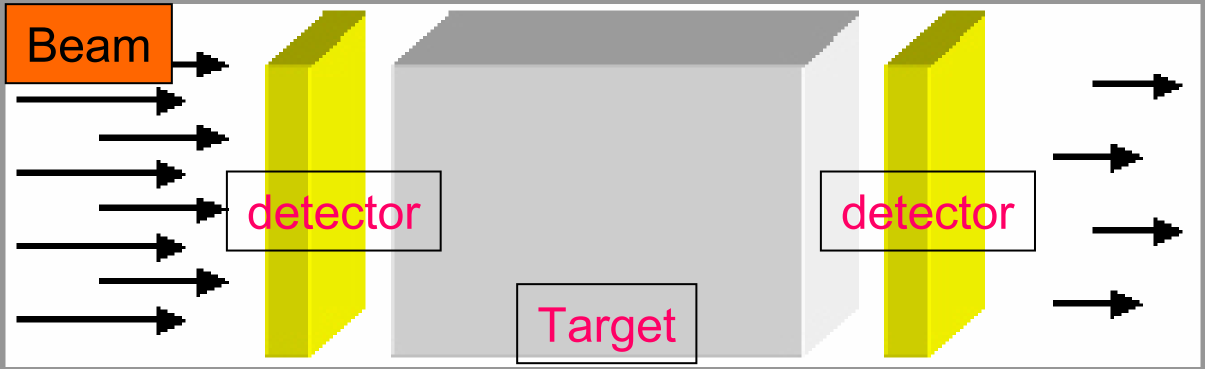


Radiobiology



Thick and thin targets

Physics



Thin target
=
cross section measurements

$$\sigma_{\text{tot}} = \frac{A_T \ln(N_{\text{in}}/N_{\text{out}})}{\rho t N_{\text{Av}}}$$

$$\sigma(Z_i, Z_f) \simeq \frac{1}{Kt} \frac{N_f}{N_i}$$

Thick target
=
fluence measurements

$$D = 1.6 \sum_i L_i \phi_i$$

$$H = D\overline{Q} = D \times \frac{1}{D} \int Q(L) D(L) dL = \sum_i Q(L_i) L_i \phi_i$$

Monte Carlo Codes With Fragmentation

- **Several possibilities:**
  - GEANT4
  - SHIELD-HIT (Karolinska / Russian Acad. Of Sciences)
  - FLUKA (INFN/CERN)

Goal:

Accurate estimation of fragments produced at different energies and angles is important in order to evaluate the beam contamination.

The nucleus-nucleus interaction models should be checked and validated because responsible of the fragments yields!

MC Code used to simulate light ion fragmentation experiments for benchmarking

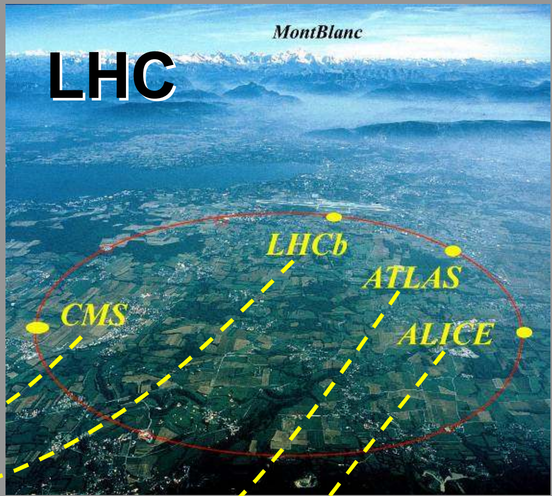
The Monte Carlo toolkit *Geant4*

Geant 4 ⇨ *Geometry and Tracking*

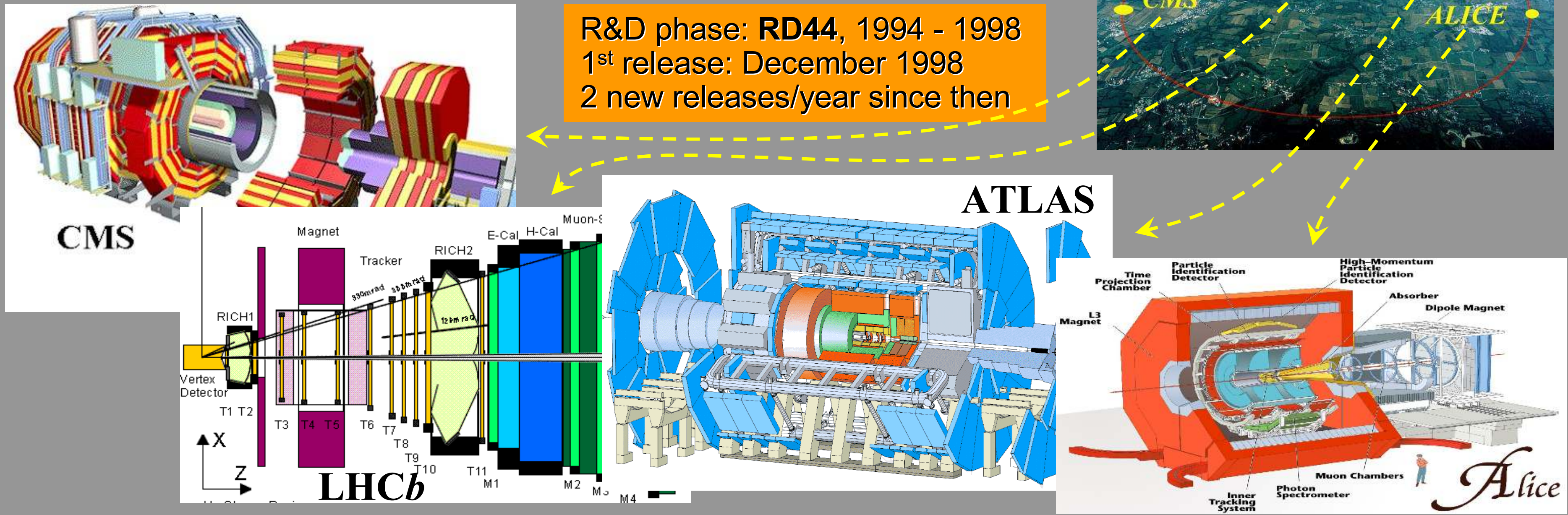
...is a toolkit for simulation of particles passing through and interacting with matter

Object Oriented Toolkit (C++) born for the simulation of large scale HEP experiments at CERN (Geneva)

Agostinelli S. et al., GEANT4-a simulation toolkit, Nucl. Inst. And Methods in Phys. Res. A 506, 250-303 (2003)



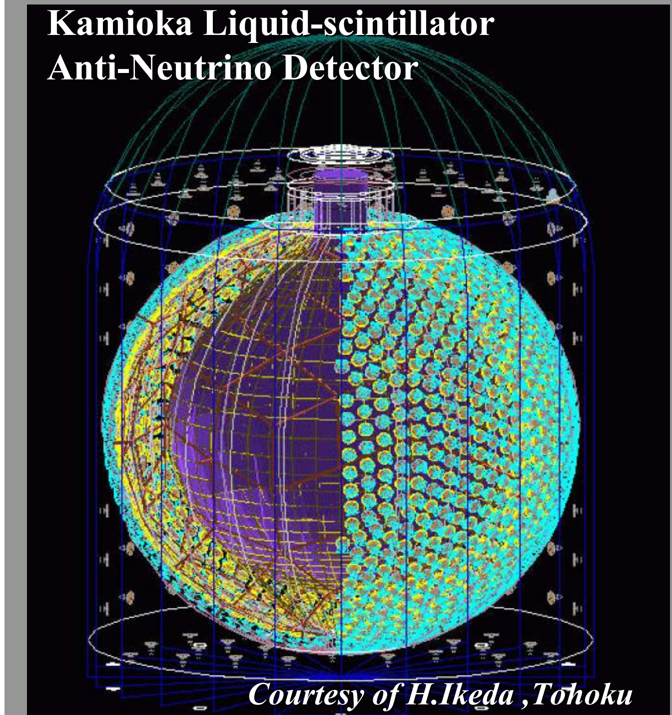
R&D phase: **RD44**, 1994 - 1998
1st release: December 1998
2 new releases/year since then



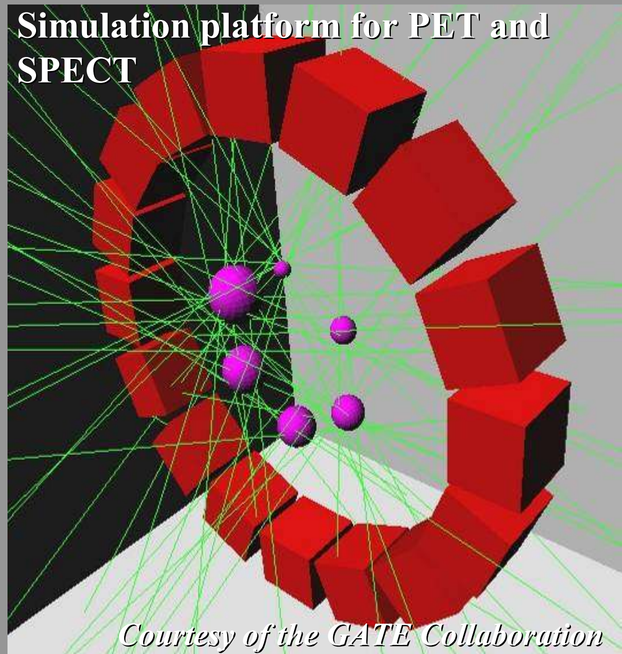
The Monte Carlo toolkit *Geant4*

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

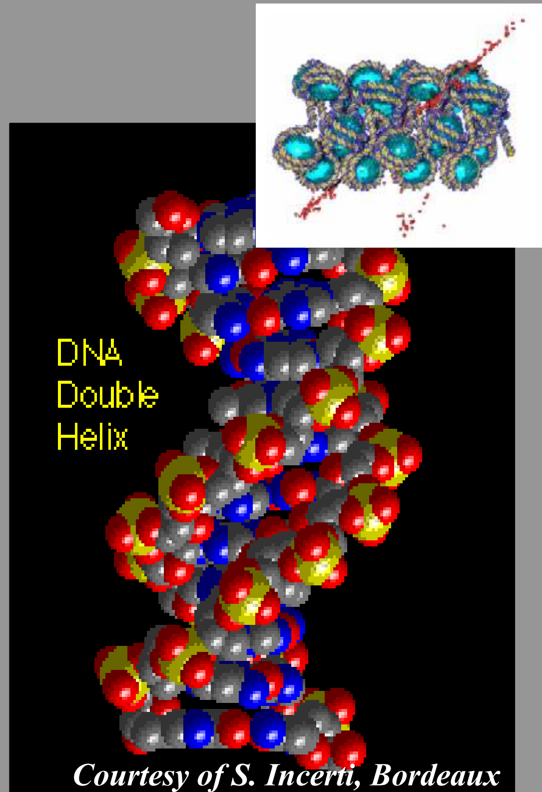
Today...



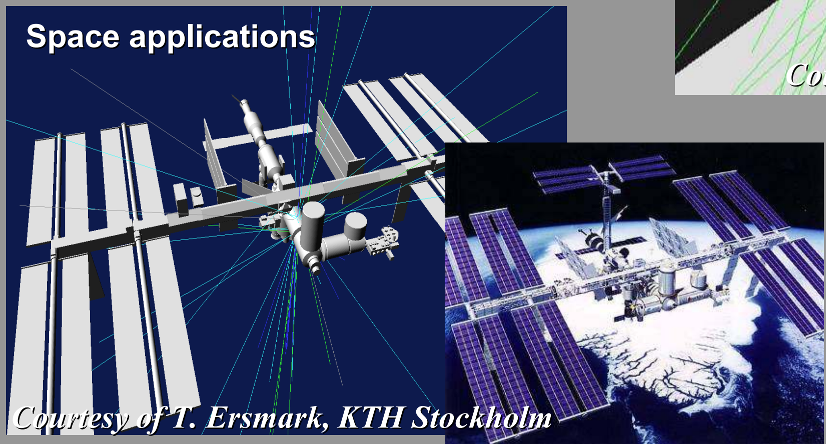
Courtesy of H.Ikeda ,Tohoku



Courtesy of the GATE Collaboration



Courtesy of S. Incerti, Bordeaux



Courtesy of T. Ersmark, KTH Stockholm

...not only for HEP detectors!!!

The Geant4 collaboration

MoU based

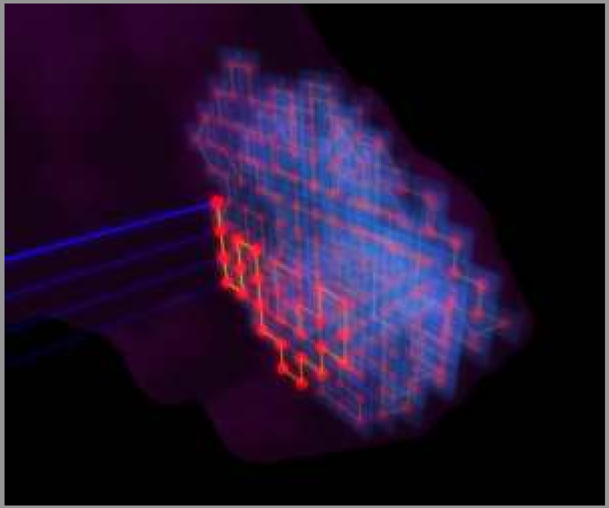
Distribution, Development and User Support of Geant4

CERN, ESA, KEK, SLAC, TRIUMF, TJNL

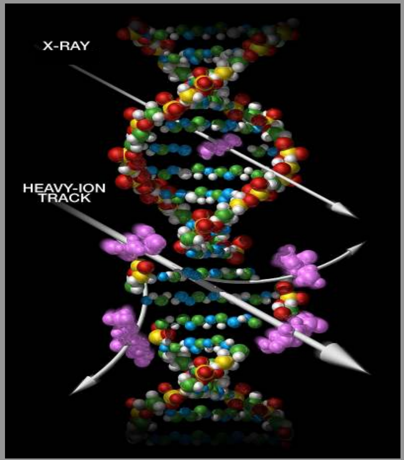
INFN, IN2P3, PPARC

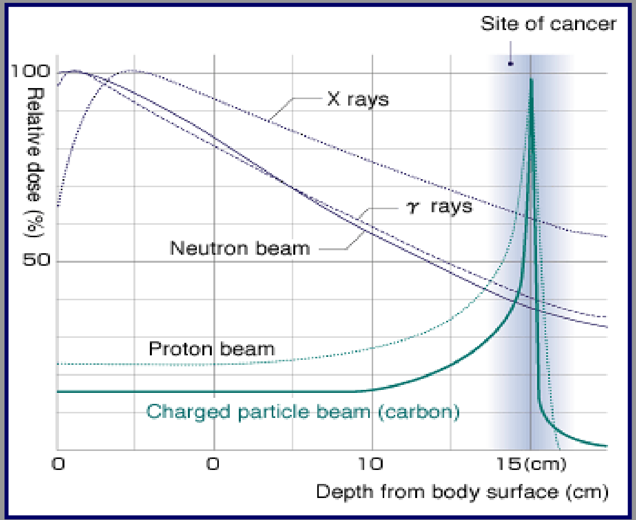
Barcelona Univ., Budker Inst., Frankfurt Univ., Karolinska Inst., Helsinki Univ., Lebedev Inst., LIP, Northeastern Univ. *etc.*

We are involved in the ***Hadronic****,* ***Low Energy*** *and* ***Advanced Example*** *WGs*



Application of the Monte Carlo Geant4 toolkit in hadrontherapy dosimetry





Fragmentation studies for carbon beams

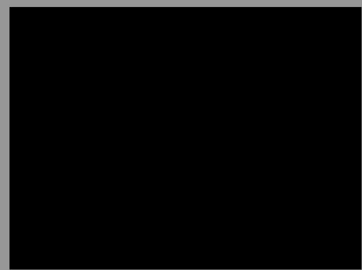
It is important to know the cross section of secondary particles production at different angles and for different target materials.
In literature there is not a complete data set in the energy range of interest for carbon ion therapy (0-400 AMeV)

Experimental data
INFN – LNS, Catania

Up to now we have performed two experimental runs with 62 and 35 AMeV carbon ion beams on graphite and gold targets.
Future expeimebts at GSI.

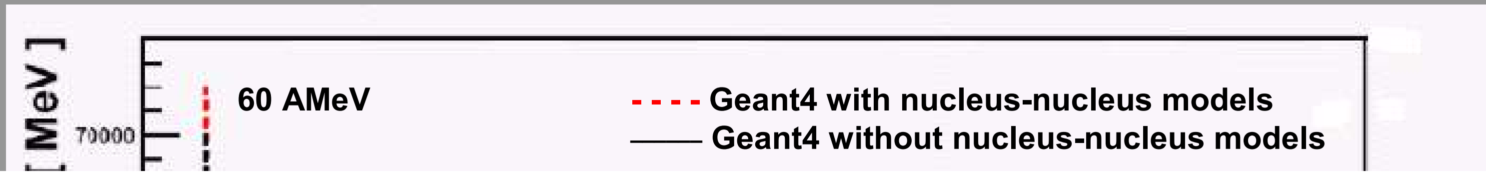
Geant4 Monte Carlo simulations and understanding of the hadronic models

Collaboration with Geant4 hadronic working group



Contribute of the hadronic processes on the physical dose

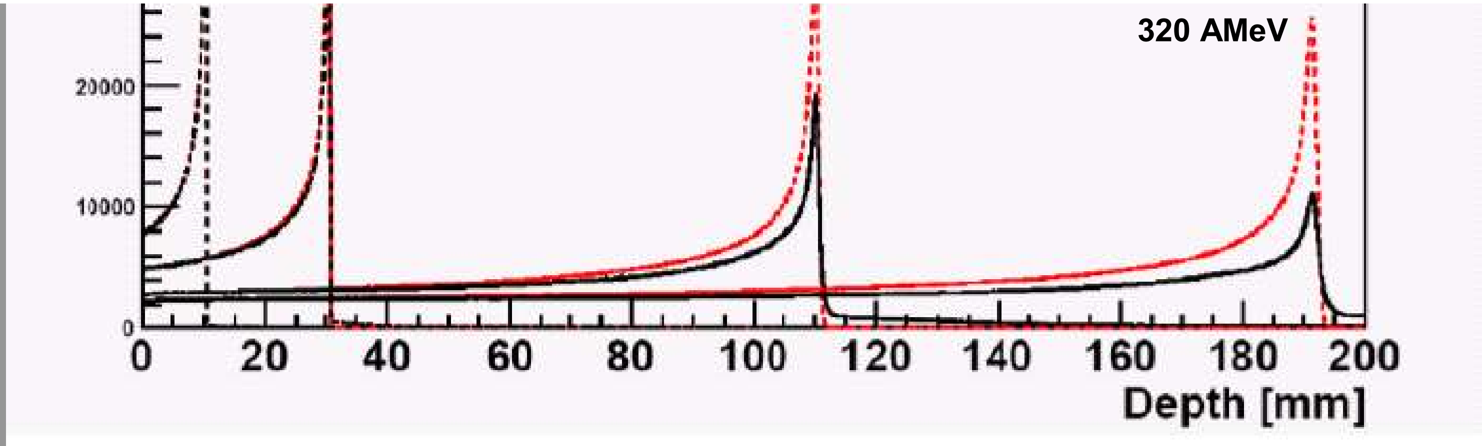
Comparison of carbon Bragg peak switching on and off the nucleus-nucleus models



Accurate estimation of fragments produced at different energies and angles is important in order to evaluate the contamination of the beam

The <u>nucleus-nucleus interaction models</u> should be checked and <u>validated</u> because responsible of the fragments yields!

This work could contribute to the development of a Treatment Planning System (TPS) for hadrontherapy (INFN project from 2009), which must consider the different biological effects of the secondary produced



Comparison of ion inelastic models

With the collaboration of the Geant4 Hadronic WG, systematic comparisons of different ion inelastic models have been performed *(in progress)*

It is important to know the cross section of secondary particles production at different angles and for different target materials.

lack of experimental data!

published data

experiments at LNS-INFN
(thin target)

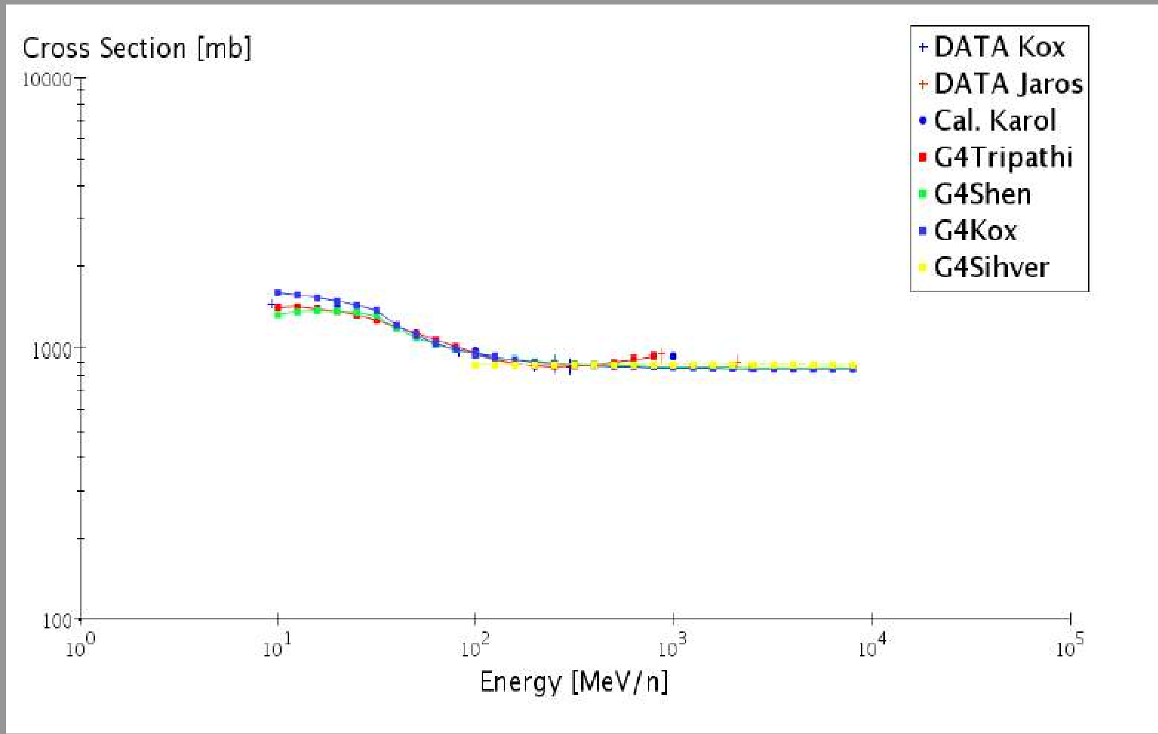
- **Secondary production data for nucleus-nucleus interactions are provided by thin and thick target experiments**
- **Published experimental data available for ion interactions at energy range of interest in the medical physics field (10 – 500 AMeV):**
  - **enough for neutron production (both for thin and thick target)**
  - **few (and sometimes not of good quality) in case of fragments production**

Inelastic cross sections in Geant4

Many cross section formulae for NN collisions are included in Geant4

- **Tripathi Formula, NASA, Technical Paper TP-3621 (1997)**
- **Tripathi Light System, NASA, Technical Paper TP-209726 (1999)**
- **Kox Formula, Phys. Rev. C 35 1678 (1987)**
- **Shen Formula, Nuclear Physics. A 49 1130 (1989)**
- **Sihver Formula, Phys. Rev. C 47 1225 (1993)**

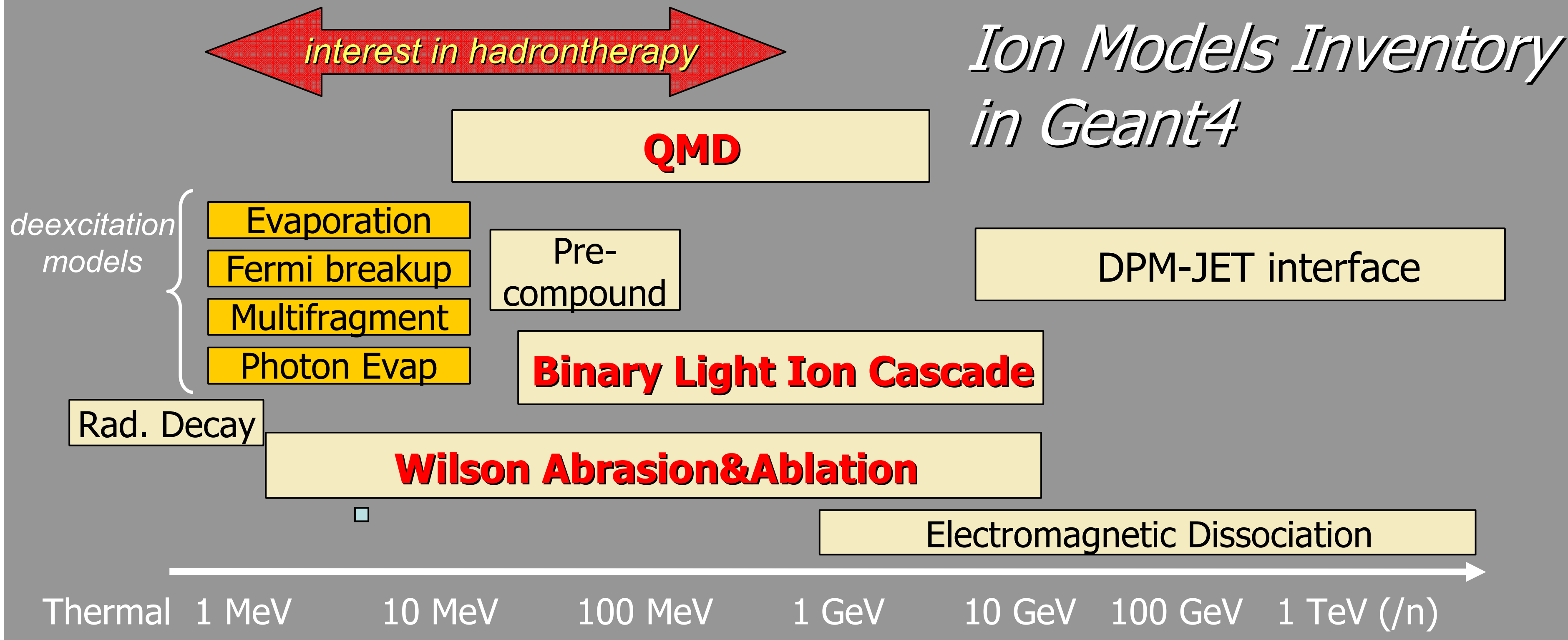
Inelastic cross sections
^{12}C on ^{12}C



These are empirical and parameterized formulae with theoretical insights.

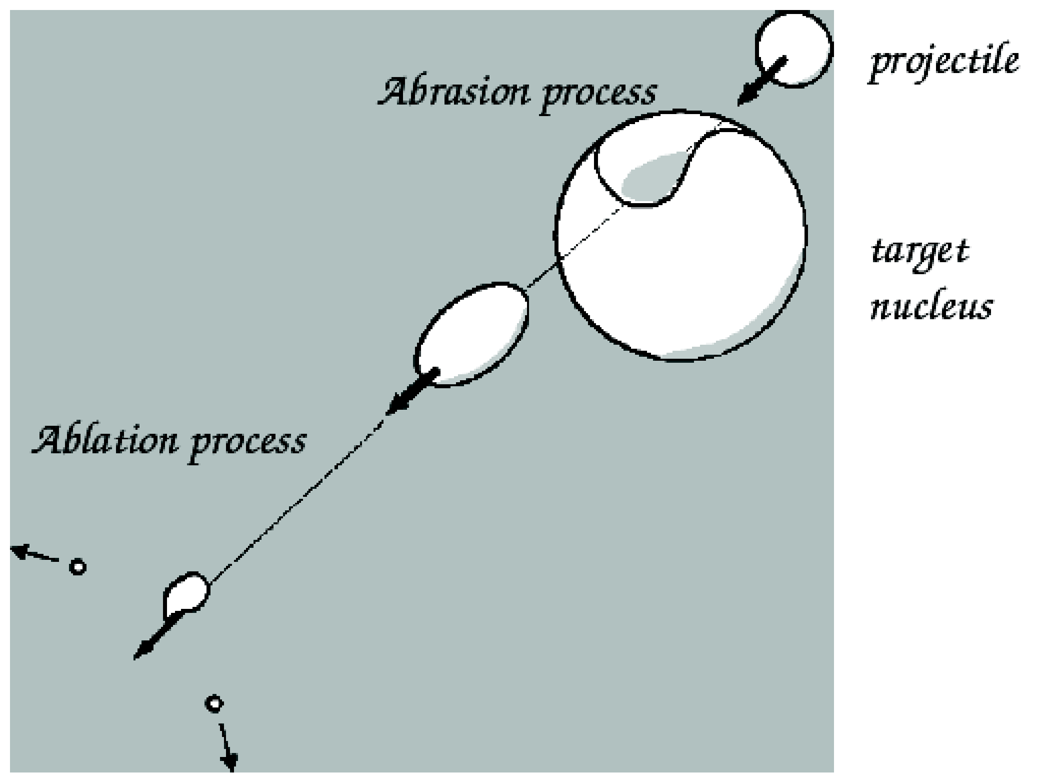
Nucleus-nucleus models in Geant4

- **geant4.9.1**
- Ion interaction models compared:
  - ***G4WilsonAbrasionAblasion model*** *(P. Truscott et al., QineticQ)*
  - ***G4BinaryLightIonCascade model*** *(G. Folger et al., CERN)*
  - ***G4QMD model*** *(T. Koi et al., SLAC)*



G4WilsonAbrasionAblation model

- G4WilsonAbrasionModel is a simplified macroscopic model for nuclear-nuclear interactions based largely on geometric arguments
- A nuclear ablation has been developed to provide a better approximation for the final nuclear fragments from an abrasion interaction.
- Performing an ablation process to simulate the deexcitation of the nuclear pre-fragments, nuclear deexcitation models within Geant4 (default).



- G4WilsonAblationModel uses the same approach for selecting the final-state nucleus as NUCFRG2 (NASA TP 3533)
- The speed of the simulation is found to be faster than other Geant4 models but at the cost of accuracy.

G4QMD model

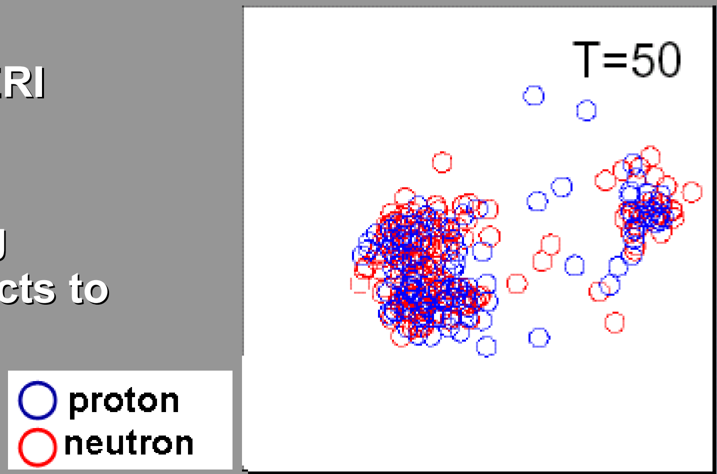
QMD (Quantum Molecular Dynamics) is a
quantum extension of classical molecular-dynamics model.

- Each nucleon is seen as a Gaussian wave packet
- Propagation with scattering term which take into account Pauli's principle

QMD model is widely used to analyze various aspects of heavy ion reactions, especially for many-body processes in particular the formation of ***complex fragments*** *(enable to simulate real HZE reactions).*

- G4QMD create ground state nucleus based on JQMD, which can be used in MD
- Potential field and parameters of G4QMD is also based on JQMD with Lorentz scalar modifications – "*Development of Jaeri QMD Code*", Niita et al, JAERI Data/Code 99 042
- Self generating potential field is used in G4QMD.
- G4QMD includes Participant-Participant Scattering
- After the QMD reaction calculation, G4QMD connects to Evaporation models of Geant4

Fe 290 MeV/n on Pb



couertesy of T. Koi, SLAC

VALIDATION ACTIVITY AT INFN - LNS

G.A.P.Cirrone, G.Cuttone, F.Di Rosa, Z.Quiwei, F.Romano

"INFN- Laboratori Nazionali del Sud" -Catania (I)

1. **Proton and carbon Bragg peak compared versus experiment**
    - **Use of the Hadrontherapy**
    - **Choice of the best parameters**
    - **Choice of the more accurate physic**
2. **LET calculation for proton beam: comparison with other analytical models**
3. **Validation of migrated Lowenergy and Standard models against data libraries**
    - **At moment validation of photon models is in progress**
4. **Advanced example activity and coordination**

VALIDATION ACTIVITY AT INFN - LNS

62 AMeV proton and carbon beam is acquired in water with an high precision, air-free ionisation chamber

Using Hadrontherapy we compared different physic models also using the built-in physic lists and packages.

We are now able to suggest a set of transport parameters and physic models to be used in proton and carbon Brag peak reconstruction

Collection volumecase	Slices of 200 um in thickness
Production cut	≤ of the half of slice dimension (≤ 100 um) but best agreement with 10 um
Step max	No set of the step max is necessary if production cut is ≤ 100 um
Electromagnetic models	G4EmStandardOption3 (also Lowenergy Livermore models but too time consuming)
Hadronic models	Binary Cascade (protons and neutrons) + BinaryLigthIon or QMD (for ion-ion interaction)
Package	QGSP_BIC but G4EmStandardPhysicOption3 must be forced

VALIDATION ACTIVITY AT INFN - LNS

DEPTH DOSE DISTRIBUTIONS WITH THE NEW VERSION OF THE HADRONTHERAPY EXAMPLE

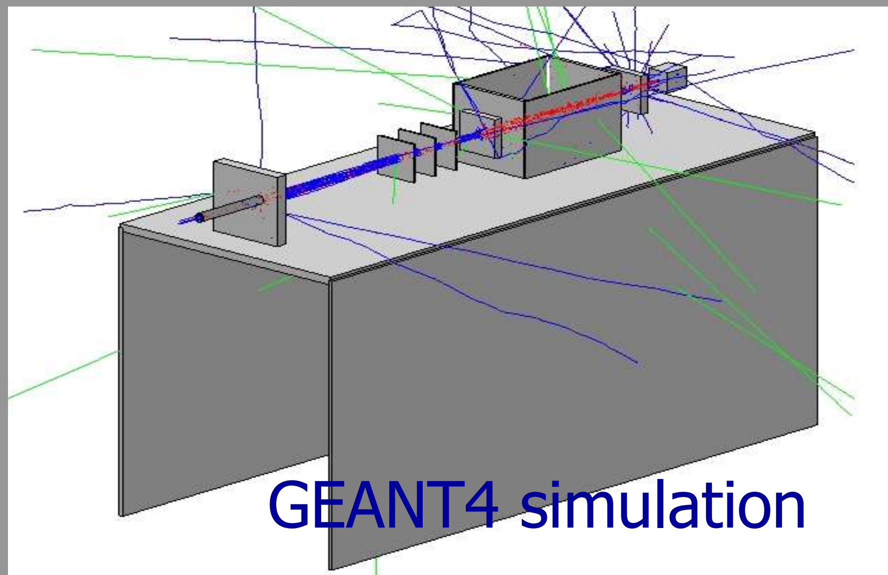
GEANT4 Simulation

Monte Carlo Simulation of the entire beam line using GEANT4:

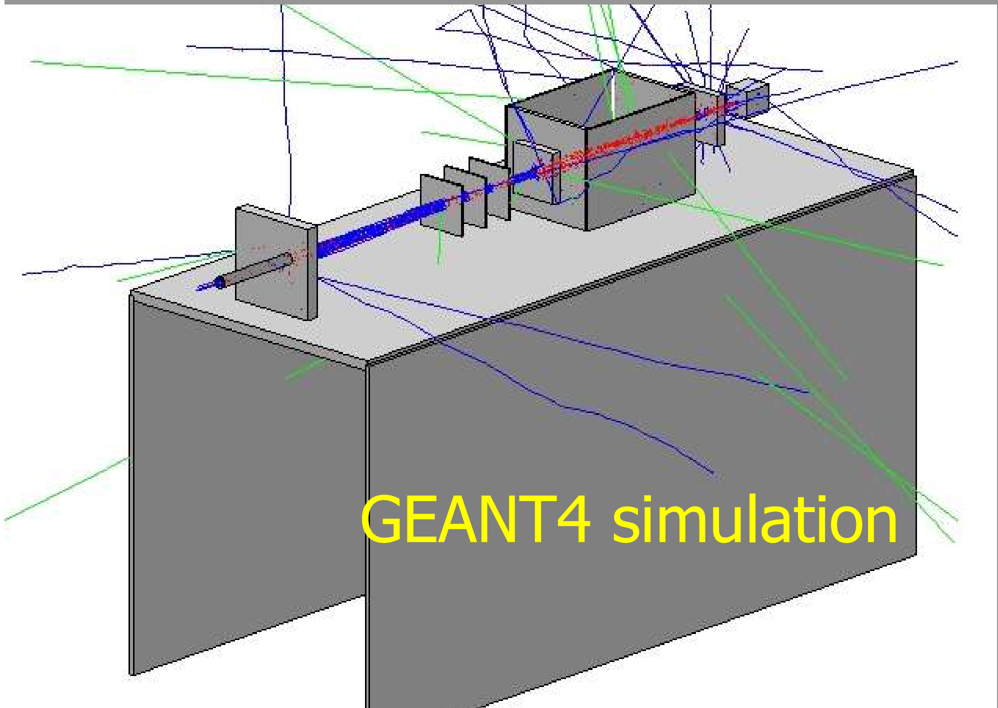
Improvement of our beam line and dosimetry

Give a general purpose tool for the design of new hadron-therapy beam line

Validation of the treatment system software



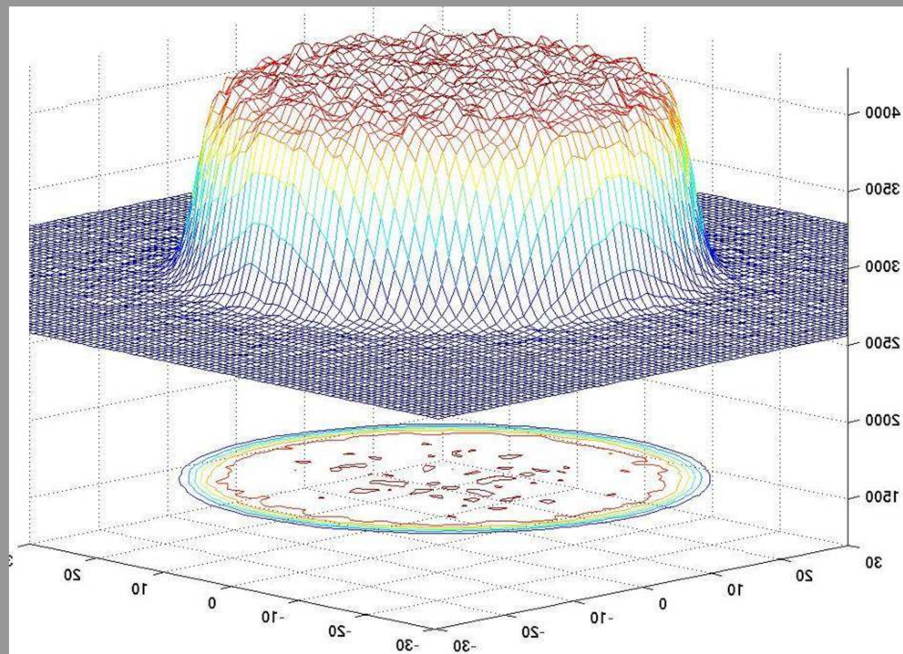
GEANT4 Complete simulation of the CATANA beam line:



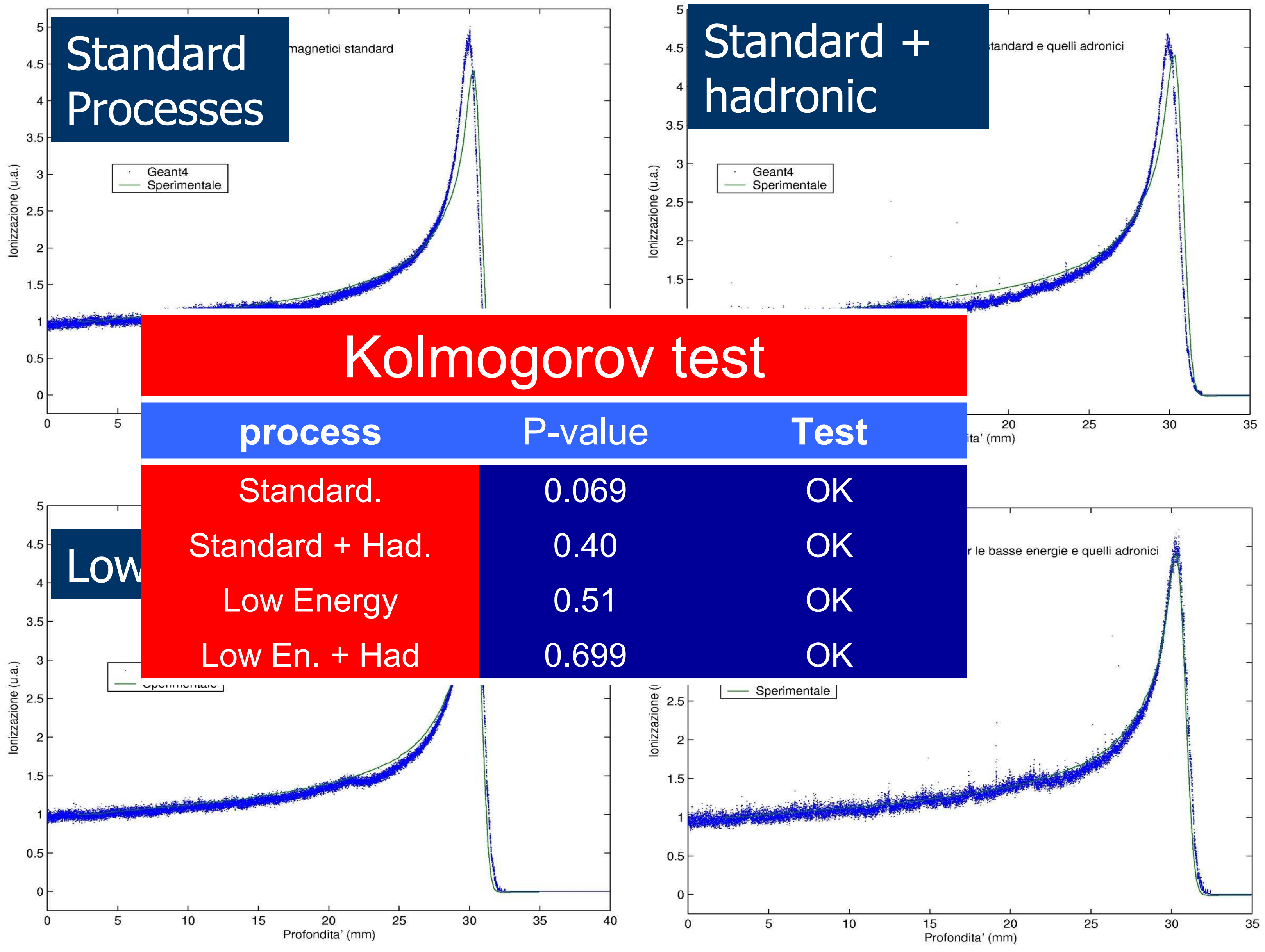
Design possibility of a general hadron therapy beam line

Optimization of its elements

TPS check respect the very precise Monte Carlo method



Physics models

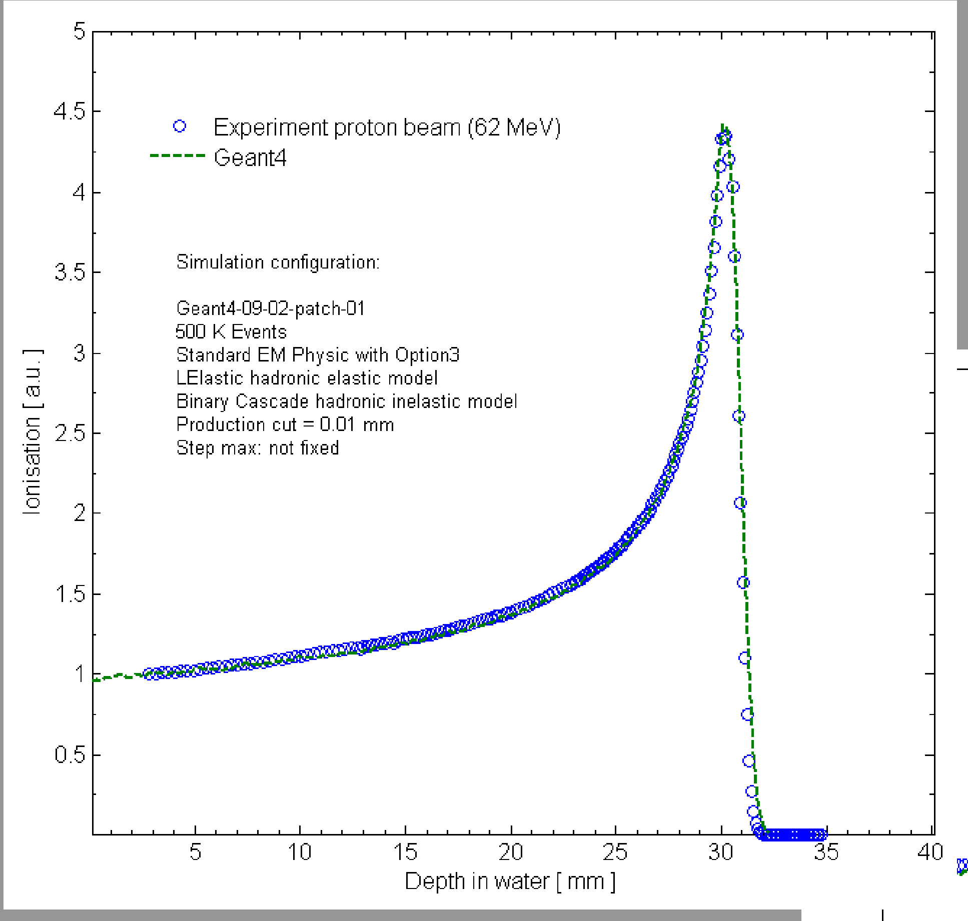


Kolmogorov test

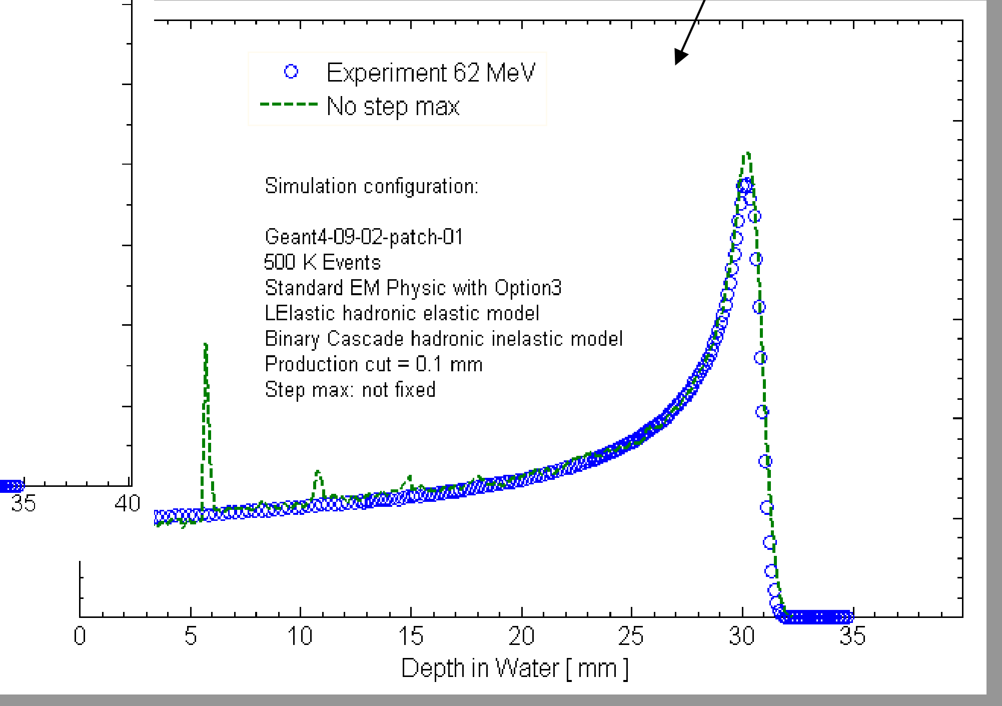
process	P-value	Test
Standard.	0.069	OK
Standard + Had.	0.40	OK
Low Energy	0.51	OK
Low En. + Had	0.699	OK

VALIDATION ACTIVITY AT INFN - LNS

Depth dose in water for proton beam. 62 MeV case

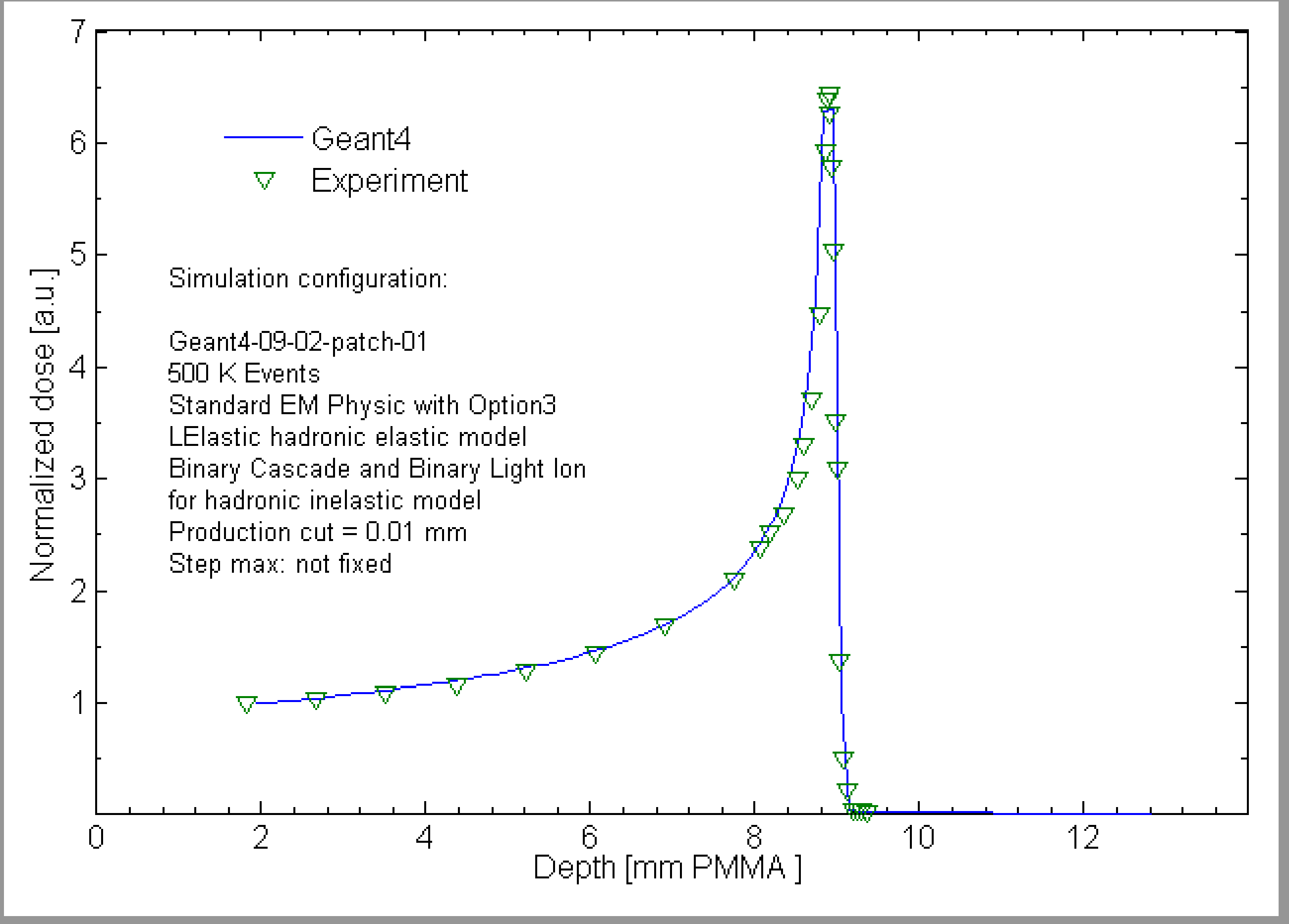


With cut = 0.1 mm that agreement is a little bit worse with some instability



VALIDATION ACTIVITY AT INFN - LNS

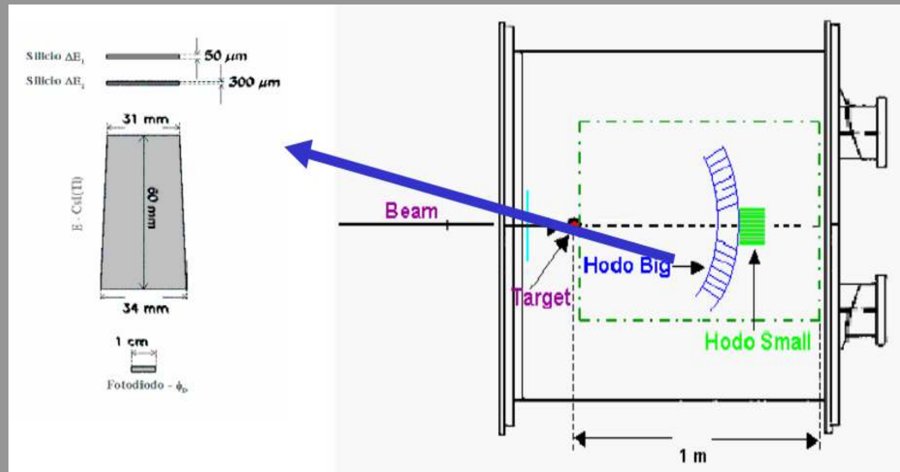
Depth dose in PMMA for carbon beam. 62 MeV case



Comparison of charged fragments production cross sections

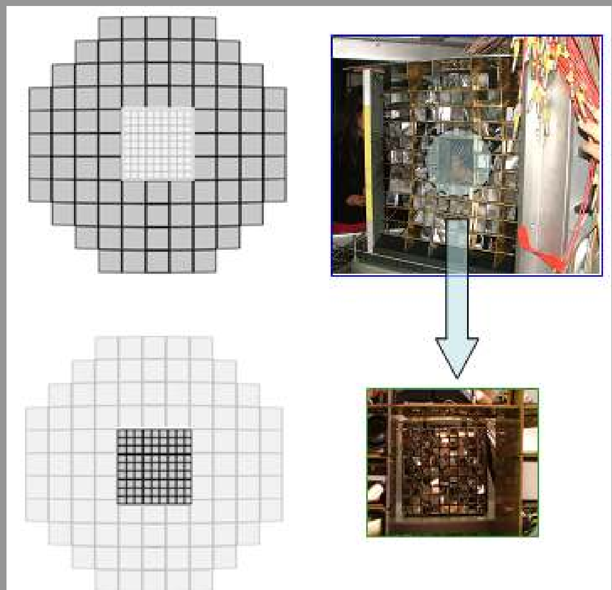
^{12}C Fragmentation measurements at 62 MeV/A (LNS - INFN)

In order to perform a systematic study of projectile fragmentation cross section at intermediate energies, we measured the ^{12}C fragmentation cross section on Au and C targets at 62 MeV/A.



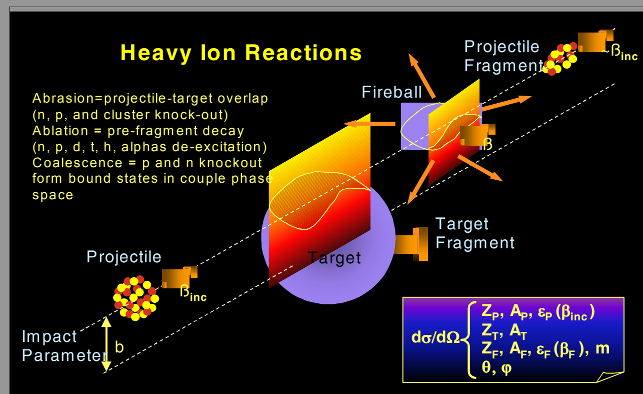
hodo big
5° < θ < 21.5°

Si-ΔE_1	50 μm	3x3 cm²
Si-ΔE_2	300 μm	3x3 cm²
CsI(Tl)-E	6 cm	3x3 cm²



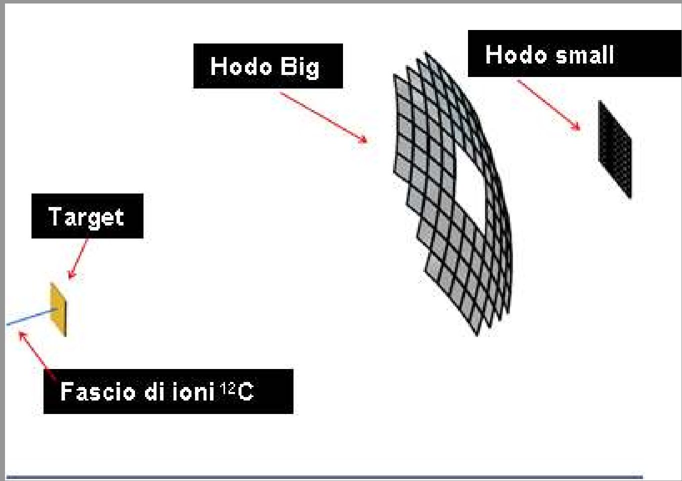
hodo small
0° < θ < 5°

Si-ΔE	300 μm	1x1 cm²
CsI(Tl)-E	10 cm	1x1 cm²



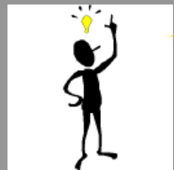
Comparison of charged fragments production cross sections

Monte Carlo simulation of the detector and the experimental setup

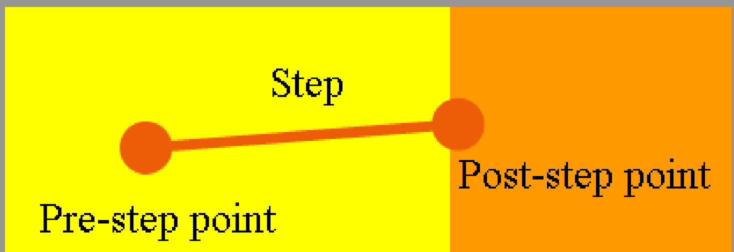


Implemented Physic	
EM Physic	**Hadronic Physic**
Photoelectric Effect	Ions Inelastic Scattering (*Binary Light Ion*)
Compton Effect	Elastic nuclear Scattering
Pair Production	
Multiple Diffusion	
Ionization (electrons, hadrons and ions)	
Bremsstrahlung	

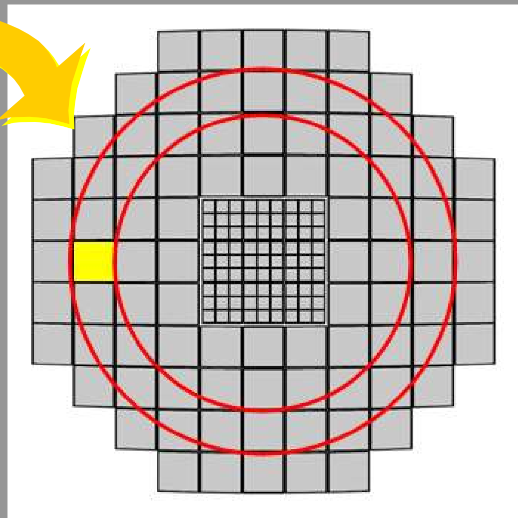
...but time consuming!!!



Azimuthal detector simmetry allows to the integration for 2π



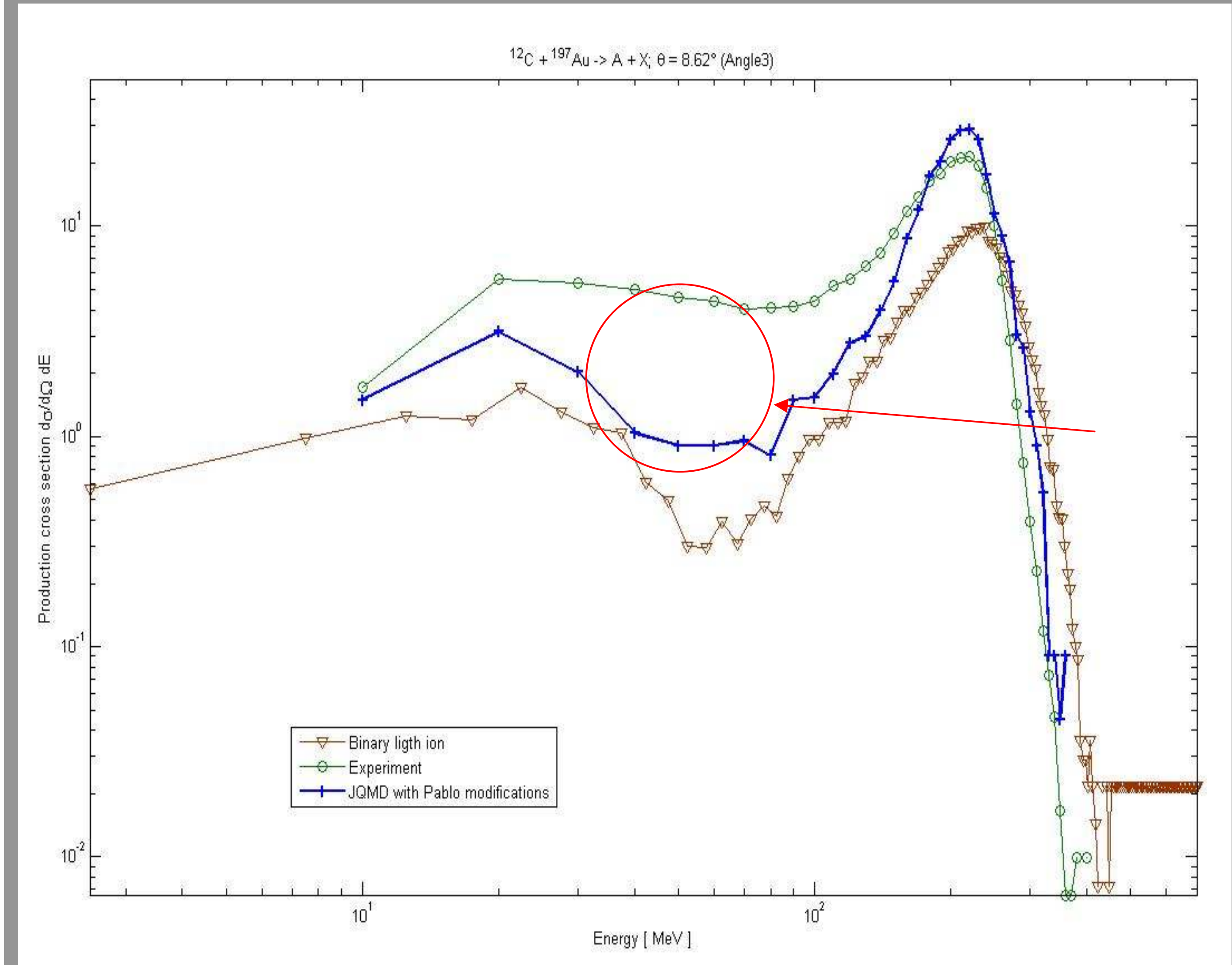
Particles are registered and deleted when they got the right distance R.



Circular crowns corresponding to the angles

Comparison of charged fragments production cross sections

- Measured vs MC double differential cross sections

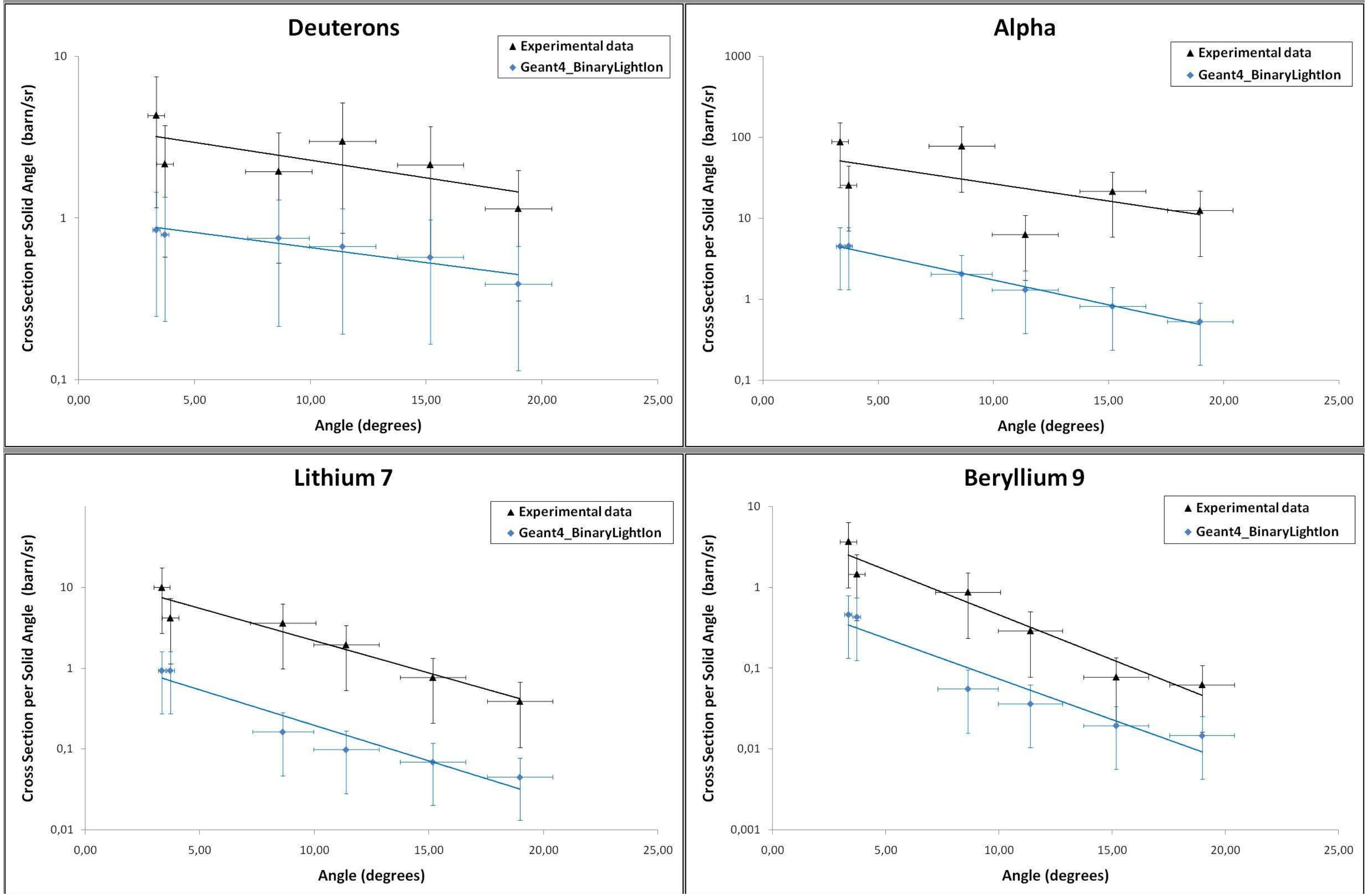


alpha production

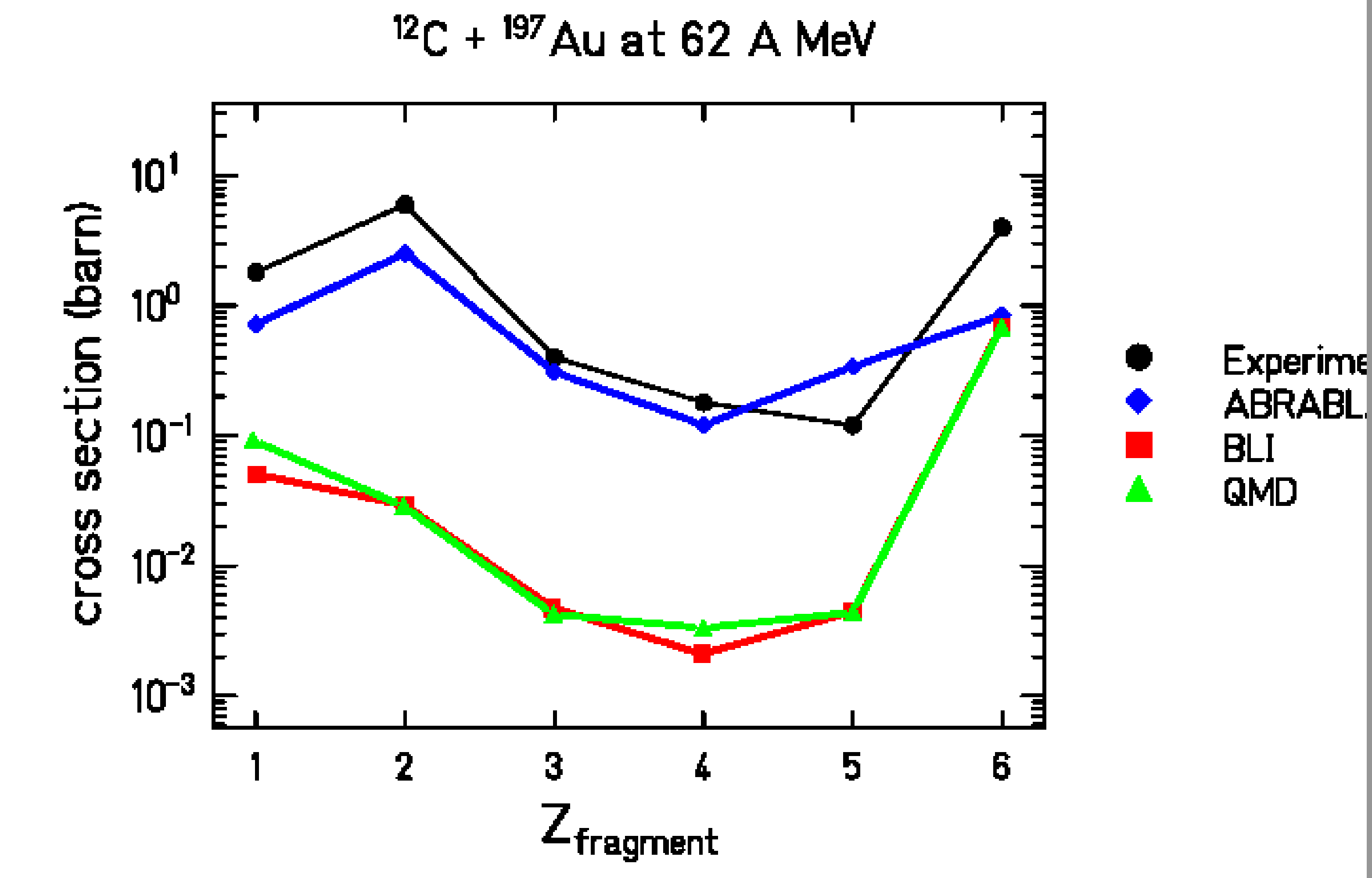
General better agreement of JQMD with our modifications but still worse agreement in the intermediate part of the spectra

Comparison of charged fragments production cross sections

- Measured vs MC angular differential cross sections



Comparison between experimental data and MC simulations



Modelling has to be benchmarked and improved

INFN Istituto Nazionale di Fisica Nucleare

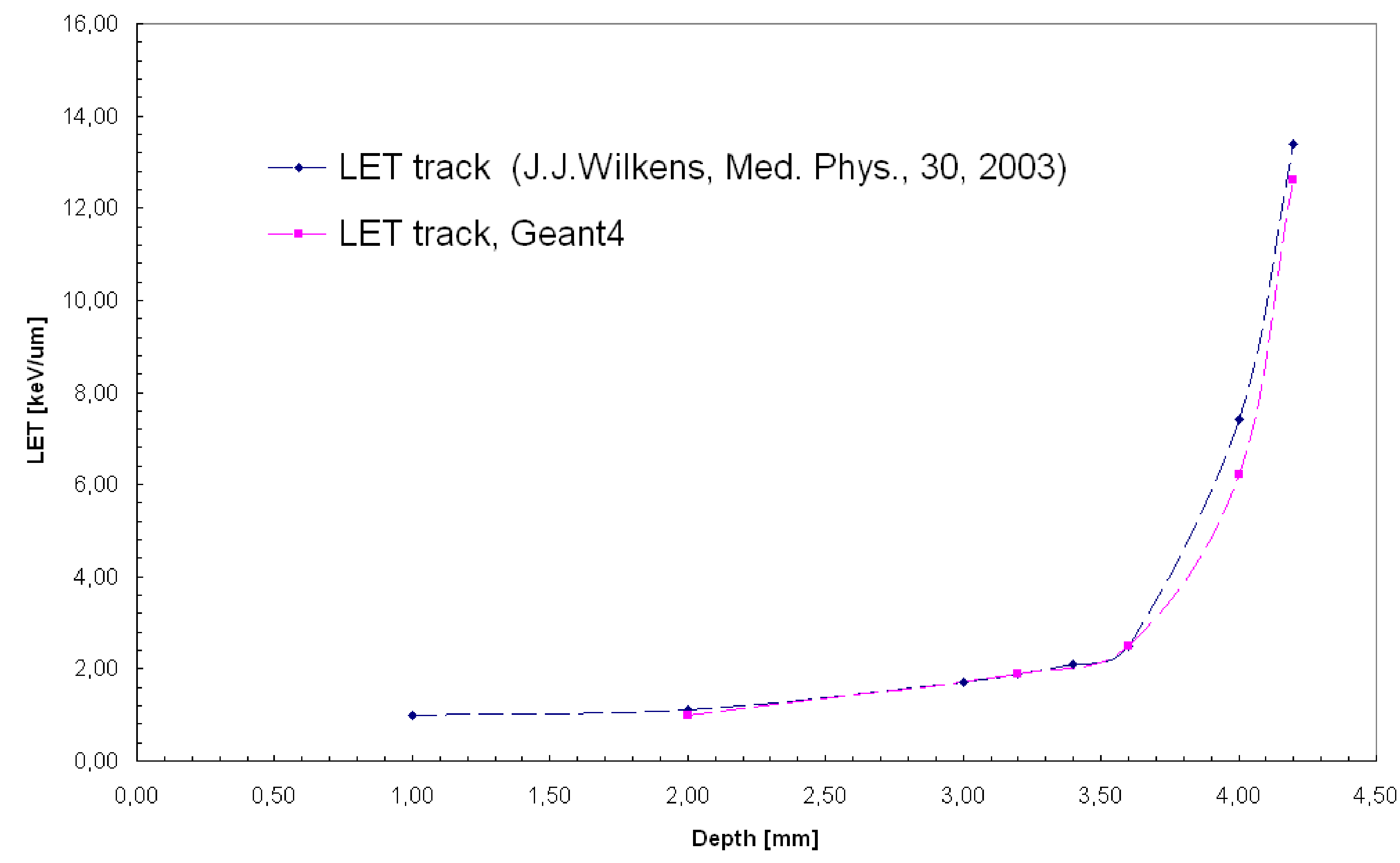
VALIDATION ACTIVITY AT INFN - LNS

LET CALCULATION WITH THE HADRONTHERAPY EXAMPLE:

A FIRST STEP TOWARDS THE INTRODUCTION OF RADIOBIOLOGICAL MODELS IN GEANT4

VALIDATION ACTIVITY AT INFN - LNS

LET "track" values calculated with Hadrontherapy for proton beams



Optimization of the physical dose: LET calculation for clinical proton beams

The physical dose is not the only parameter one should look at in treatment planning
(the biological effect does not depend on the physical dose alone)

→ At least the increased effectiveness at the end of the range of proton beams should be accounted for in treatment planning

In protontherapy a constant relative biological effectiveness (RBE) is widely used (…the effects of a variable RBE would be clinically significant…)

→ It could be to develop very efficient models for RBE calculation (NOT only constant value!?)

RBE depends on dose, tissue type, the biological endpoint and the local energy spectrum. The latter is often referred to as ‘‘radiation quality’’ characterized by the Linear energy transfer (LET)

↓

It is reasonable to provide 3D LET distributions (in addition to the physical dose distributions). This might help to localize high LET regions, where the greatest variations in RBE are expected (RBE is surely not a linear function of LET (not a function of LET alone))

Optimization of the physical dose: LET calculation for clinical proton beams

The LET for monoenergetic protons is easily obtained from tables

The calculation of the mean local LET for realistic clinical proton spectra (SOBP) is **a more complicated task**

This task can be accomplished by Monte Carlo simulations

For our purpose, the term LET is employed to describe a mean value of the stopping power. This mean can be calculated either along the track of a single particle or by averaging the stopping powers of all particles at a certain point in a radiation field

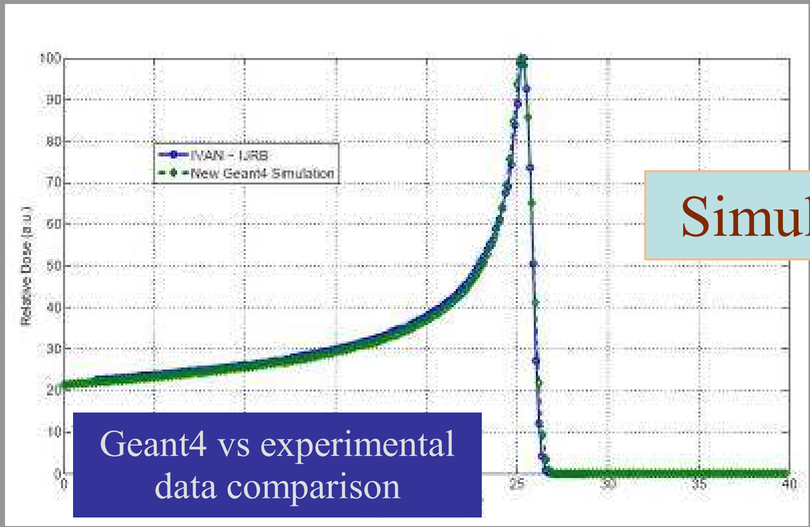
$$L_t(\mathbf{x}) = \frac{\int_0^\infty \varphi_r(\mathbf{x}) S(r)\,\mathrm{d}r}{\int_0^\infty \varphi_r(\mathbf{x})\,\mathrm{d}r}$$

$$L_d(\mathbf{x}) = \frac{\int_0^\infty \varphi_r(\mathbf{x}) S^2(r)\,\mathrm{d}r}{\int_0^\infty \varphi_r(\mathbf{x}) S(r)\,\mathrm{d}r}$$

r*: residual range, $\varphi_r(x)$: local spectrum, $\varphi_r(x)\mathrm{d}r$ gives the fluence of protons at x with residual ranges between *r* and *r* + d*r*. The total particle fluence at x will be $\int \varphi_r(x)\mathrm{d}r$. *S*(*r*) is the stopping power of protons with residual range *r

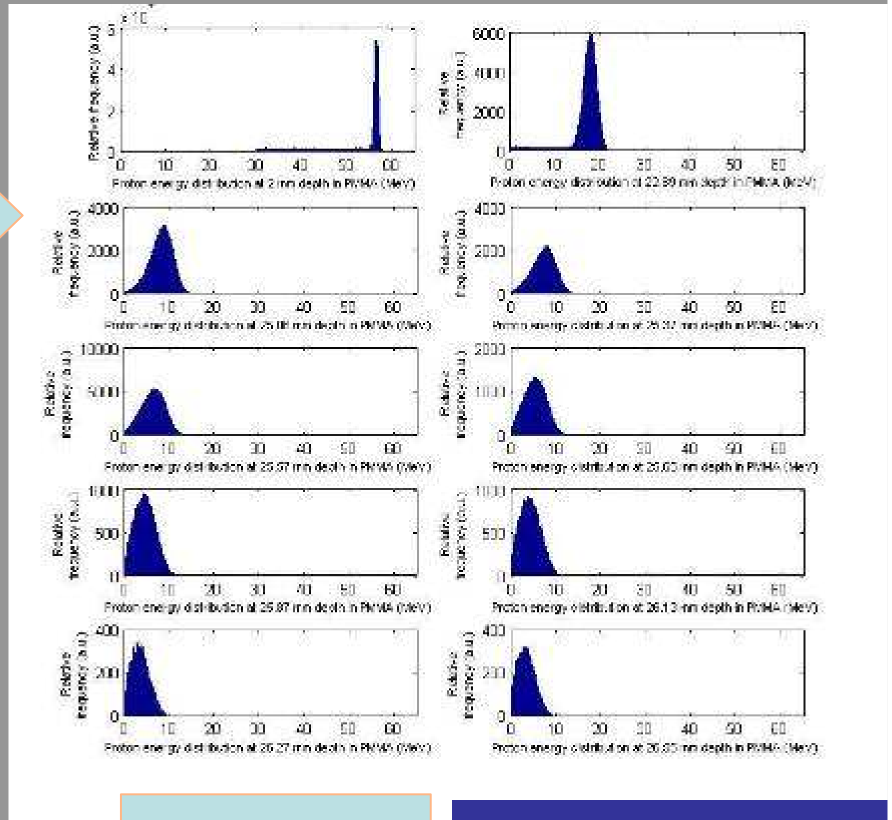
Optimization of the physical dose: LET calculation for clinical proton beams

LET CALCULATION IS A FEATURE OF HADRONTHERAPY



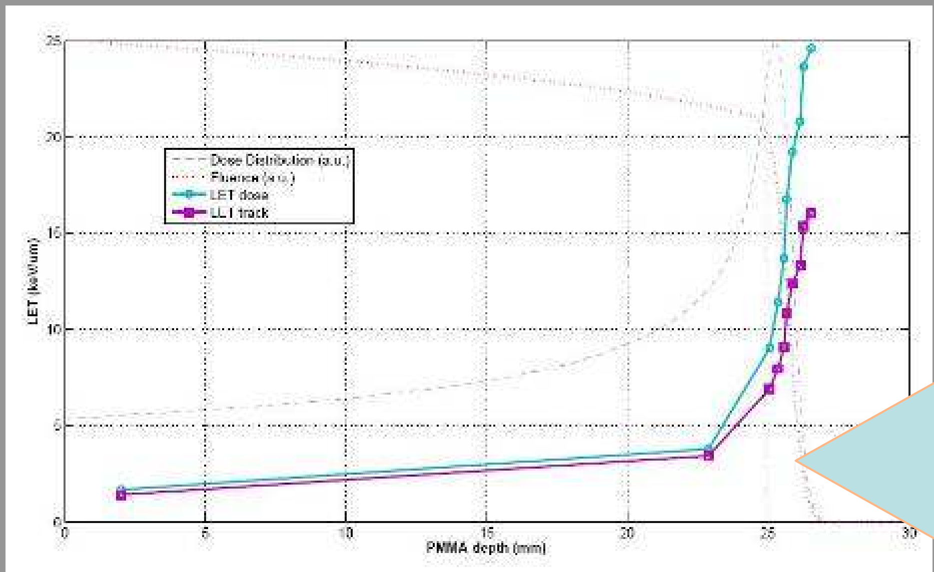
Geant4 vs experimental data comparison

Simulation

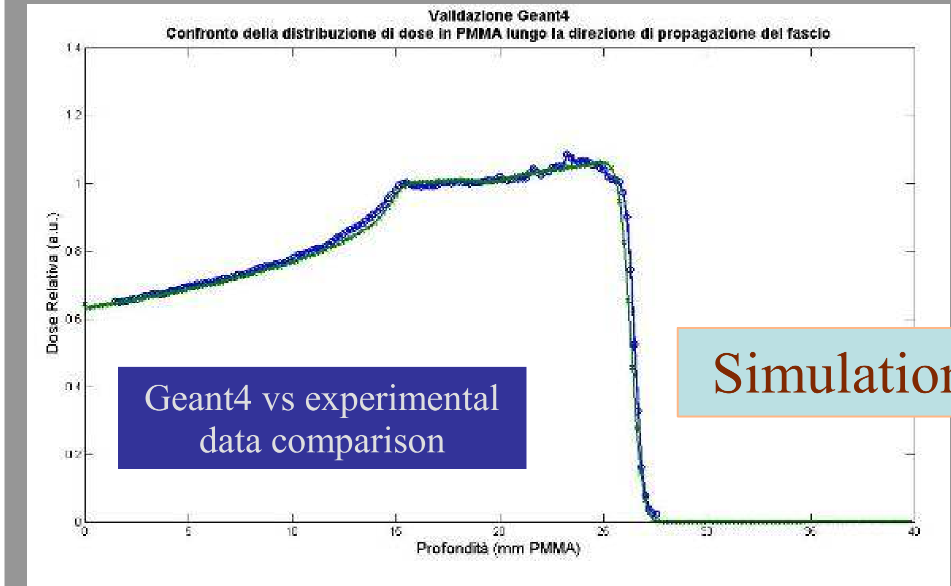


Geant4 proton depth kinetic energy simulation

LET Calculation

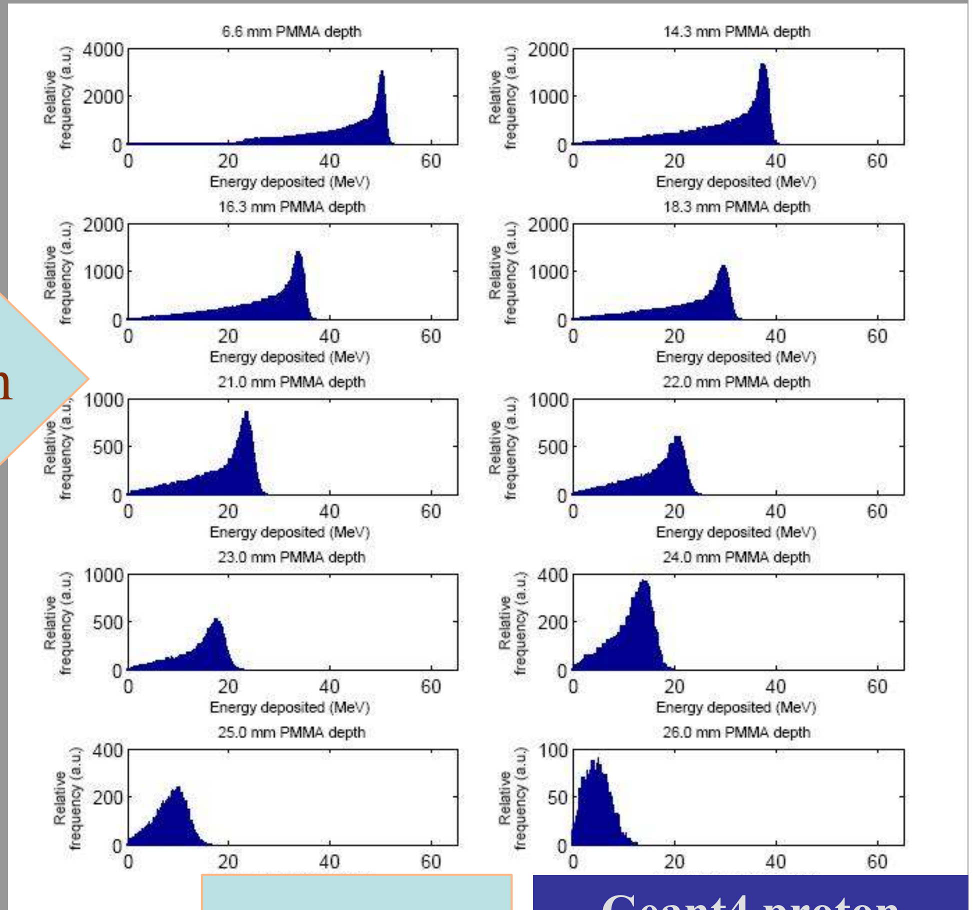


Optimization of the physical dose: LET calculation for clinical proton beams



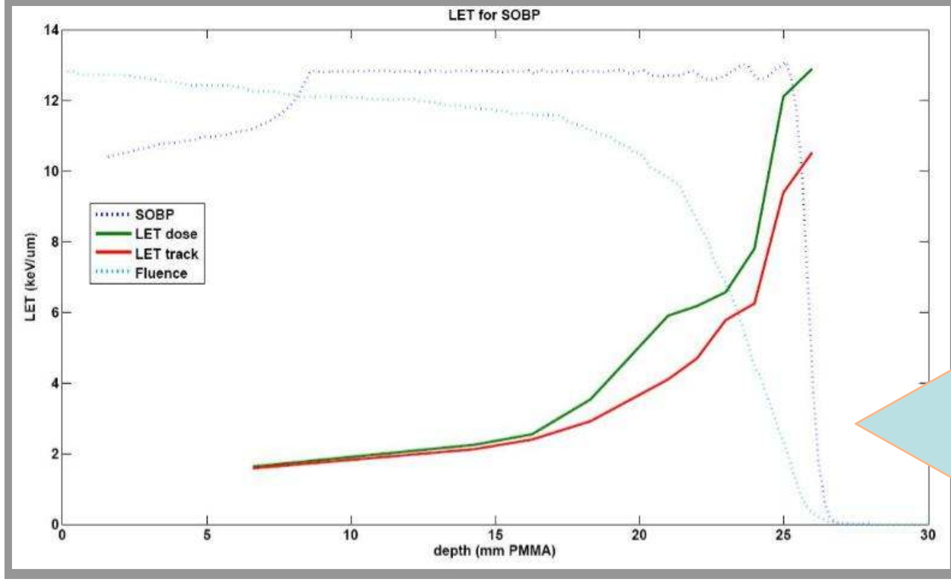
Geant4 vs experimental data comparison

Simulation



Geant4 proton depth kinetic energy simulation

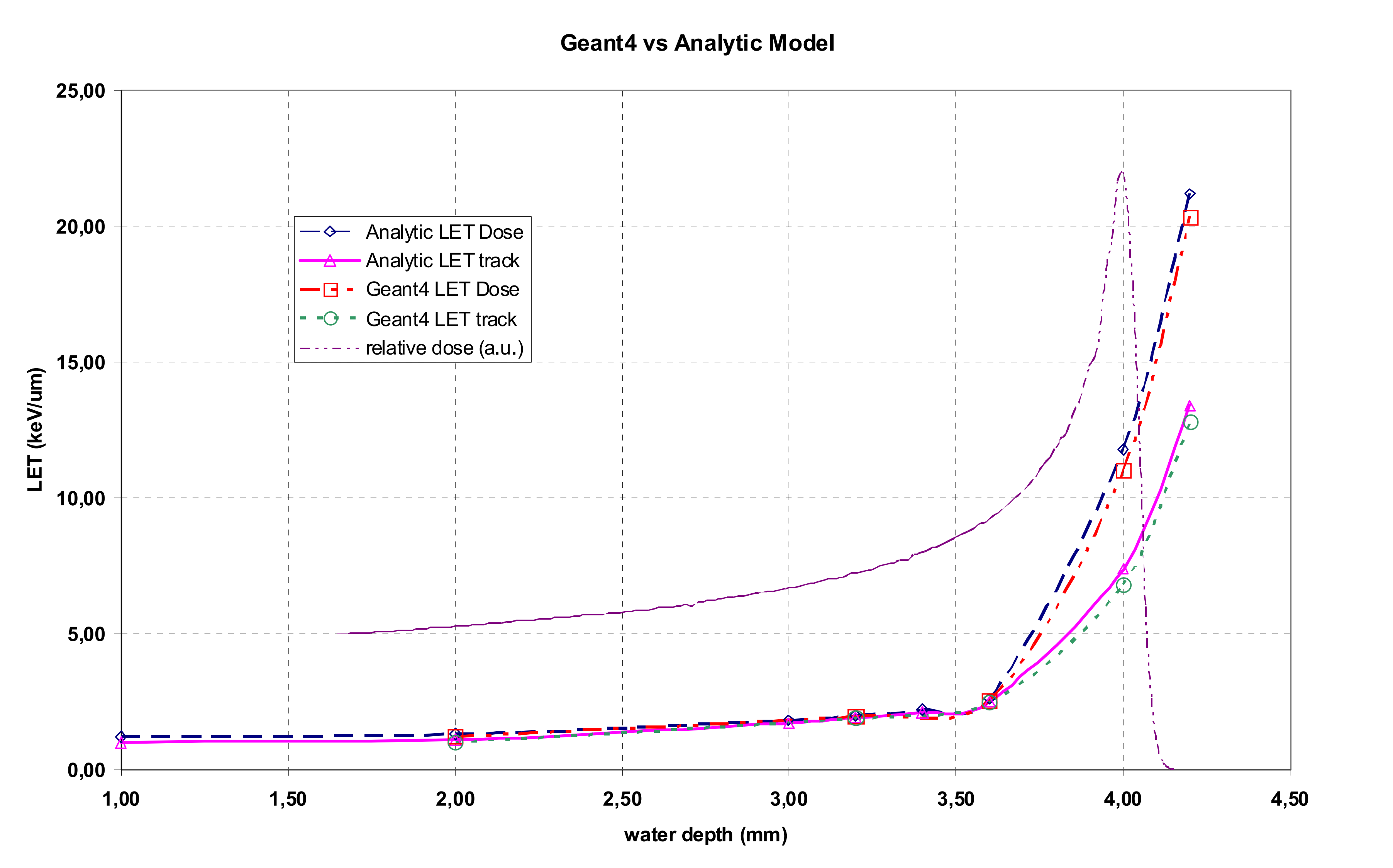
LET Calculation



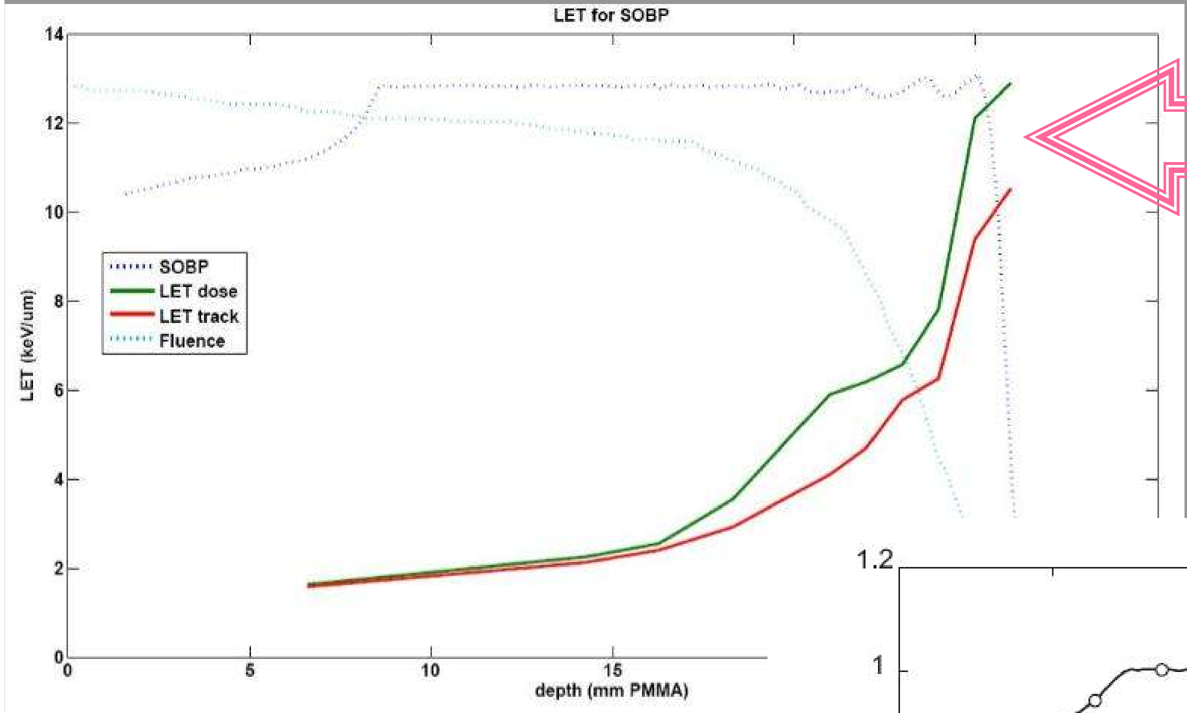
Optimization of the physical dose: LET calculation for clinical proton beams

Comparison with literature data*

*J. J. Wilkens and U. Oelfke - Medical Physics, Vol. 30, No. 5, May 2003

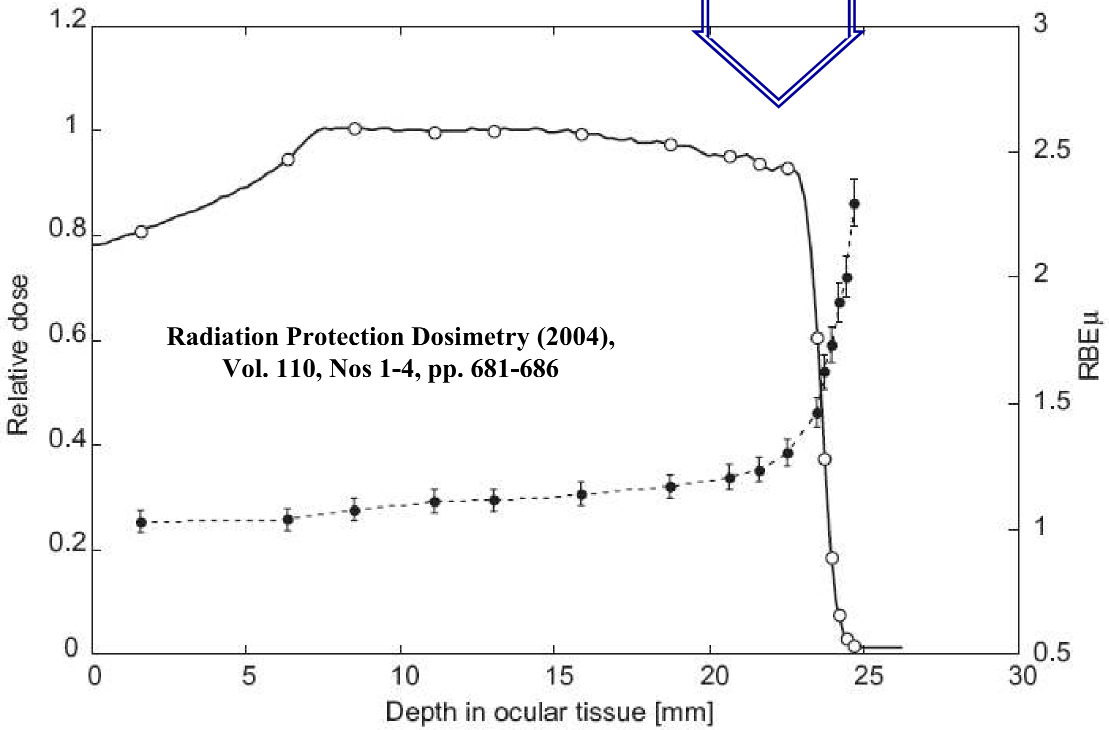


Optimization of the physical dose: LET calculation for clinical proton beams



In this region we expect the greatest RBE variations

Experimental RBE data confirm our prediction



In clinical situation, for the optimization of the physical dose is desirable to use a variable RBE as counting our initial hypothesis

Optimization of the physical dose: LET for heavy ions

Fast protons in soft tissue reach a local LET maximum of about 80 eV/nm over a few microns just before the particle comes to rest

→

However, since this high LET track segment is very short compared to the range straggling, the RBE of high energy protons is very close to that of photons

Heavy ions are tested mainly due to the low oxygen enhancement ratio OER. These ions have a high LET and high RBE in the beam entrance and the plateau region

The nuclear fragmentation processes of these heavier ions increase with atomic number and the produced secondary particles will also give an increasing dose of high LET behind the target

Various investigations on ion beam radiation quality have been carried out considering the absorbed dose and LET distributions as well as fragmentation processes

Optimization of the physical dose: LET for heavy ions

Unlike the proton beam, the LET calculation for mixed radiation qualities (like those produced by ions heavier than protons) is a more and more complicated task.

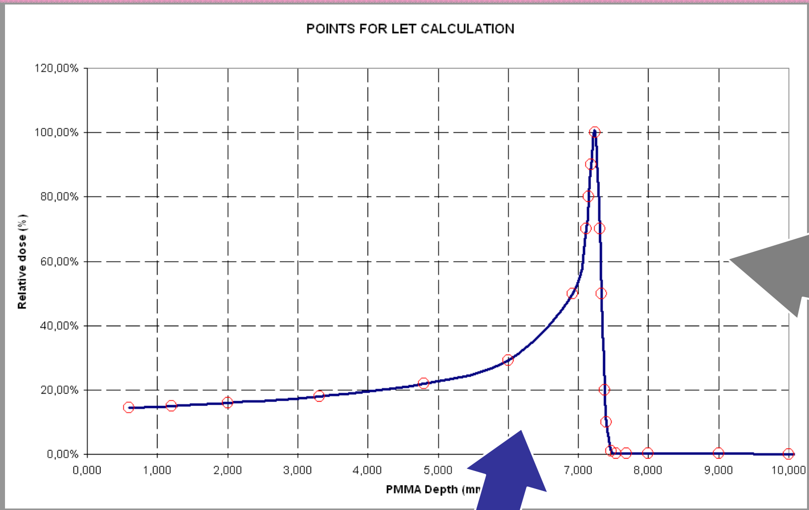
It is difficult to expect a simple dependence between LET and RBE

So a more complicate model need in order to predict the biological response with the accuracy necessary for physical dose optimization

For the case of carbon ion beams, inside **Hadrontherapy** we are implementing a new model for LET calculation

This model takes in account the secondary particles distribution due to the carbon beam fragmentation. The single contribute of each fragment is collected and pondered in order to calculate a unique LET track and dose value for each point of the depth dose distribution

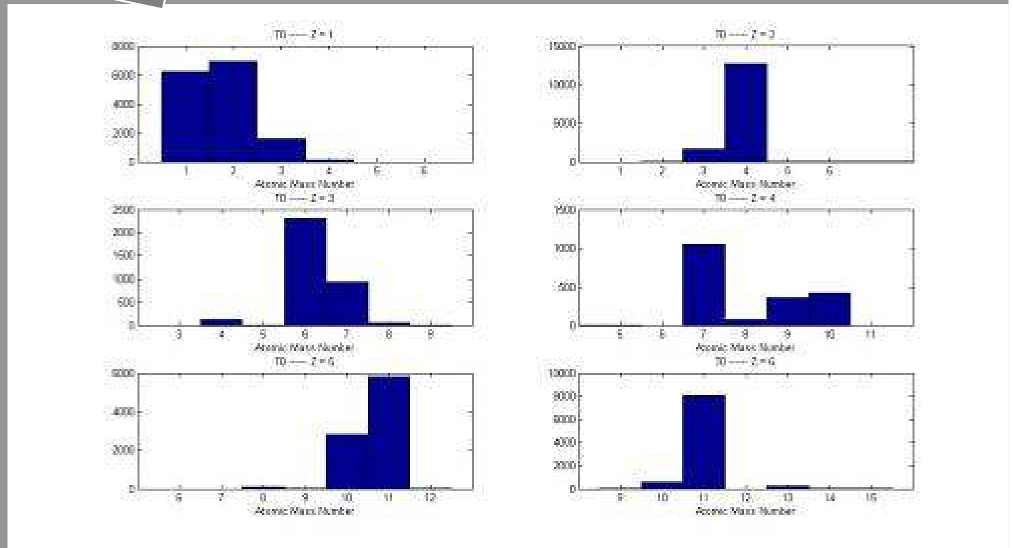
Optimization of the physical dose: LET for heavy ions

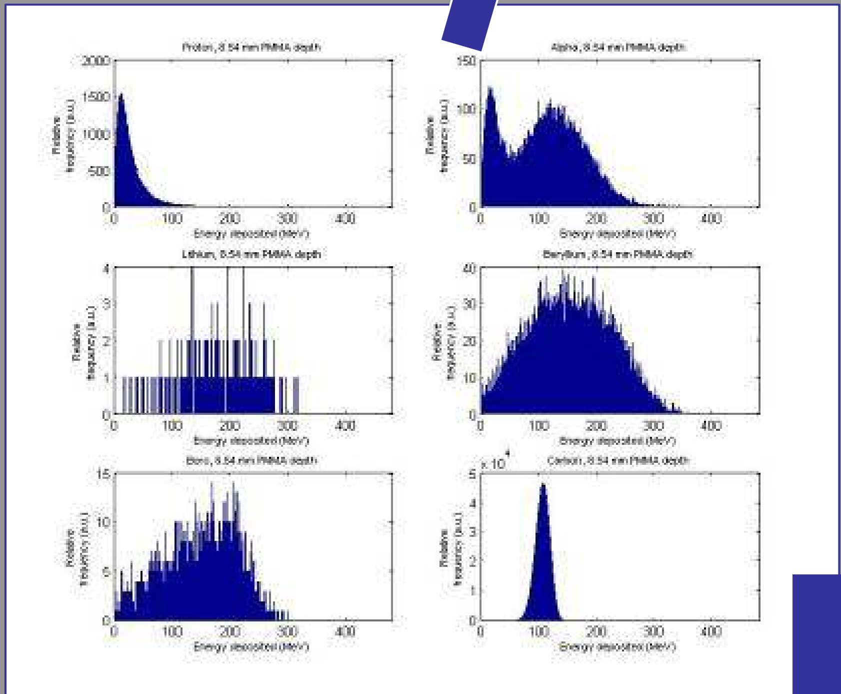


Points for LET calculations:

1) Secondary particles

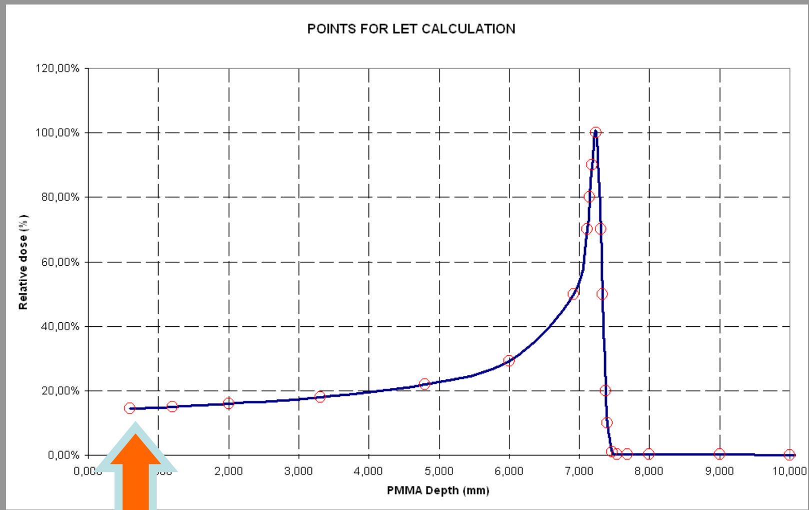
2) Kinetic energy spectra of these particles



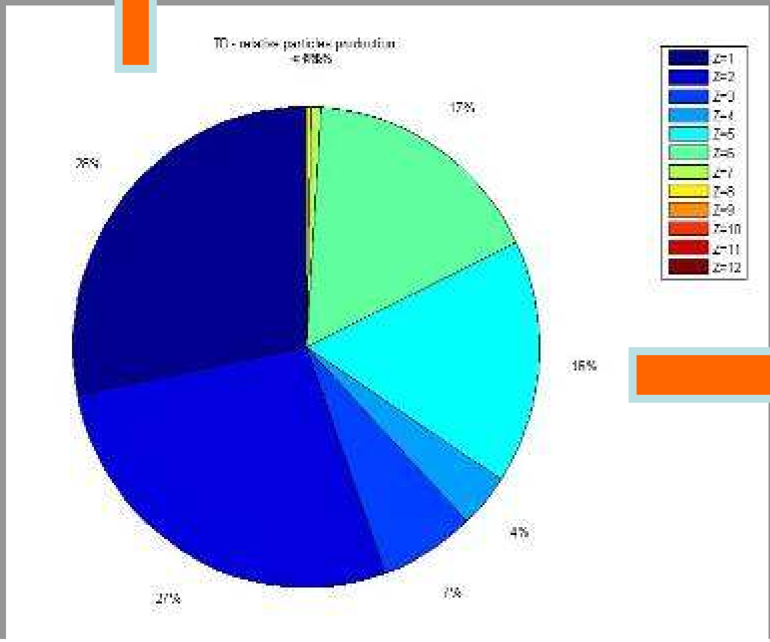


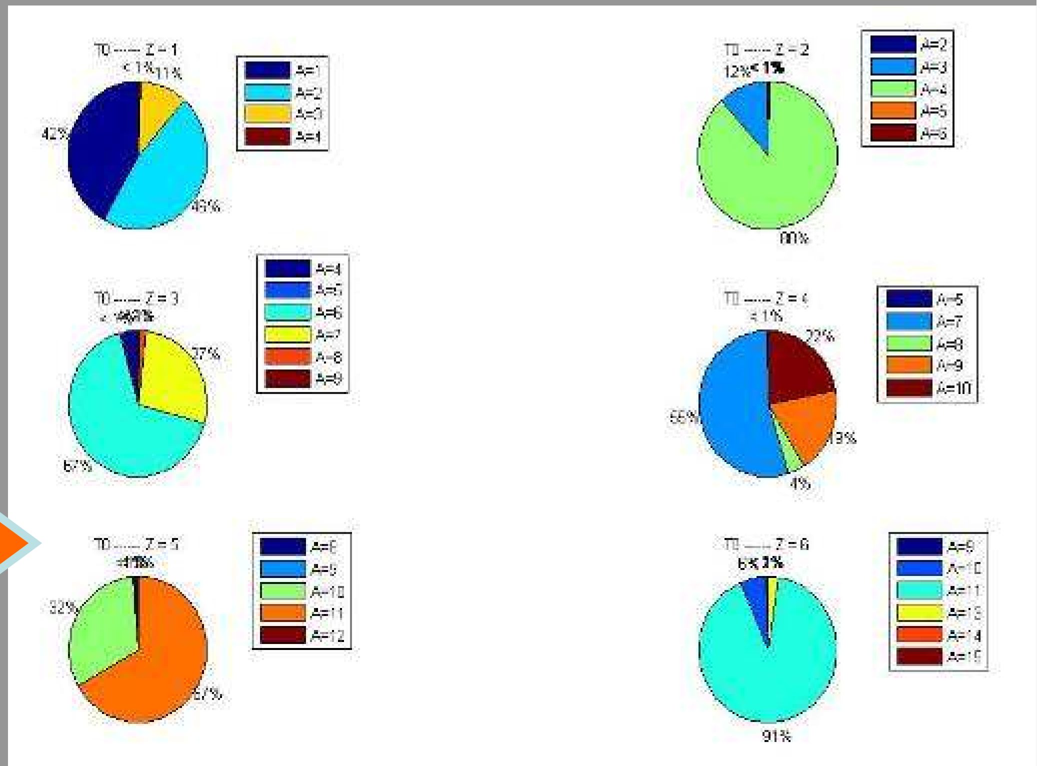
Geant4 particles kinetic energy distribution

Multifragmentation contributions

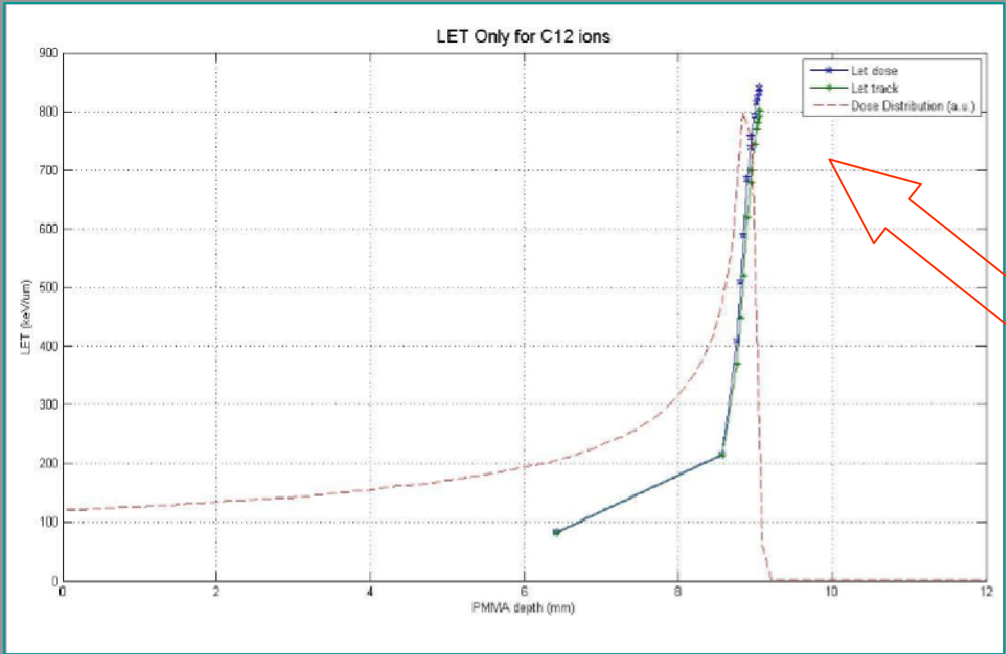


EXAMPLE OF ION AND ISOTOPIES PRODUCTION AT FIRST PMMA DEPTH POSITION FOR LET CALCULATION

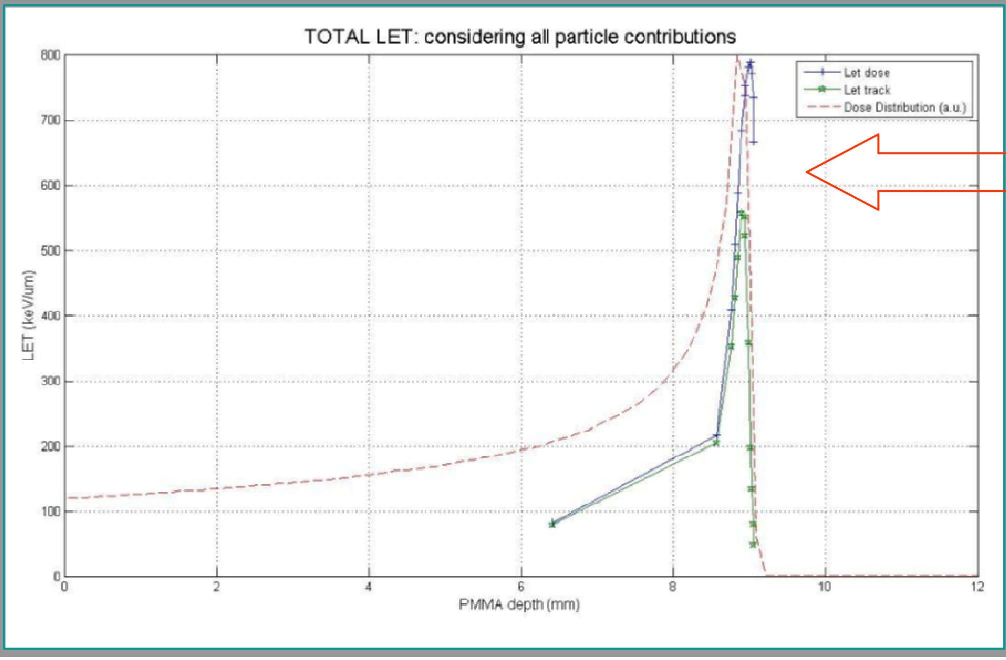




Optimization of the physical dose: LET for heavy ions



Without Multifragmentation contributions (only primary Carbon ion)



Multifragmentation contributions

A Monte Carlo (MC) code can be used to entire commissioning and validation of a proton therapy treatment planning system.

BUT:

1) MC validation versus experimental data is a fundamental step.

2) The computation time for the entire virtual commissioning process is enough long for clinical routine

Commissioning of a Treatment Planning System

1. Eyeplan analytical ocular proton treatment planning

- Feature
- Algorithm
- Output

2. MC code to verify dose distribution

- Validation Procedure
- GEANT4
- Beam Line
- Analysis

3. Dosimetric TPS validation: Measured and Monte Carlo data

- Experimental Setup
- Measured Data
- Dose distribution Comparison

4. Results

- Discussion
- Computation Time

Commissioning of a Treatment Planning System: EYEPLAN

EYEPLAN developed by T. Miller, M. Goitien (1983), now manteined by M. Sheen (2000)

Main Eyeplan features (as treatment planning program in general):
Three – dimensional definition of the tumor volume and normal structures
Possibility of delivering the treatment beam from any direction in space
Provision of arbitrary viewpoints including a beam's eye point of view

Ultra Simplified Broad beam method to get out a non-divergent beam, large enough beam so that the relative depth-dose curve on the central axis does not depend on the field amplitude

INPUT NEED (configuration of Enviroment file)

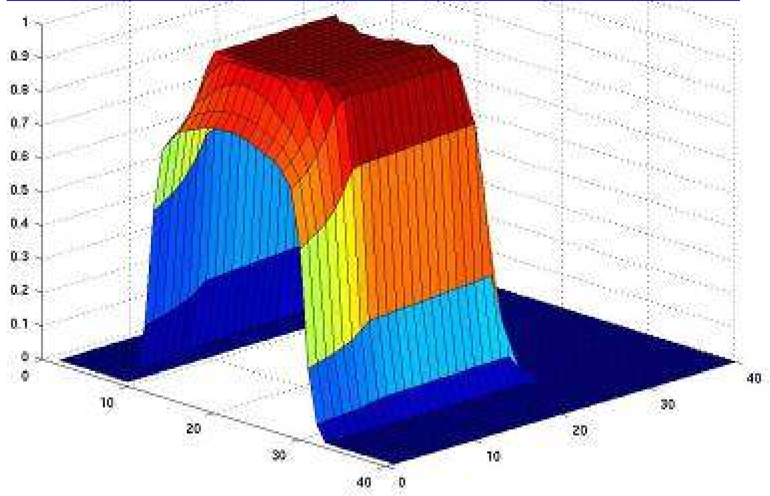
TWO GEOMETRIC PARAMETERS (Virtual source – isocenter, Final collimator – isocenter)

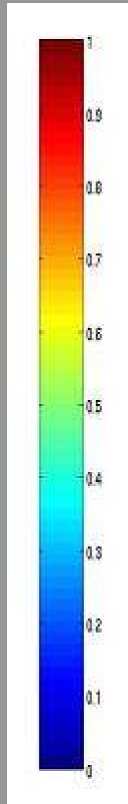
THREE DOSIMETRIC PARAMETERS (Later penumbra, dose distal fall-off (Range) and Proximal Bragg Peak Points)

Eyeplan reconstructs eye dose distribution so that isodose 90% enclose totally PTV, with a security Margin of 2,5 mm
Eyeplan uses a dose plane divided in voxels (Variable dimension) to perform all 3D dose distribution in entire eye

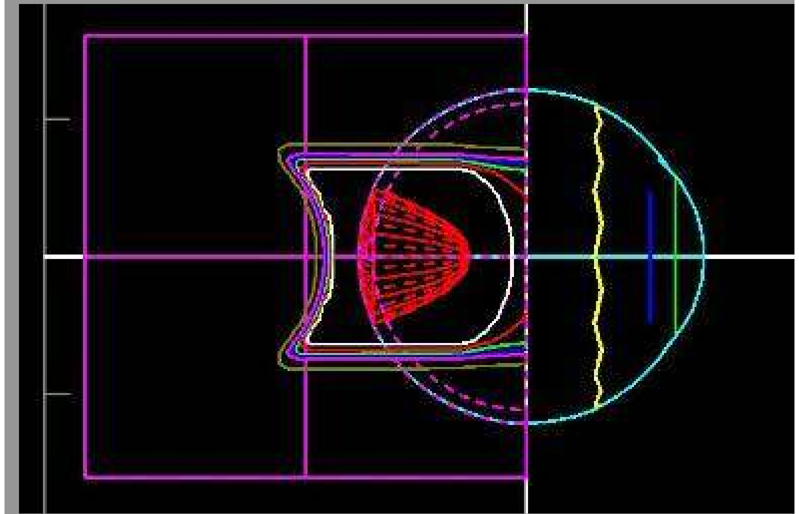
Commissioning of a Treatment Planning System: EYEPLAN

3D EYEPLAN dose distribution
(Transversal plan)



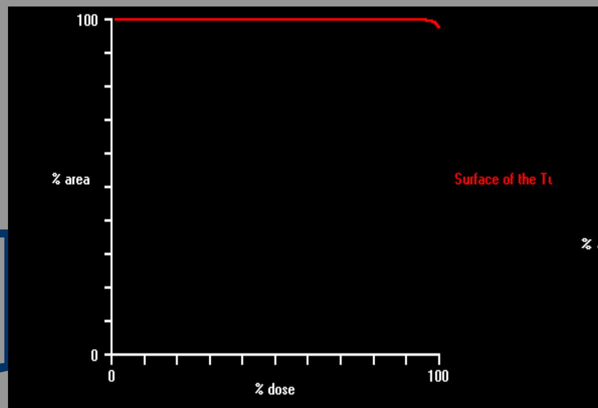


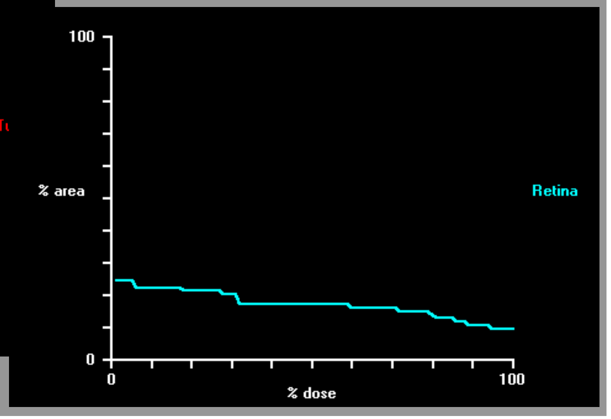
Calculation and Visualization of isodose curve in more eye section plane



Mean Spatial Resolution = 0.8 mm

Dose-Volume histogram (DVH) for PTV and important eye structure





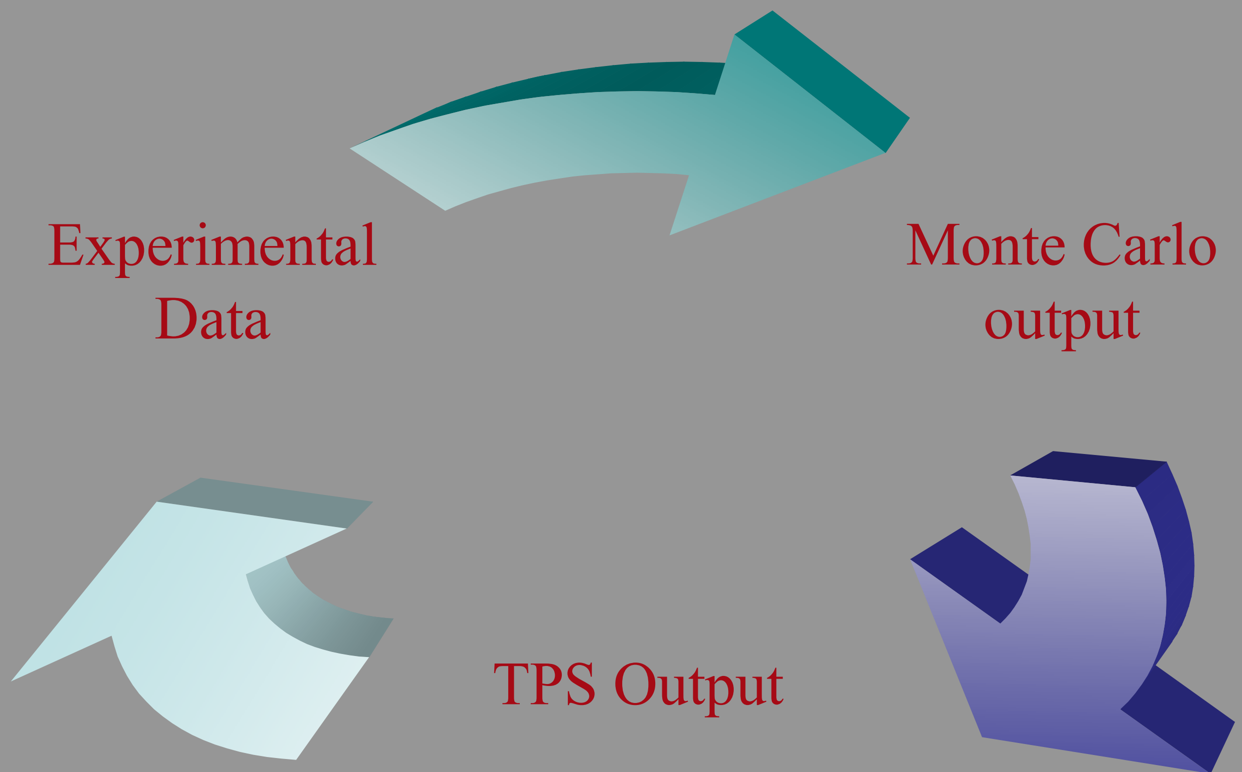
Commissioning of a Treatment Planning System: Validation Procedure

THREE ESSENTIAL STEPS

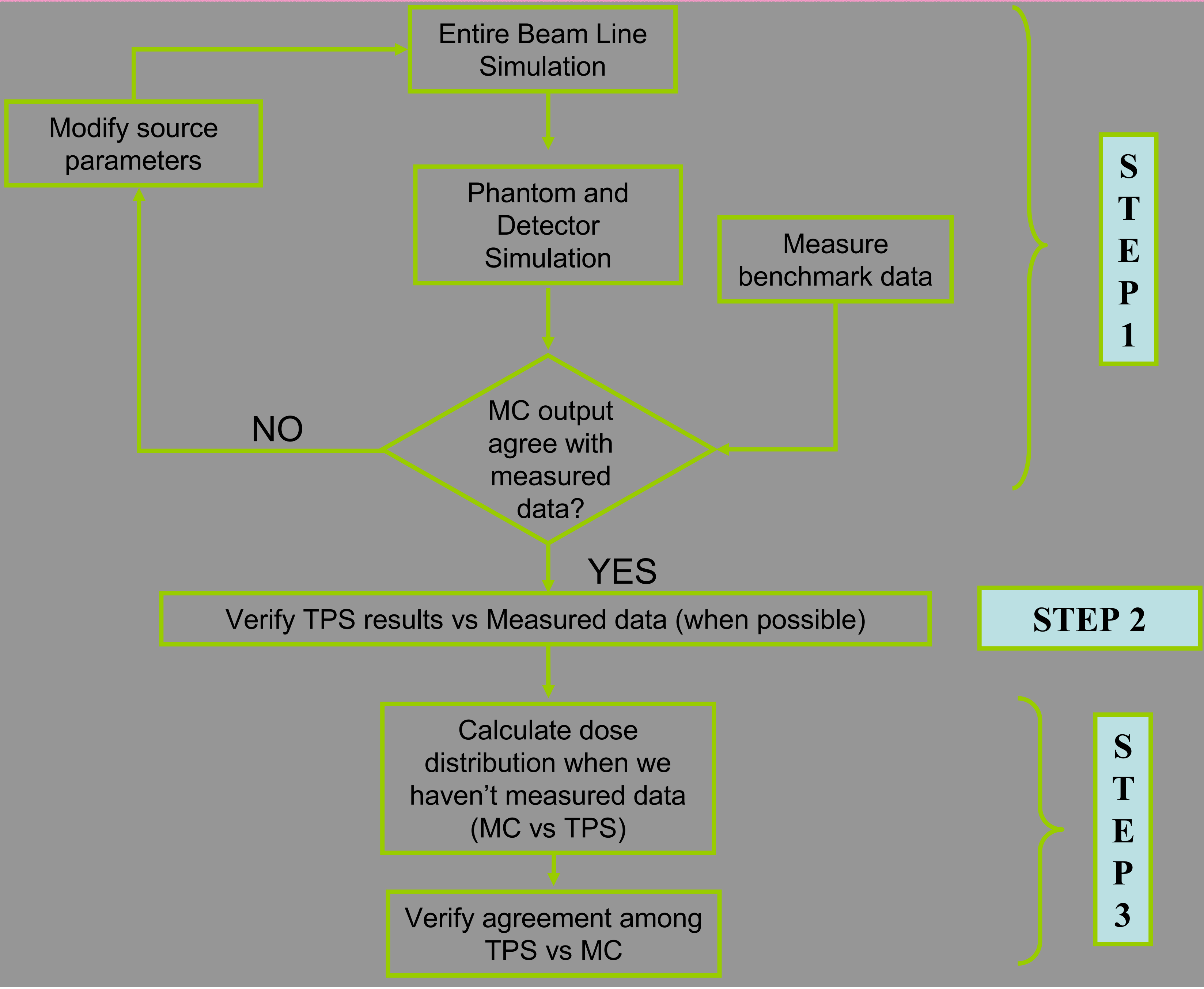
1.- GEANT4 validation versus experimental data

2.- Comparison of TPS dose distribution versus experimental data (when possible)

3.- Comparison between TPS and MC output (without measured data)



Commissioning of a TPS: flowchart with validation procedure



Commissioning of a Treatment Planning System: HADRONTHERAPY

Eyeplan Validation work is performed employing HADRONTHERPY example based on GEANT4 toolkit

Sensitive detector with cubic voxel

3D Monte Carlo simulation

High spatial resolution (0.2 mm)

[“G4ROGeometry”]

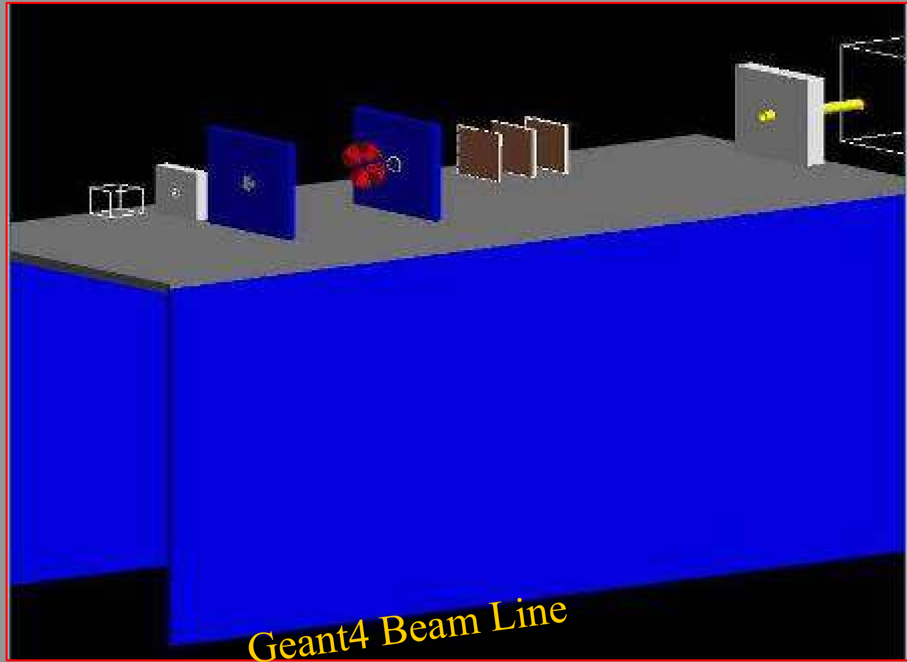
Small size of Output file

Only one output file for entire 3D dose distribution in the detector

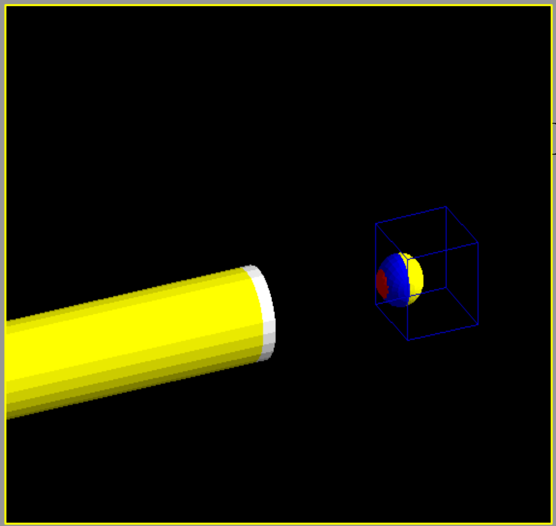
Every Eye structure can be voxelizated (DVH)

Commissioning of a TPS: CATANA beamline simulation

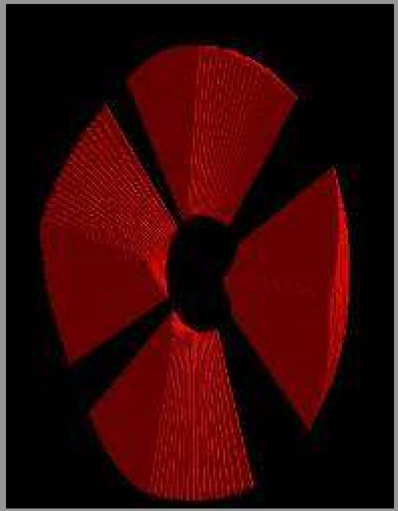
Final Nozzle in treatment room CATANA



GEANT4 Simulation of the beamline



EYE structure simulation



Time – dependent geometry

Commissioning of a Treatment Planning System: ANALYSIS COMPARISON

How compare Two dose distributions?

Composite Analysis: Dose Difference, DTA e Gamma function

D. A. Low et al.

A technique for the quantitative evaluation of dose distributions

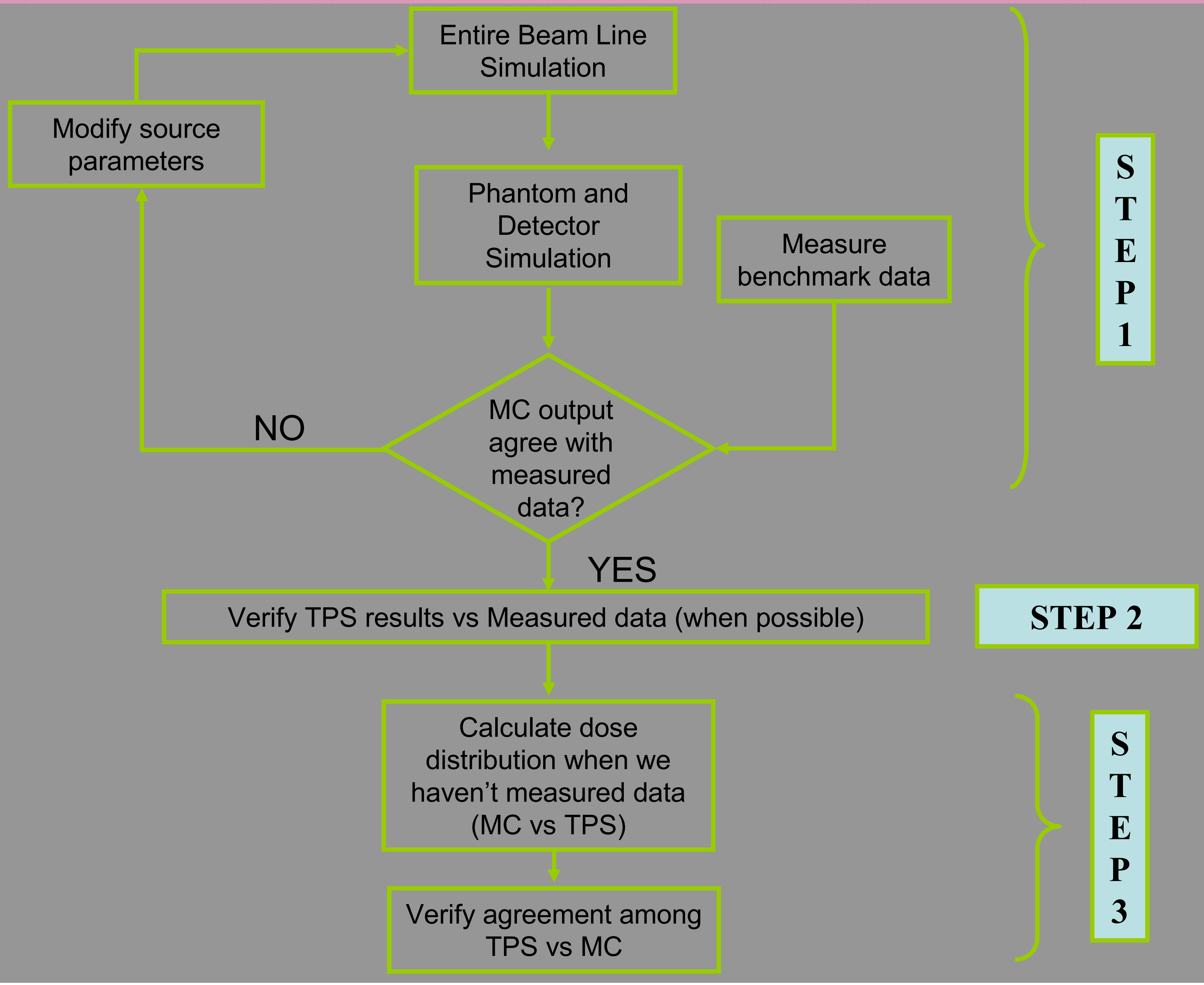
Med. Phys. 25: 656-661, 1998

If the dose-difference criterion is Δ_{DM} , and the DTA criterion is Δ_{dM}

The passing criteria shown are Δ_{DM} = 3% (5%) and Δ_{dM} = 3 mm based on clinical standards for photon and electron beams

In Proton Beams case, we performed a study to set Δ_{DM} AND Δ_{dM}

Commissioning of a treatment planning system: STEP 1



Commissioning of a treatment planning system: STEP 1

DOSIMETRIC PARAMETERS USED TO COMPARE THE AGREEMENT BETWEEN SIMULATED AND EXPERIMENTAL DATA

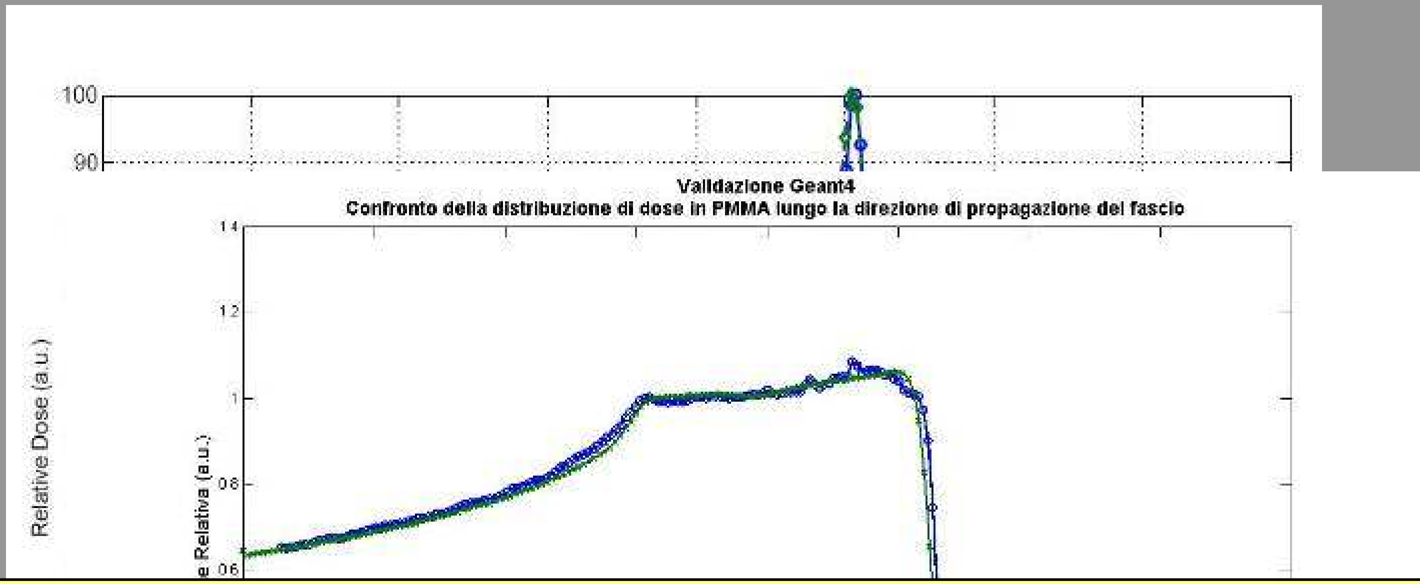
Full Energy Bragg peak and SOBP →

- **Peak – plateau Ratio**
- **Pratical Range**
- **Distal dose fall-off (90%-10 %)**
- **FWHM**
- **Modulation Range**

Profile →

- **Beam Width 50%**
- **Penumbra (80% – 20%)**
- **Homogeneity**
- **Symmetry**

Commissioning of a treatment planning system: STEP 1



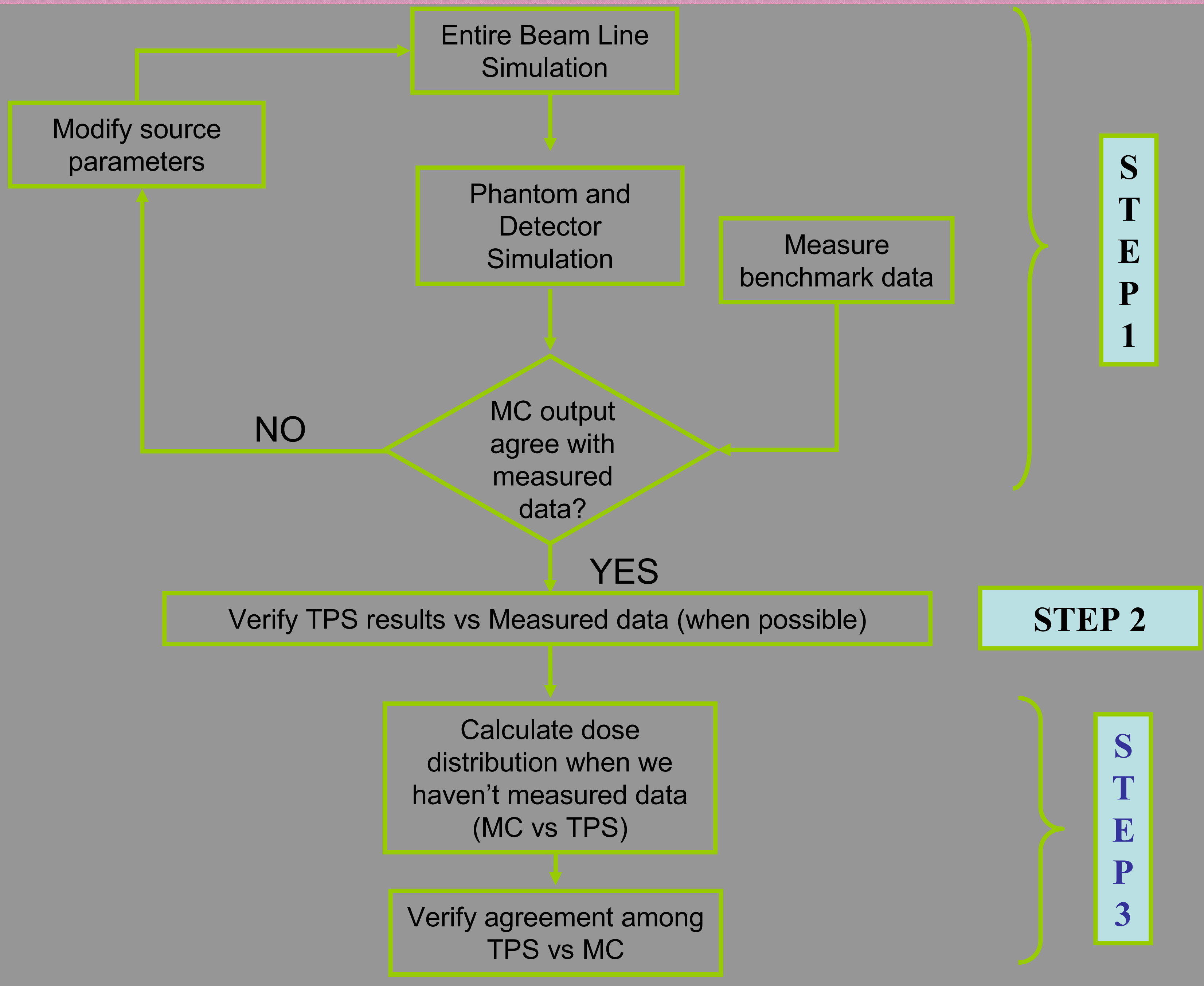
PMMA

Differences are less than 0.2 mm (voxel dimension)

Pure Bragg Peak				
Dosimetric Parameters	Peak – Plateau Ratio	FWHM (mm)	Penumbra (mm)	Pratical Range (mm)
Geant4 Simulation	4.42	2.95	0.95	26.95
Experimental Measured	4.40	3.15	0.76	26.81

SOBP			
Dosimetric Parameters	Modulation Range $d_{90\%}$ - $p_{100\% \text{ (mm)}}$	Penumbra (mm)	Pratical Range (mm)
Geant4 Simulation	9.90	1.05	26.91
Experimental Measured	10.00	0.95	26.98

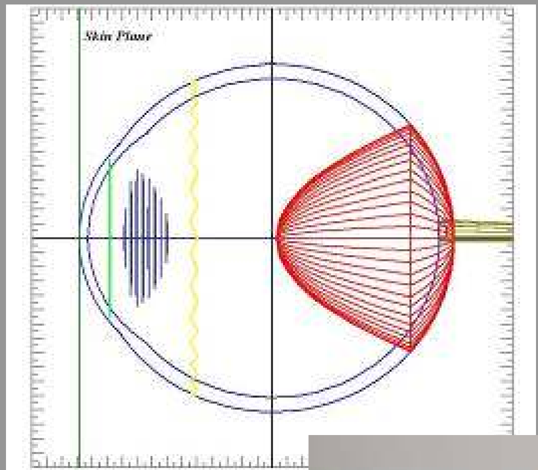
Commissioning of a treatment planning system: STEP 2

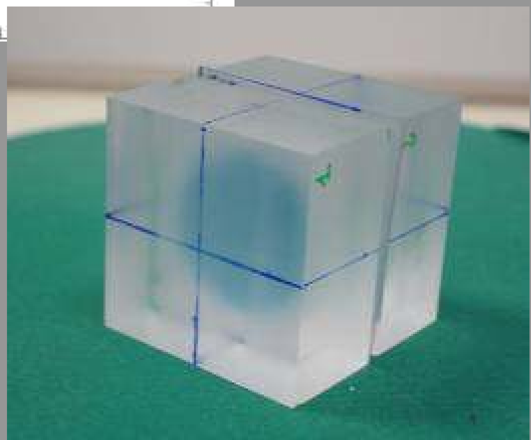


Commissioning of a treatment planning system: STEP 2

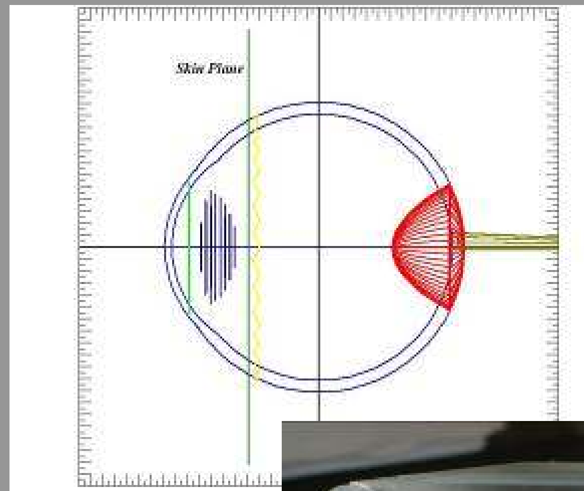
Two different configurations planned

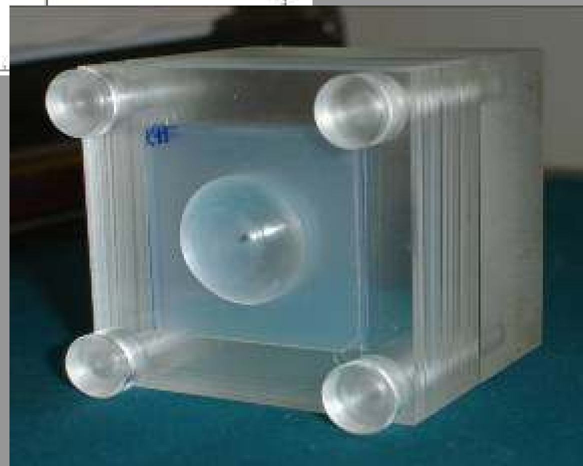
NO Clinical Case





Clinical Configuration

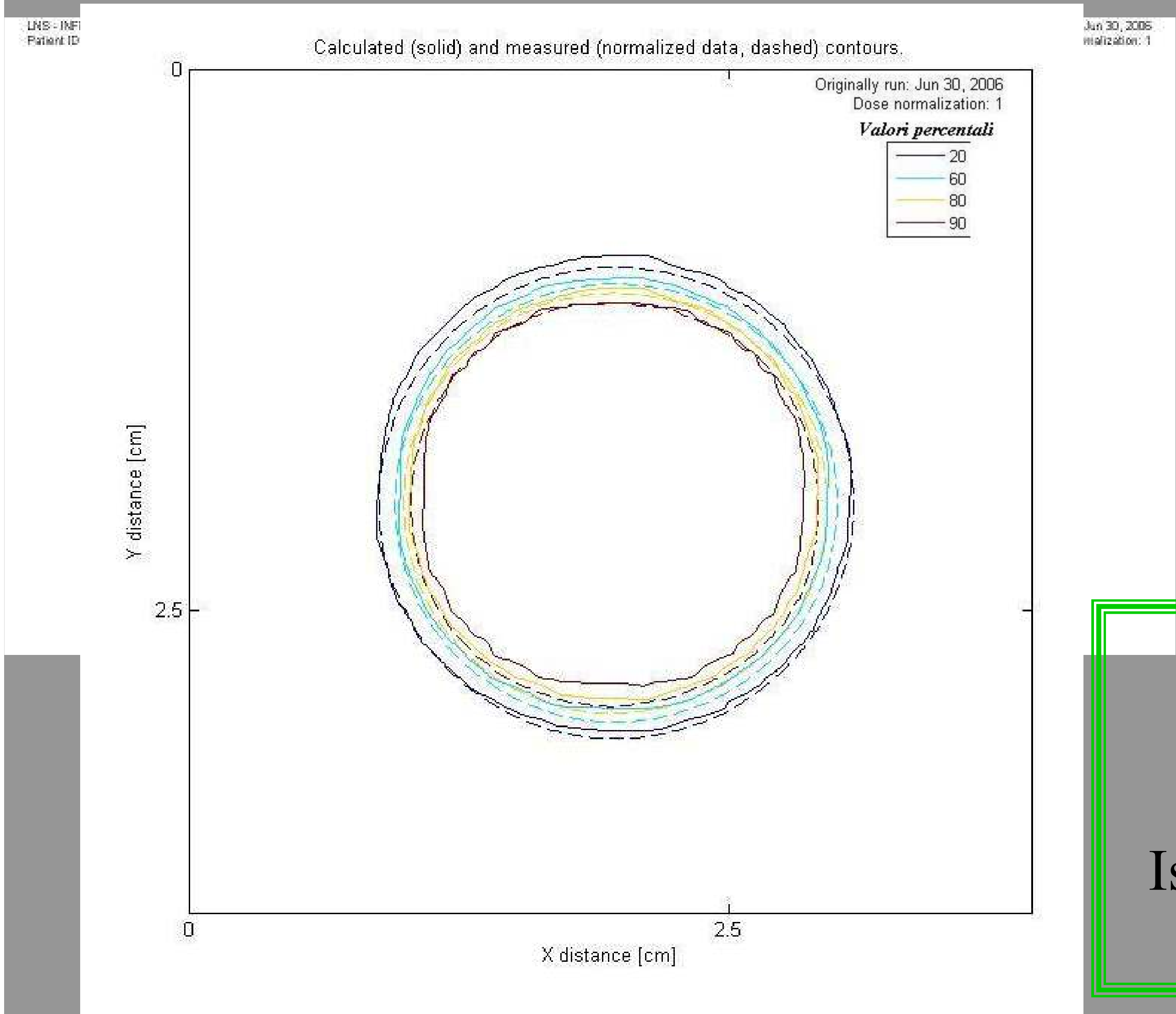




The Comparisons between dose distribution are along and perpendicular to beam direction at different PMMA depth

Commissioning of a treatment planning system: STEP 2

NO Clinical case (Perpendicular to beam direction)

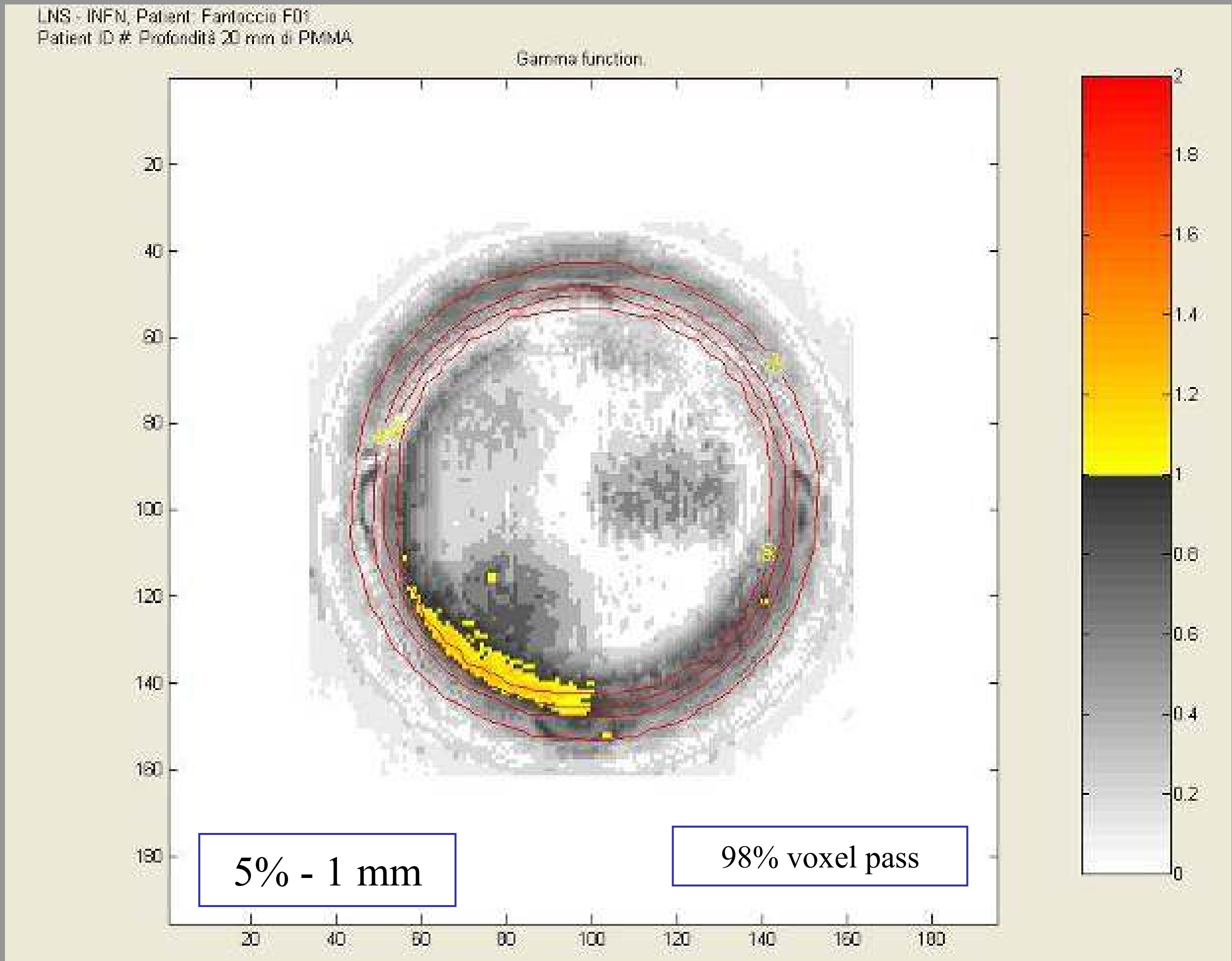


Direct Comparison between Isodoses levels

GOOD Agreement among TPS and Measured Data. Isodose level Maximum difference = 1 mm

Commissioning of a treatment planning system: STEP 2

NO Clinical case (Perpendicular to beam direction)

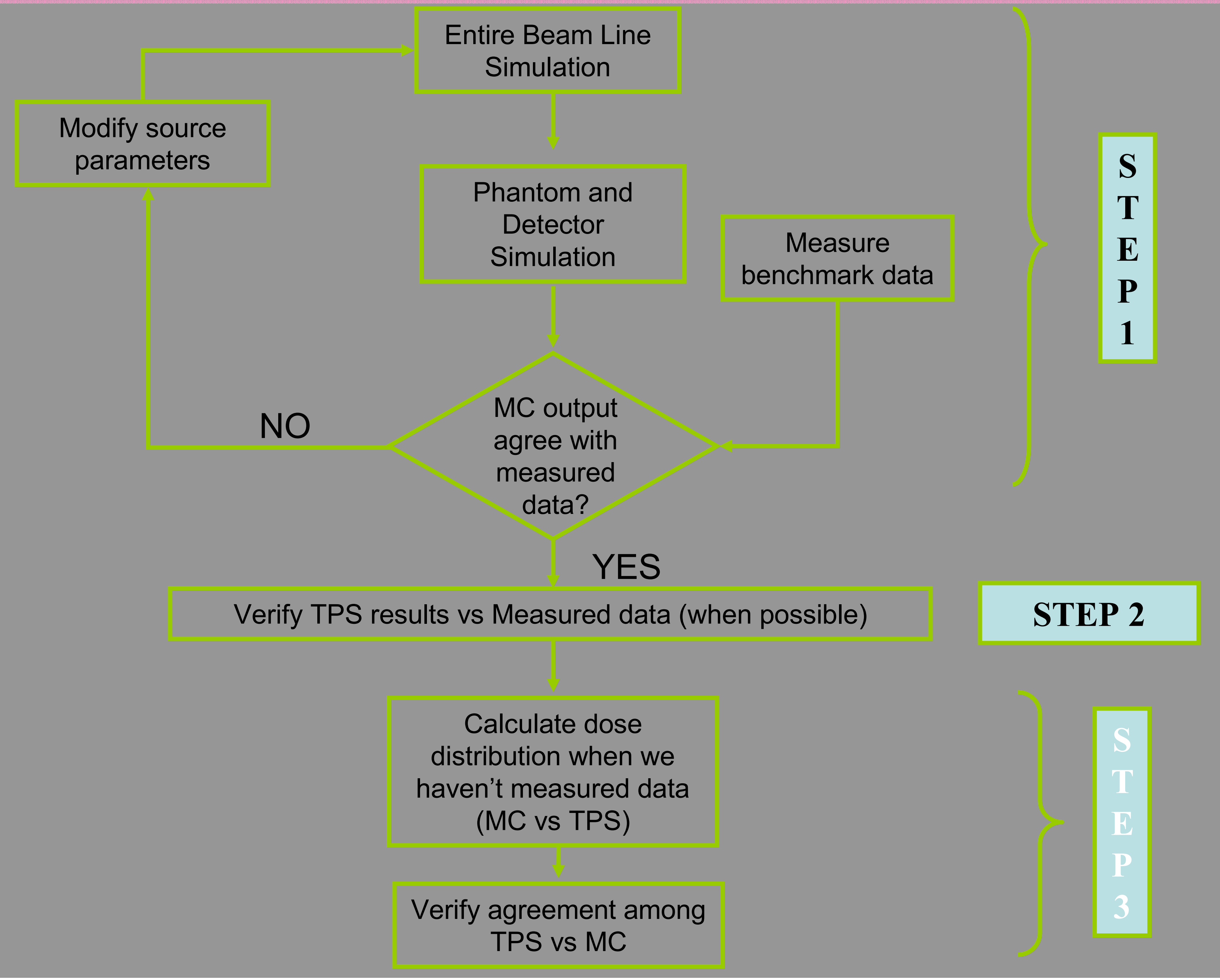


2D gamma function distribution

Gamma function distribution is not uniform, the values fails criteria are focused around 90 % isodose level

This difference can be due to a non accurate phantom centering. In the same mode, local spot near to unit gamma value (inside 90% isodose level) are given by a non ideal detector homogeneity

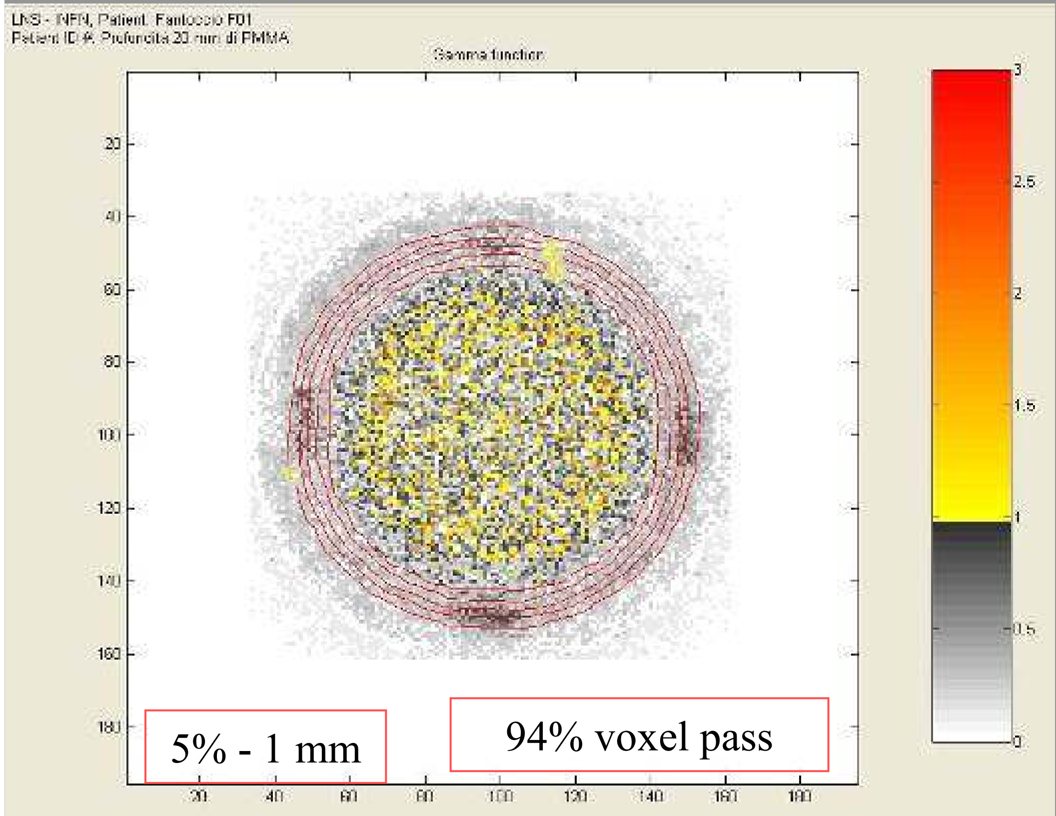
Commissioning of a treatment planning system: STEP 3



Commissioning of a treatment planning system: STEP 3

NO Clinical case (Perpendicular to beam direction)

TPS dose distribution is in agreement to Measured data => MC dose distribution can be directly compared to TPS output



Good agreement among MC and TPS
Maximum differences < 0.2 mm

This comparison can be used as a additional validation test to confirm that Monte Carlo predictions reproduce measured dose distribution in a phantom

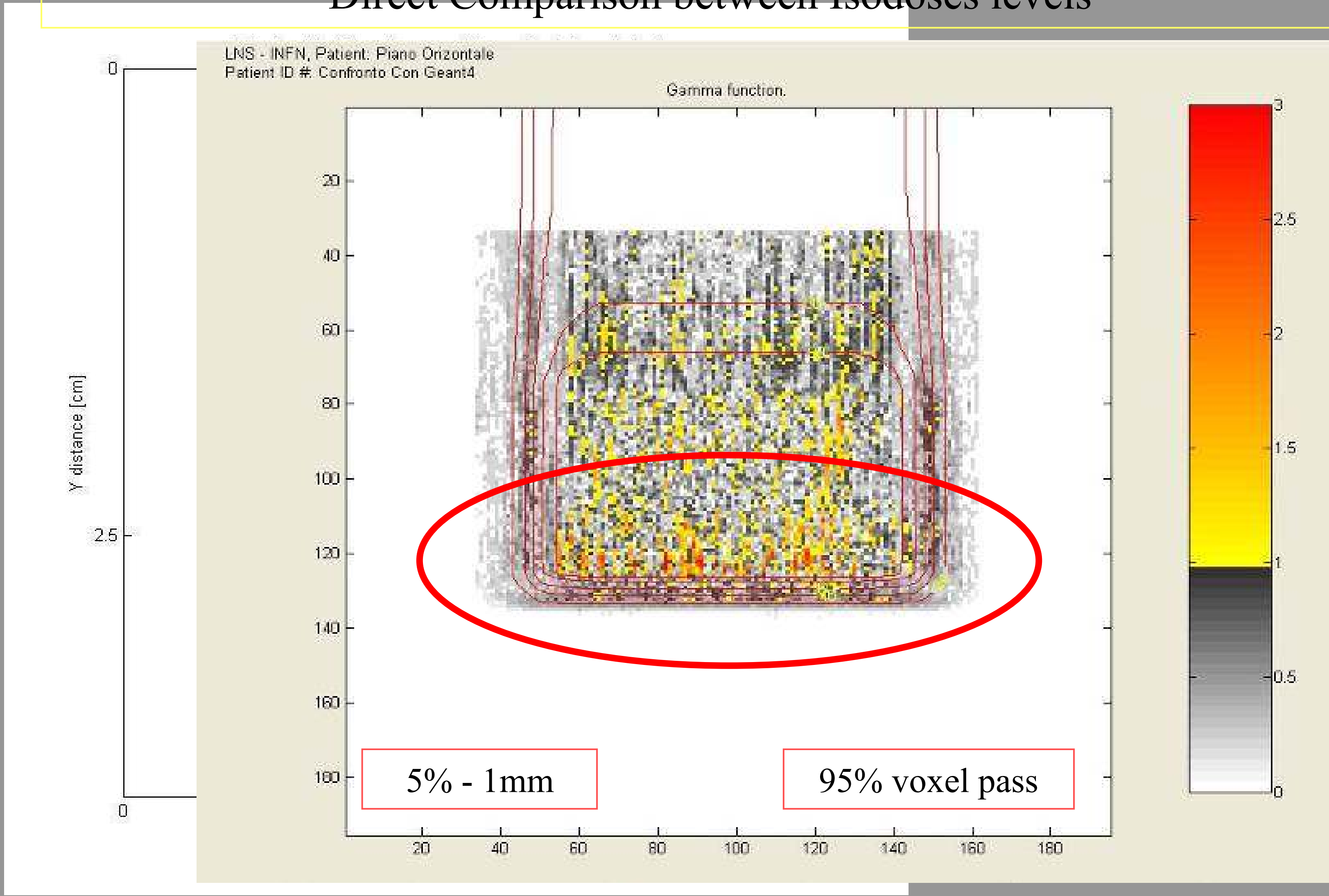
It also possible to exclude the position errors and inhomogeneity detector

The gamma voxel distribution, when the test fails, is uniform on the whole gamma function distribution inside the 90% dose level (Statistic fluctuations in the MC simulation)

Commissioning of a treatment planning system: STEP 3

NO Clinical case (Along beam direction)

Direct Comparison between Isodoses levels



ersus MC
= 0.6 mm

ce
2 mm

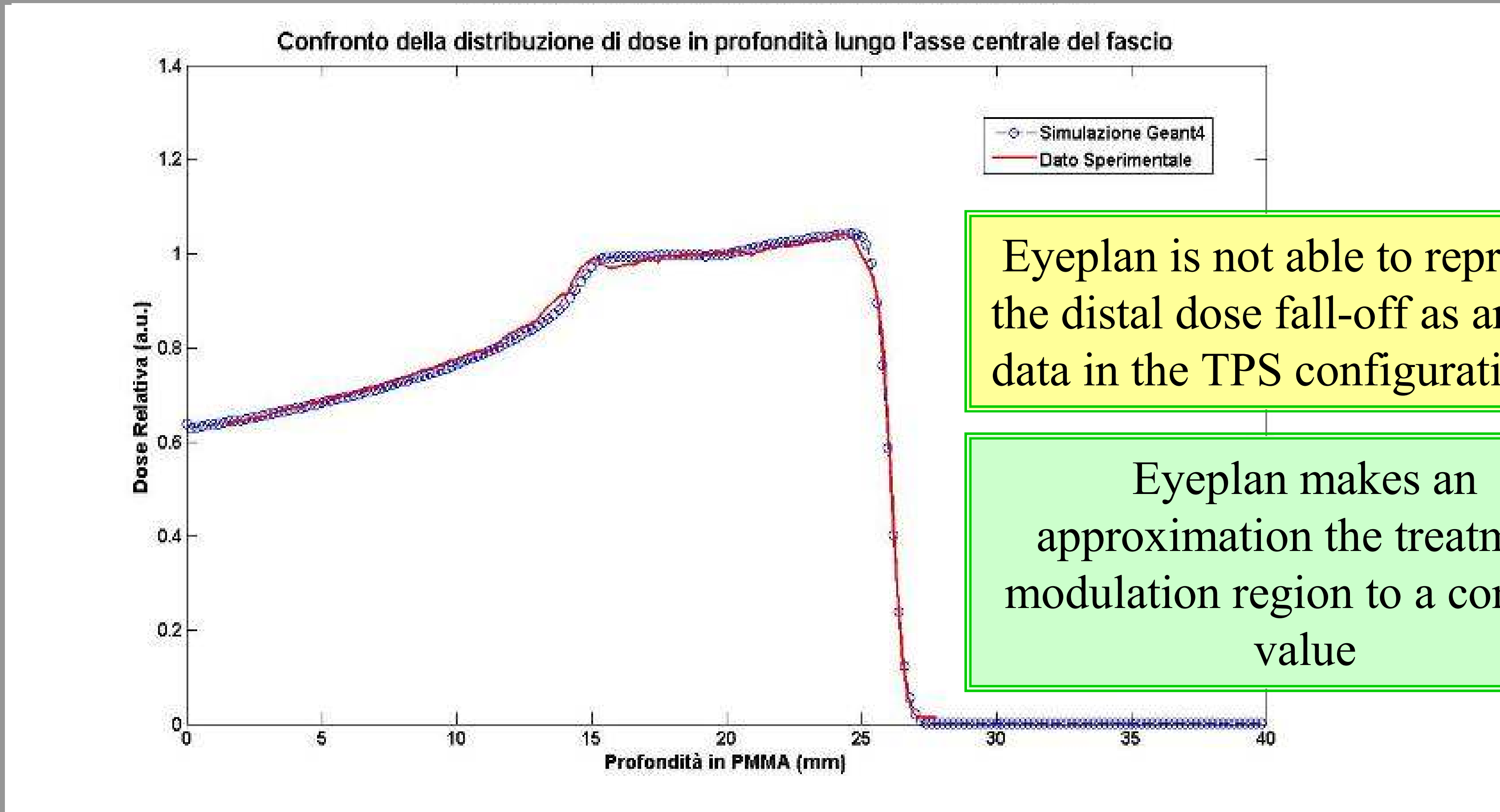
)% Isodose
irection

nces????

Commissioning of a treatment planning system: STEP 3

NO Clinical case (Along beam direction)

The accuracy of Monte Carlo simulations is superior to that of EYEPLAN

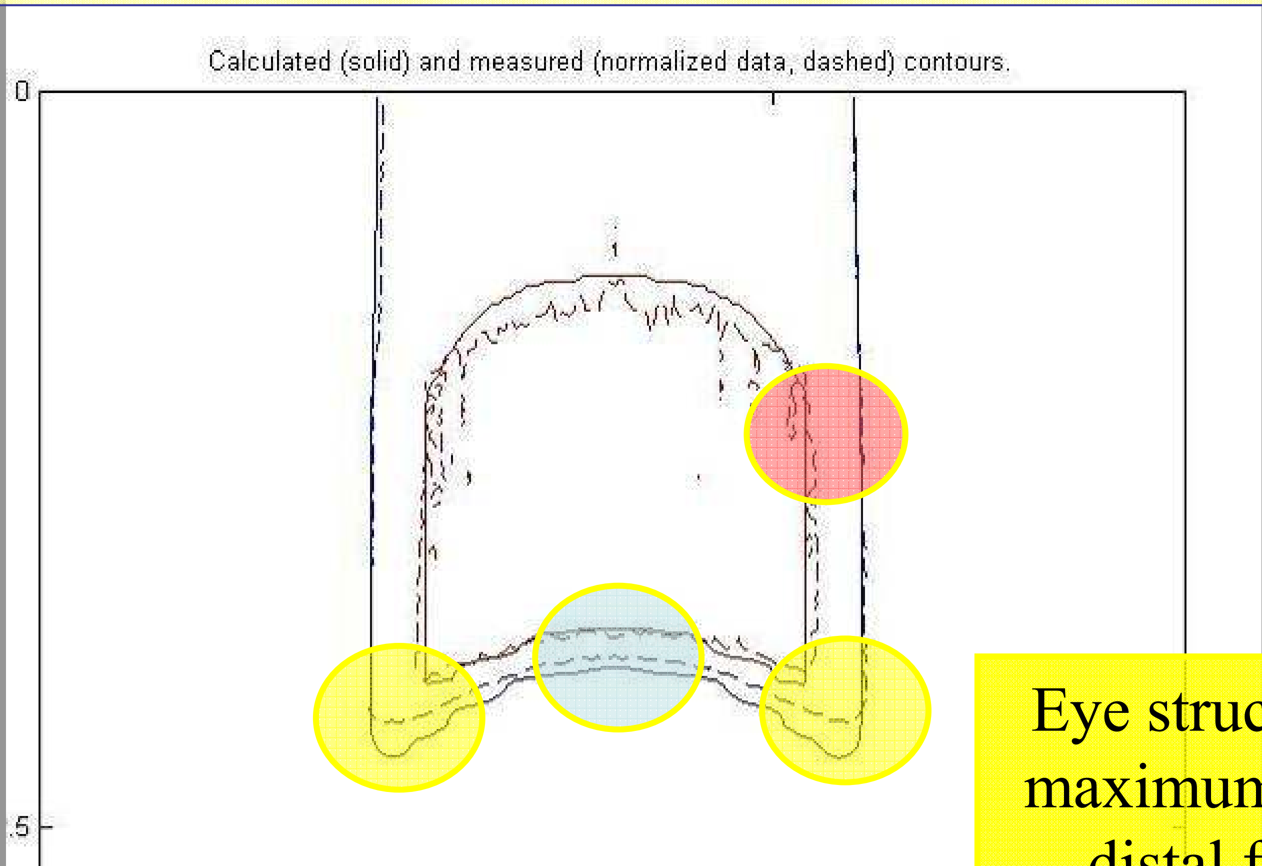


Eyeplan is not able to reproduce the distal dose fall-off as an input data in the TPS configuration file

Eyeplan makes an approximation the treatment modulation region to a constant value

The complexity of the EYE structure, in a realistic clinical case, can modify the results found?!

Clinical Configuration (Along beam direction)



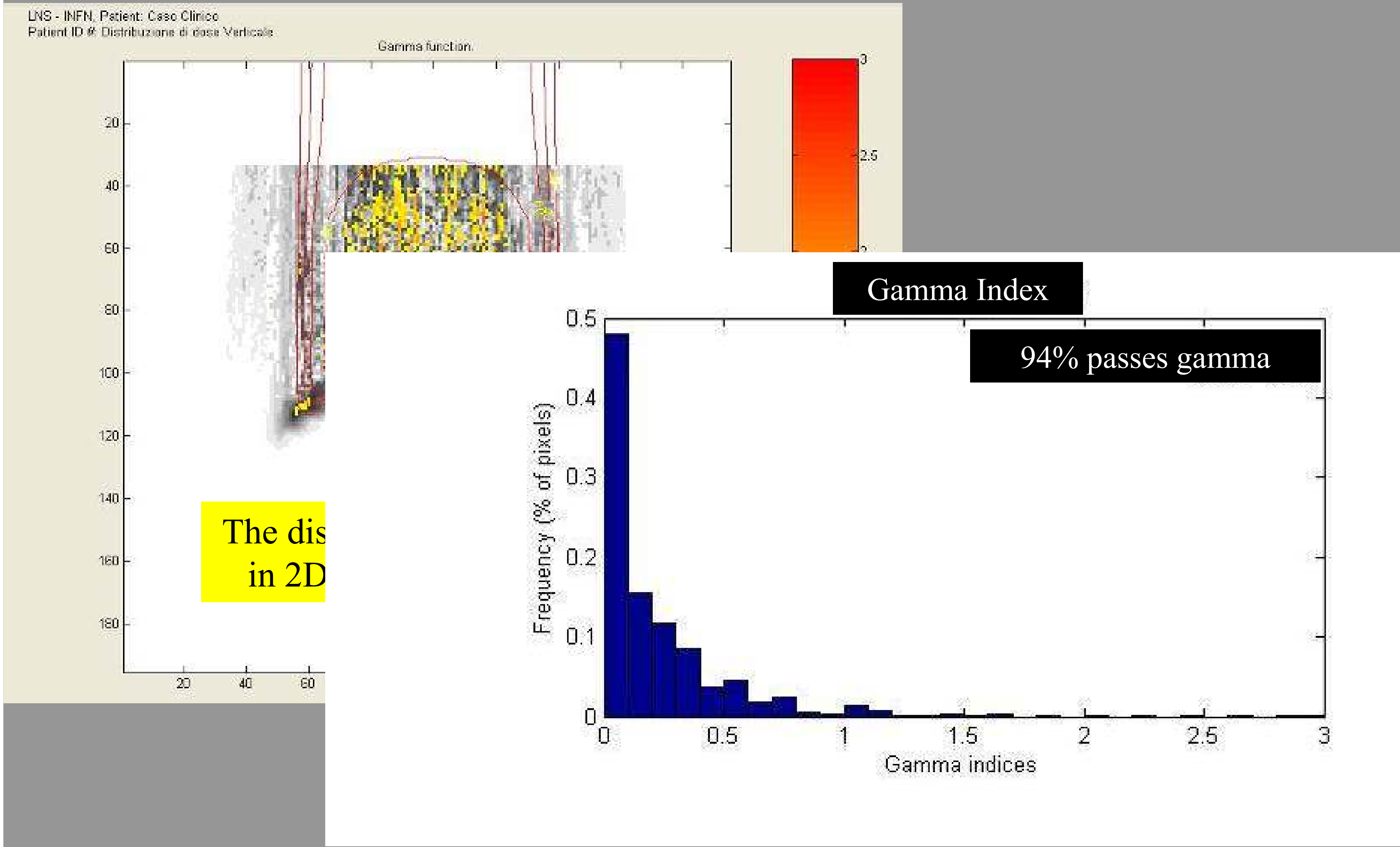
Range Difference (90% Isodose level) < 0.2 mm

Difference in lateral penumbras < 0.2 mm

Eye structure emphasizes the maximum differences in dose distal fall-off calculation

Commissioning of a treatment planning system: STEP 3

Summary of the results for the clinical configuration (along beam)



Commissioning of a treatment planning system: DISCUSSION

OUR RESULTS SUGGEST THAT THE GEANT4 MONTE CARLO CODE IS SUITABLE TO VALIDATION PROCEDURE

THE COMPARISON DEMONSTRATE SOME DIFFERENCES AMONG MC RESULTS AND TPS OUTPUT. THESE DIFFERENCES ARE DUE TO TPS LIMITS:

LOW SPATIAL RESOLUTION

ESTIMATE MAXIMUM DOSE TO CONSTANT VALUE

NO MULTIPLE SCATTERING

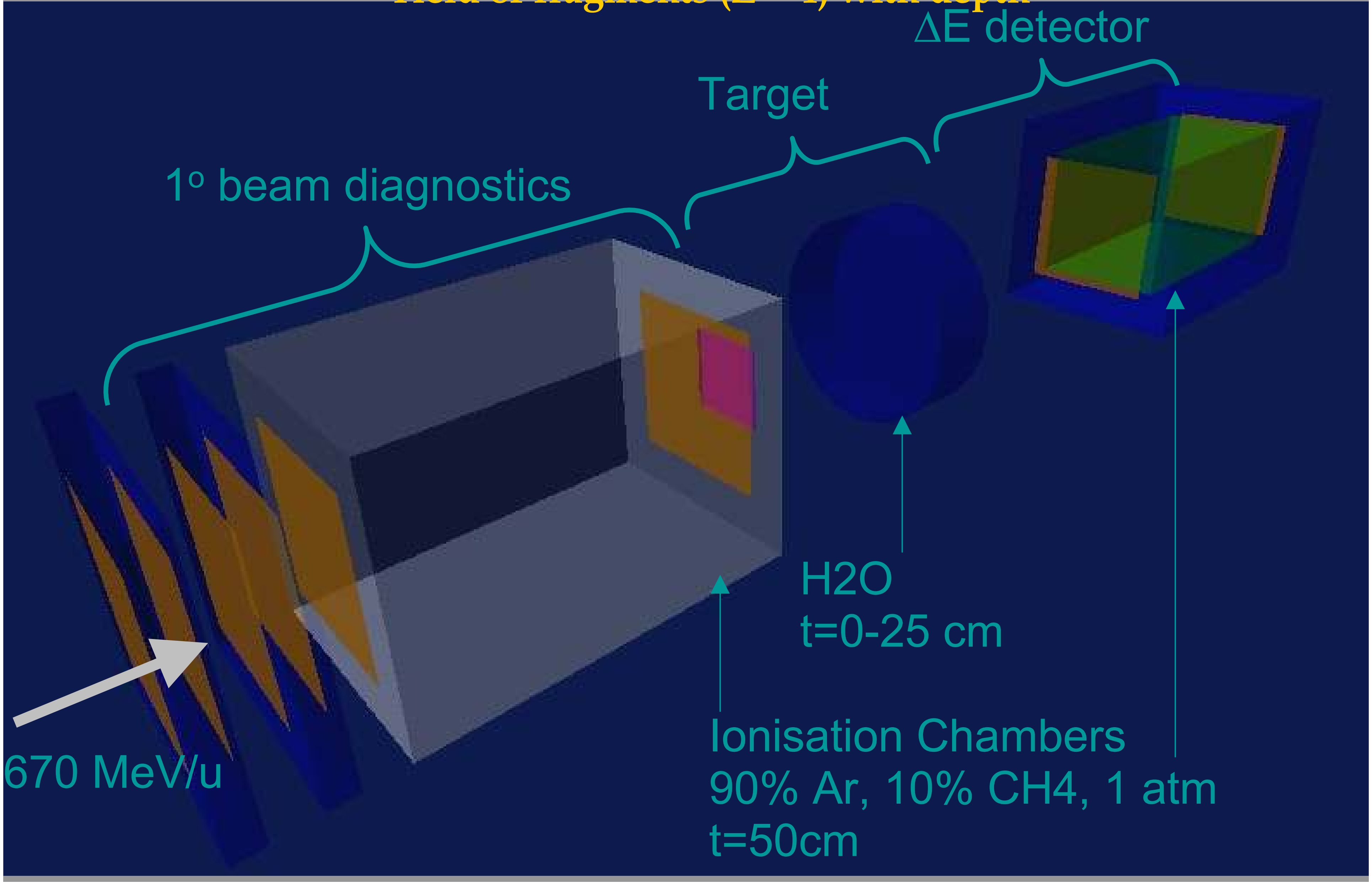
THE EYE STRUCTURE IN EYEPLAN INVOLVES A MORE INACCURACY. HOWEVER, THE DIFFERENCES REVEALED ARE VERY CONTAINED AND CLINICALLY ACCEPTABLE

THE ENTIRE PROCEDURE FOR THE COMMISSIONIG IS VERY TIME COMSUMING:

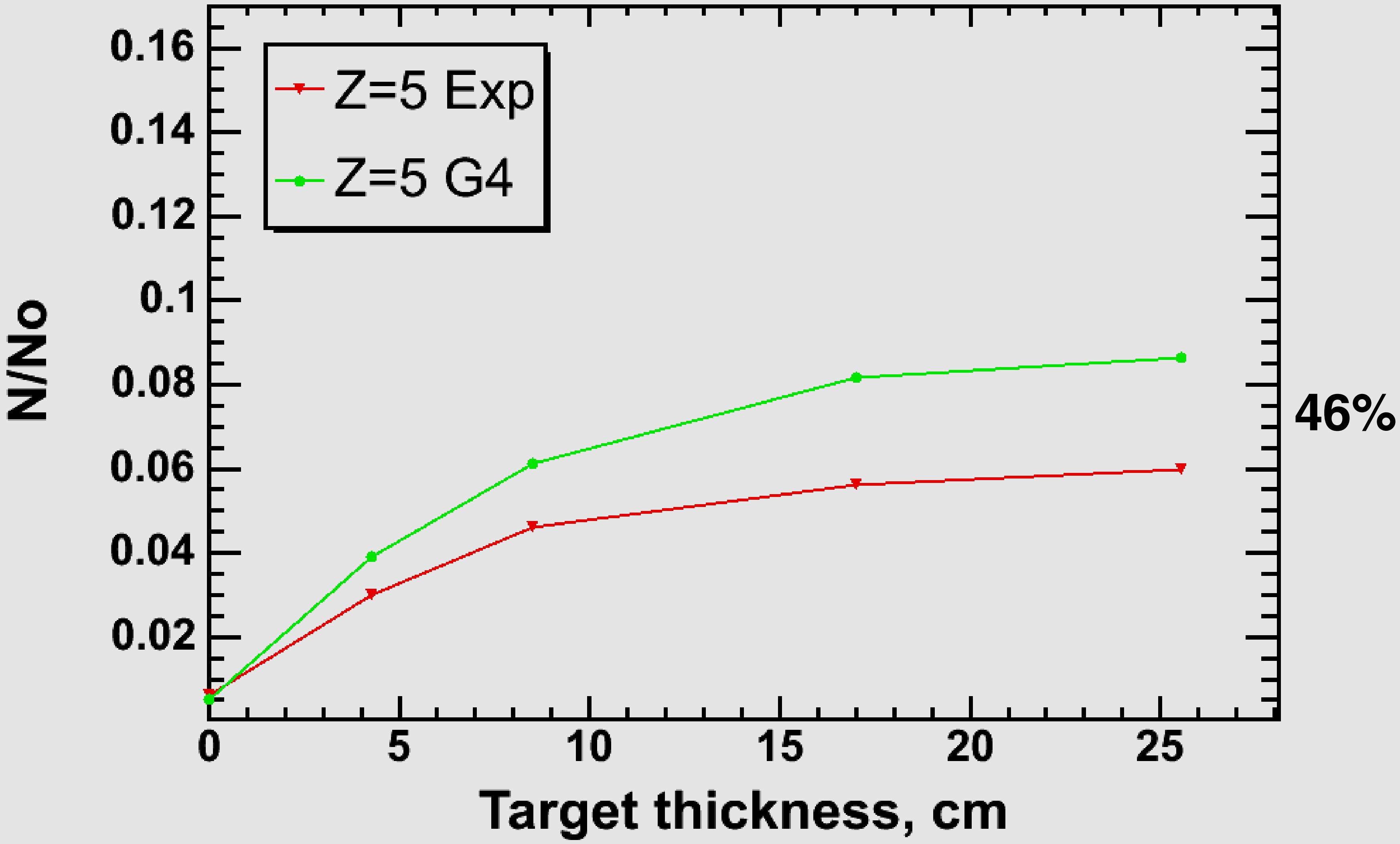
USING A 12-NODE CLUSTER SYSTEM (DISTRIBUTION CALCULATION)

ENTIRE 3D EYE DOSE DISTRIBUTION: 1 WEEK!!!

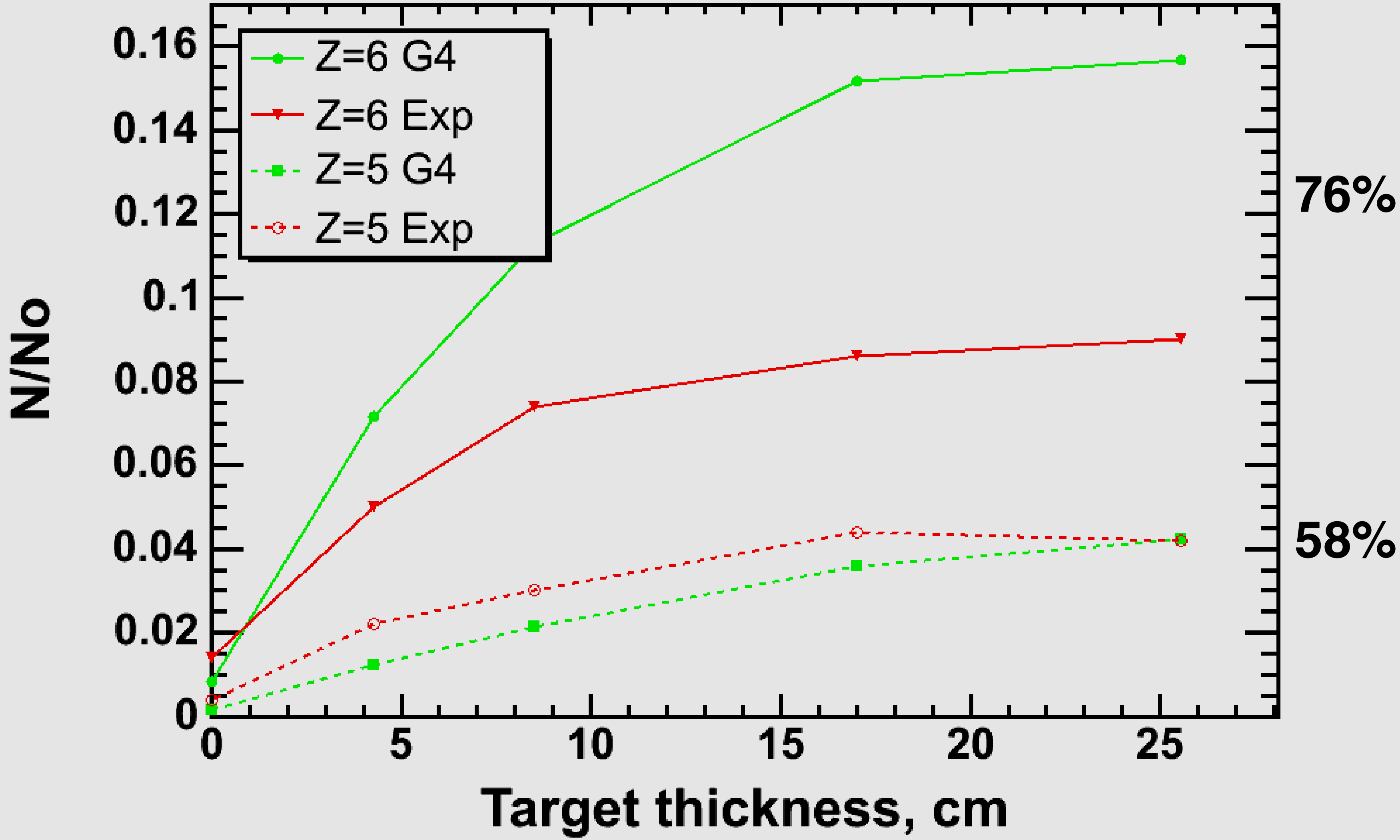
Schall et al 1996 (GSI)
Fragmentation of light ion beams in water
Yield of fragments (Z > 4) with depth



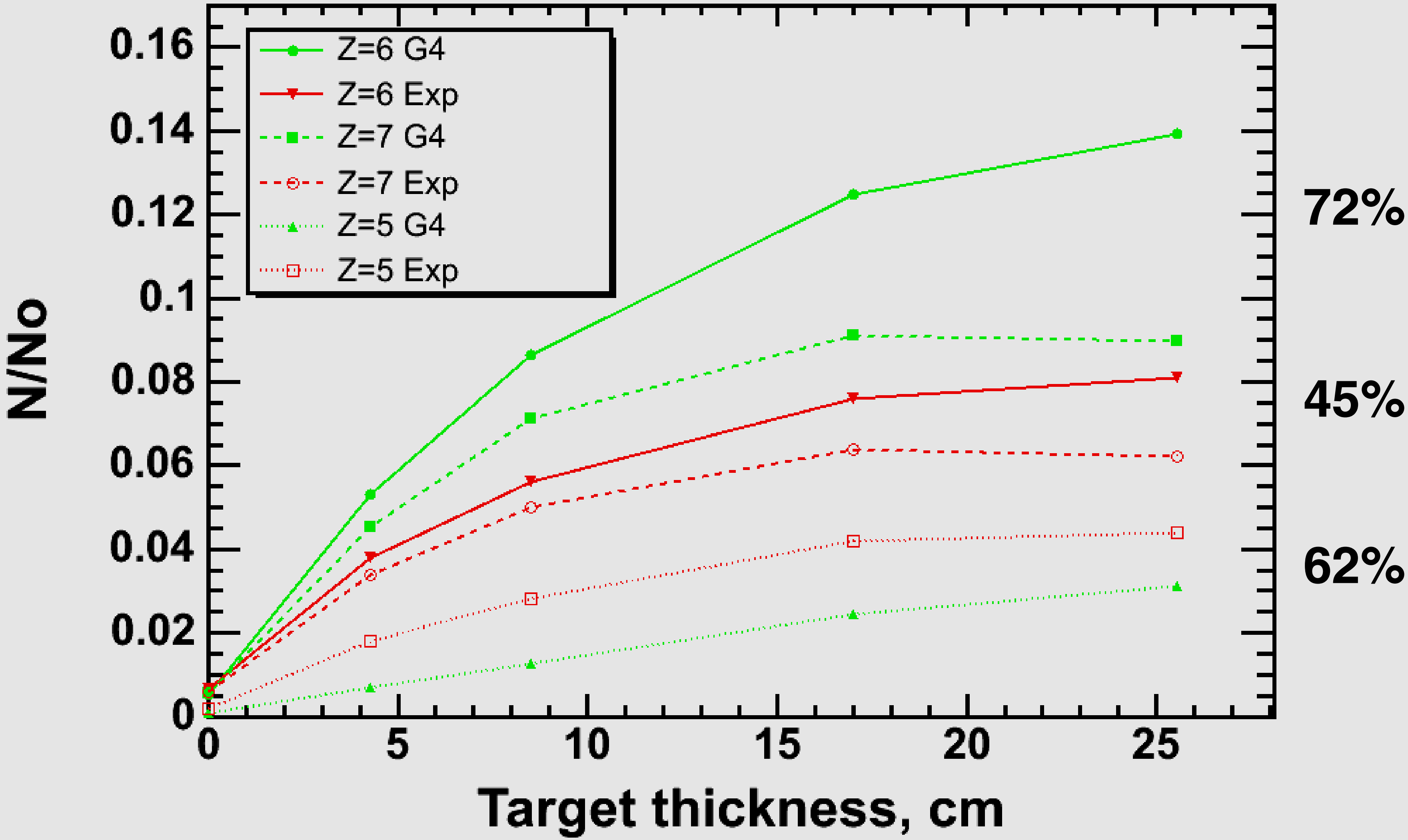
2. Results: C^{12}



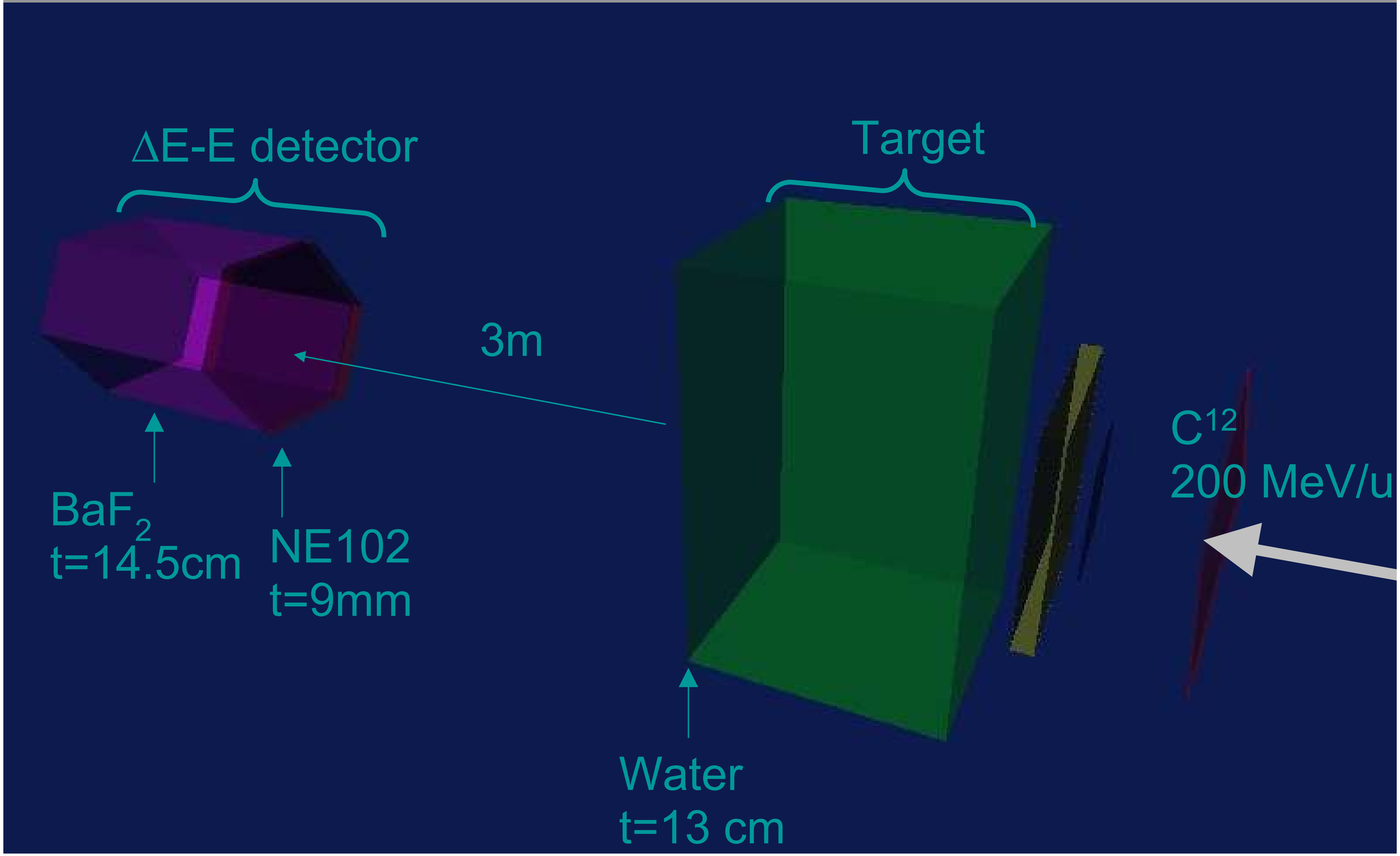
2. Results: N^{14}



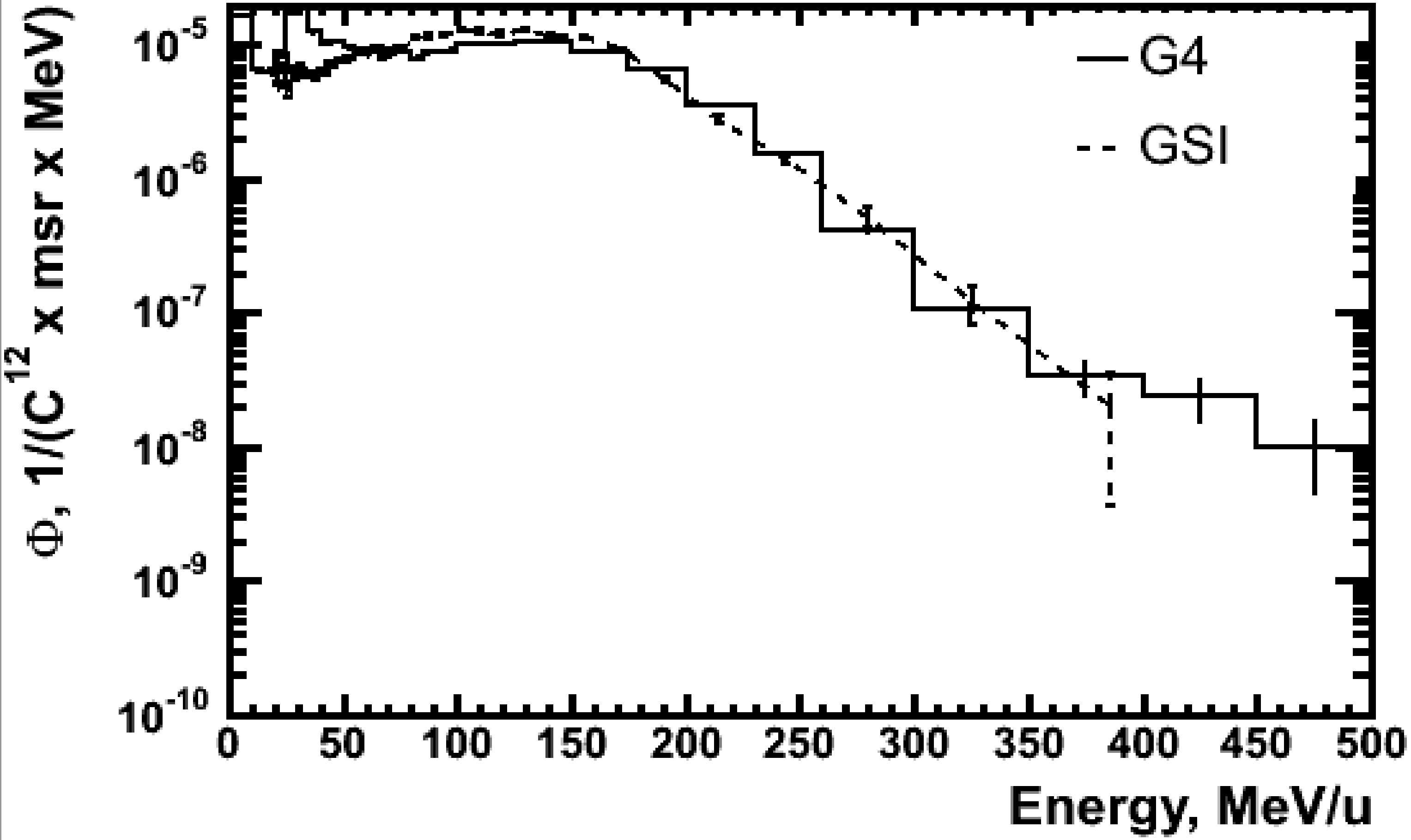
2. Results: O^{16}



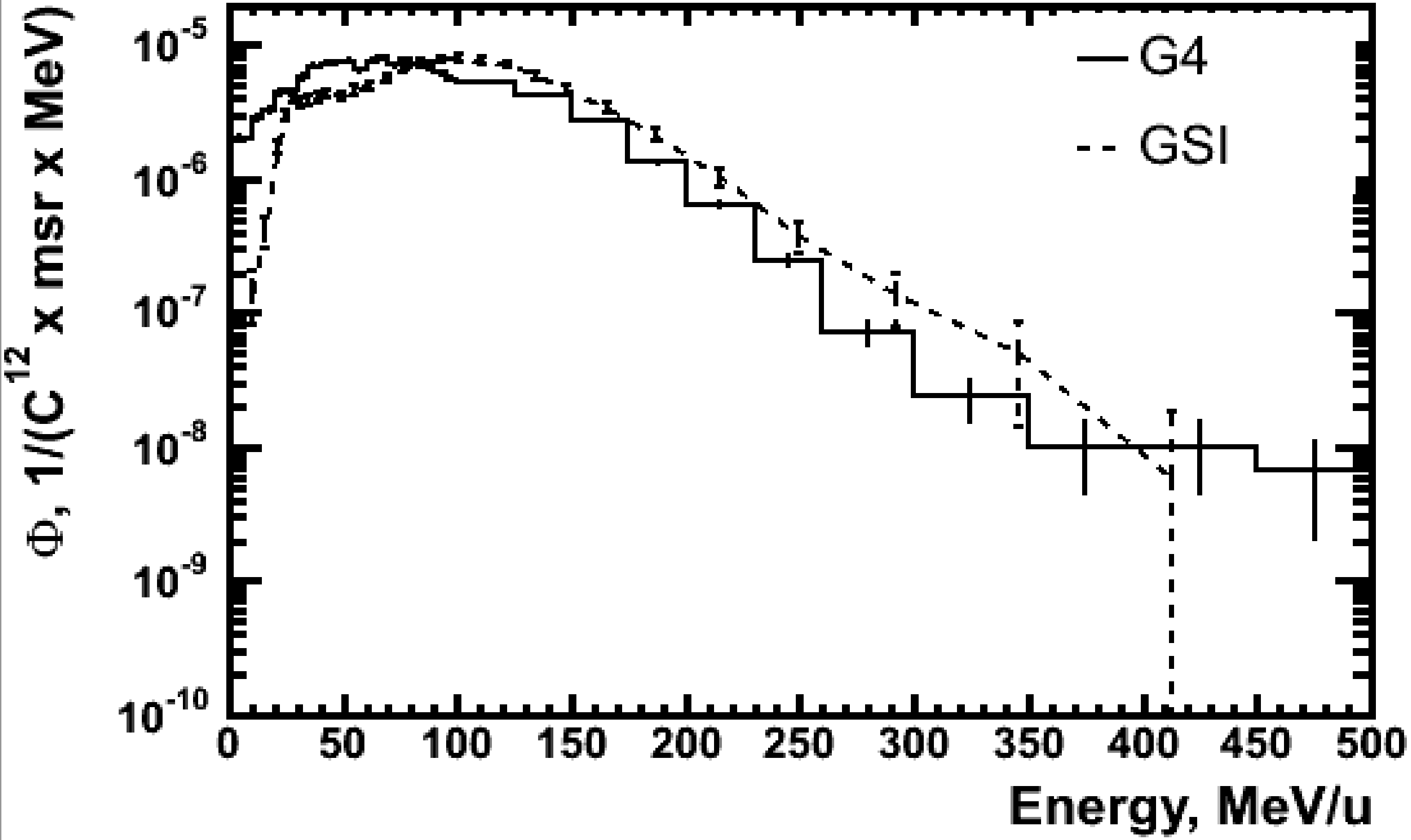
Gunzert-Marx et al 2003 (GSI)
Fragmentation of a carbon beam in water
Spectroscopy of light fragments (A < 4)



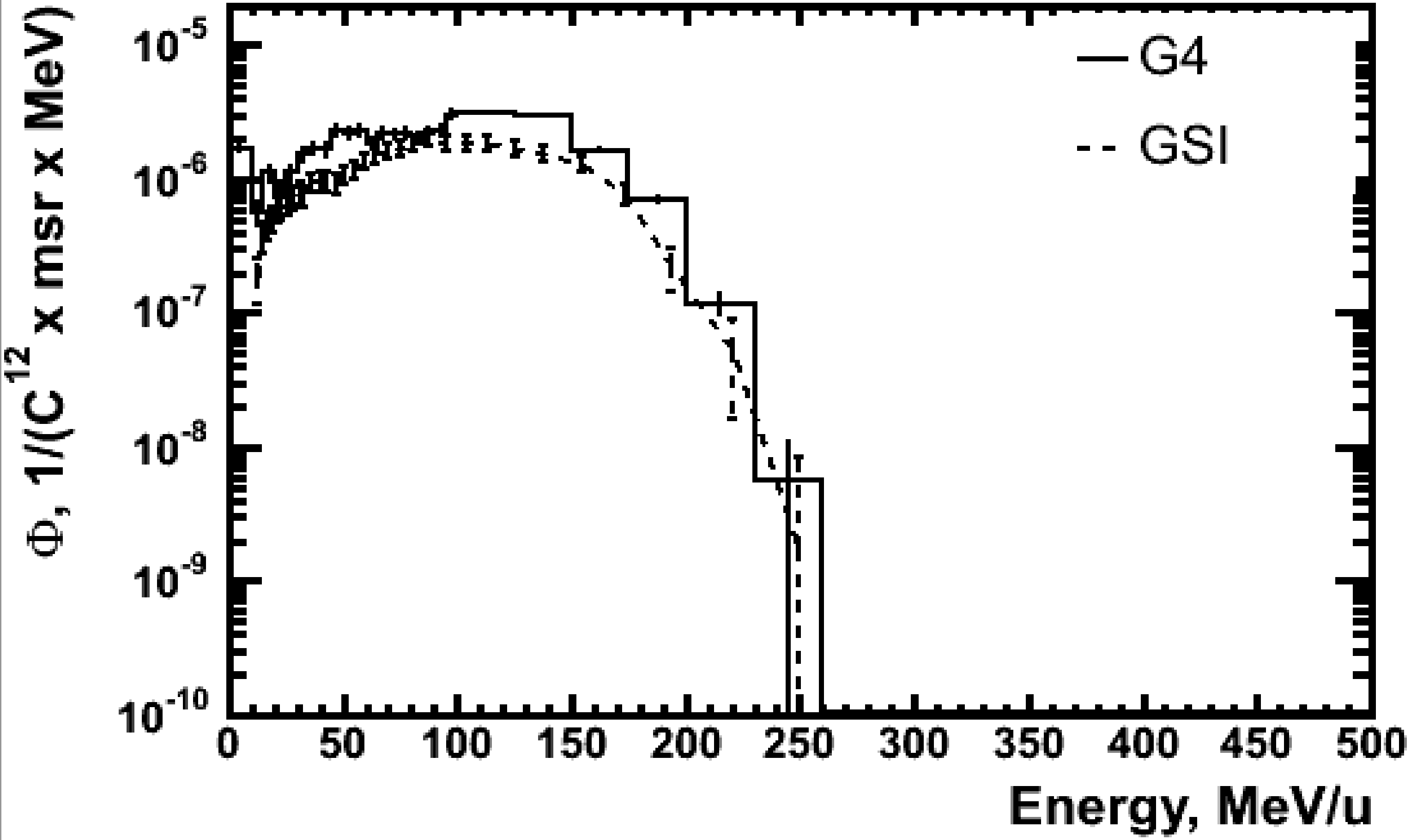
3. Results: neutrons



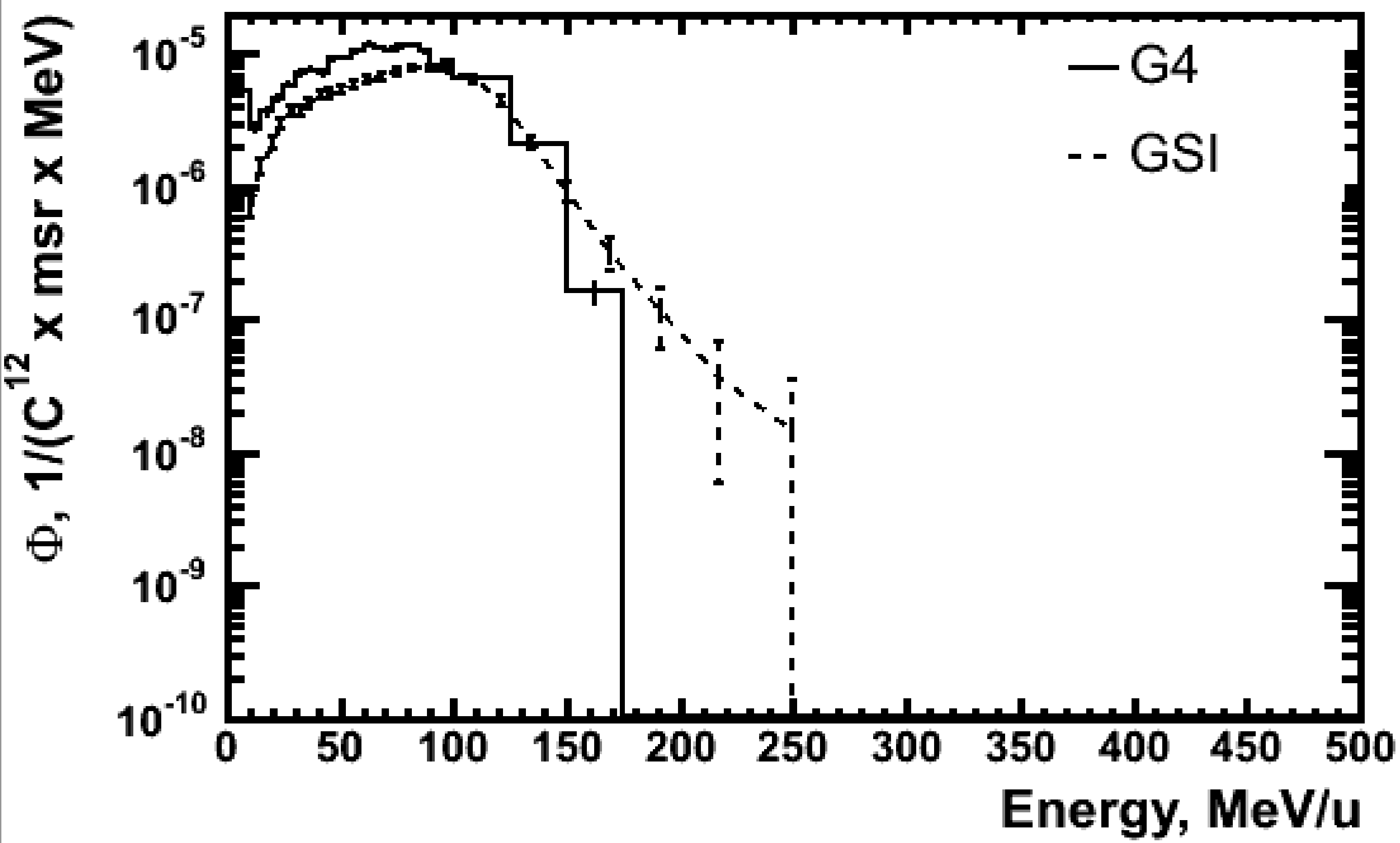
3. Results: protons



3. Results: deuterons



3. Results: alpha



Next Geant4 workshop held in Catania (15-22 October)

SHIELD-HIT (Heavy Ion Therapy): medical version of the SHIELD.

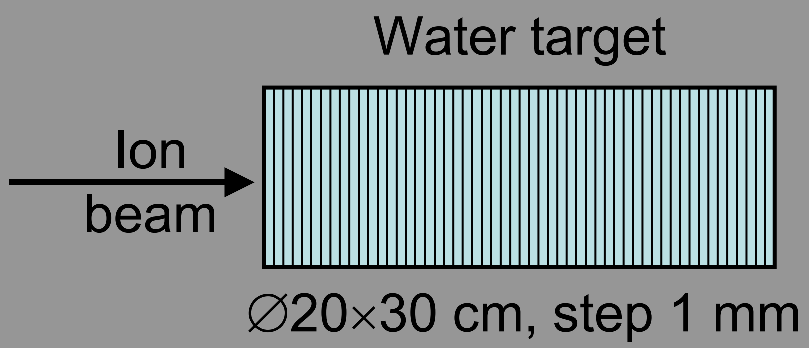
1.Fluctuations of energy loss and multiple Coulomb scattering are taken into account.

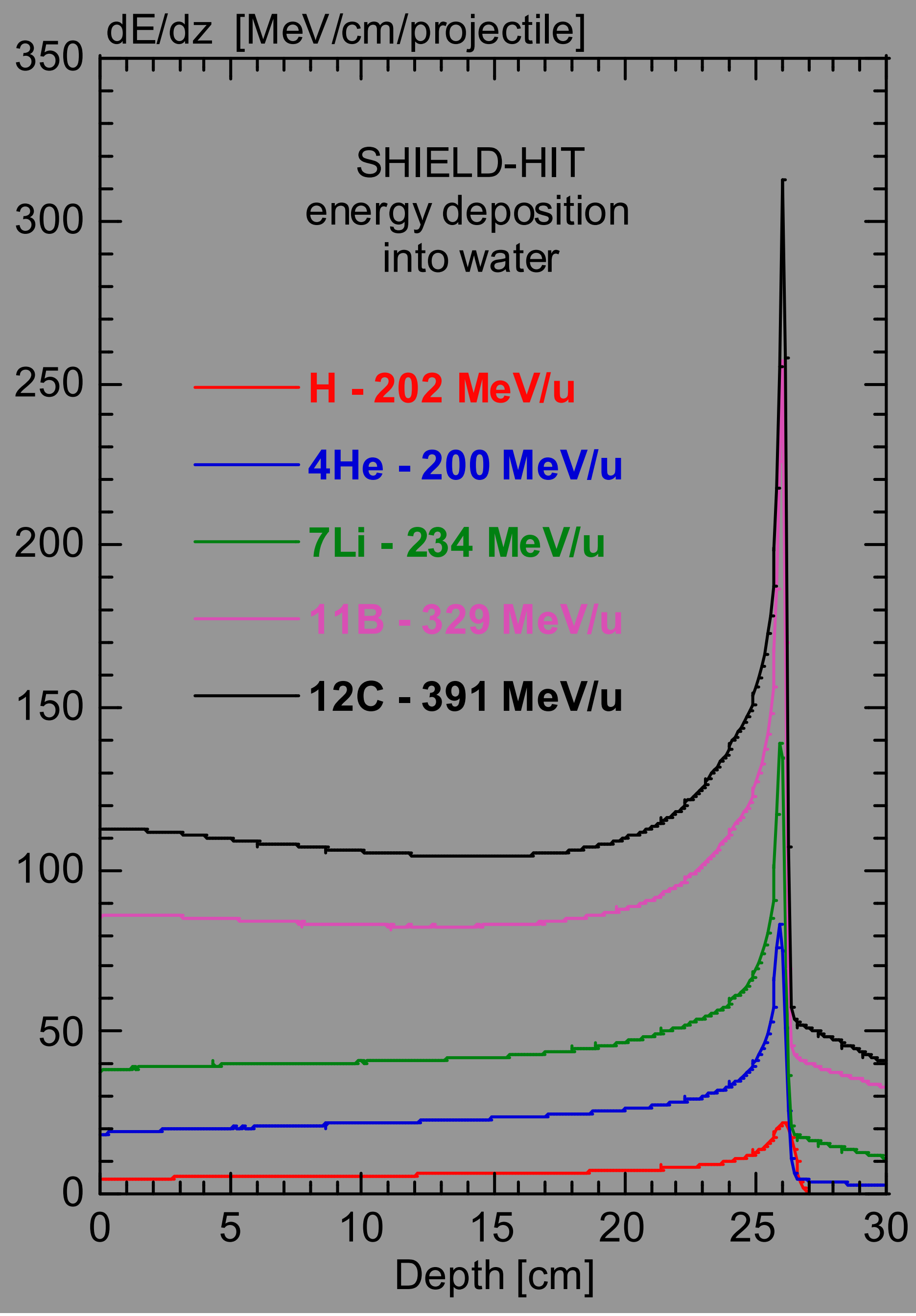
2.Stopping power calculation dE/dx according to ICRU49 (1993).

3.Detailed energy grids for more precise interpolation of particle ranges and cross sections.

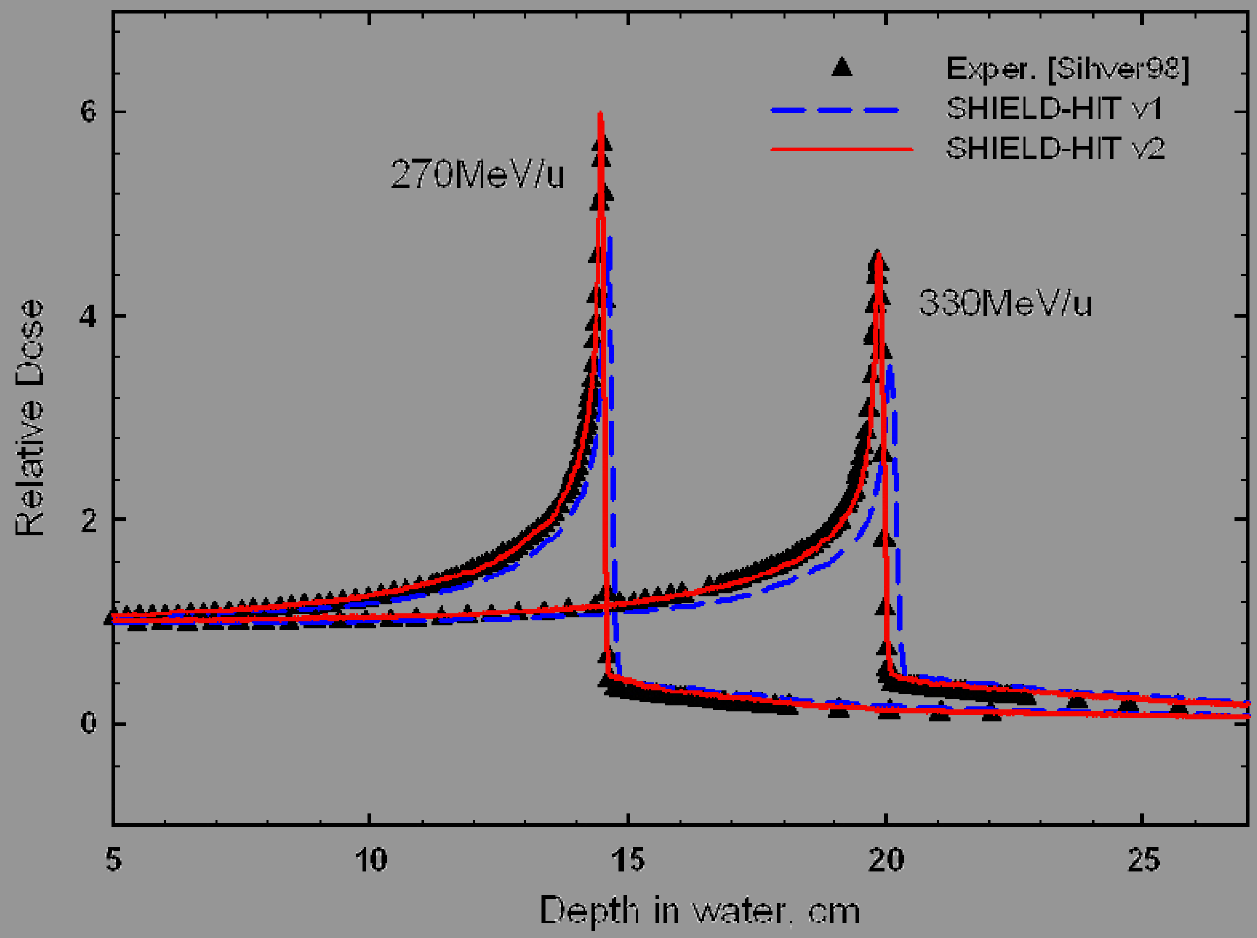
Track length estimation of fluences of all particles in all target zones.

5.Possibility to «switch off» various physics processes etc.

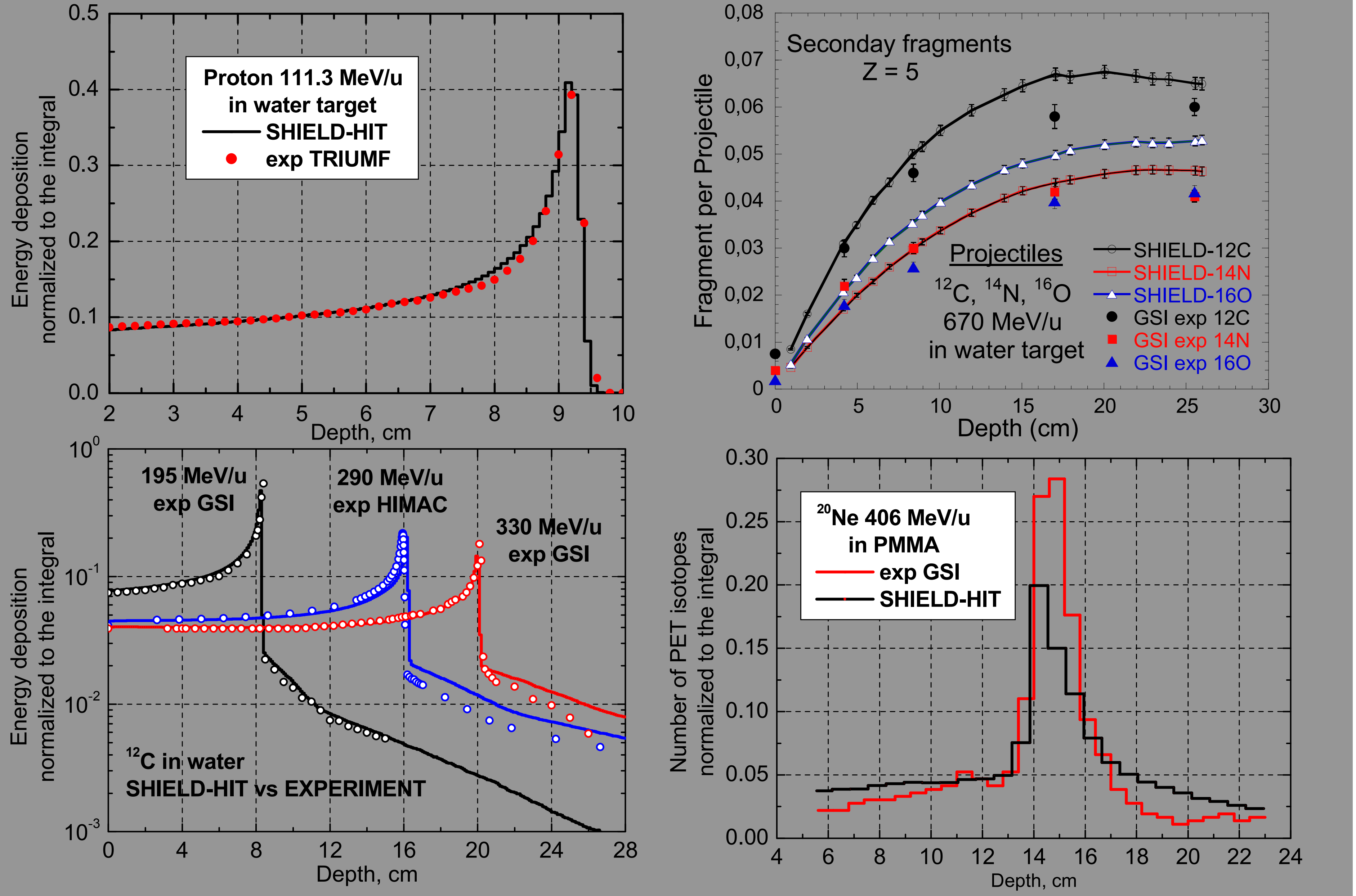




Verification of SHIELD-HIT V2
Depth dose of C-12 ions



Shiled-Hit Comparison with experiment

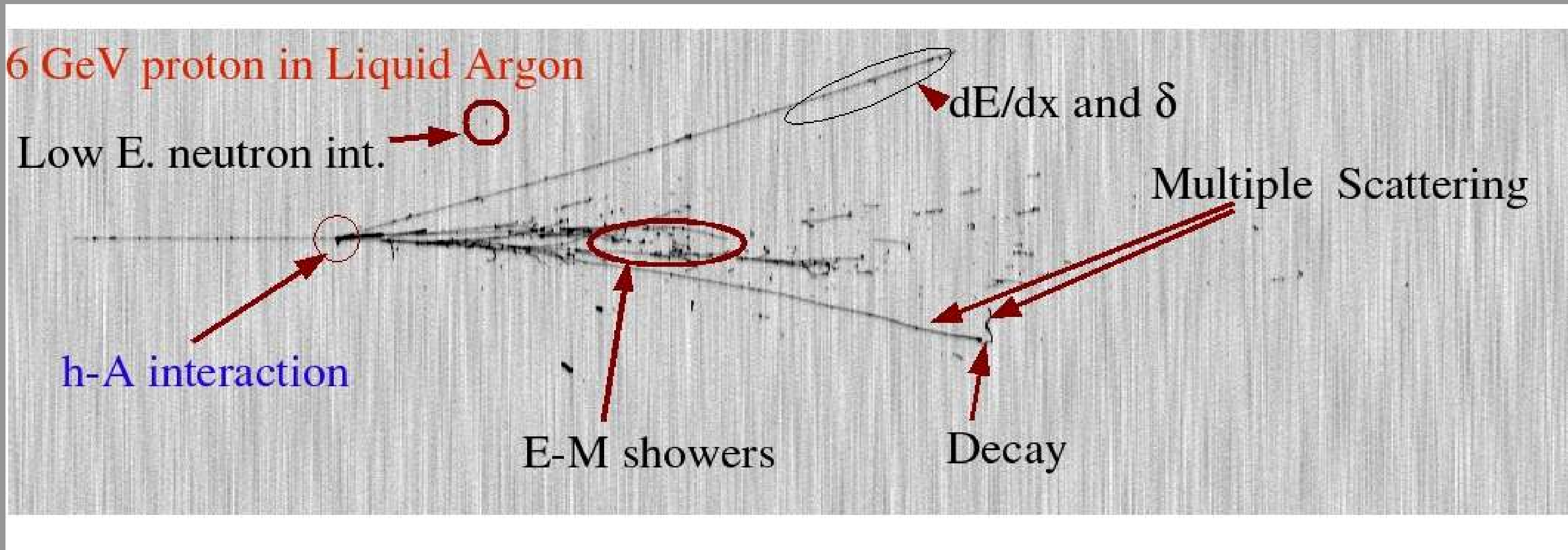


FLUKA

FLUKA

Main authors: **A. Fassò, A. Ferrari, J. Ranft, P.R. Sala**

Contributing authors: **G.Battistoni, F.Cerutti, T.Empl, M.V.Garzelli, M.Lantz, A. Mairani, V.Patera, S.Roesler, G. Smirnov, F.Sommerer, V.Vlachoudis**



Developed and maintained under an INFN-CERN agreement

>2000 users **http://www.fluka.org**

The FLUKA international Collaboration

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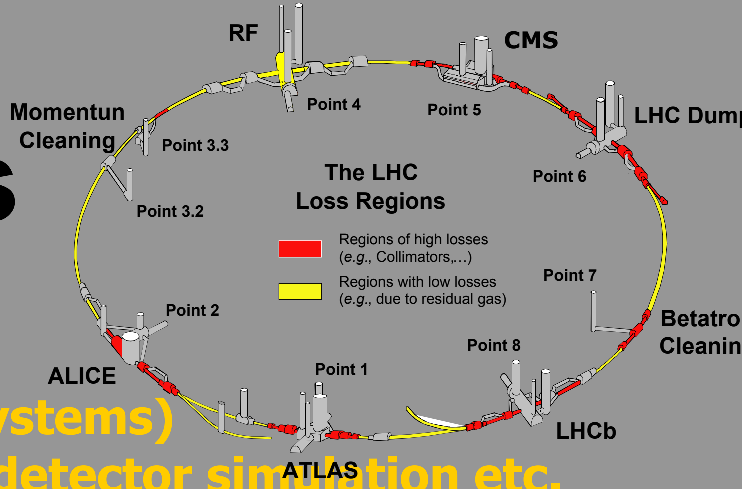
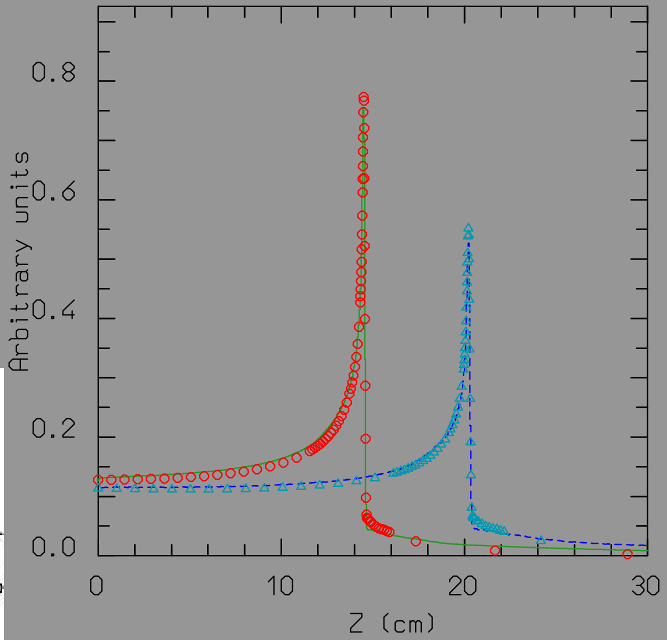
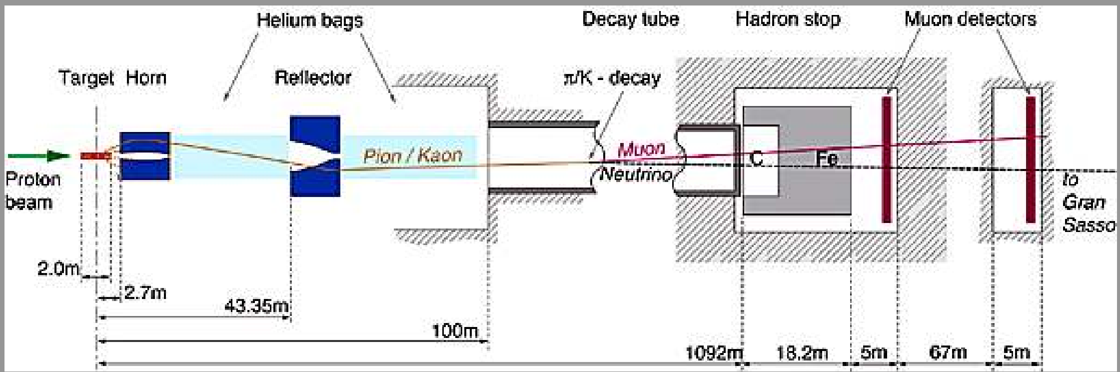
FLUKA Applications



- Cosmic ray physics
- Neutrino physics
- Accelerator design (→ n_ToF, CNGS, LHC systems)
- Particle physics: calorimetry, tracking and detector simulation etc. (→ ALICE, ICARUS, ...)
- ADS systems, waste transmutation, (→"Energy amplifier", FEAT, TARC,...)
- Shielding design
- Dosimetry and radioprotection
- Space radiation
- Hadrontherapy
- Neutronics





The FLUKA Code design

- Sound and updated physics models
  - Based, as far as possible, on original and well-tested microscopic models
  - Optimized by comparing with experimental data at single interaction level: ***"theory driven, benchmarked with data"***
  - Final predictions obtained with minimal free parameters fixed for all energies, targets and projectiles
  - Basic conservation laws fulfilled "a priori"
  - ➔ ***Results in complex cases, as well as properties and scaling laws***, arise naturally from the underlying physical models
  - ➔ ***Predictivity where no experimental data are directly available***
  - Full cross-talk between all components: hadronic, electromagnetic, neutrons, muons, heavy ions
  - Effort to achieve the same level of accuracy:
    - for each component
    - for all energies
  - ➔ Correlations preserved fully within interactions and among shower components
  - ➔ ***FLUKA is NOT a toolkit! Its physical models are fully integrated***

FLUKA hadronic models

Hadron-Hadron

Elastic, exchange:	P<3-5GeV/c:	low E π,*K*:	High Energy:
Phase shifts analyses data, eikonal approximation	Resonance prod. and decay	Special	DPM + Hadronization

Hadron-Nucleus

E < 5 GeV		High E (< 20 TeV)
PEANUT Sophisticated GINC Preequilibrium Coalescence	E X T E N S I O N	Glauber-Gribov multiple interactions + Coarser GINC + Coalescence High E (> 20 TeV) DPMJET

Nucleus-Nucleus

E< 0.1GeV/u	0.1< E< 5 GeV/u	E> 5 GeV/u
BME Complete fusion + peripheral	modified rQMD-2.4 new QMD	DPMJET DPM + Glauber + GINC

Evaporation/Fission/Fermi break-up

γ deexcitation

The Physics Content of FLUKA

- Nucleus-nucleus interactions 100 MeV/n – 10000 TeV/n

  New model (BME, under development): from Coulomb Barrier
- Electromagnetic and μ interactions 1 keV – 10000 TeV
- Hadron-hadron and hadron-nucleus interactions 0–10000 TeV
- Neutrino interactions NEW! (new DIS and RES generator!)
- Charged particle transport including all relevant processes
- Transport in magnetic field NEW! new library with 260 groups
- Neutron multigroup transport and interactions 0 – 20 MeV
- Analog calculations, or with variance reduction

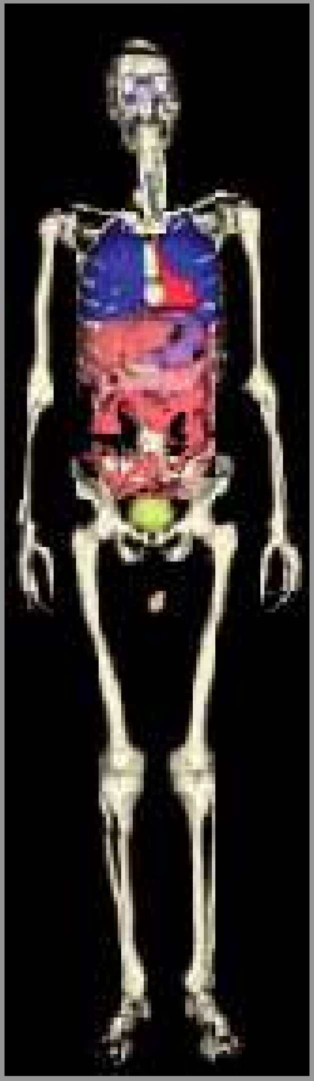
FLUKA for medicine and hadrotherapy

Using the information from the patient CT in the MC I

The Voxel Geometry

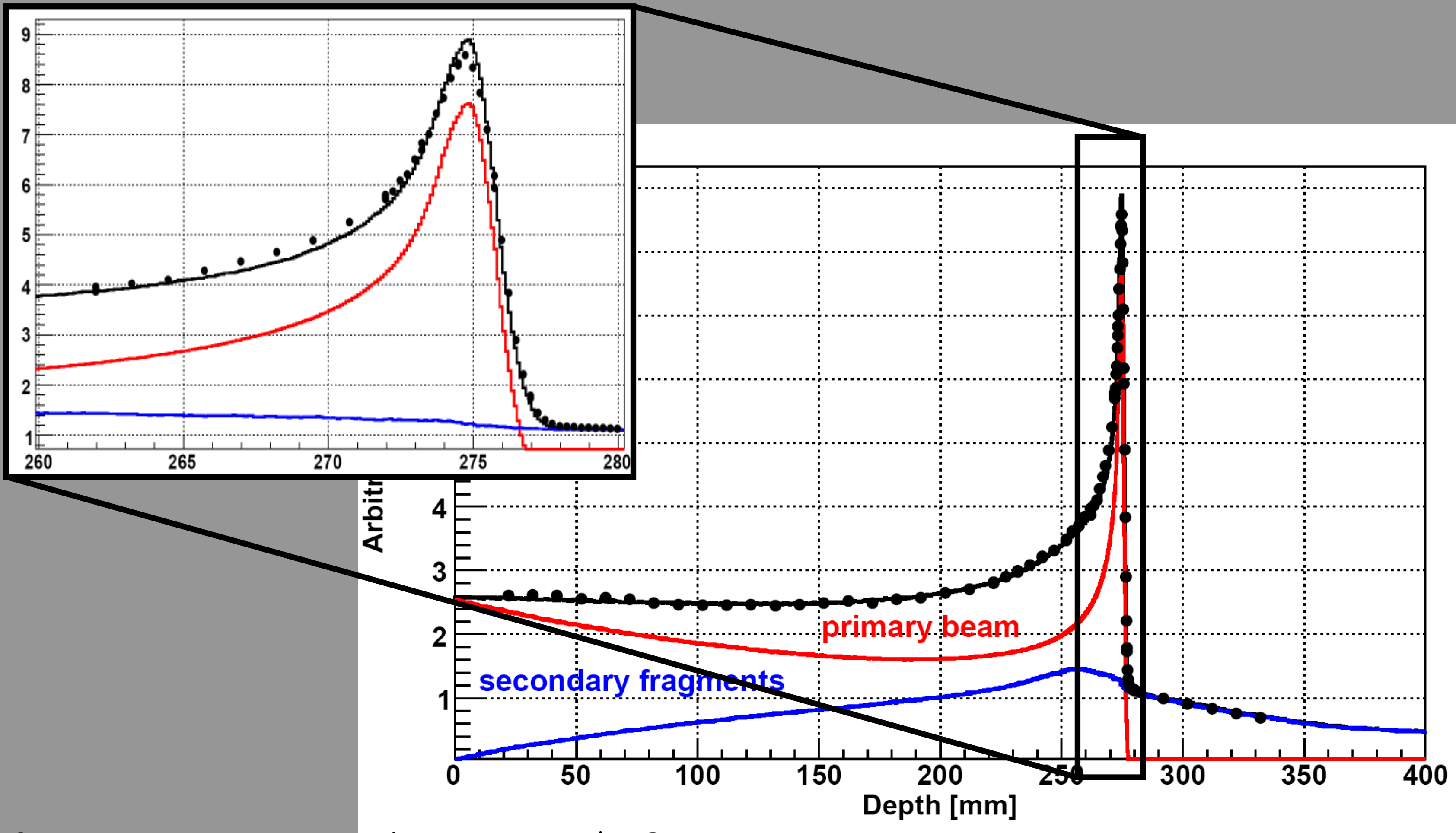
- FLUKA can embed voxel structures within its standard combinatorial geometry
- Transport through the voxels is optimized and efficient
- Raw CT-scan outputs can be imported

The GOLEM phantom
Petoussi-Henss et al, 2002



Heavy ions

^{12}C @ 400 MeV/n on water: Bragg peak

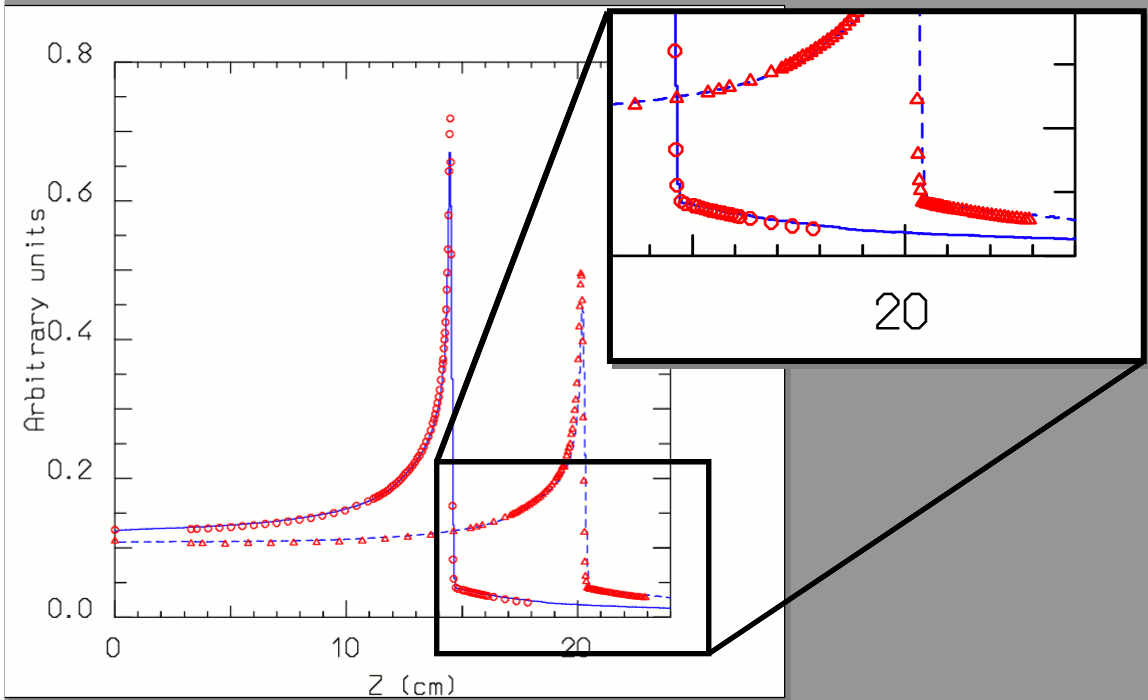


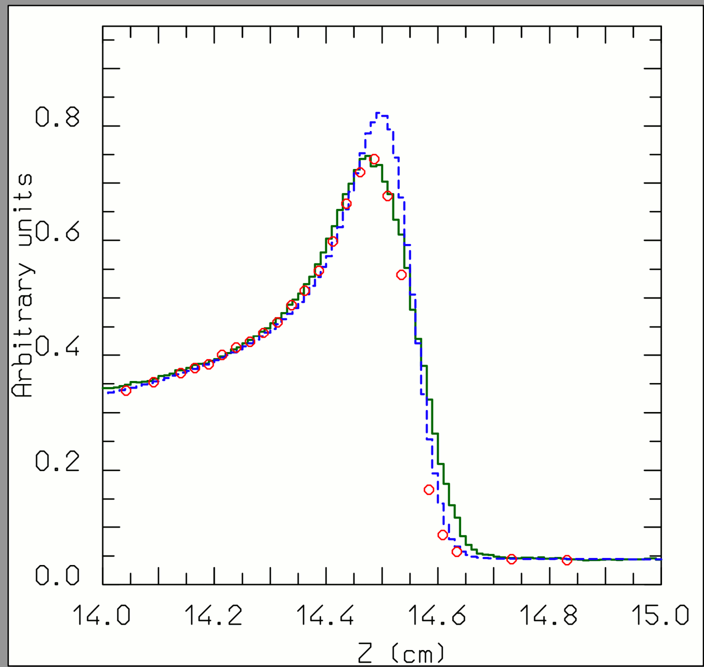
Beam energy spread: 0.2 MeV/n FWHM

*Preliminary exp. data courtesy of E.Haettner (Diploma thesis), D.Schardt, GSI, and S.Brons, K.Parodi, HIT. **FLUKA** simulations: A.Mairani PhD thesis*

^{12}C Bragg peaks vs exp. data[1]

[1]Sihver et al. Jpn.J.Med.Phys. 18, 1,1998





- Experiment: circles (270 AMeV) and triangles (330 AMeV)
- FLUKA: lines

Zoom: 270 AMeV

Blue: no spread

Green: 0.15% Energy spread (σ)

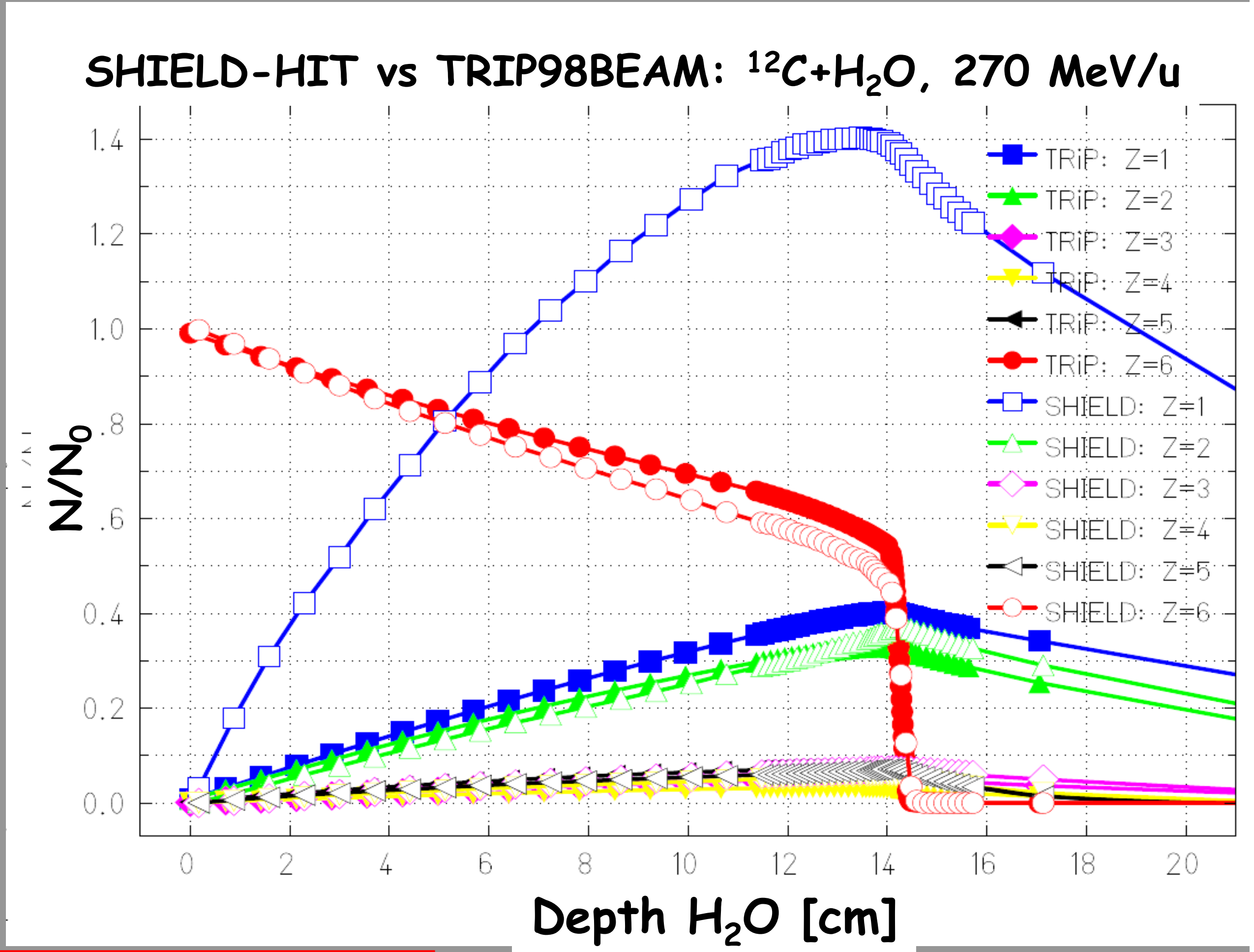
Sommerer *et al*: Phys. Med. Biol. **51** 2006

Heavy ion therapy vs (projectile) fragmentation

- A significant fraction of the primary beam undergoes nuclear interactions

- Importance of secondary fragments: RBE and tail after the peak (mostly p and α's)

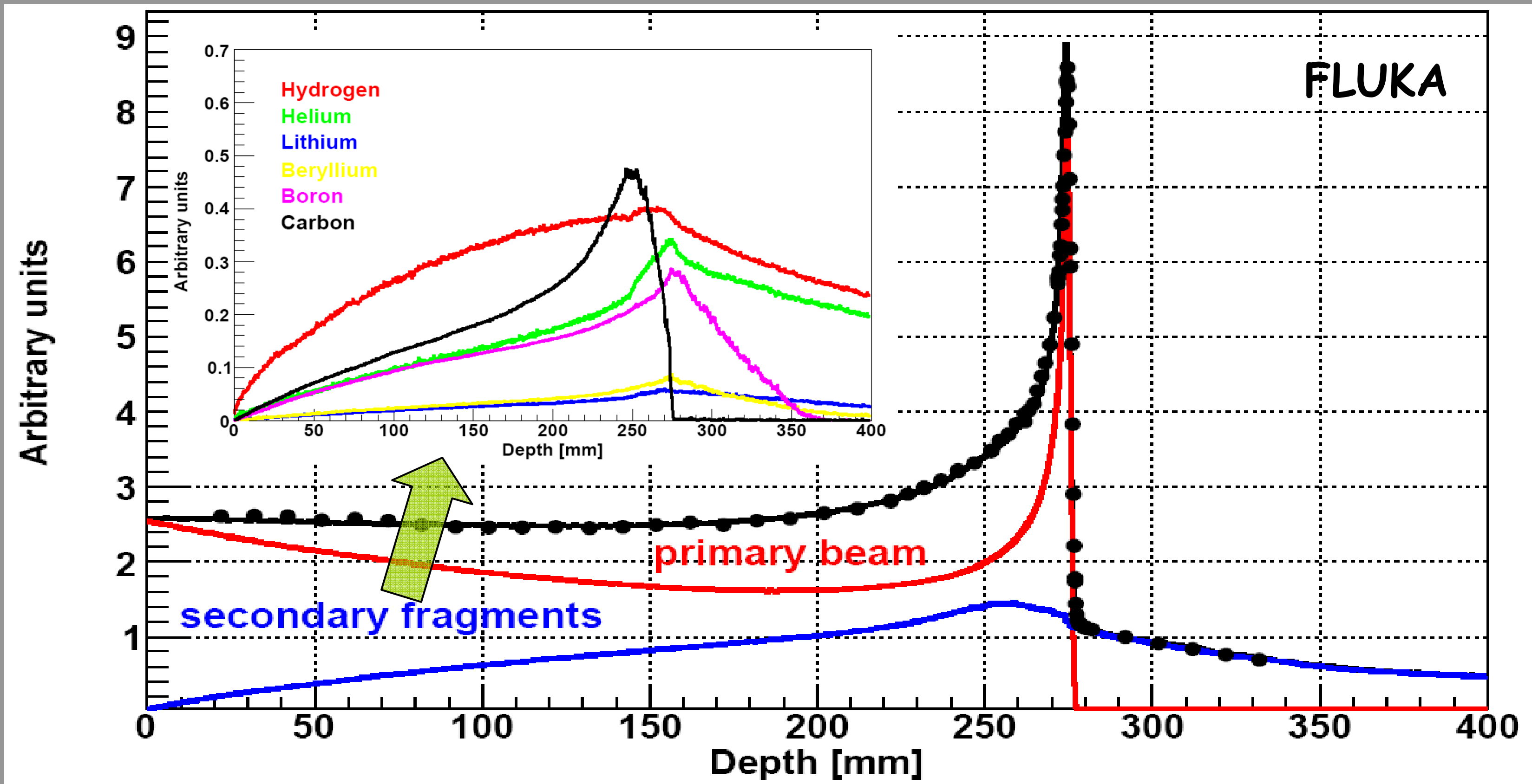
- Such topics, particularly the tail, are key for therapy



Accurate knowledge of ion beam fragmentation is critical for therapy

The experimental validation against measured Bragg curve in Carbon ion therapy

^{12}C ions (400 MeV/u) on Water phantoms



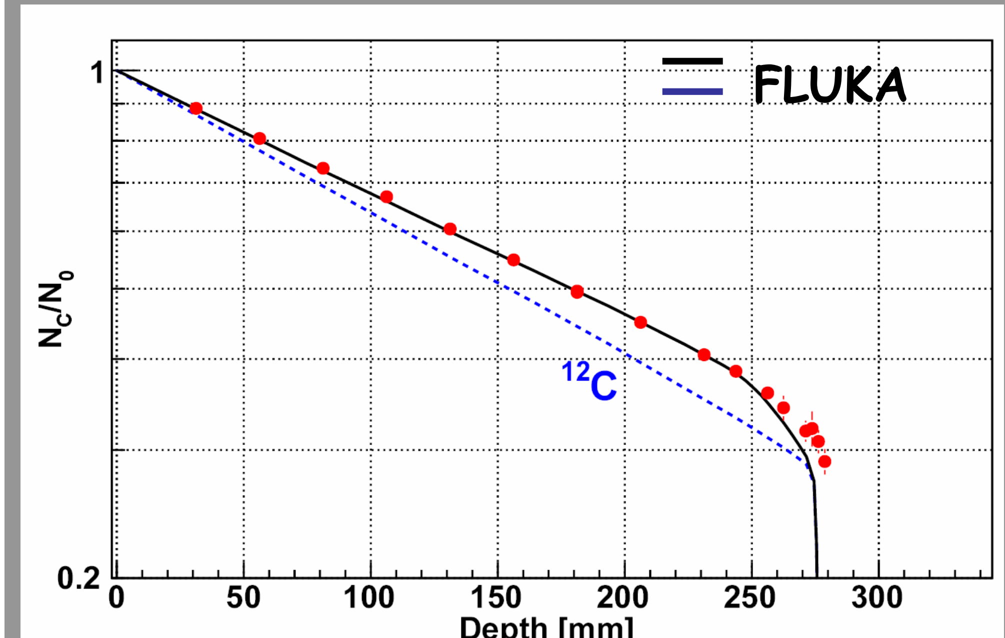
Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006

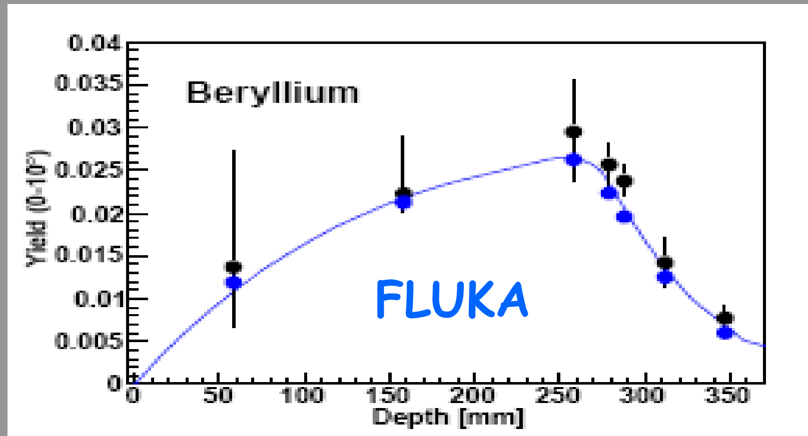
Simulation: A. Mairani PhD Thesis, Pavia, 2007

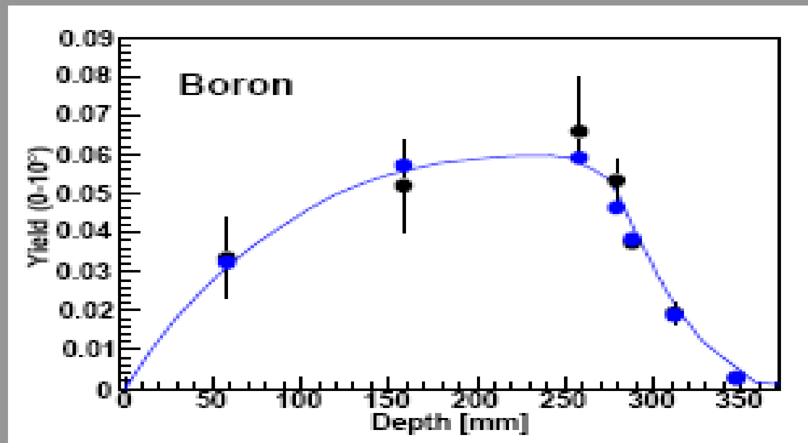
Carbon beam fragmentation:

^{12}C ions (400 MeV/u) on Water phantoms

Carbon Beam Attenuation   Build-up of secondary fragments

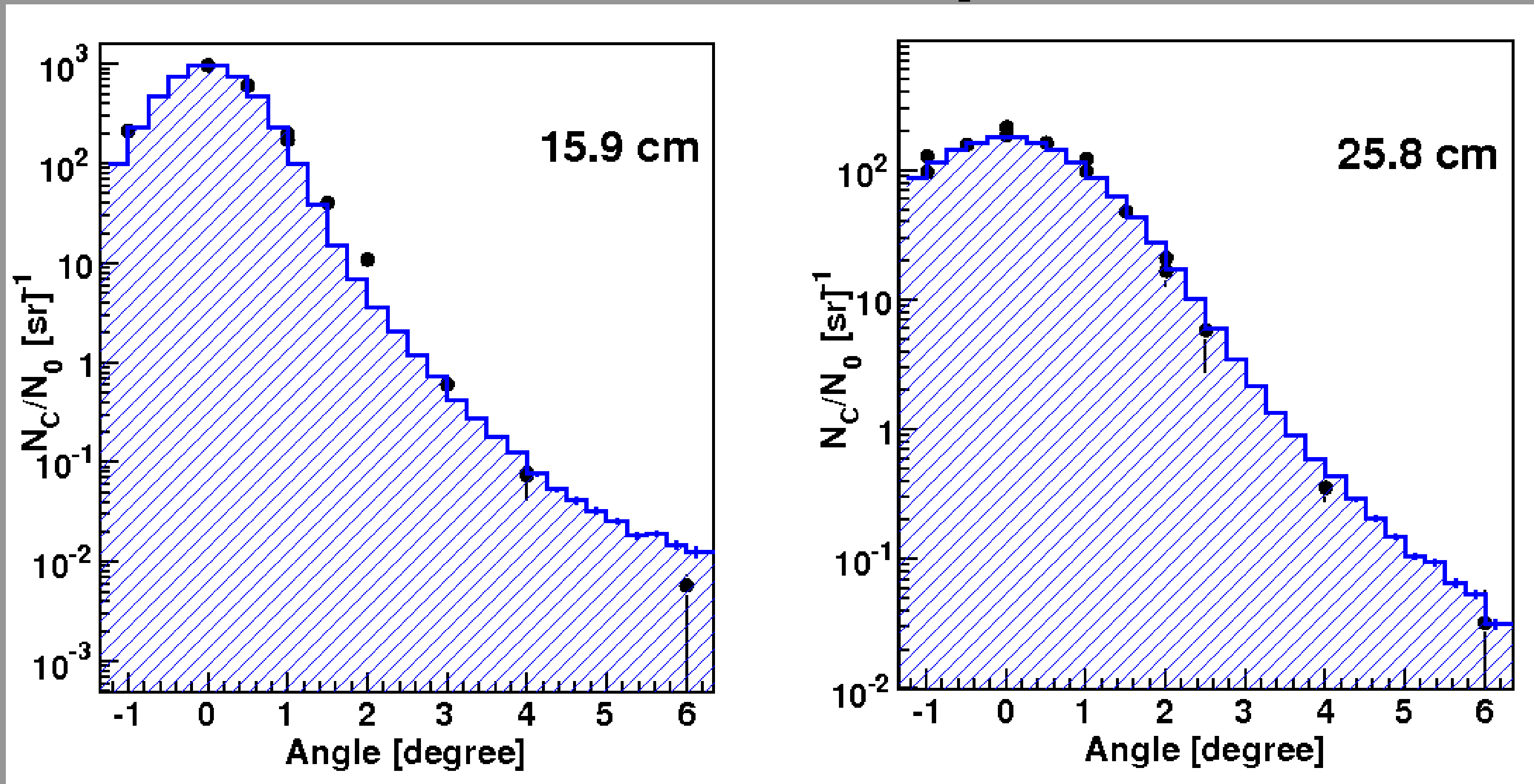






Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006

^{12}C @ 400 MeV/n: C ions angular dist. at various depths

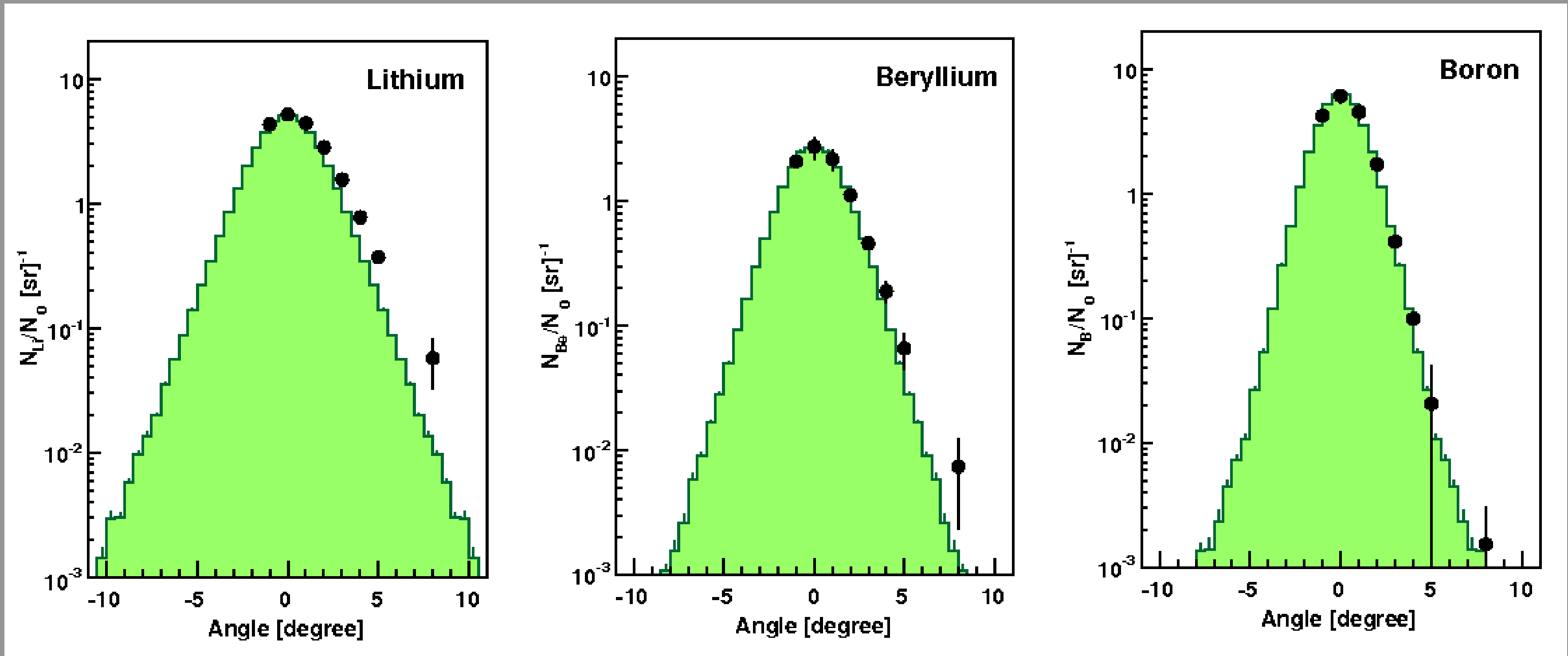


Preliminary exp. data courtesy of E.Haettner (Diploma thesis), D.Schardt, GSI, and S.Brons, K.Parodi, HIT. Simulations: A.Mairani PhD thesis

The experimental validation against mixed field measurements in Carbon Ion therapy.

^{12}C ions (400 MeV/u) on Water phantoms

Angular Distributions at 31.2 cm



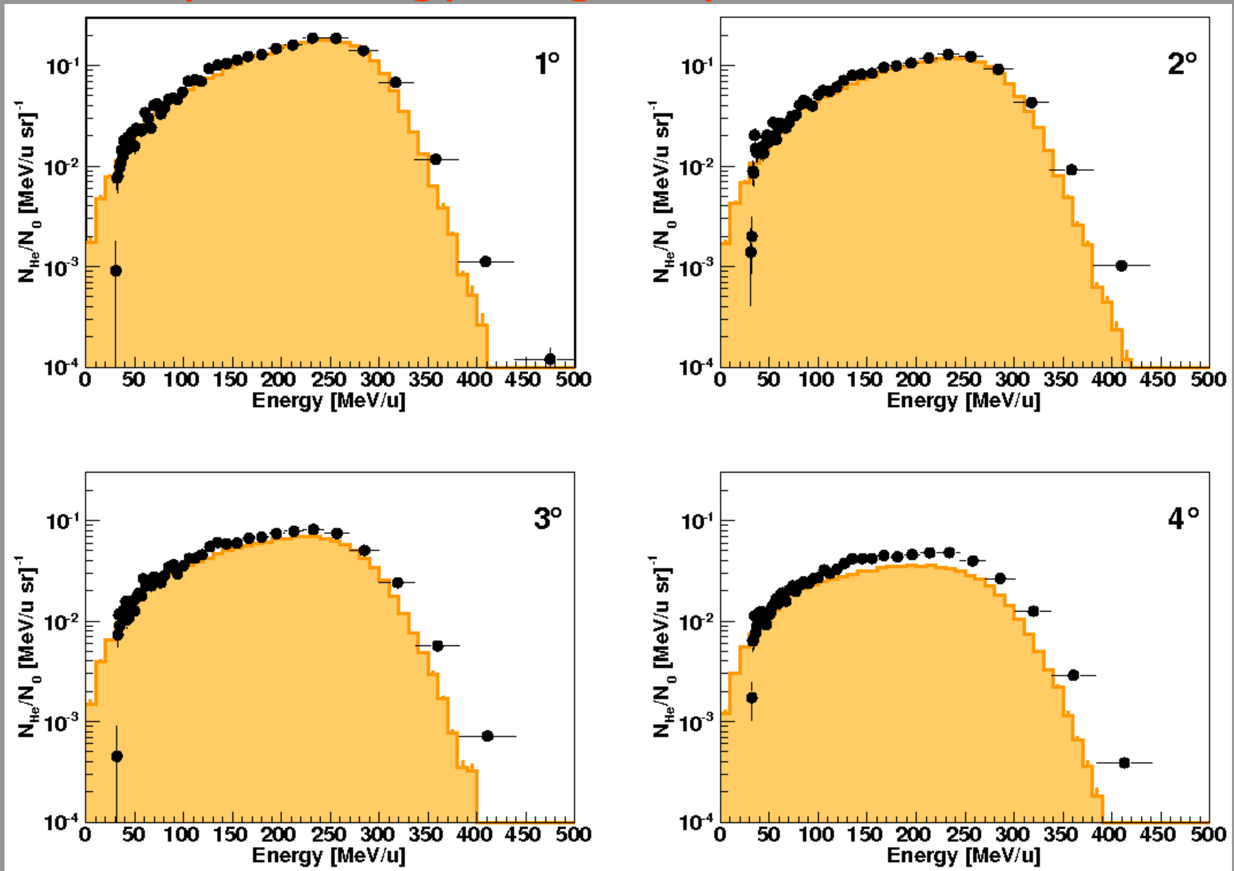
Exp. Data (points) courtesy of E. Haettner, D. Schardt, GSI, and S. Brons, K. Parodi, HIT.

FLUKA Simulations: A. Mairani, PhD Thesis, Pavia, 2007

The experimental validation against mixed field measurements in Carbon Ion therapy.

^{12}C ions (400 MeV/u) on Water phantoms

Alpha Energy-Angle Spectra at 28.8 cm



FLUKA
Simulation: A. Mairani, PhD Thesis, Pavia 2007

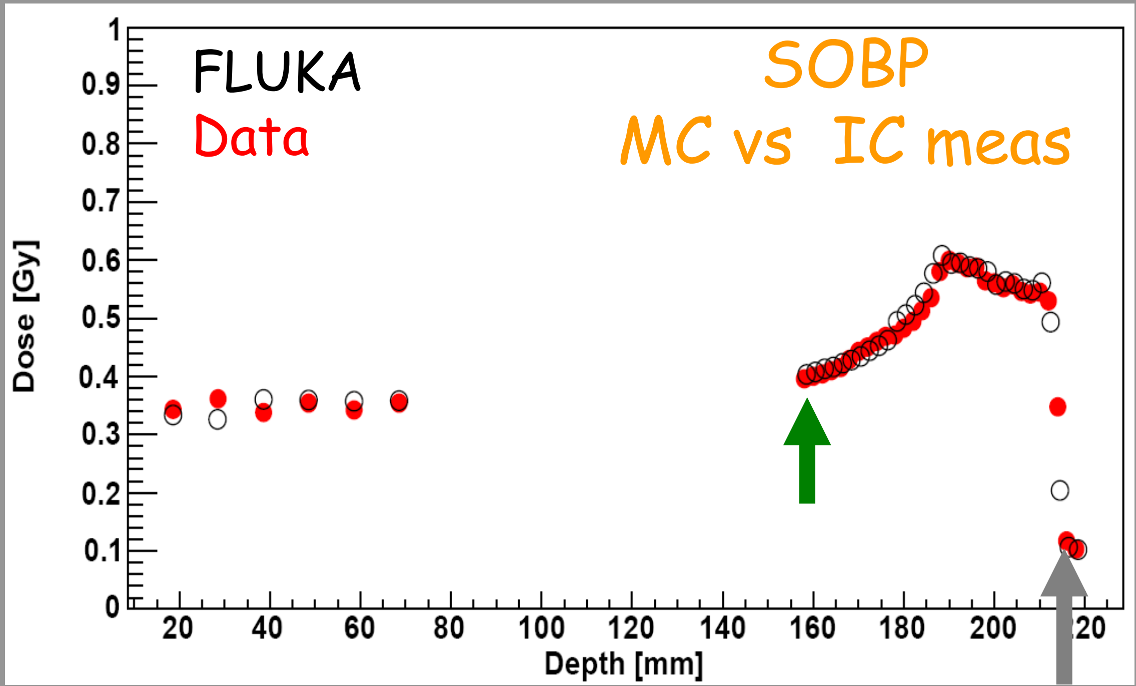
Preliminary data (points) courtesy of E. Haettner, D. Schardt, GSI, and S. Brons, K. Parodi, HIT.

Applications to carbon therapy @ GSI

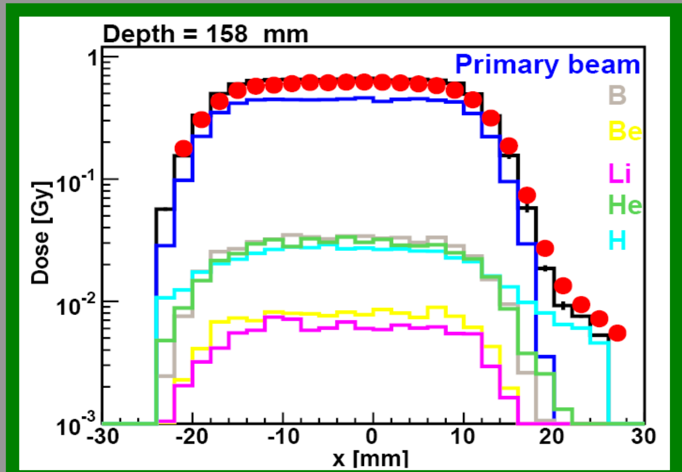
FLUKA coupled with control file of raster scanning system and modeling ridge filter

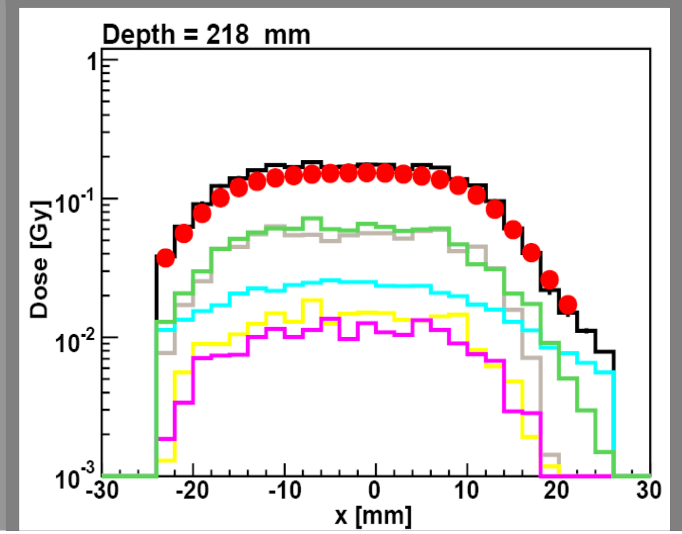
Simulations by F. Sommerer, A. Mairani, K. Parodi, and A. Ferrari

Experimental data (points) from S.Brons (HIT)

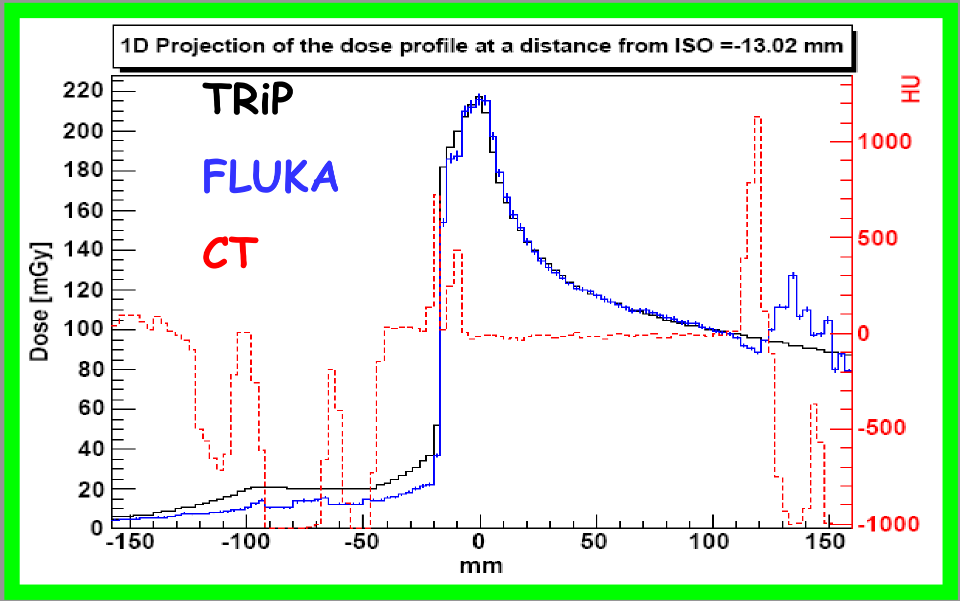


Lateral Profiles



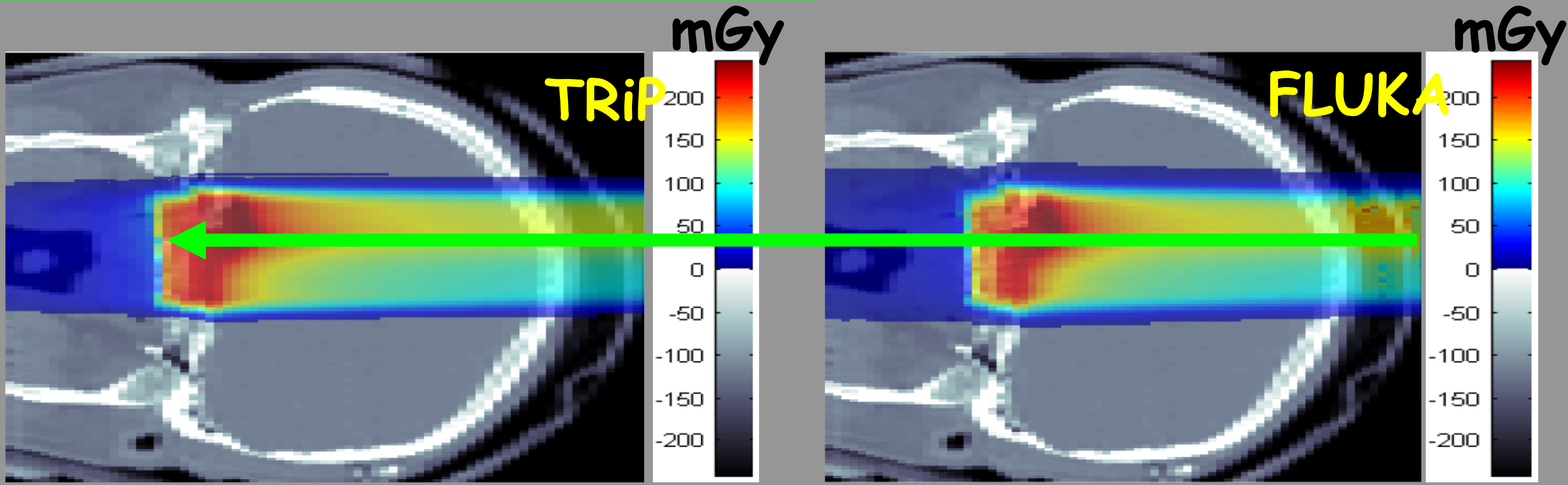


Clivus Chordoma Patient @ GSI
Absorbed dose distributions



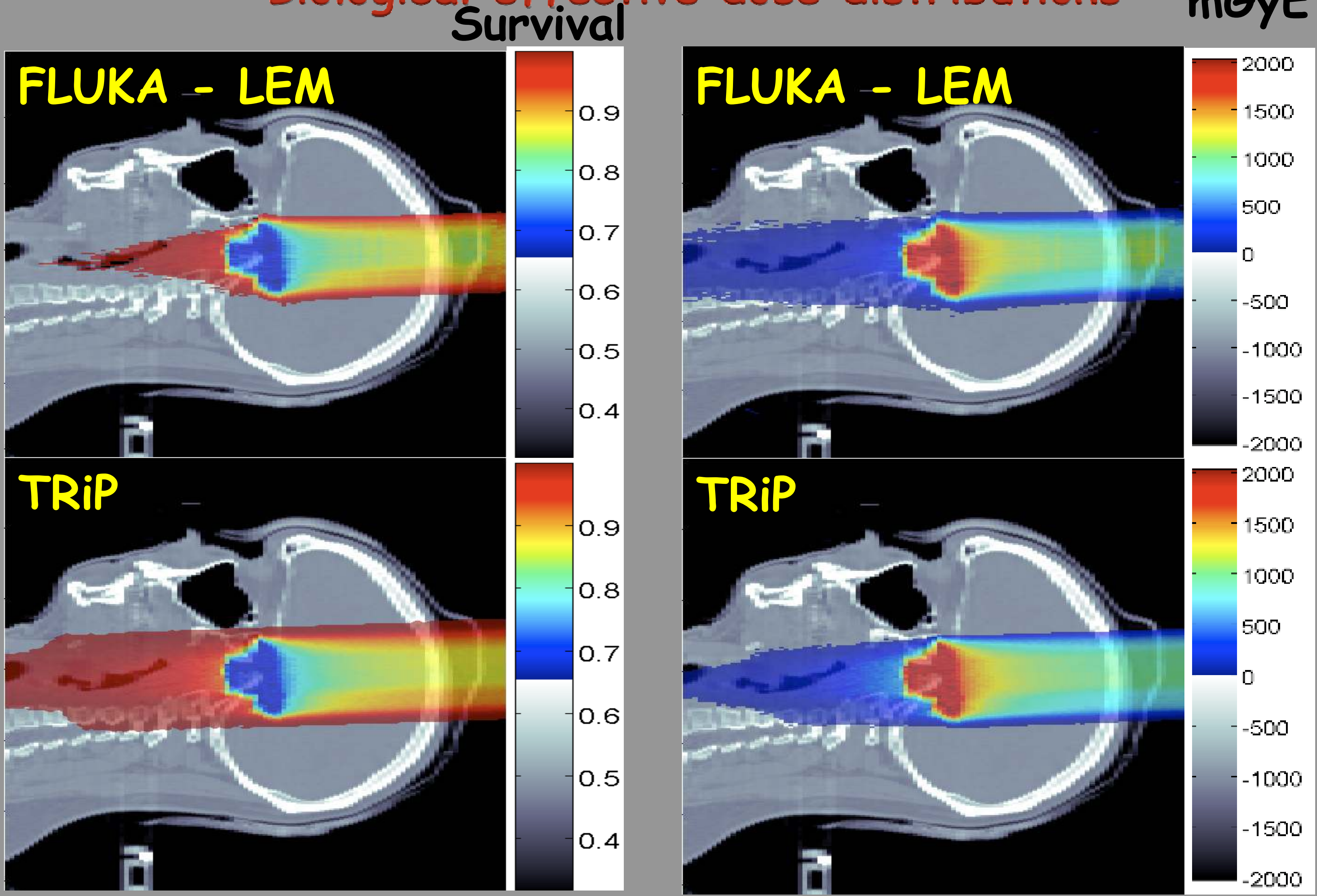
A. Mairani PhD thesis 2007, Pavia

Absorbed Dose Spread-Out Bragg Peak in the patient



Clivus Chordoma Patient @ GSI

Biological effective dose distributions



A. Mairani et al, to be published

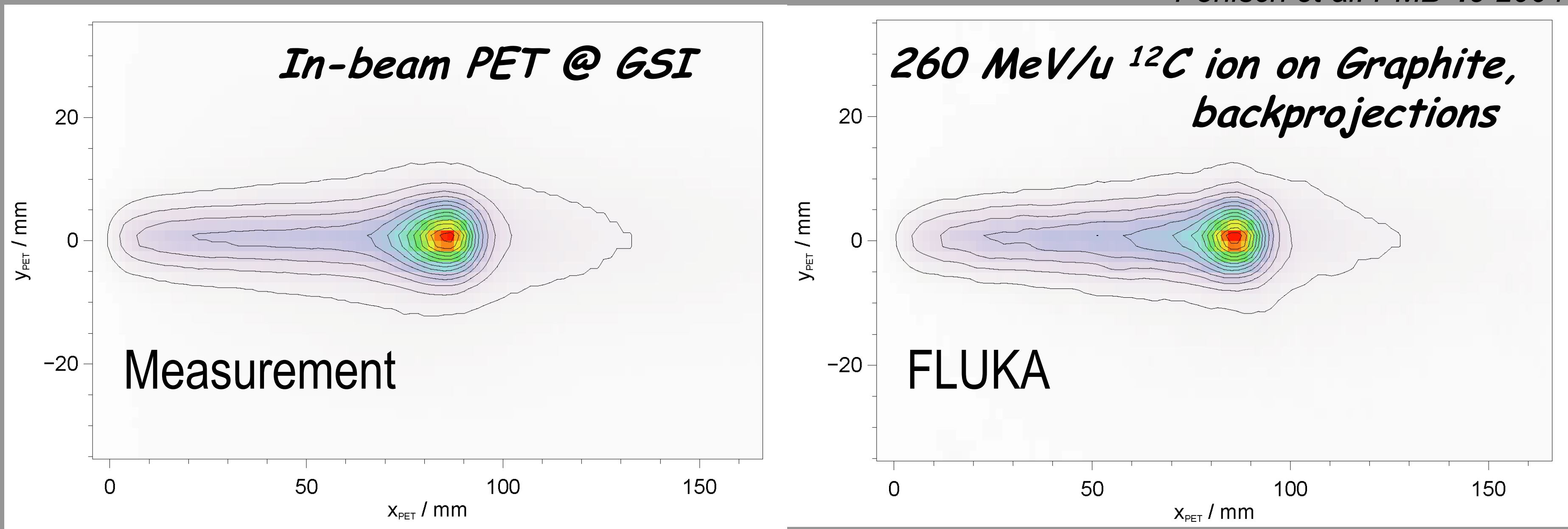
β^+ emitters for ion beams: phantom experiments

Application of FLUKA to PET monitoring of ion species (e.g. ^{12}C, ^{16}O) based on *internal nuclear models*

Simulation of *imaging process* (β^+-decay, propagation of e^+ and annihilation photons, detection) same as for measured data

- ✓ Exact replica of the experimental setup, PET heads included
- ✓ FLUKA irradiation+decay features exploited
- ✓ MC γ's reaching PET heads converted to list-mode data by modified PETSIM[1]
- ✓ Backprojection with same routines as in experiment

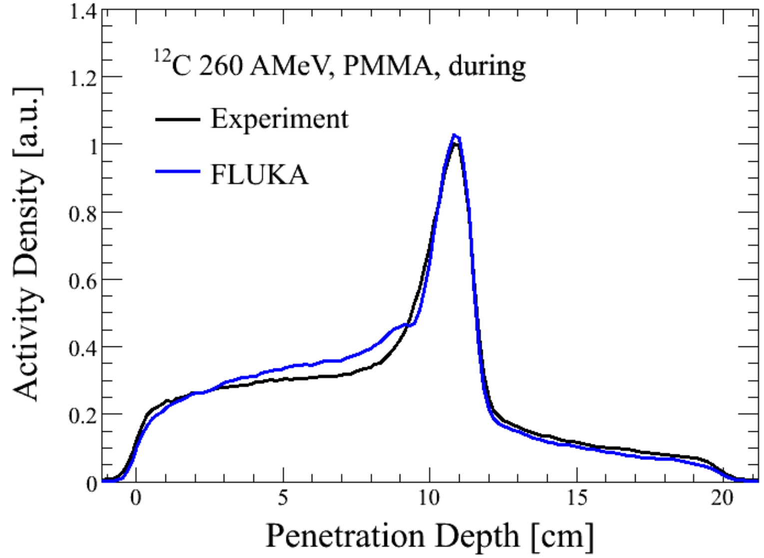
[1]Pönisch et al. PMB **49** 2004

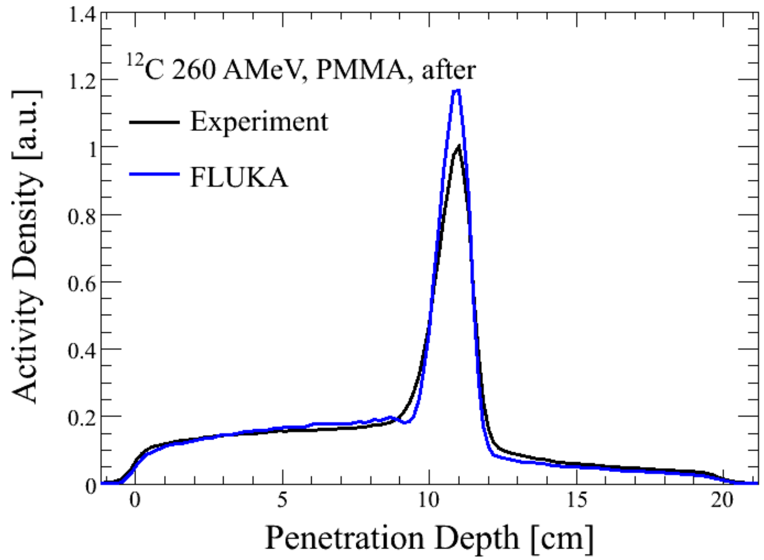


F. Sommerer PhD Thesis, 2007

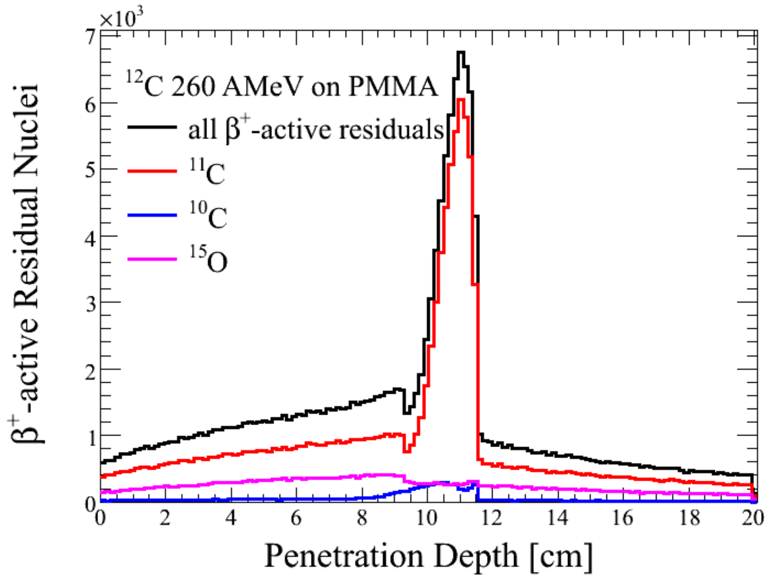
Backprojections: FLUKA vs Exp data

^{12}C 260 MeV/A on PMMA





^{12}C 260 MeV/A on PMMA, simulated relative production rate of different isotopes

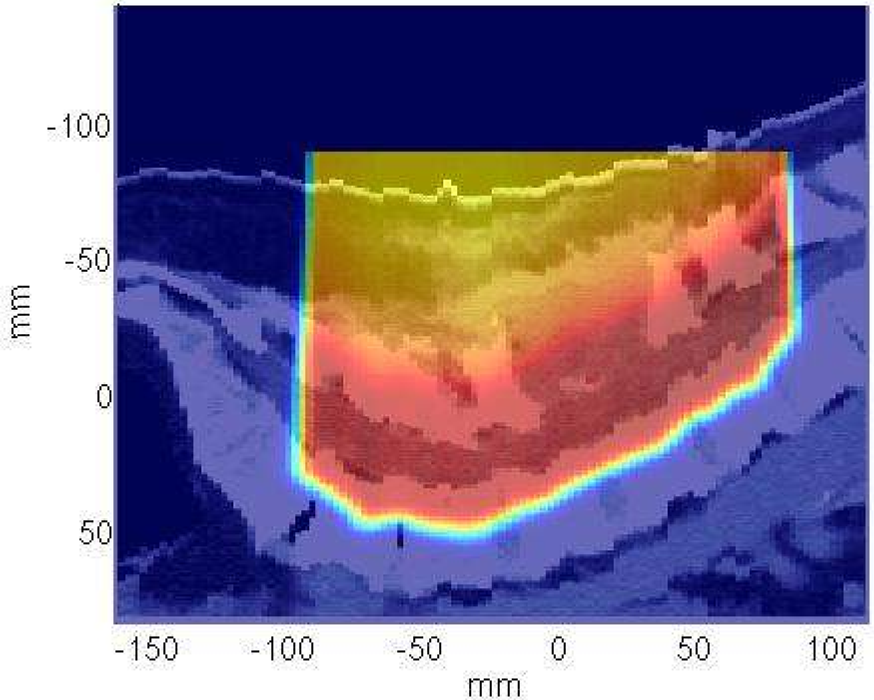


Both the data and the FLUKA calculations are normalized to the same area

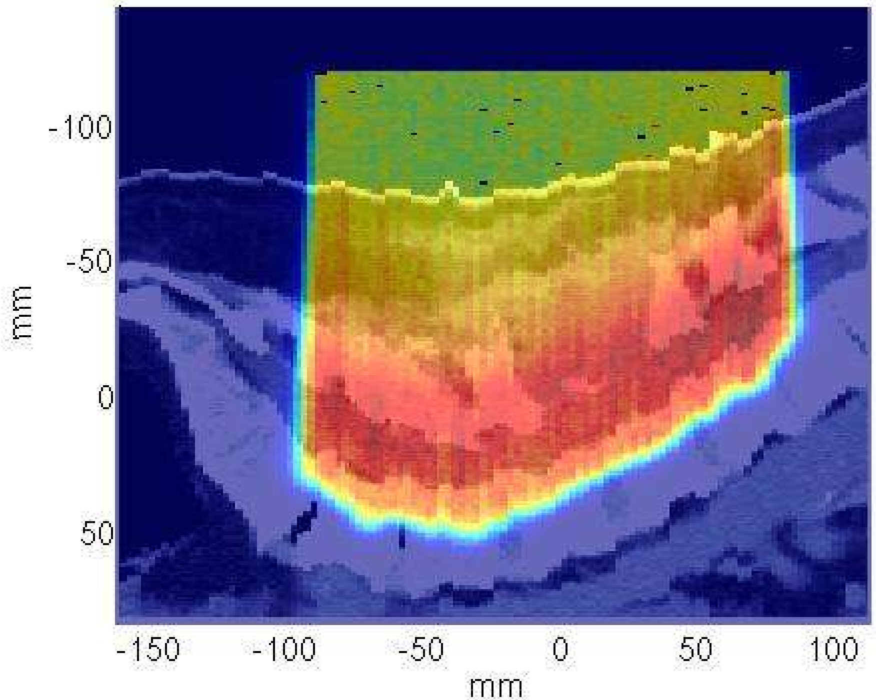
F. Sommerer PhD Thesis, 2007

Applications to proton therapy at MGH (USA)

Treatment planning system



FLUKA simulation



Planned dose distribution in a patient with a spinal tumor (planning with FOCUS/XiO; data were recorded on slightly different regions for the two plots). Both calculations are directly performed on the planning CT.

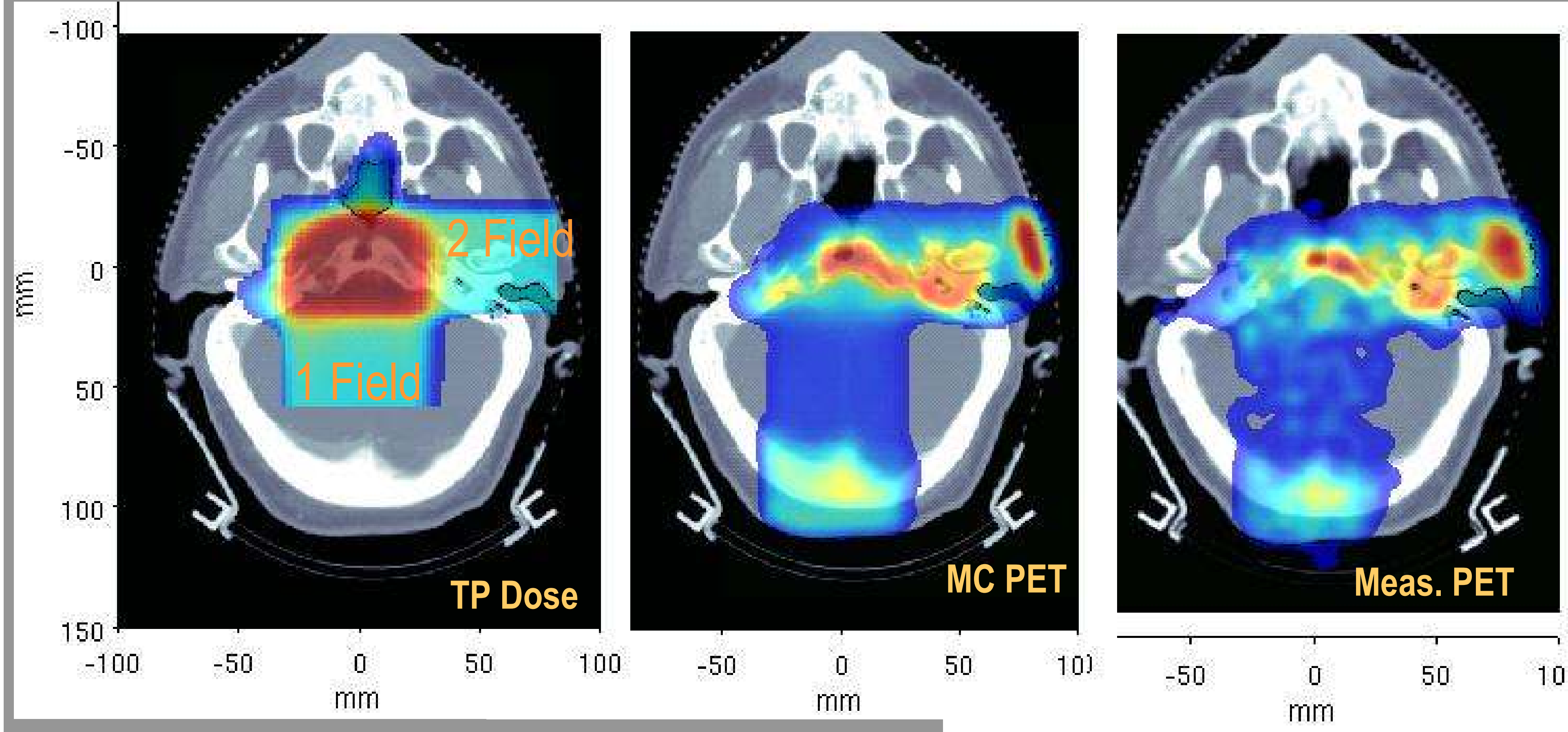
K. Parodi, H. Paganetti and T. Bortfeld, **M**assachusetts **G**eneral **H**ospital

K. Parodi et al, PMB 52 (2007)

Applications to proton therapy at MGH

PET/CT imaging after irradiation

Clival Chordoma, 0.96 GyE / field, ΔT_1 ~ 26 min, ΔT_2 ~ 16 min



K. Parodi et al, IJROBP, 2007

What is still missing ??

Extensive Measurements in ”Thin-Target” Configuration!

Bench marking and verfication of the *physics models* in the transport codes !

To increase the reliability of the calculated results of un-measured systems !

What should be necessary ??

Very few experimental data are available, especially regarding charged particles production.

Few data for incident ion energy greater than 35 AMeV and below 1 AGeV.

See our public database reporting collection of actually available data:

http://workgroup.lngs.infn.it/geant4lns

TODAY (only) AT GSI WE CAN HAVE THE RIGHT BEAMS AND THE RIGHT DETECTORS!

INFN Istituto Nazionale di Fisica Nucleare

INTERNATIONAL SCENARIO

- **IAEA Benchmark of Spallation Models** (Detlef Filges, Forschungszentrum Jülich, Germany, Sylvie Leray, CEA Saclay, France, Gunter Mank, IAEA Vienna, Austria, Yair Yariv, Soreq NRC, Israel, Alberto Mengoni, IAEA Vienna, Austria)

- **IAEA "Heavy Charged Particle Interaction Data for Radiotherapy"** (G. Cuttone INFN, O.Jaekel DKFZ, A. Ferrari CERN, A. Heikkinen Univ. of Helsinki, T. Lomax PSI, H. Palmans NPL, H.Paganetti. MGH, M.C. Morone INFN & Univ. of Rome Tor Vergata, M. Quesada Sevilla Univ.,R. CapoteNoy & S. Vatnisky IAEA Vienna,)

- **ESA SEENoTC** (Energetic particle radiation and its effects on systems, payloads and humans) Field of Interest: Ion fragmentation (50 AMeV → 1000 AMeV)

INFN Istituto Nazionale di Fisica Nucleare

Proposal of Experiment at SIS

Extensive study of nuclear reactions of interest for medical and space applications.

G.Cuttone, F.Marchetto, G.Raciti, E.Iarocci, V.Patera, C.Agodi, C.Sfienti, E.Rapisarda, M. De Napoli, F. Giacoppo, M.C. Morone, A. Sciubba, G.Battistoni, P.Sala, G.A.P.Cirrone, F.Romano

INFN: LNS, LNF, Roma1, Milan, Turin, Roma Tor Vergata

S.Leray, M.D. Salsac, A.Boudard, J.E. Ducret, M. Labalme, F. Haas, C. Ray

DSM/IRFU/SPhN CEA Saclay, IN2P3_Caen, Strasbourg, Lyon

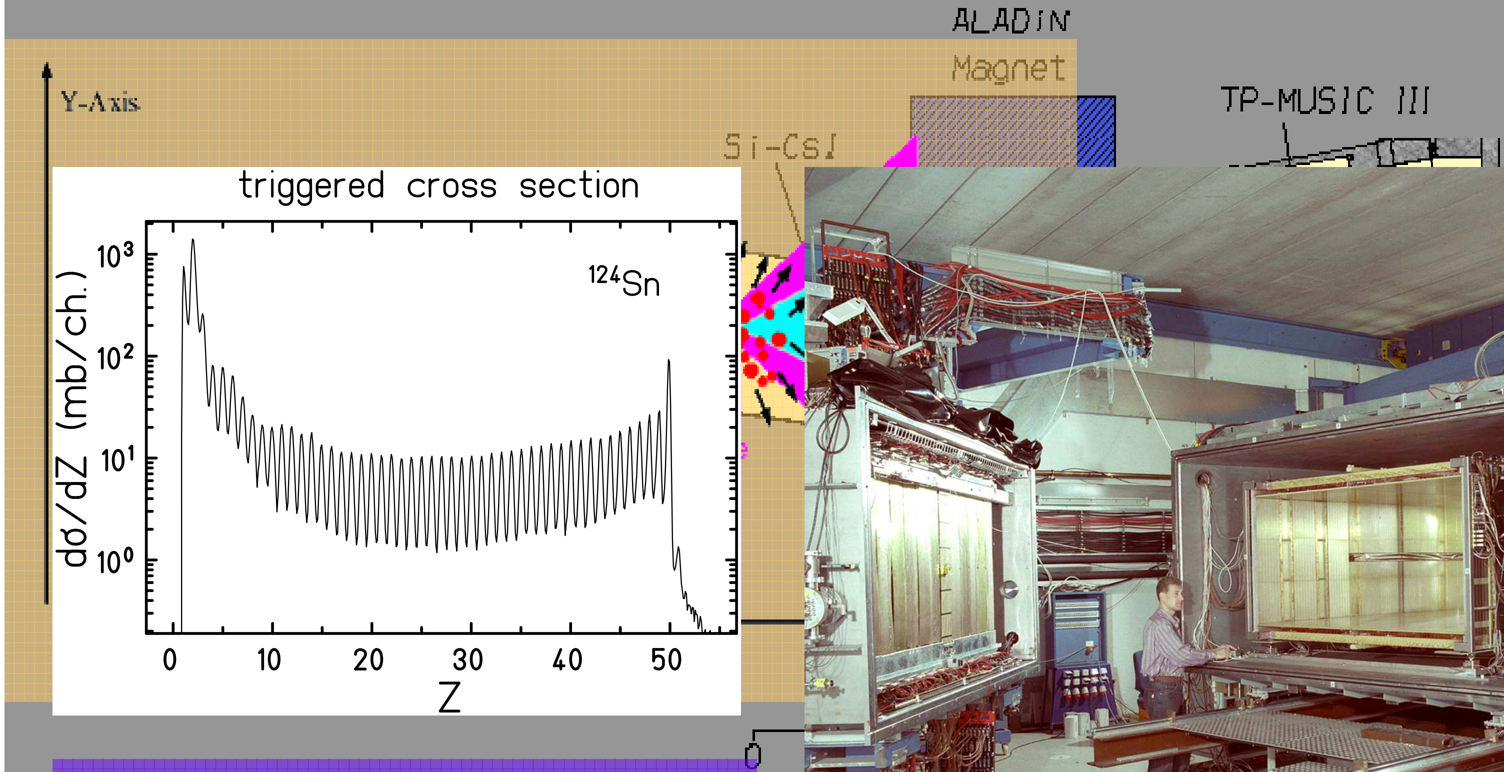
M. Durante, D. Schardt, R. Pleskac, T. Aumann, C. Scheidenberger, A. Kelic, M.V.Ricciardi, K.Boretzky, M. Heil, H. Simon, M. Winkler

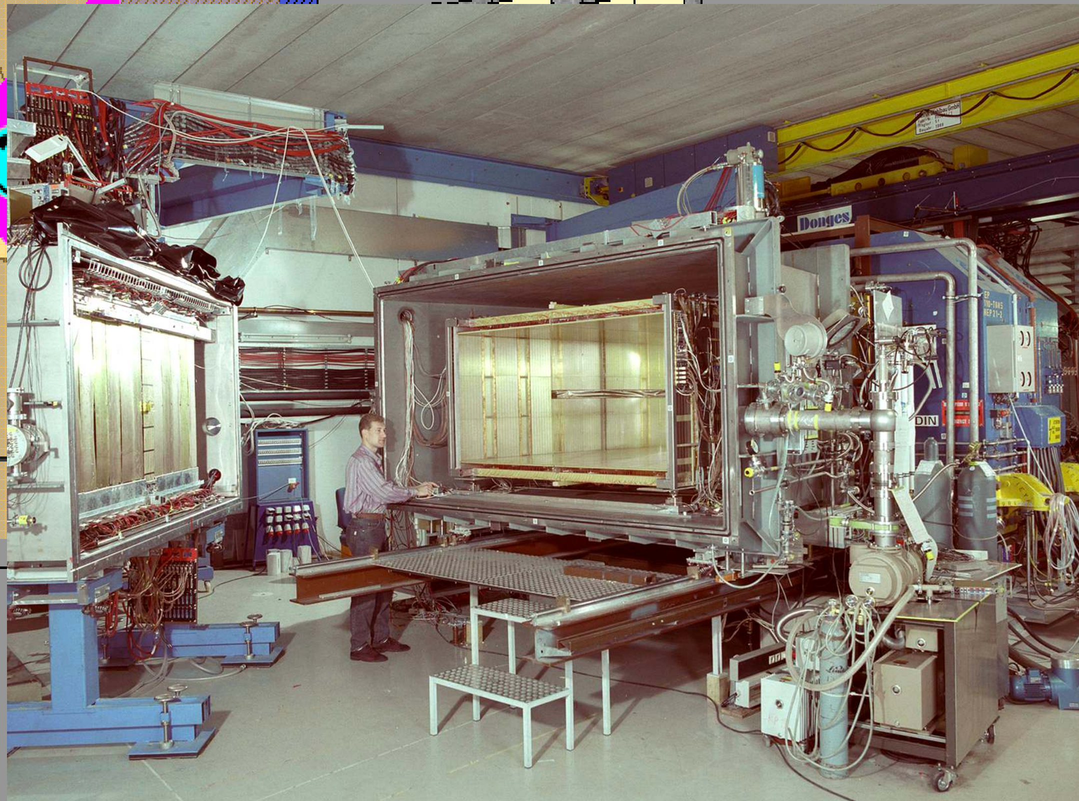
GSI

P. Nieminen, G. Santin

ESA

The ALADiN Spectrometer





- ALL Fragments (Z≥ 2)
- Isotope Resolution
- Protons...(but TOF)

Beam time request

•Control of setup	1 day per period of beam
•C+C @ 0.2, 0.4 and 1.0 AGeV	6 days
•C+Au @ 0.2, 0.4	4 days
•O+C @ 0.2, 0.4	4 days
•Fe+Si @ 0.5 and 1.0 AGeV	4 days
•Fe+C @ 1.0 AGeV	2 days
•Calibration	2 days

**The total request amount to 25 days (75 BTU).
We prefer to distribute the entire amount in 3 periods in 2 months**

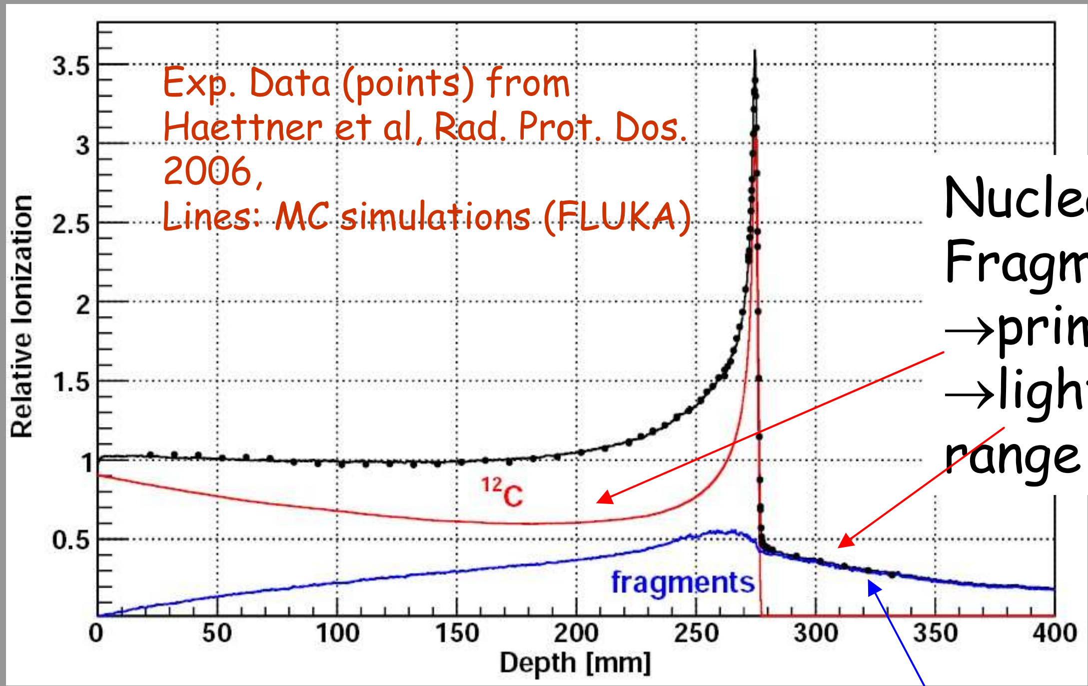
INFN and Medicine

- INFN has developed for more than 15 years competences in the application of nuclear and particle physics to medicine (hadron therapy, detectors, imaging...)
- A strategic project, INFN-MED, is now starting with the aim of coordinating those activities which, having completed the main R&D phase, are now mature for immediate application. 5 main areas:
  - Medical imaging
  - Detectors for diagnostics
  - BNCT
  - Accelerator systems for hadron therapy
  - Treatment Planning System

The TPS project of INFN

for the development of new
Treatment Planning Systems
in hadron therapy with light ion beams

The challenging aspects of therapy with ^{12}C beams



Nuclear Physics:
Fragmentation of Projectile
→primary attenuation
→lighter fragments with longer range

Dosimetry:
Mixed field complexity

Radiobiology:
RBE of primary and fragments

Possible damage to healthy tissues outside the target volume

Other aspects contributing to the complexity of Treatment Planning in hadron therapy

- Management of interfaces/corrections
- Elemental composition of materials
- Integration with local beam delivery systems
- Need for “fast” calculation; possibility of producing alternative plans in due time
- Production of general and flexible analysis tools for the inspection of isodose curves on CT scans and Dose-Volume histograms (DHV), etc
- The 4D issue...

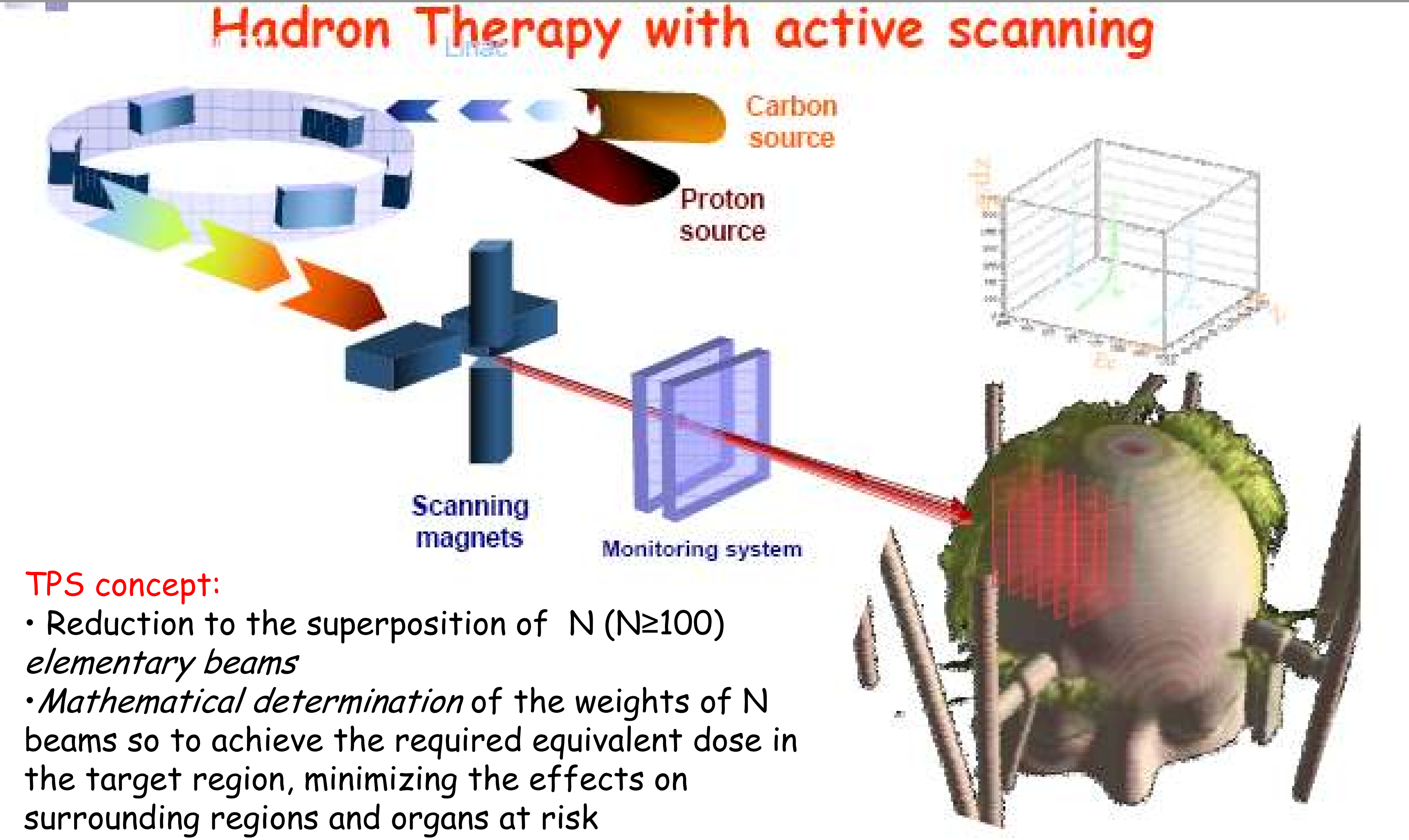
Possibility of feedback

- Production of active nuclides, particle emission

  $\rightarrow$ possibility of in-beam monitoring

  $\rightarrow$ possibility of feed-back correction to Planning

A T.P. for active scanning environment



TPS concept:

- Reduction to the superposition of N (N≥100) *elementary beams*
- *Mathematical determination* of the weights of N beams so to achieve the required equivalent dose in the target region, minimizing the effects on surrounding regions and organs at risk

Aim and features of the INFN project

- **Contribute to the development of innovative Treatment Planning Systems for therapy with ion beams (in particular ^{12}C, but not exclusively) for active voxel scanning applications**

- **To produce a well defined, certified and ready-to-use deliverable in collaboration with an industrial partner → IBA** (through associated Elekta-CMS)

- **Collaboration with CNAO in Italy for testing**

- **Scientific collaboration with other European Institutes for aspects concerning nuclear physics and radiobiology**

INFN Participants

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P. Guarino, V. Mongelli, F. Pansini, V. Patti, M.G. Sabini, V. Salamone
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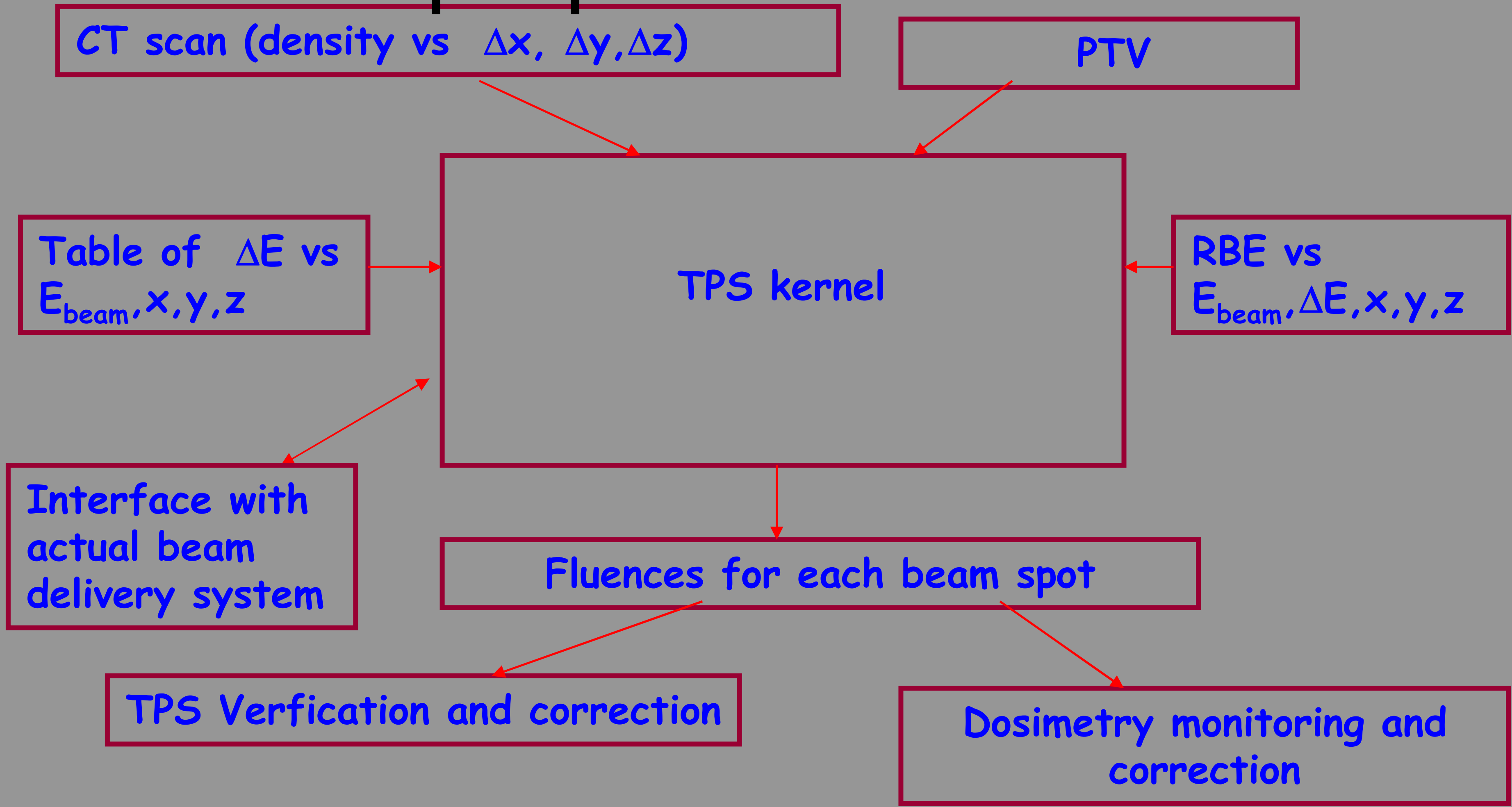
INFN - Sez. di Roma Tre e Dipartimento di Biologia, Università di Roma Tre

Areas of relevant competences within INFN

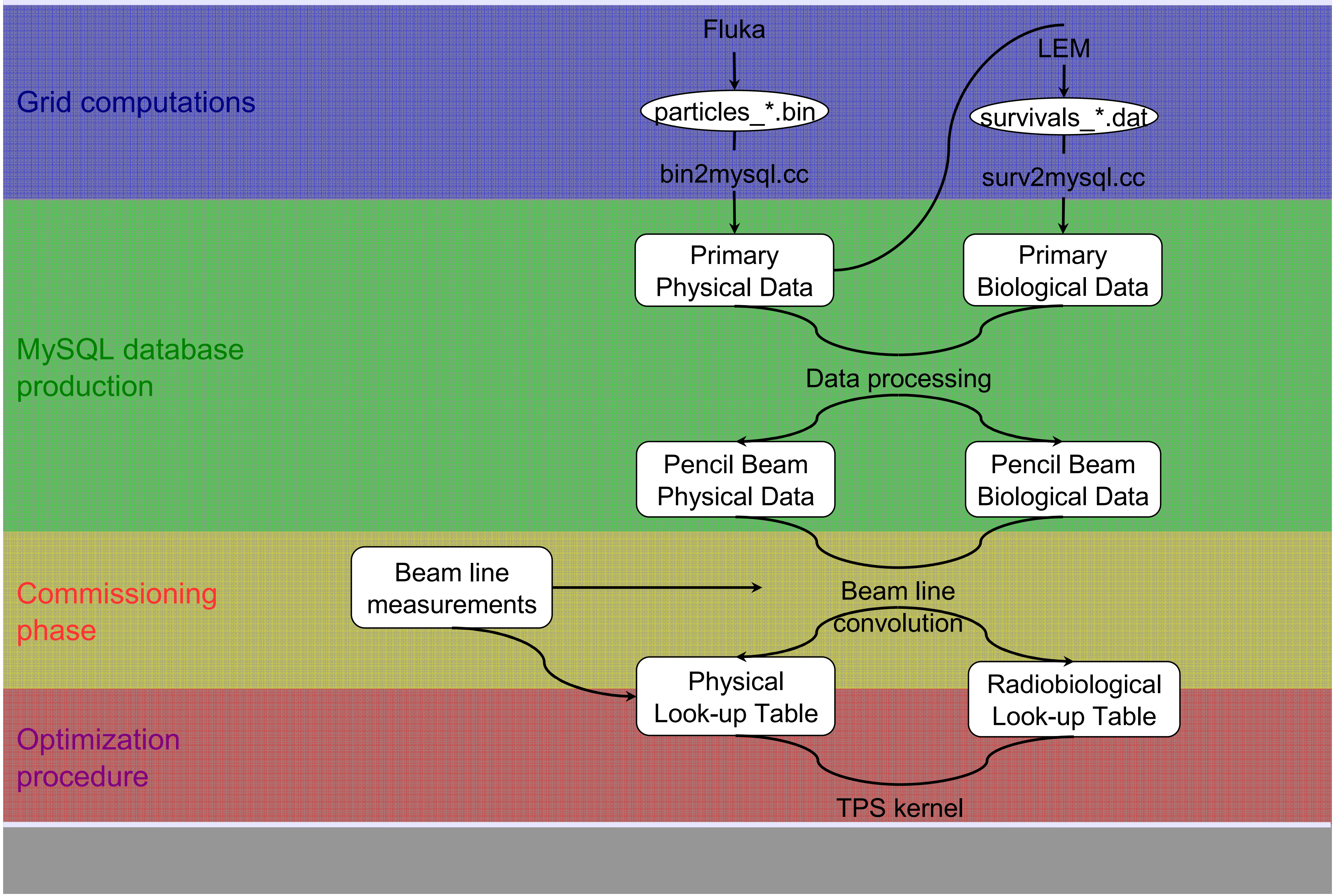
- Nuclear Physics
- MC simulation
- Optimization algorithms
- Experimental Radiobiology
- Monitoring “in beam”

these are the 5 tasks of the INFN TPS project

A simplified scheme of the proposed TPS



A first step: Database Construction



The Structure of Physics Database

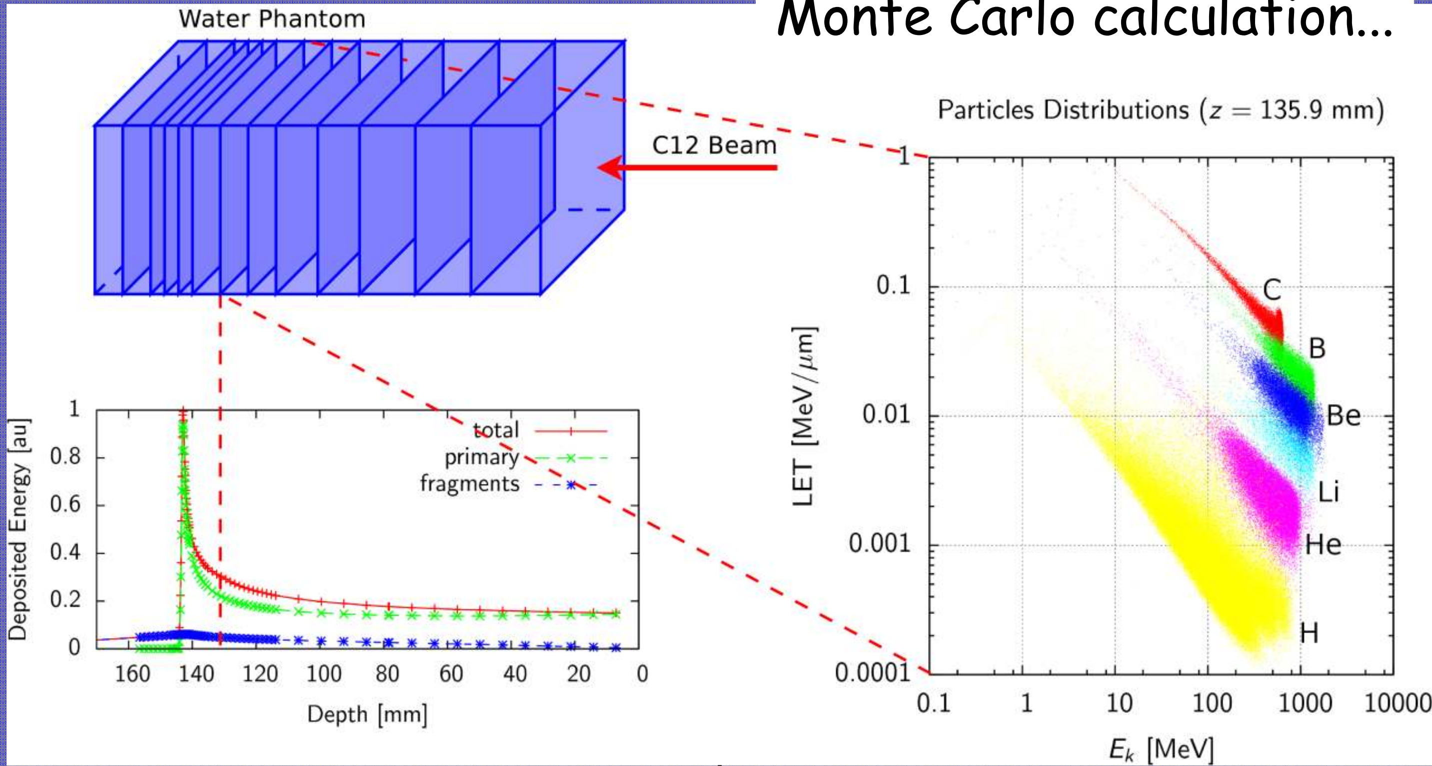
Grid computations

MySQL database production

Commissioning phase

Optimization procedure

Monte Carlo calculation…



particles_*.bin

depth, eventID, trackID, parentID, charge, restEnergy, x_in, y_in, z_in, x_out, y_out, z_out, e_in, e_d

Thank you for your attention!!!

Why carbon therapy

Because carbon beams have:

- Reduced lateral spread of the beam
- Higher L.E.T. (→ RBE)
- Permits a more accurate spatial conformation

Dose released to the patient → uncertainties:

- ***the fragments production on different angles and depths***
- ***the radiobiological efficiency (RBE) of ions in biological matters***

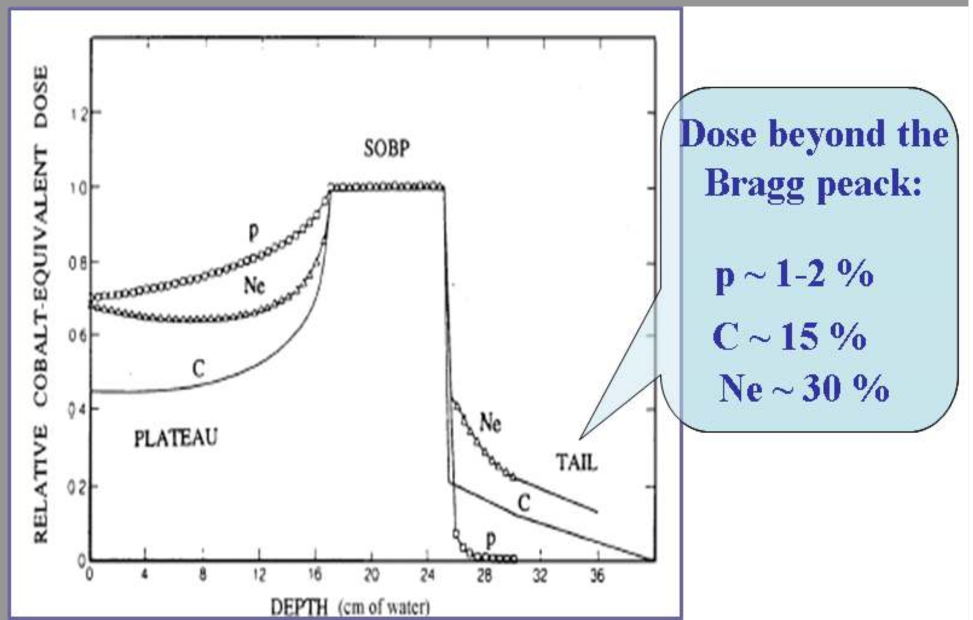
but:

- Secondary fragments production:

^{12}C ^{11}C ^{11}B ^{10}B ^{9}Be ^{7}Be
^{7}Li ^{6}Li ^{6}He ^{4}He ^{3}He t d p

Different contribution on peak (target)

Extra tail dose behind the peak (sane tissues)



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