^{12}C Fragmentation

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Outline

- Introduction
- Fragmentation and models
- Effects of fragmentation
  - Tail after Bragg Peak
  - Enhanced RBE in entrance channel
  - Secondaries and monitoring
- Experimental methods
- Monte Carlo

please stop me
if you have questions!

Definitions…

- **Stopping power:** energy lost by projectile per unit length

$$\frac{dE}{dx}$$

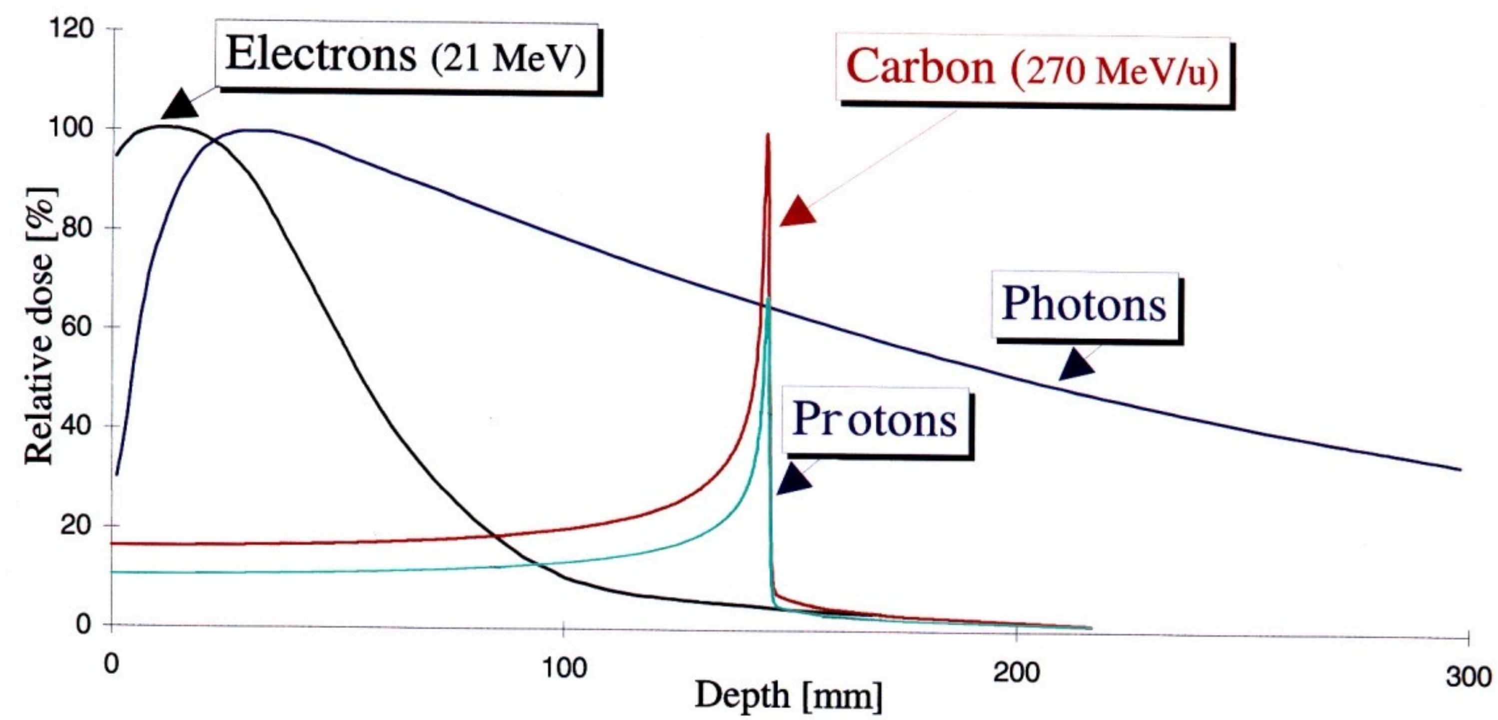
- **Linear Energy Transfer (LET):** energy transferred locally to the material per unit length

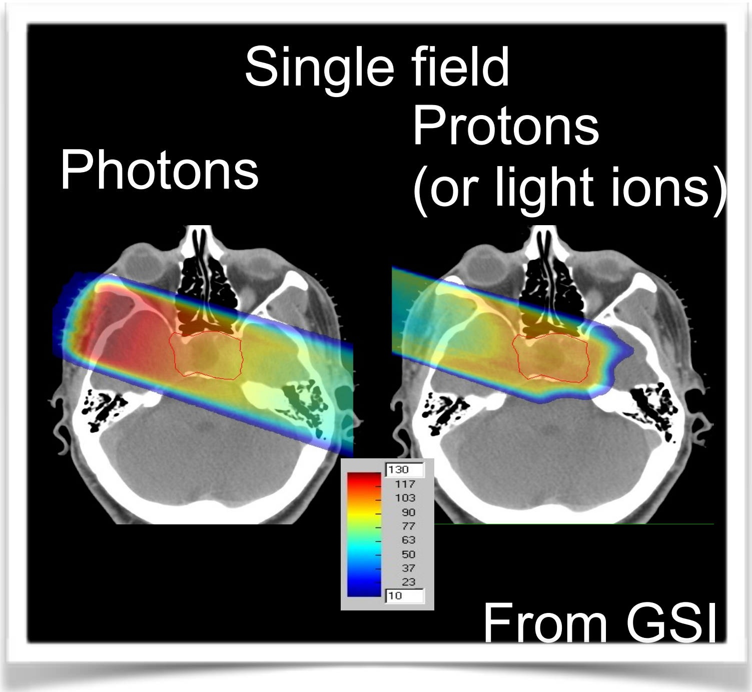
- it is the dE/dx minus the energy of δ rays

$$\mathrm{LET} = \frac{dE}{dx} - \sum E(\delta)$$

- for heavy ions δ rays contribution is negligible

Hadrontherapy

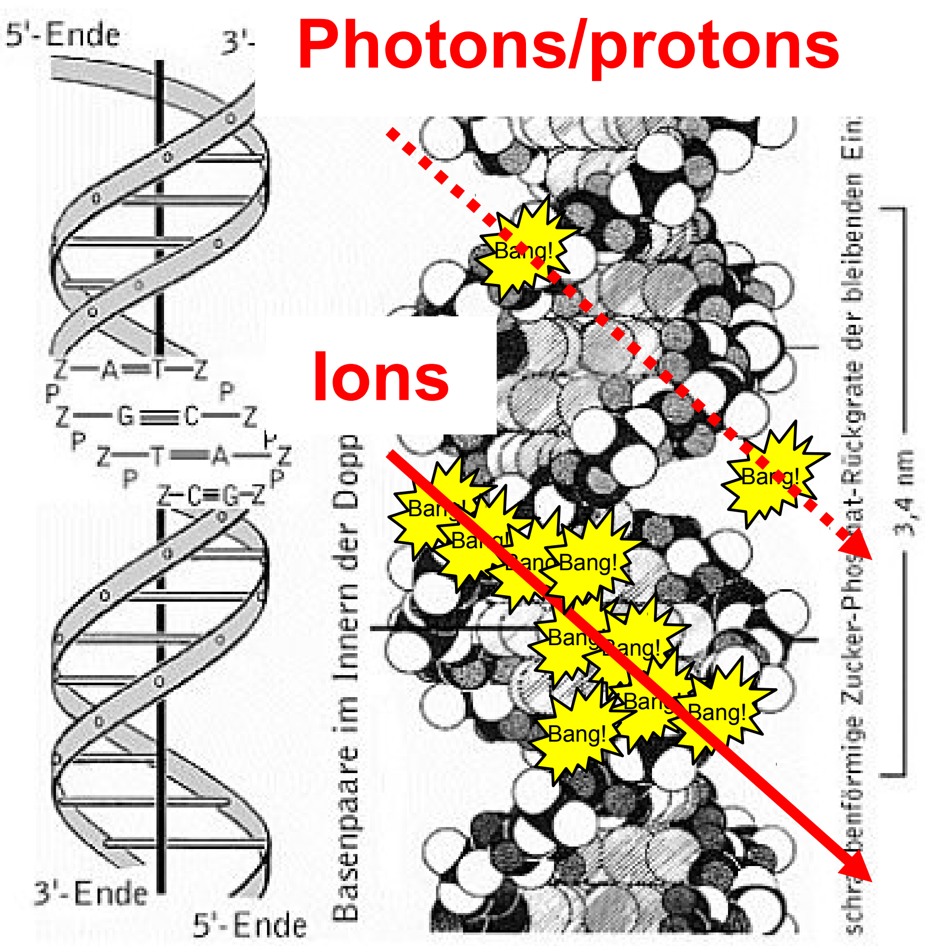




- Hadrons deposit the maximum dose close to the end point of their path (the Bragg peak)
- It is possible to damage depth tumours limiting the impact on healthy tissues

Hadrontherapy with Carbon ions

- C ions directly damage the DNA with double strand damages
- It allows to treat also tumours resistant to conventional radiotherapy



Fragmentation

- The Serber approximation:

$$\psi(p) = \frac{4\pi B(\hbar c)^2}{(2\pi\hbar)^{3/2}} \frac{1}{p} \quad \ldots \quad 1\Big)$$

$$-\cos\frac{pc(b+}{\hbar c} \quad \ldots$$

$$+\frac{1}{(\hbar Kc)^2 -} \quad \ldots \quad \sin\frac{pc(b+R)}{\hbar c}$$

$$-pc\sin Kf\,c \quad \ldots$$

$$+\frac{\sin K}{(\hbar c/R_o)^2} \quad \ldots \quad \Big]\Big\}$$

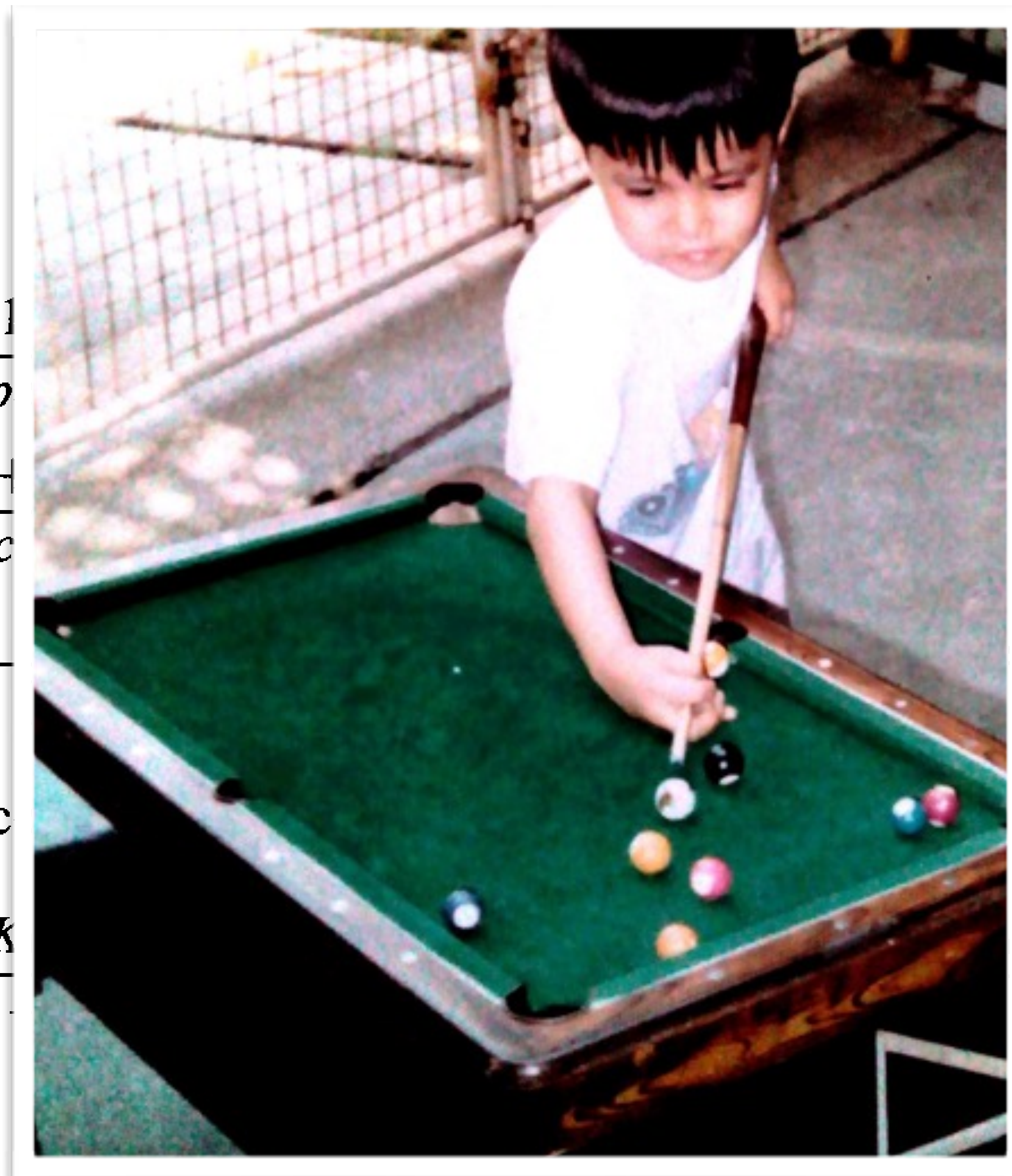
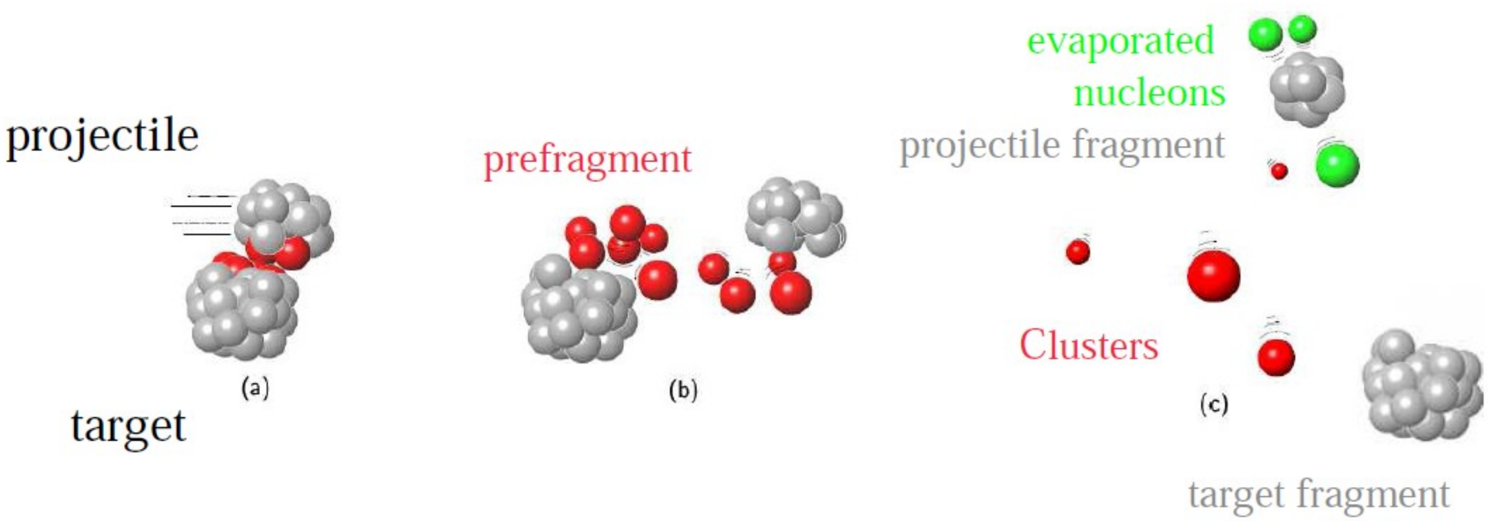
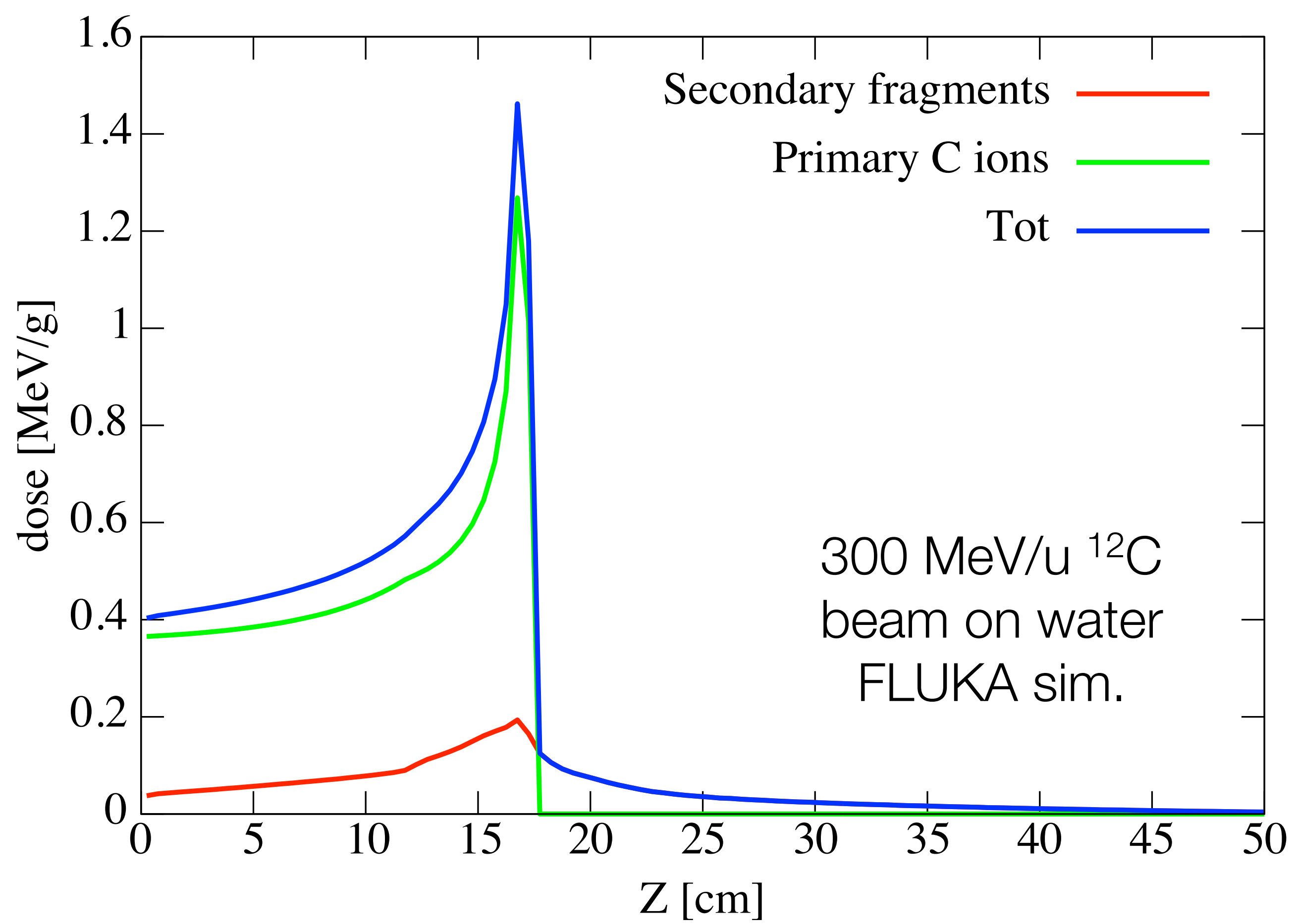


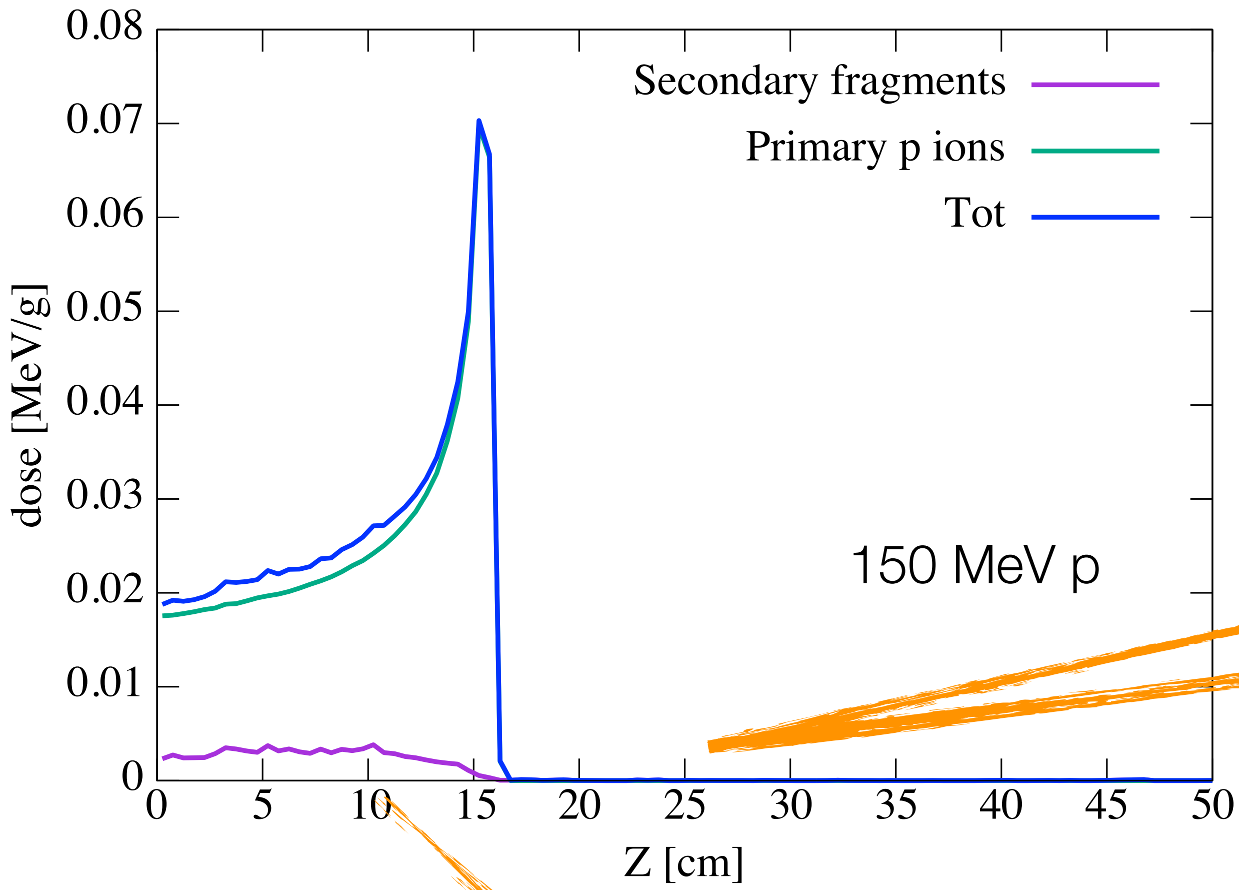
image from: https://en.wikipedia.org/wiki/Billiard_table#/media/File:Kid%27s_toy_billiard_table.jpg

Carbon could fragment

- C ions could fragment in lighter particles
- The fragments contribute significantly to the total dose
- Fragments are responsible of the tail behind the Bragg peak



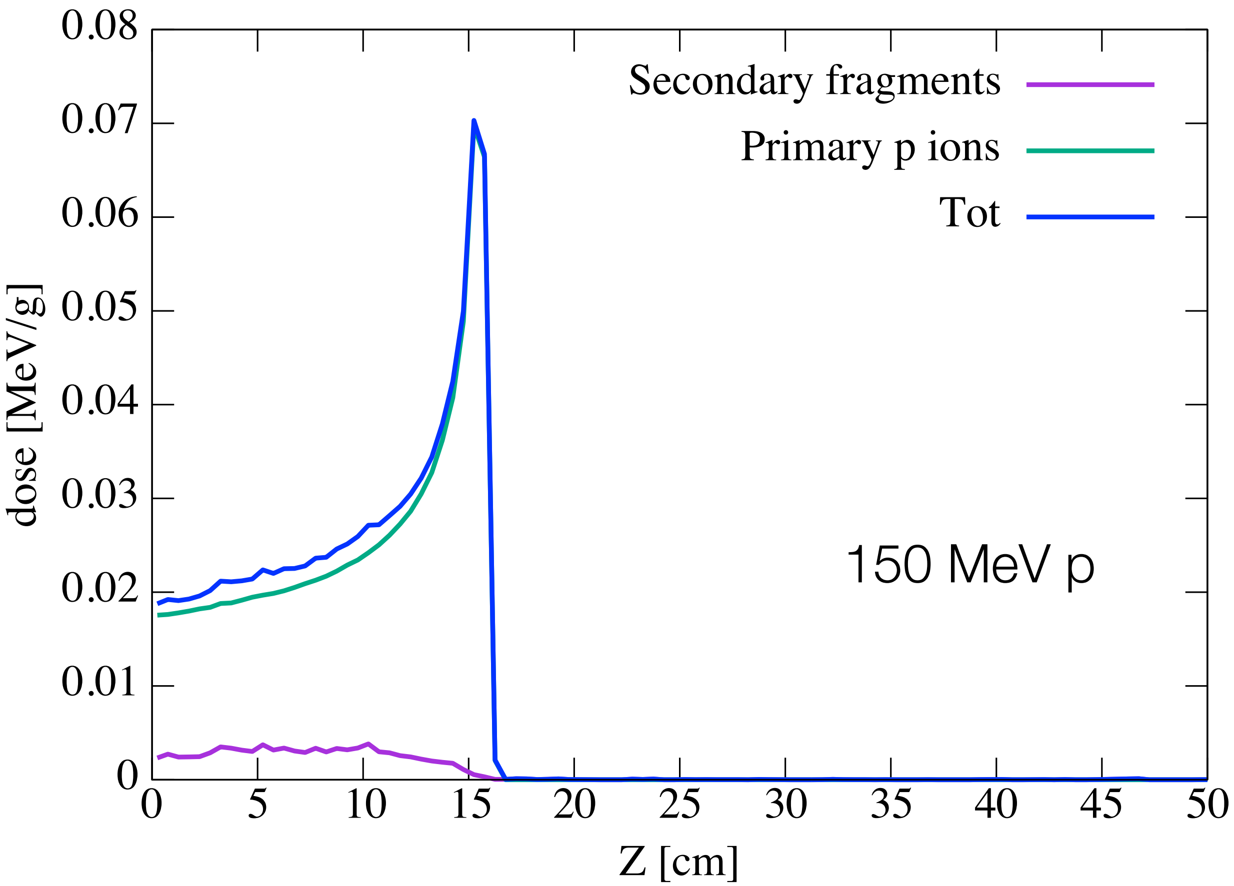


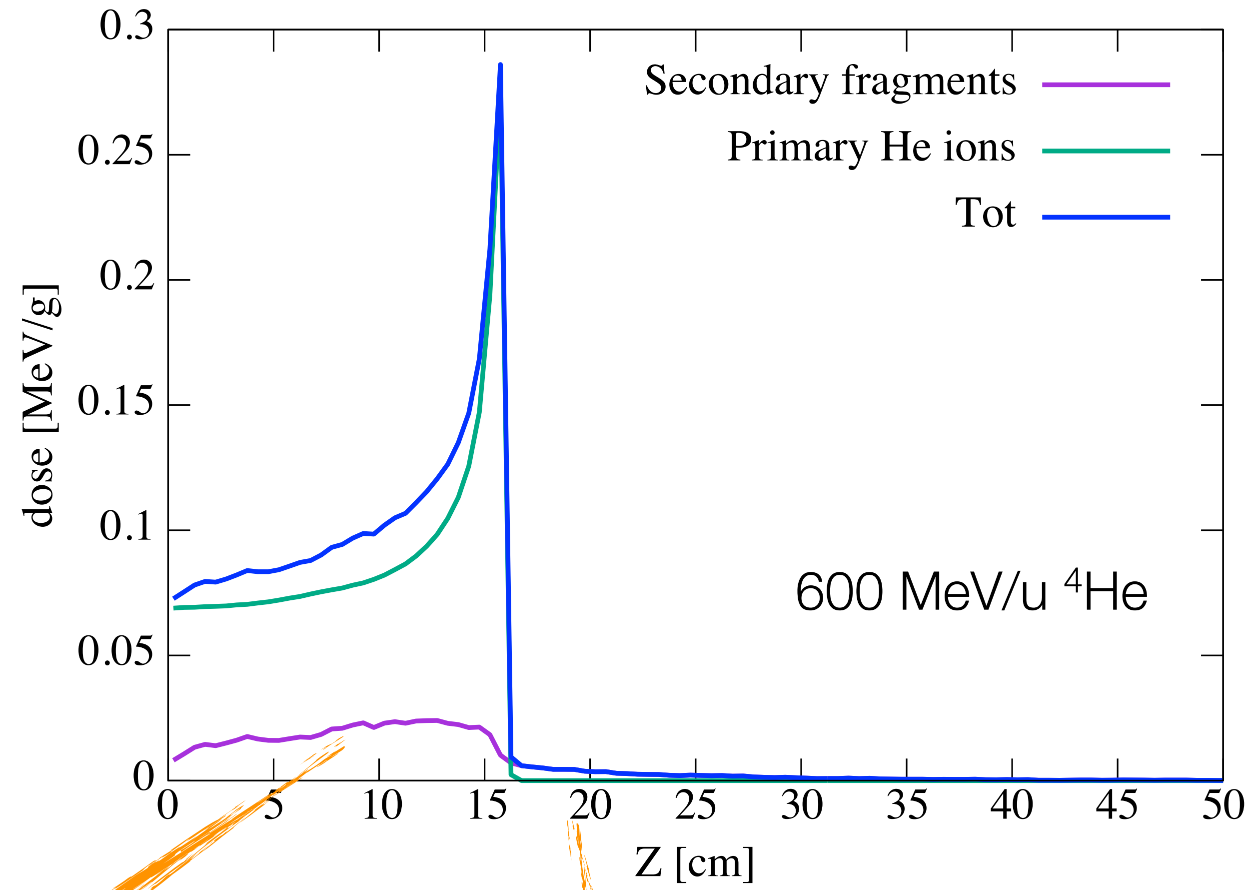


Sharp end beyond the Bragg Peak

Target fragmentation increase RBE

FLUKA simulations on water target

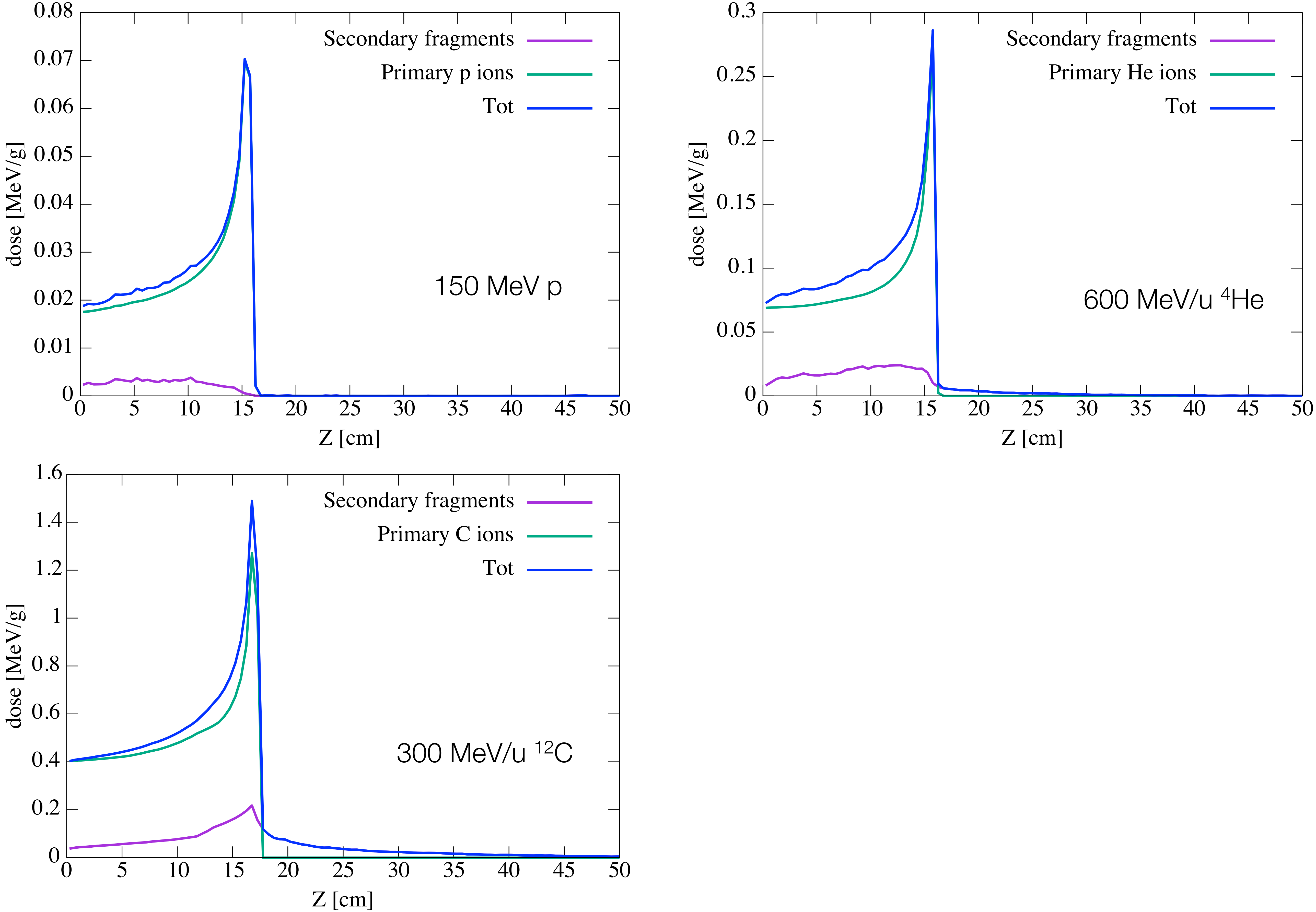




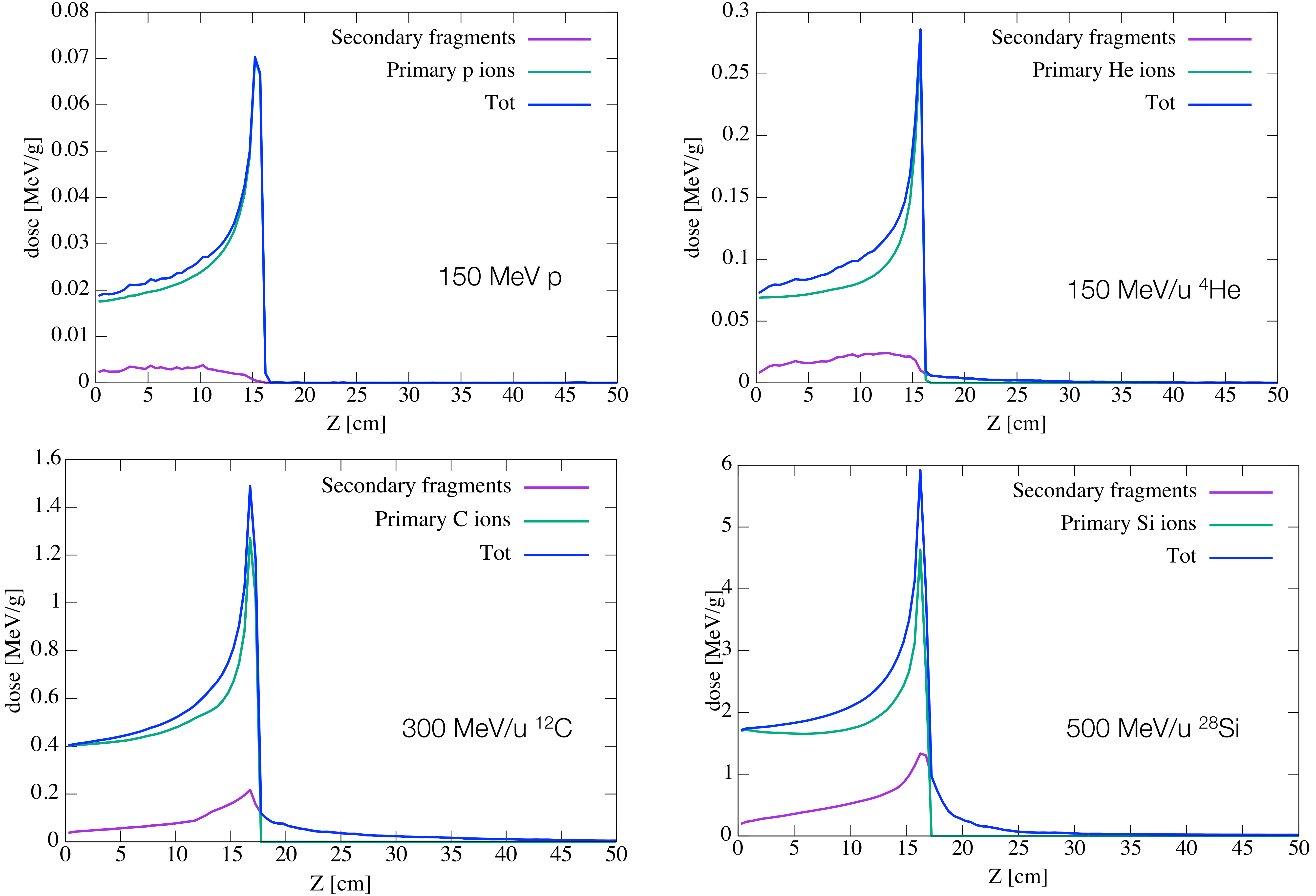
Target fragmentation increase RBE

Small tail beyond the Bragg Peak

FLUKA simulations on water target



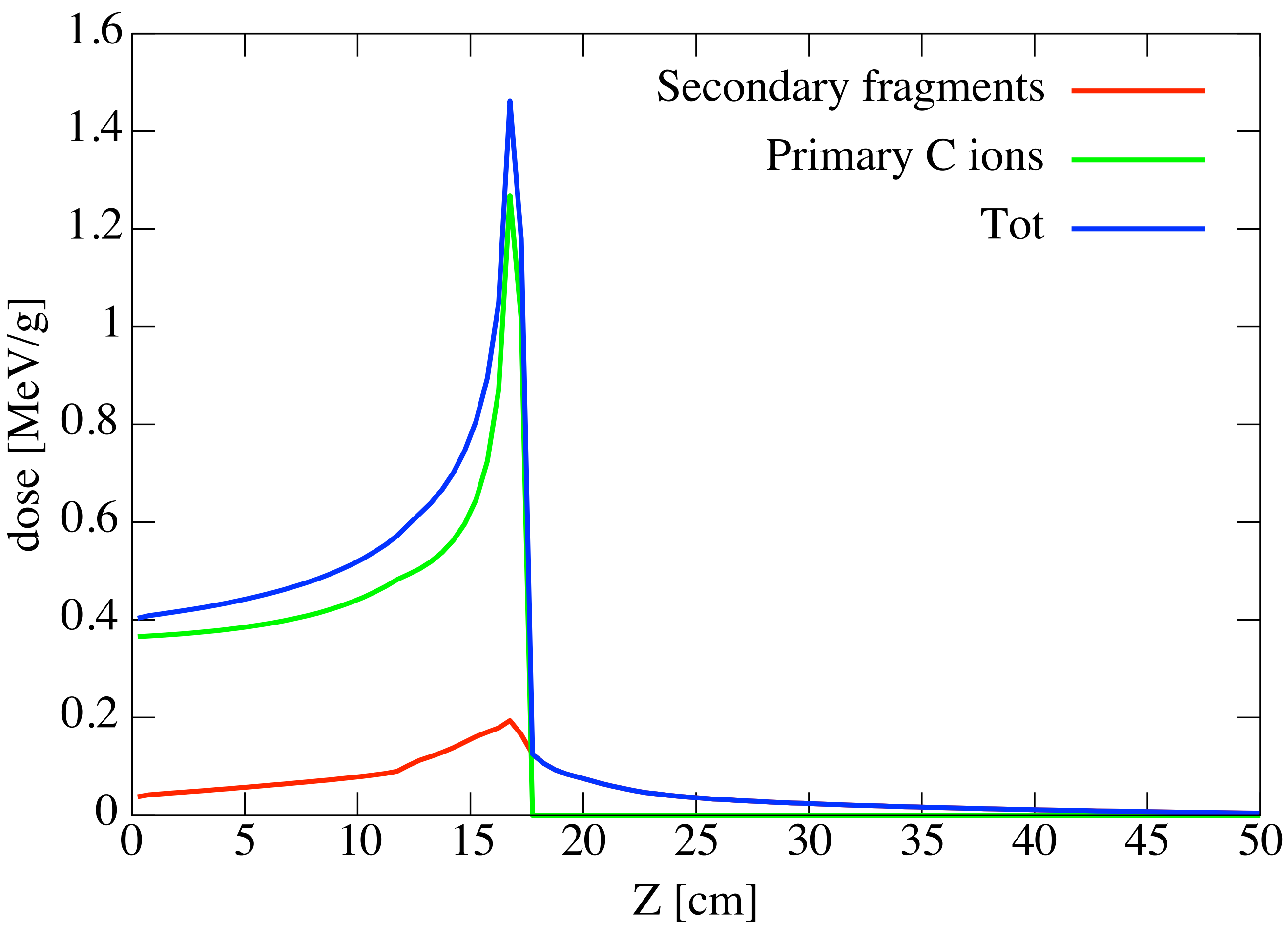
FLUKA simulations on water target



FLUKA simulations on water target

Nuclear interaction effects

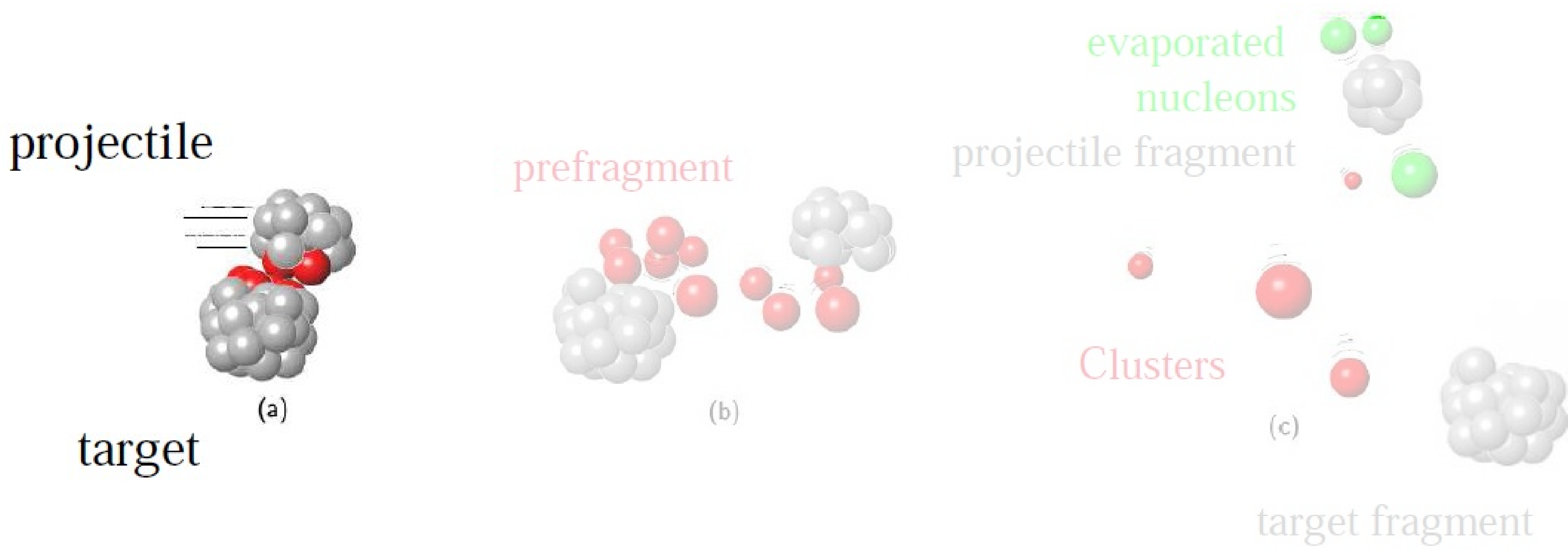
- Disappearance of projectile
  - it will not reach the Bragg Peak



- secondary particle production
  - smaller than projectile
  - if from projectile with a speed close to the beam
  - energy deposition beyond the Bragg Peak (because of the A/Z^2 scaling of the range)

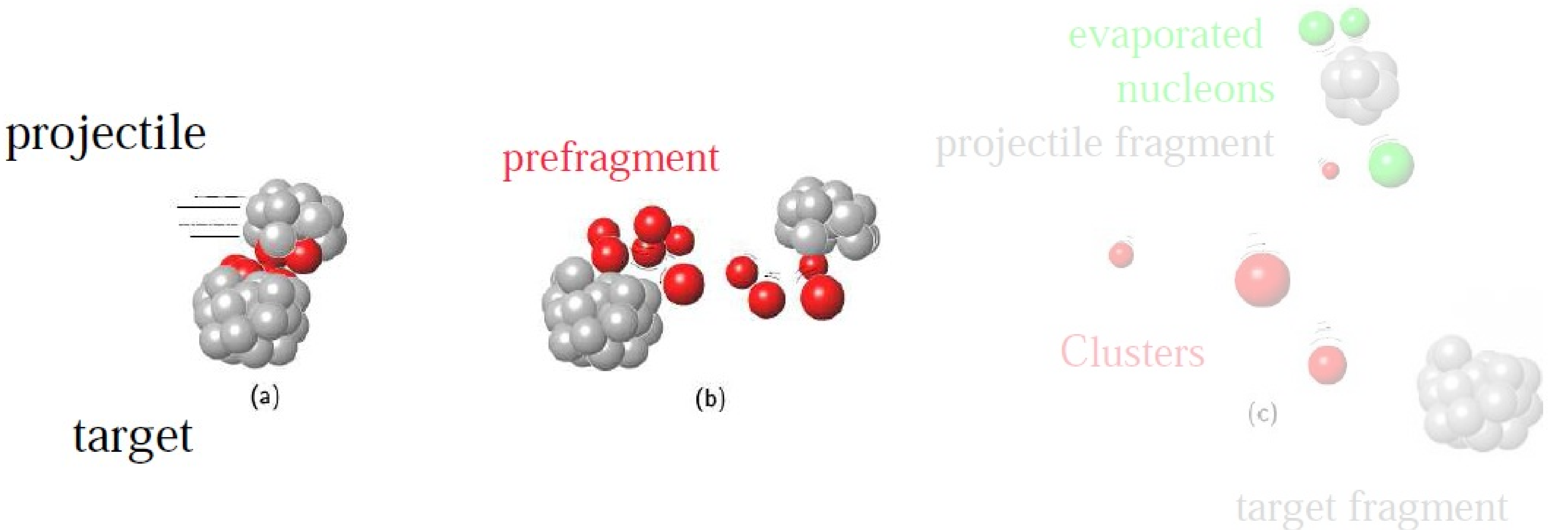
Nucleus-nucleus interaction

- Hadronic interactions are simulated in two different stages



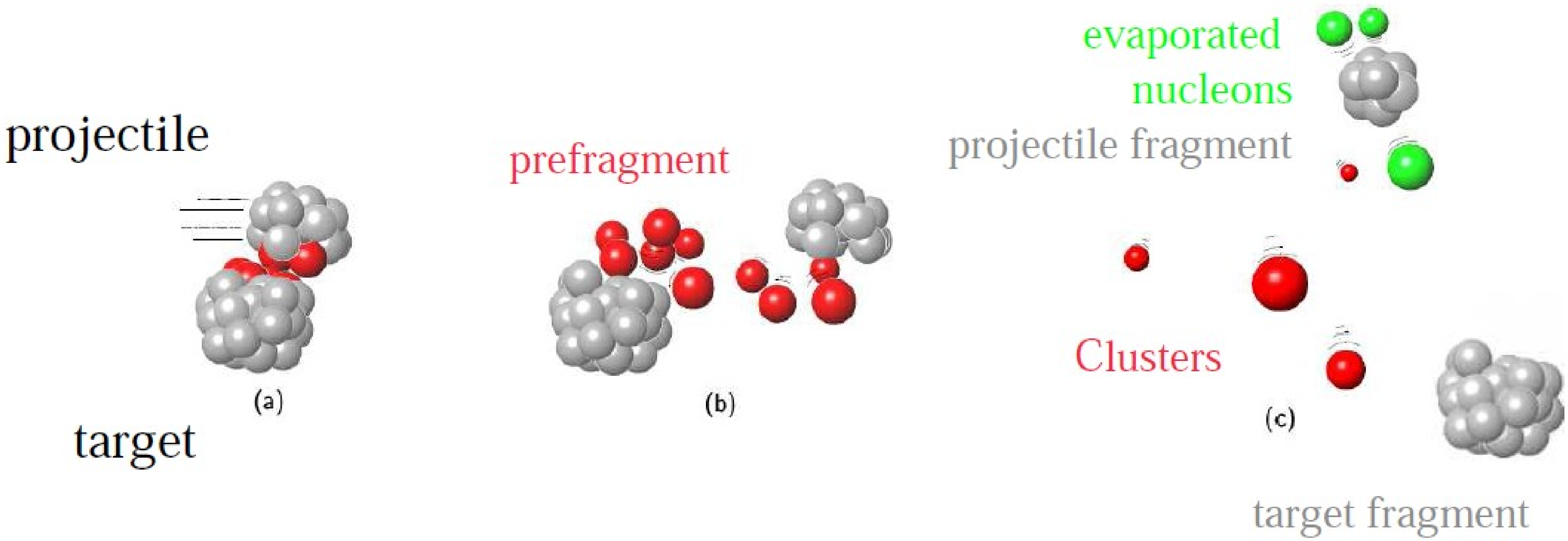
Nucleus-nucleus interaction

- the first one describes the interaction from the collision until the excited nuclear species produced in the collision are in equilibrium



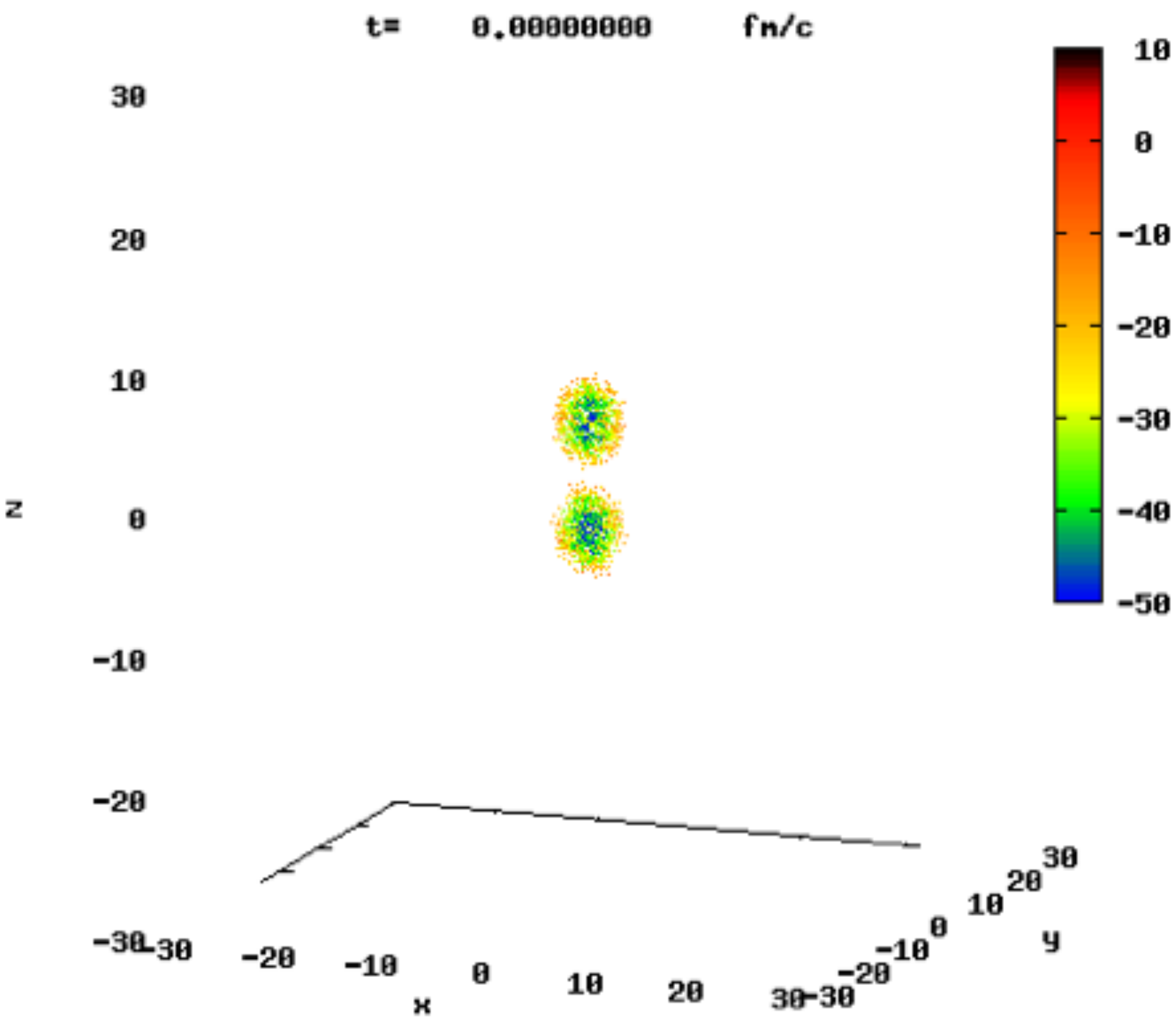
Nucleus-nucleus interaction

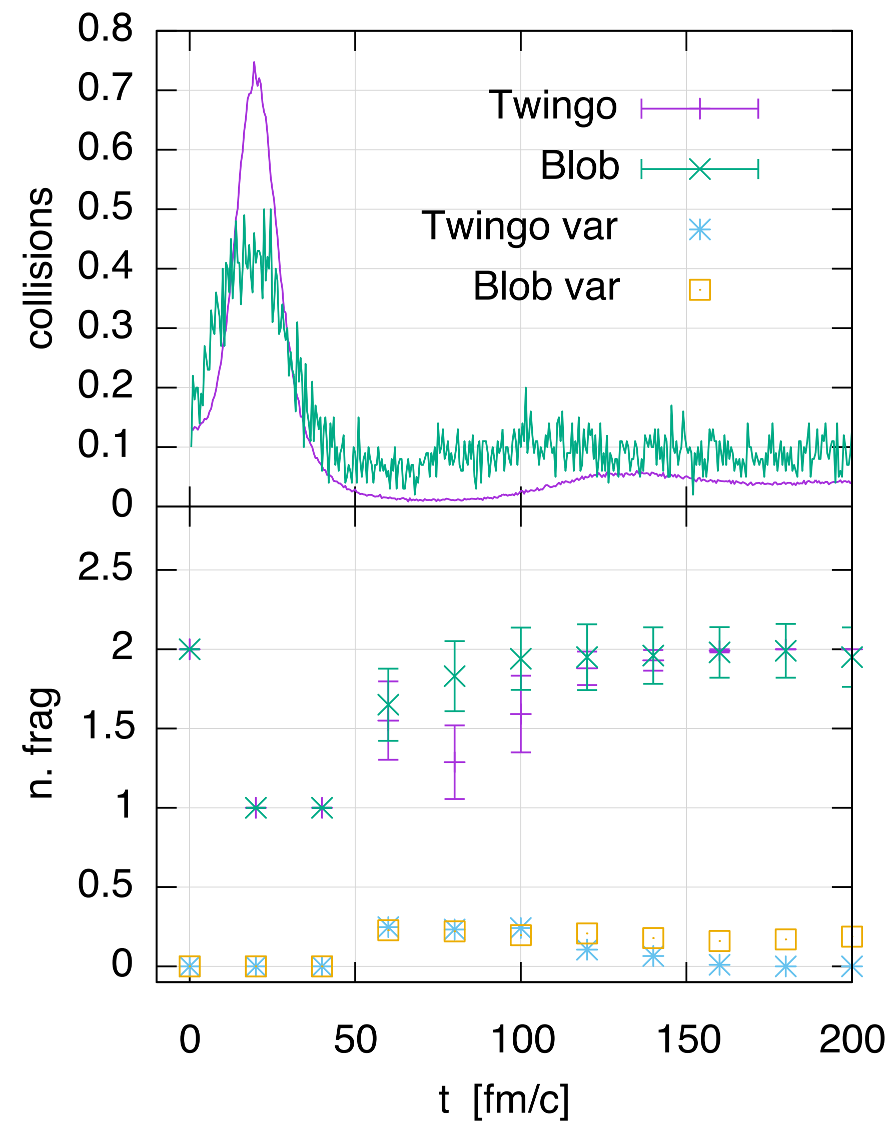
- the second one models the emission of such excited, but equilibrated, nuclei



First stage of nuclear interaction

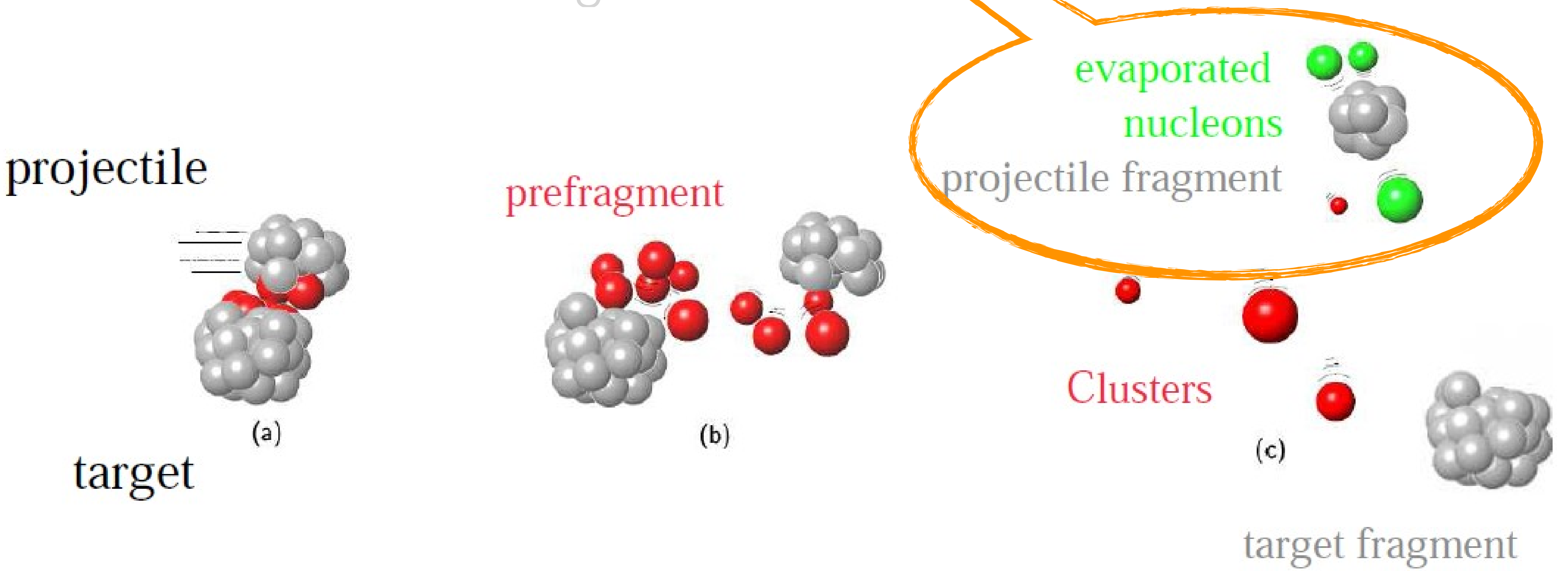
- Models for the first stage of a nuclear interaction
- The fragments are produced within 120 fm/c





Nucleus-nucleus interaction

- Projectile like fragments → speed close to the beam
- Target like fragments → speed very small
- Intermediate-mass fragments



Nucleus-nucleus interaction

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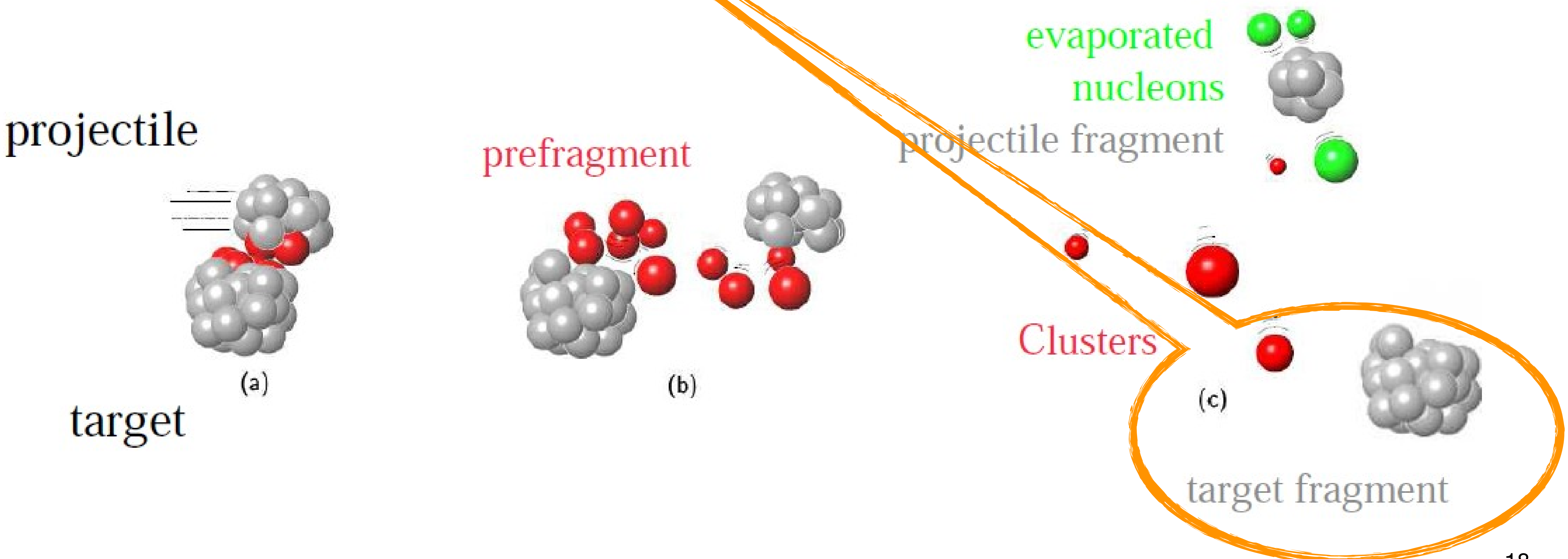

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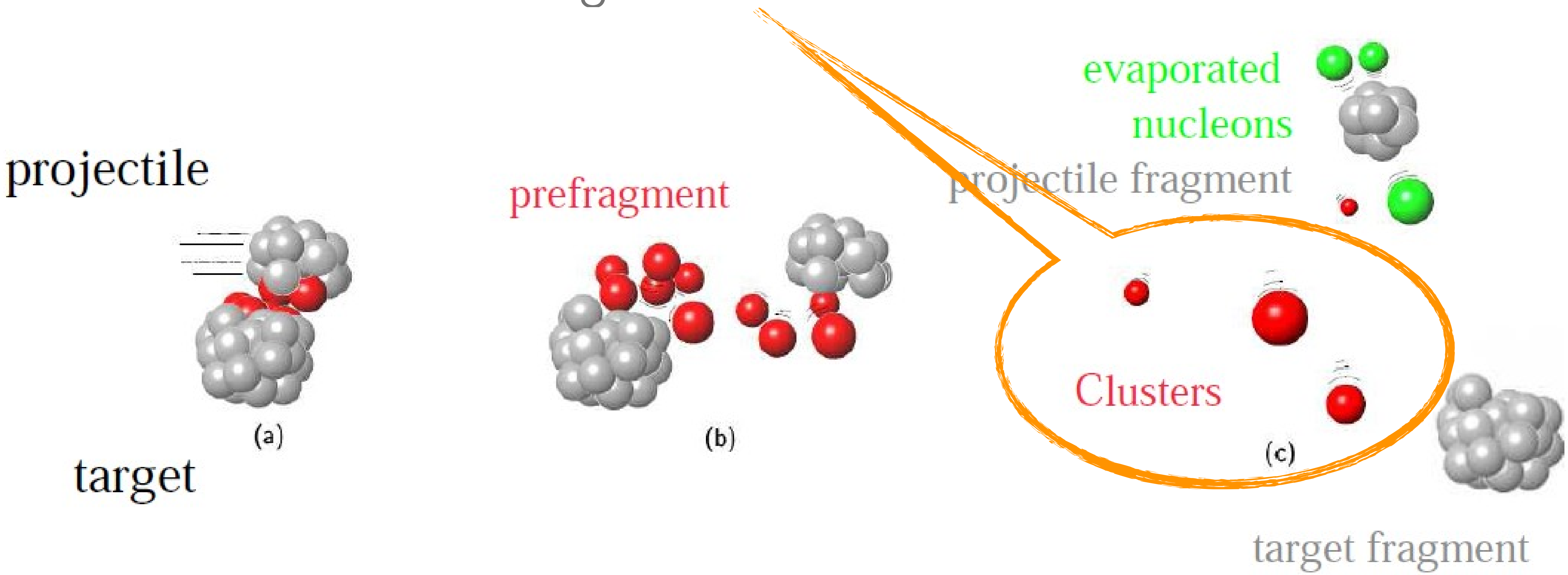
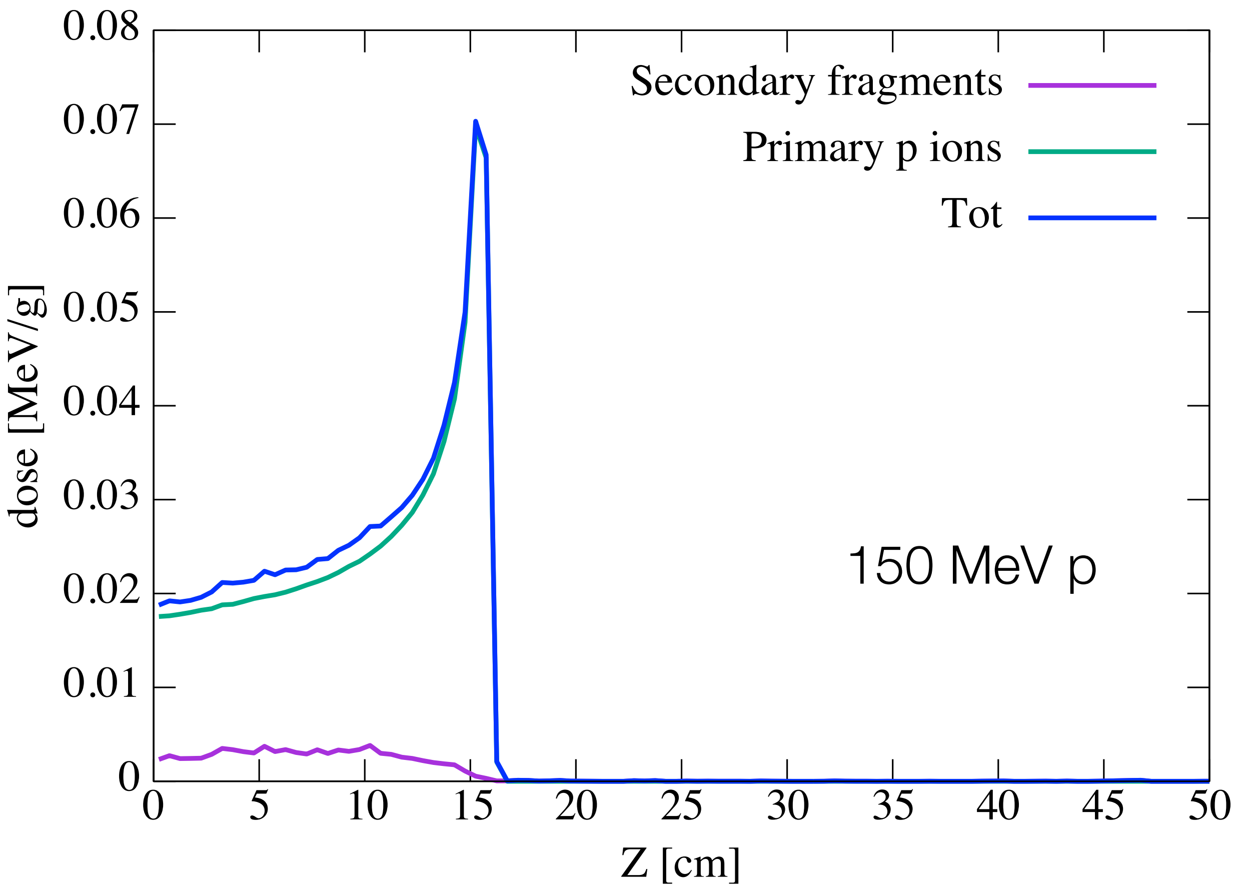
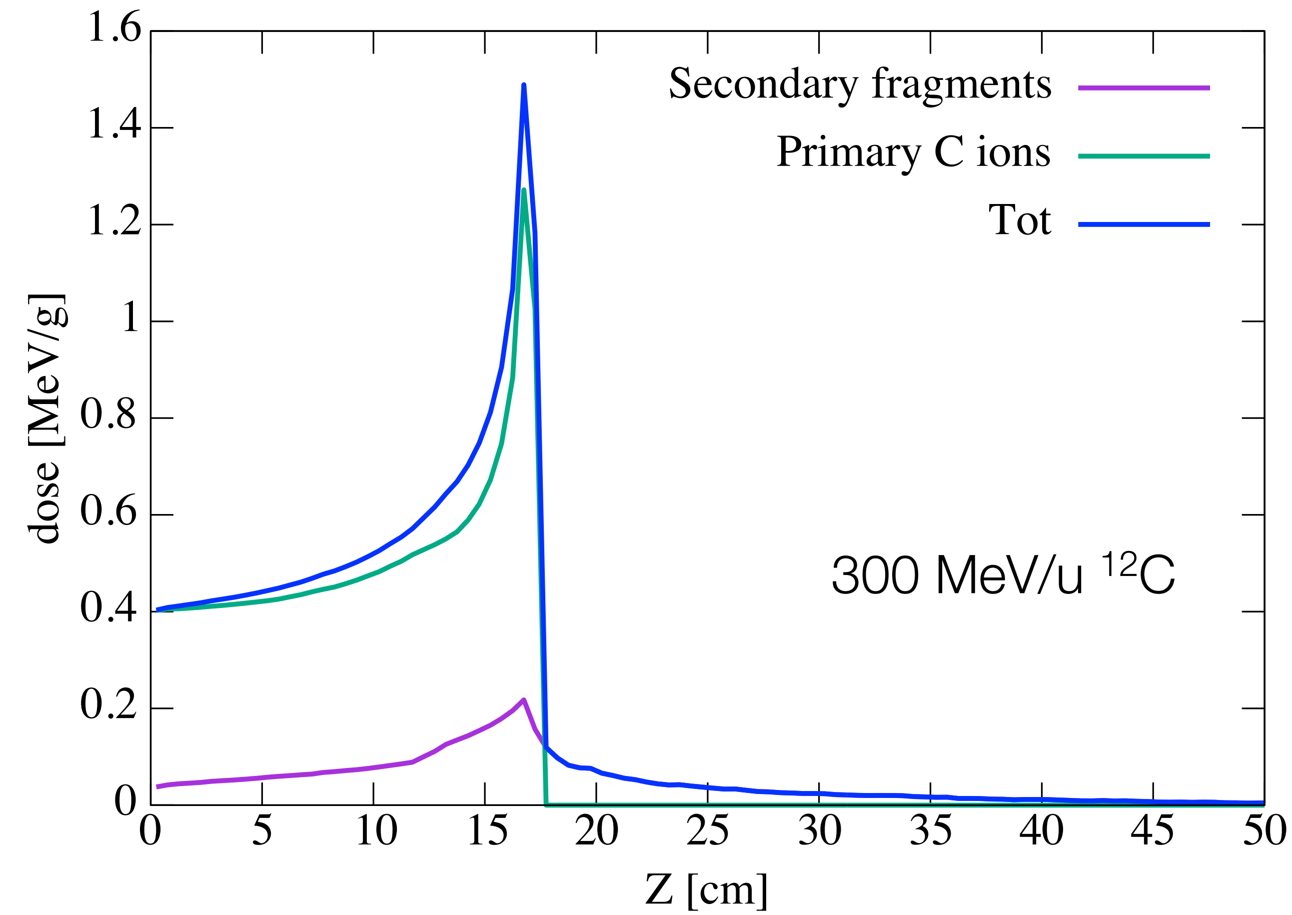




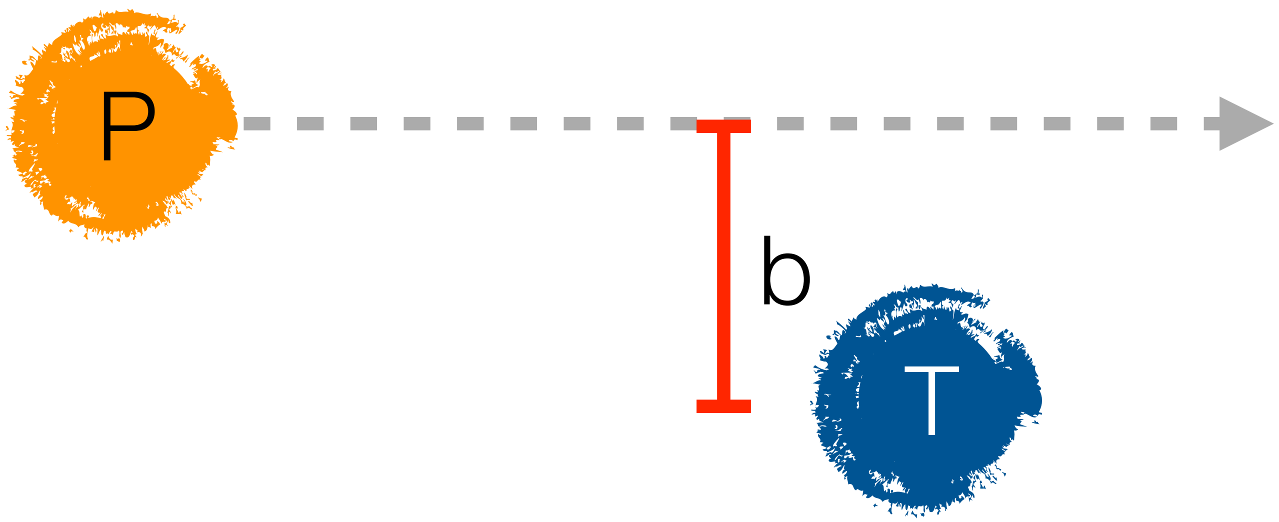


FLUKA simulations on water target

Impact parameter

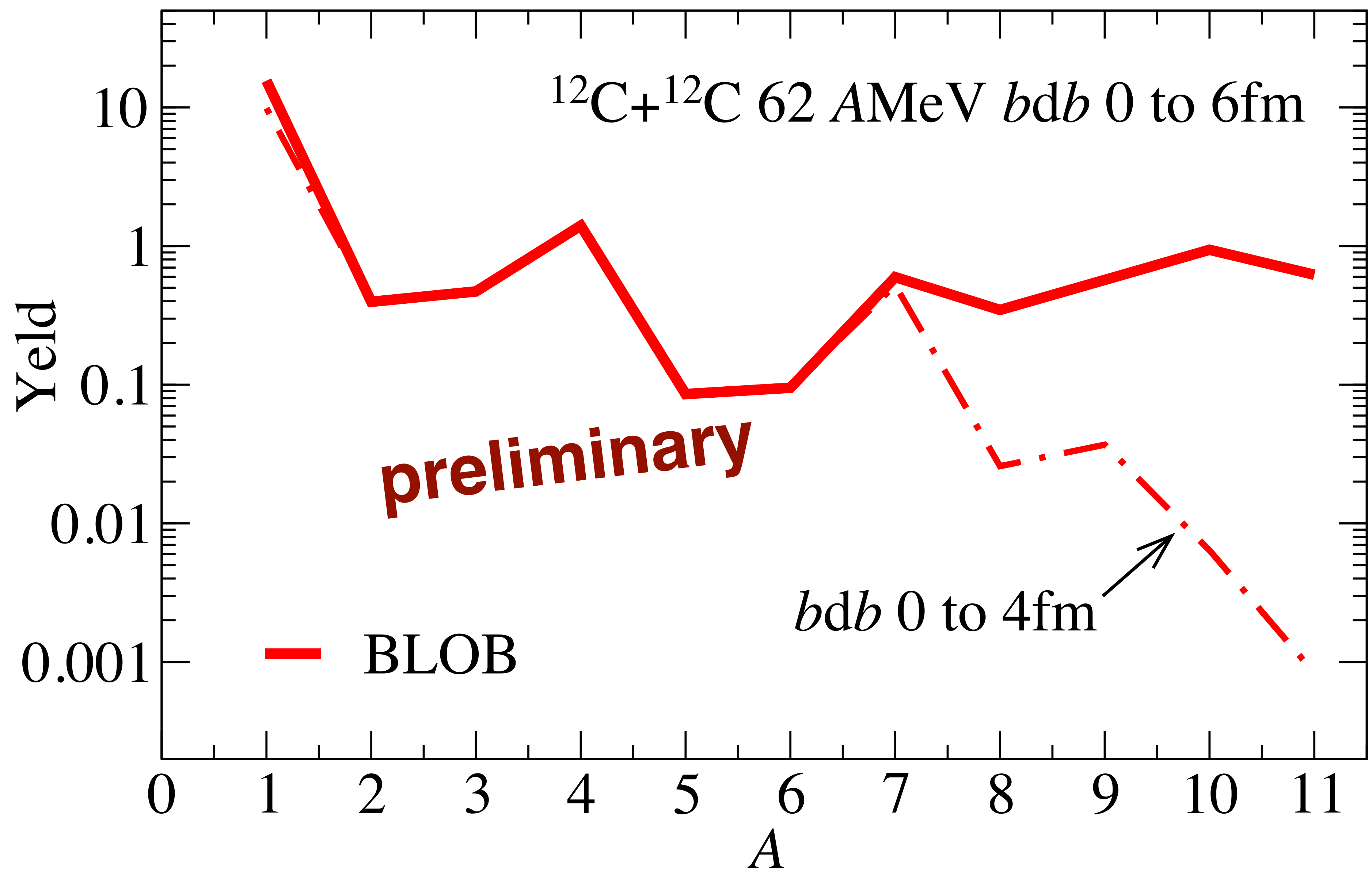
- The impact parameter b is defined as the distance between the projectile path and the the target

- Large impact parameters are more probable, because of geometrical reason



Impact parameter

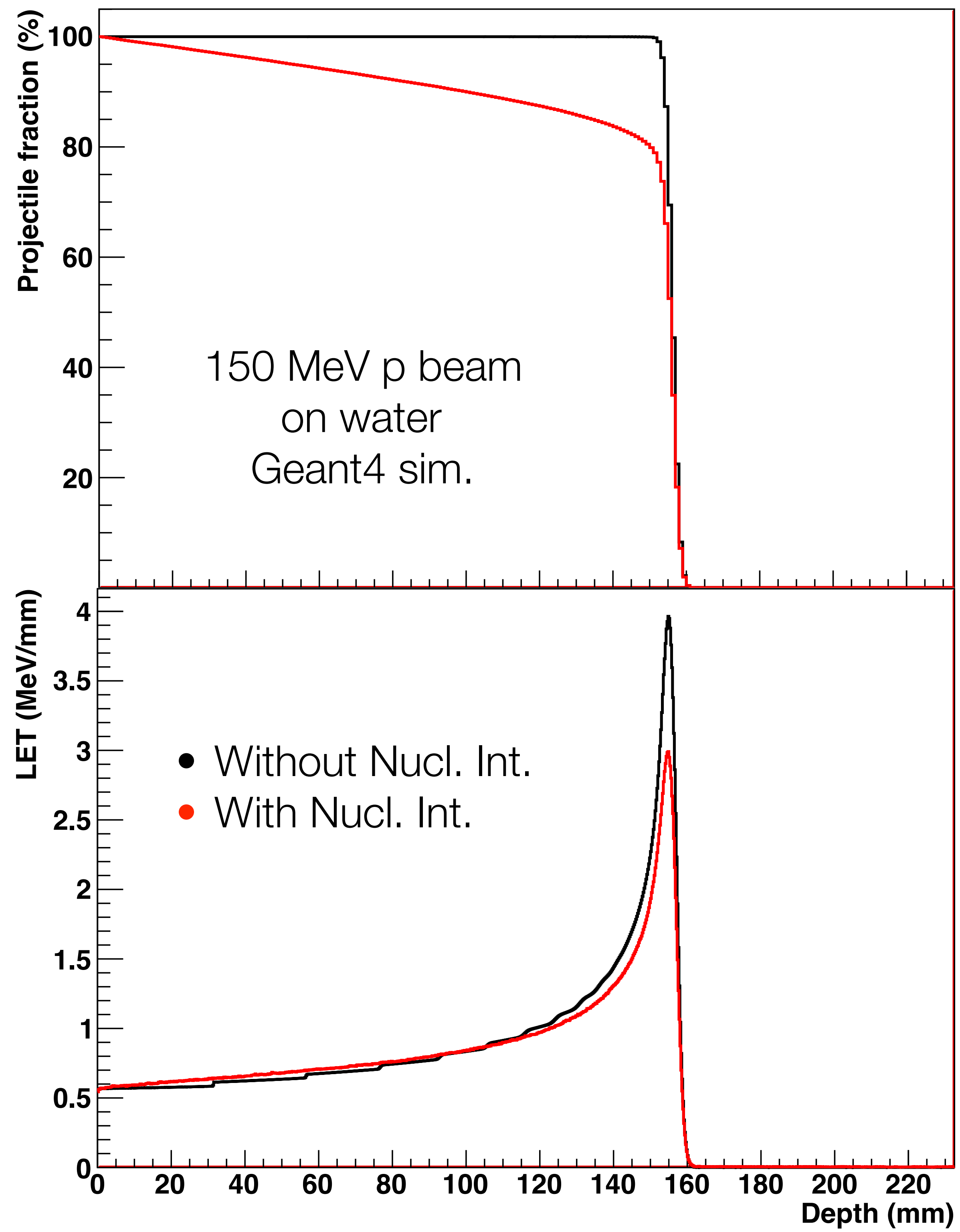
- The number of fragments with A >=9 (and <=2) increases with b



Work done in collaboration with
M. Colonna (LNS Catania) and P. Napolitani (IPN Orsay)

Effects of Nuclear interactions for p

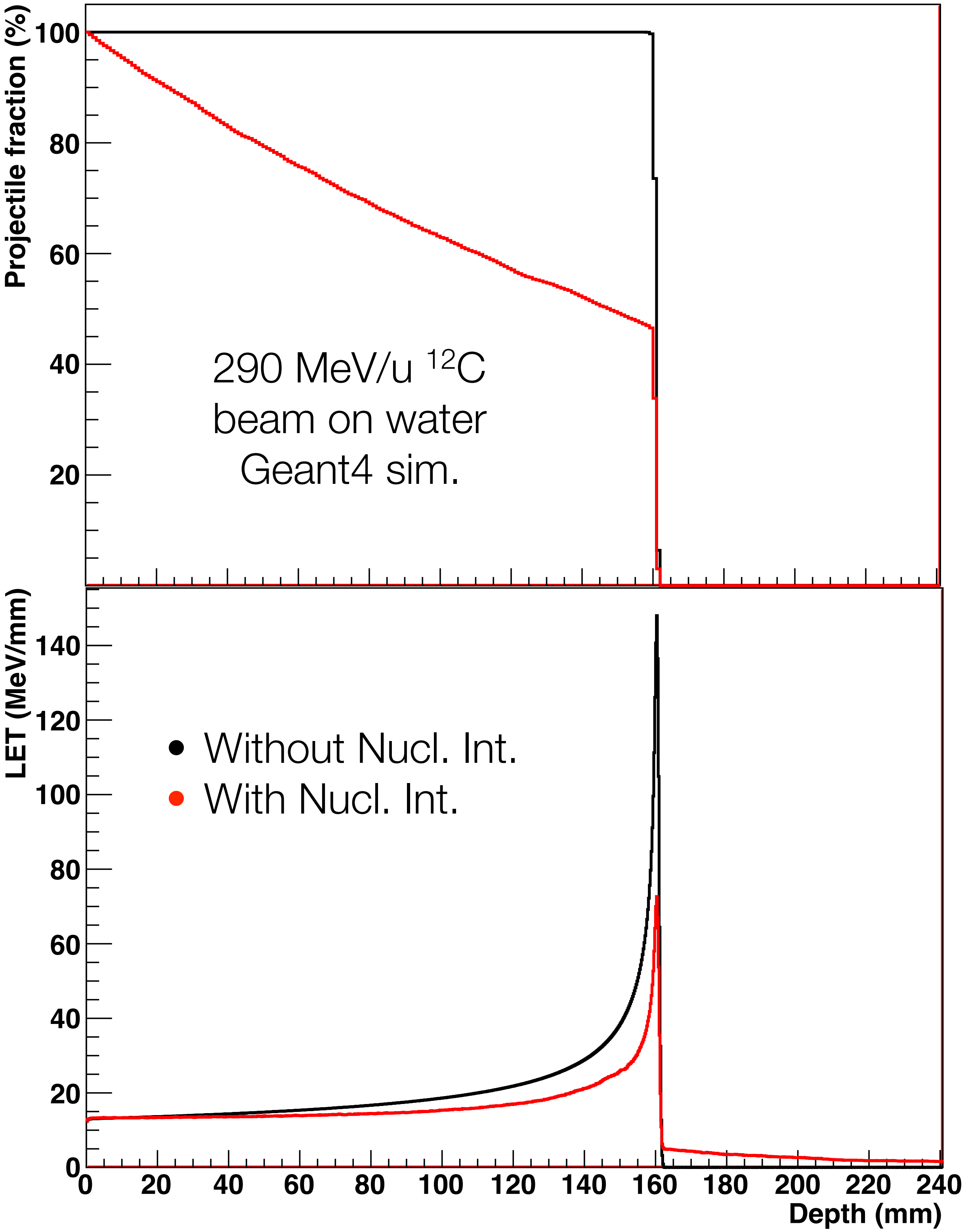
- 80% of the primary p ions reach the Bragg Peak
- Nuclear interactions do not change the Bragg Peak position
- Secondary fragments are issued from the target only
- Their velocity is very small and hence their range do not exceed few micro-meters
- They deposit their energy close to the collision location
- No significant energy deposition beyond the Bragg Peak



plot from: D. Cussol "Nuclear Physics and Hadrontherapy"

Effects of Nuclear interactions for ^{12}C

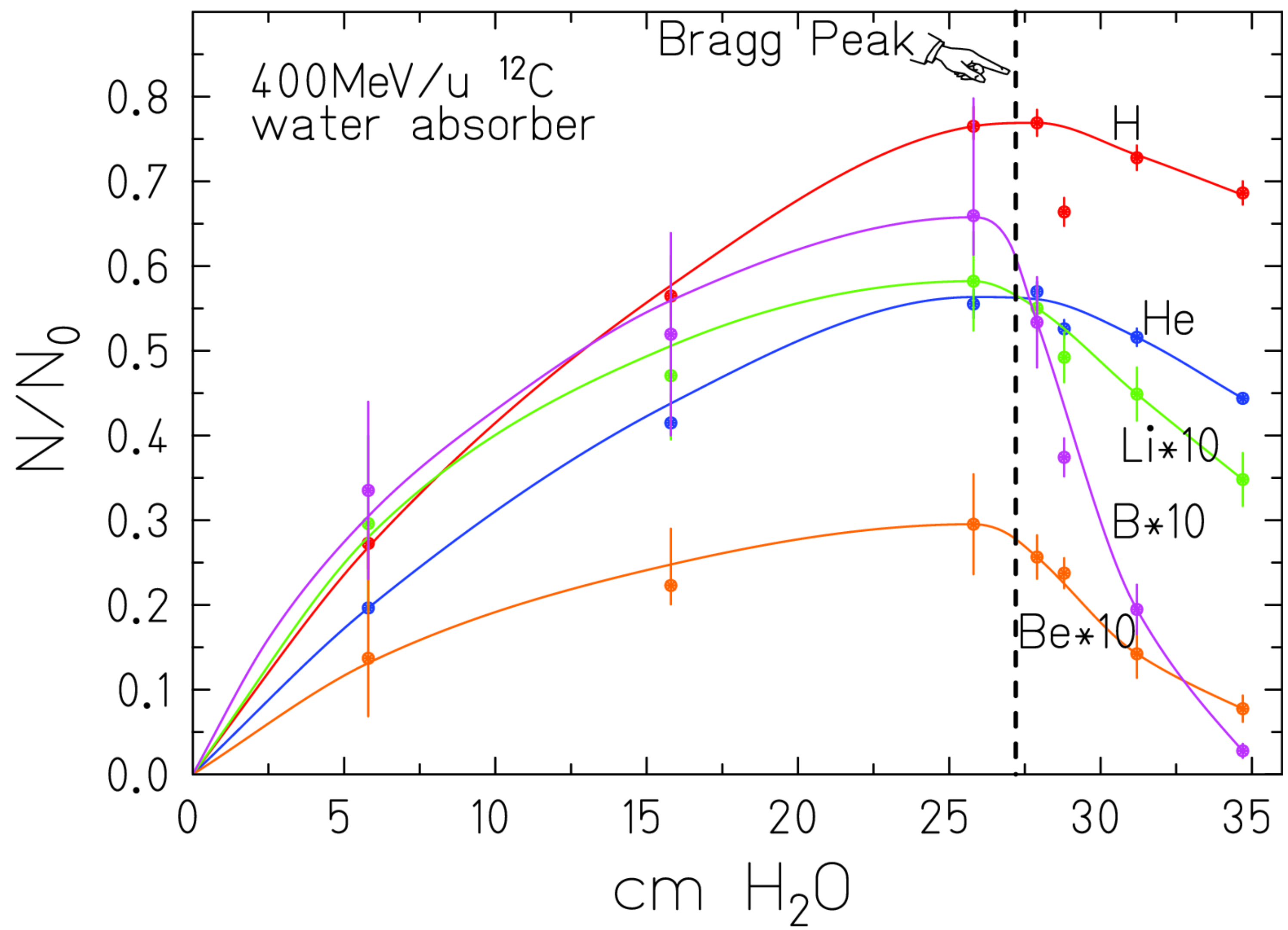
- Only 50% of the primary ^{12}C ions reach the Bragg Peak
- Nuclear interactions do not change the Bragg Peak position
- Ions which do not experience a nuclear interaction decreases exponentially with the penetration depth
- Fragments produced also from projectile
- Lighter fragments will have a much longer range



plot from: D. Cussol "Nuclear Physics and Hadrontherapy"

Secondary particles multiplicity

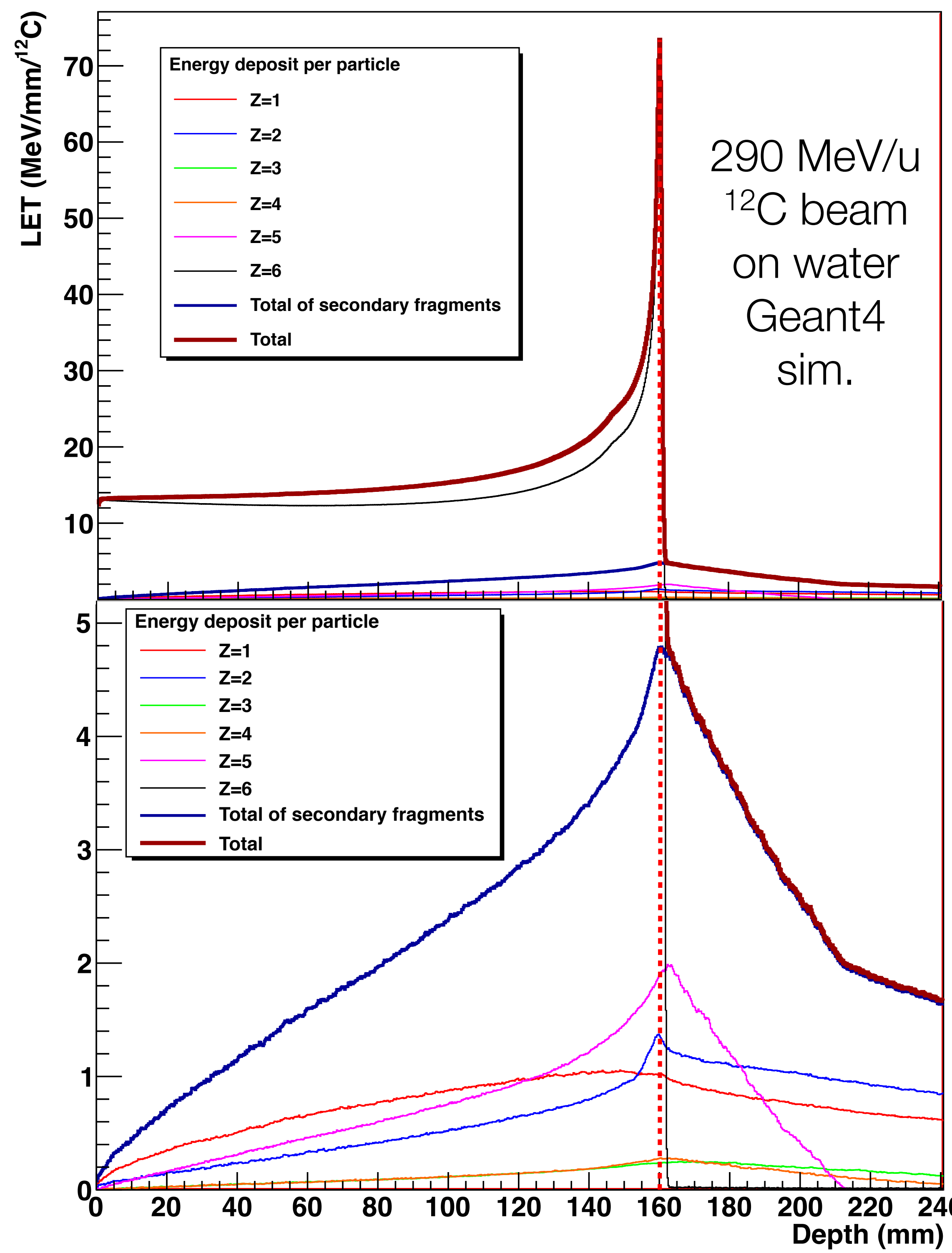
- The produced fragments are mainly H and He
- The one responsible of the tail beyond the Bragg Peak are produced in the entrance channel



plot from: E. Haettner, H. Iwase, and D. Schardt, Radiat. Prot. Dosim. 122 (2006) 485–487

Secondaries contribution to LET

- The mean LET scales roughly like Z^2
- H and He contribution is weak despite the high multiplicity
- Heavier secondary particles have a small contribution because of the smaller multiplicity
- Beyond the B.P. LET is dominated by H and He



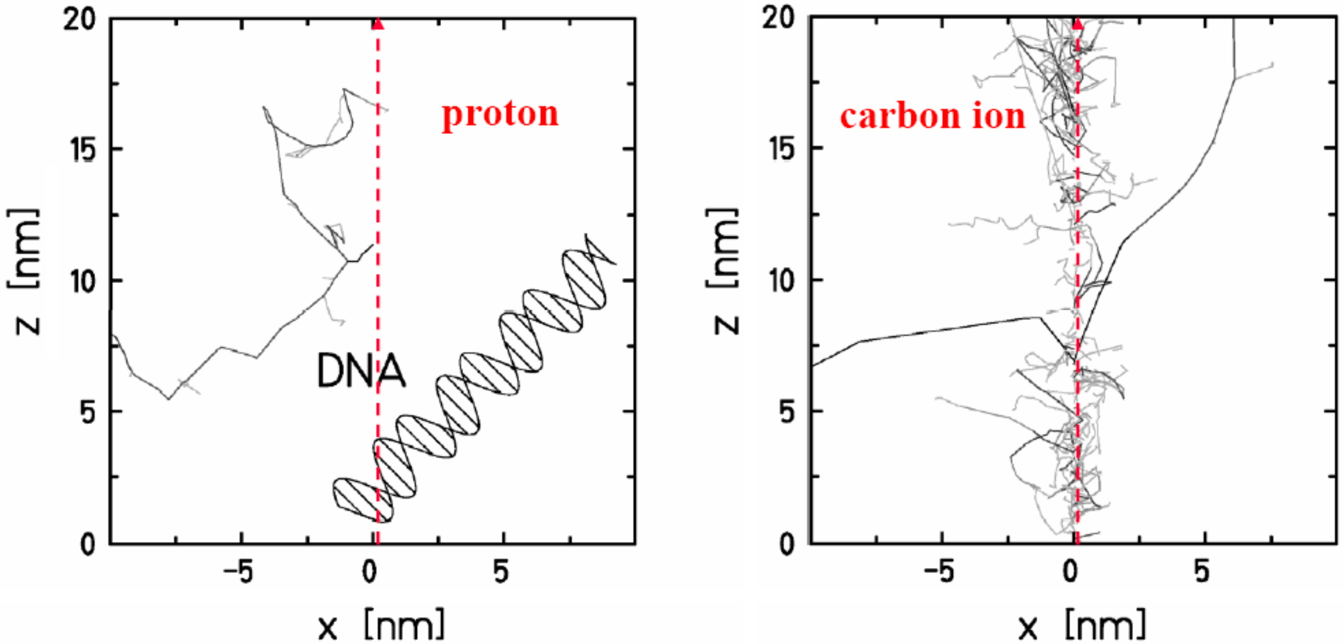
plot from: D. Cussol "Nuclear Physics and Hadrontherapy"

Secondaries production

- The contribution of secondaries to mean LET is around 7% at the Bragg Peak

- The biological effectiveness depends also on the quality of the radiation

image from: U. Amaldi and G. Kraft, Rep. Prog. Phys., vol. 68, no. 8, pp. 1861–1882, Jul. 2005.

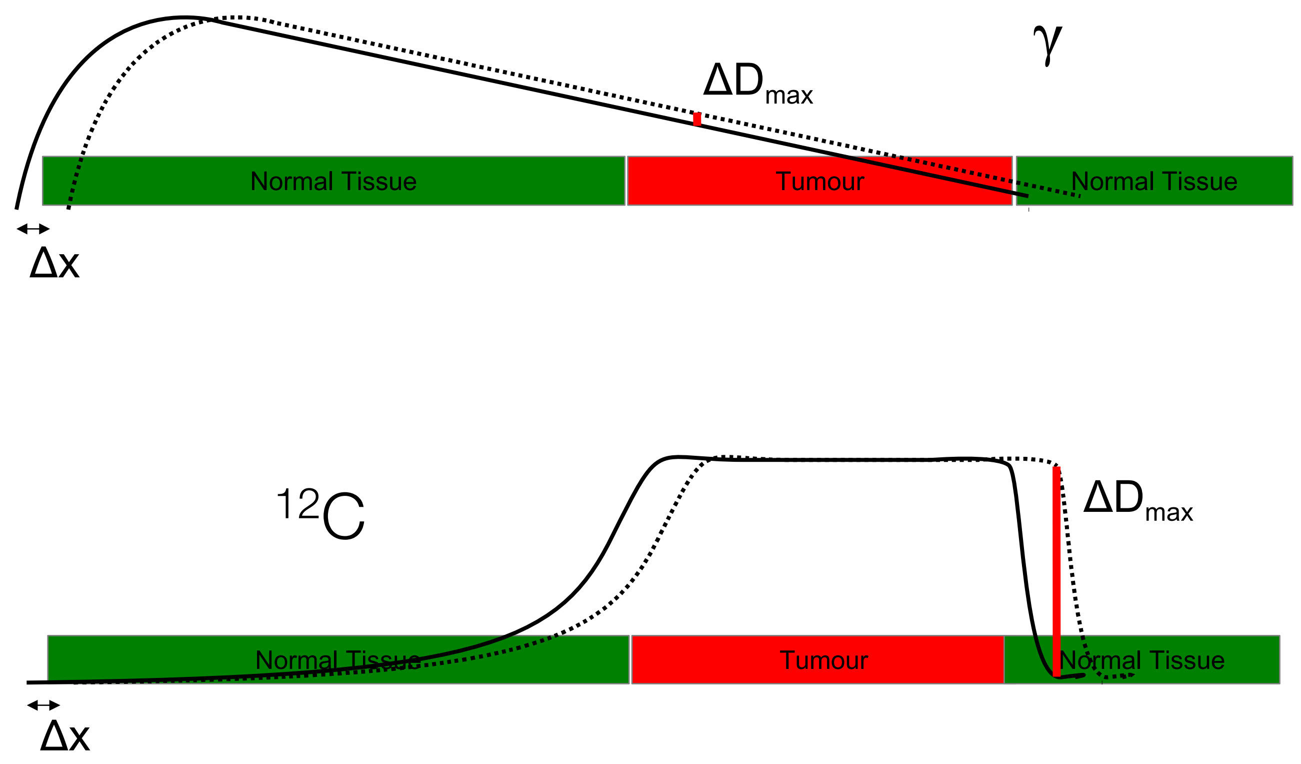


- Predicting secondary production is crucial for monitoring

Impact of range uncertainties

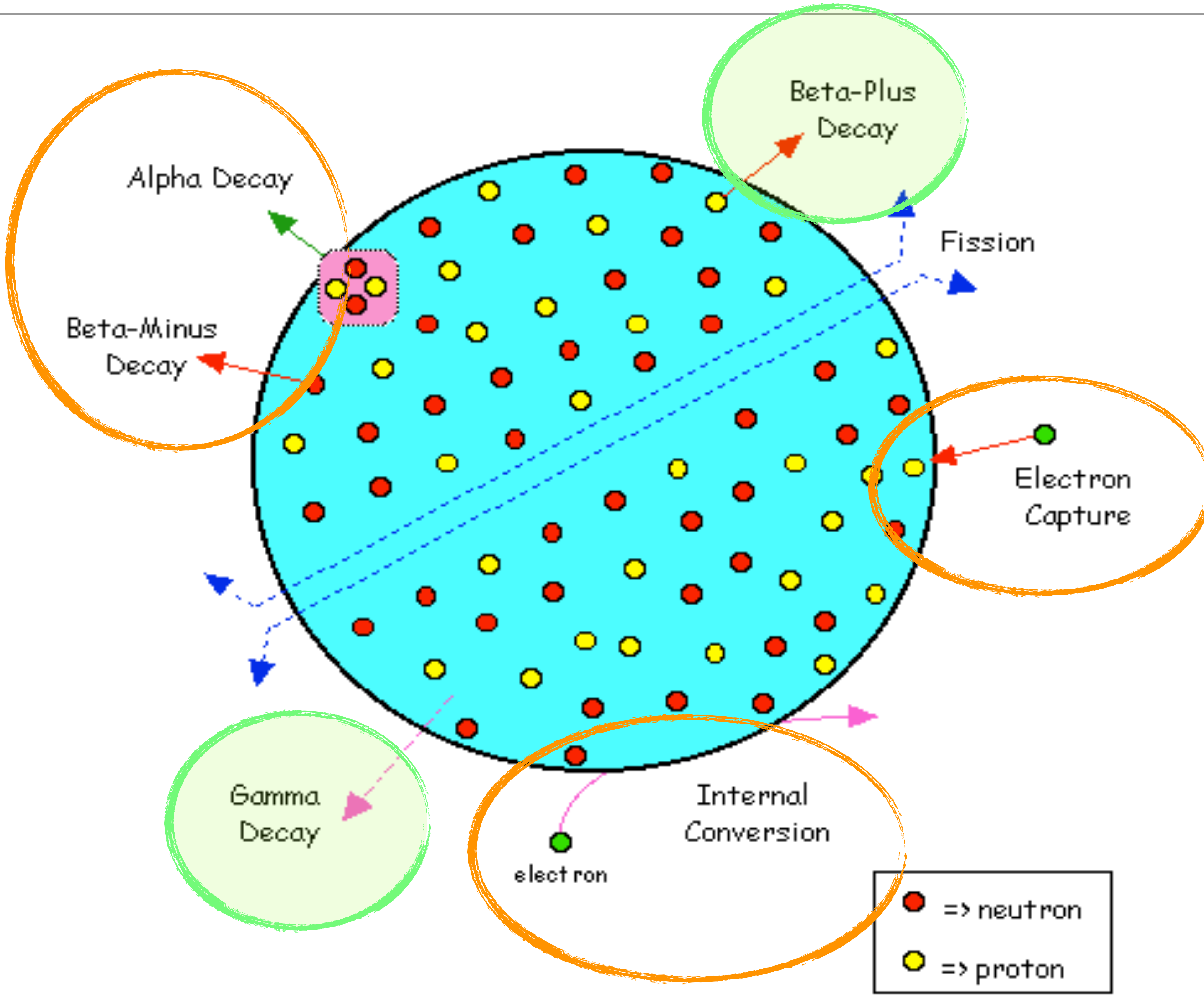
- Larger risks for dosage in ion beam therapy

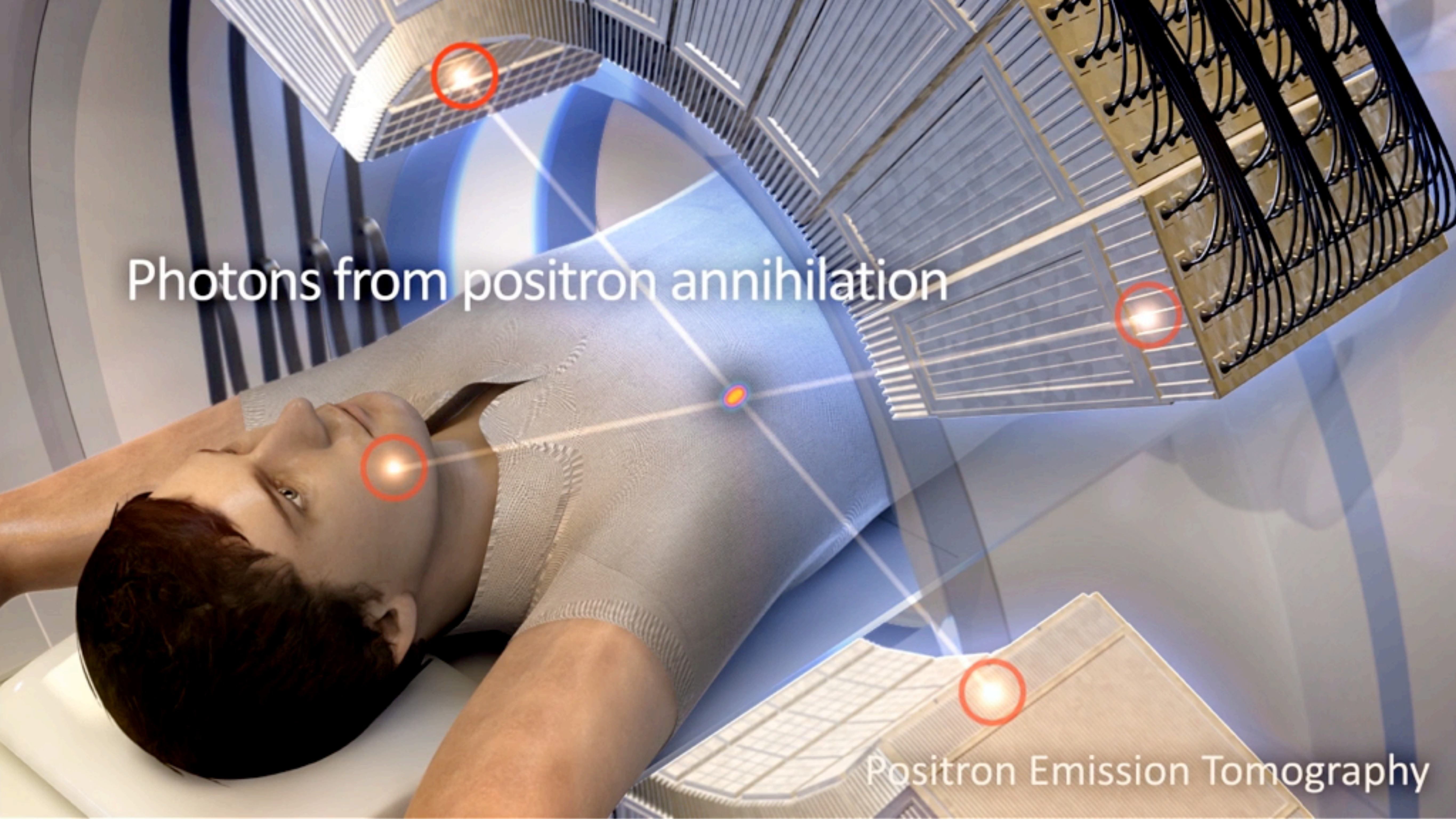
- Patient position uncertainties
- CT imaging
- HU to range conversion
- patient motion
- approximations in dose algorithms



- Beam monitoring is of utmost importance

Detectable signals



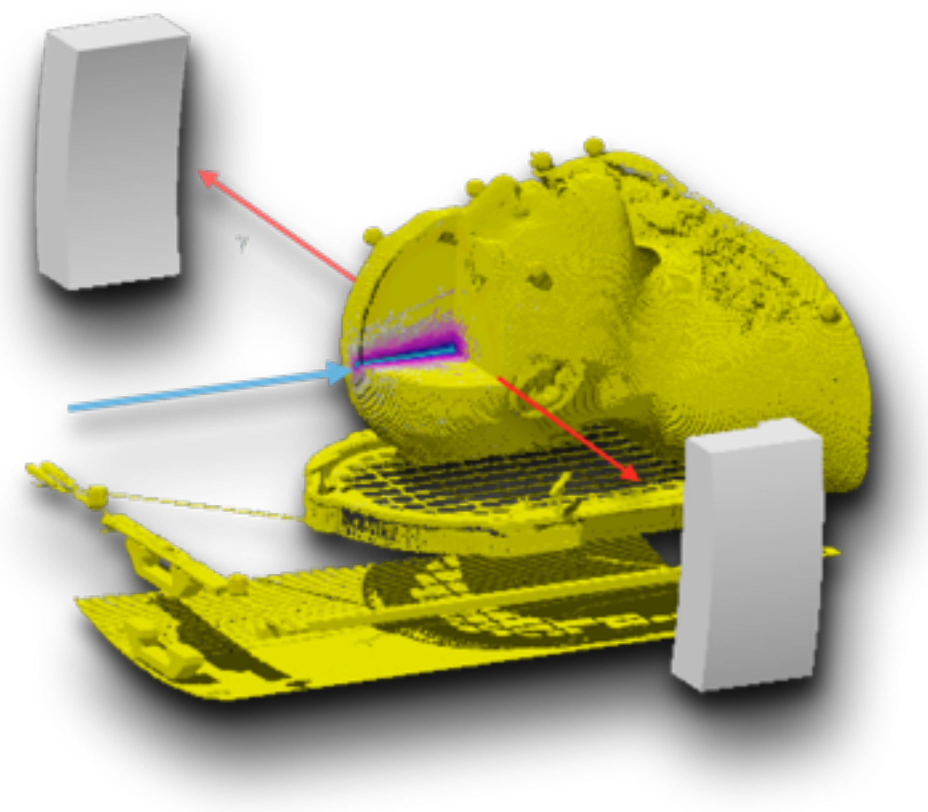


It is possible to use secondaries to infer the dose distribution

Interaction models are indispensable to link the secondaries detected with the dose distribution

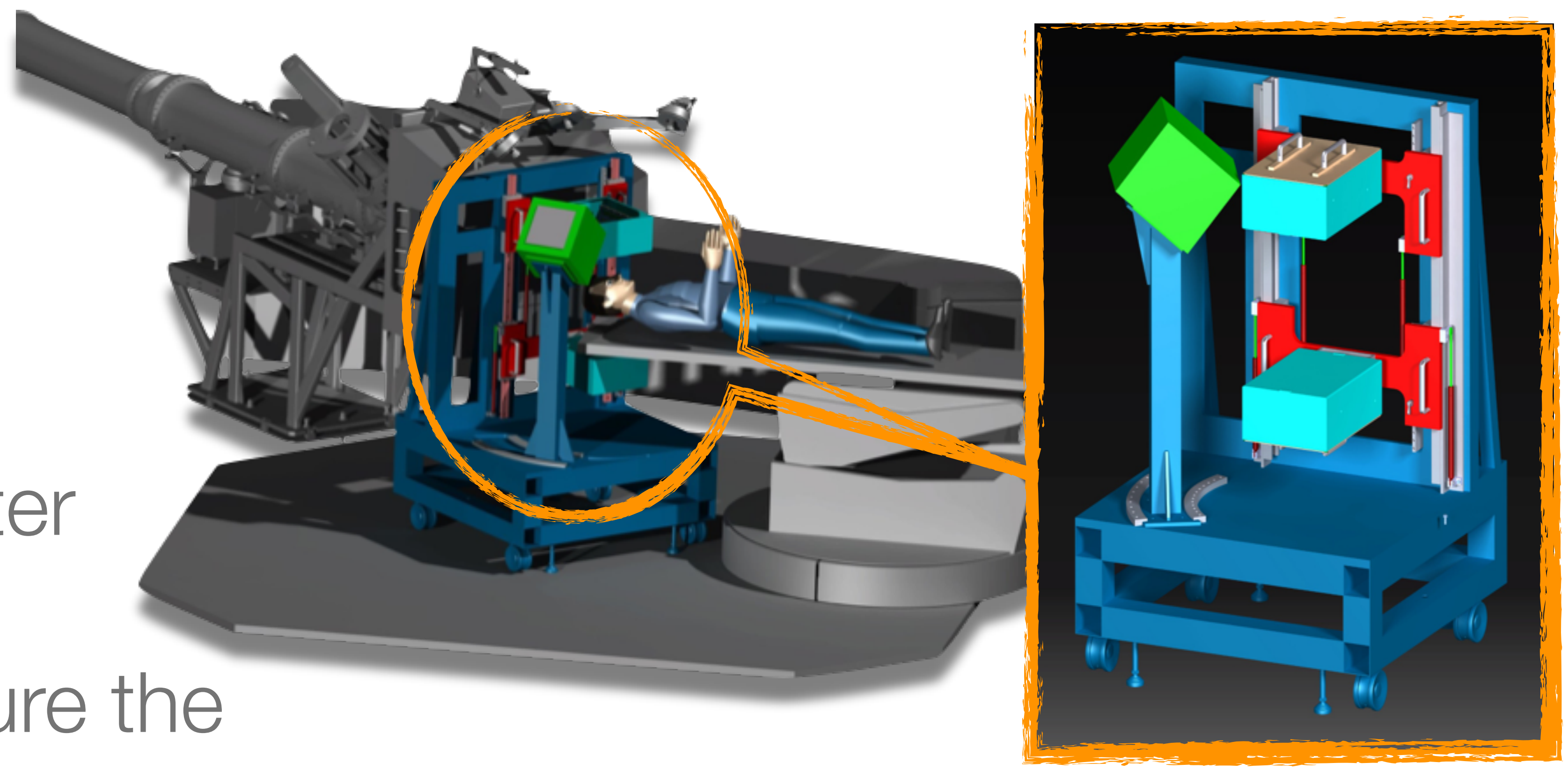
Beam monitoring

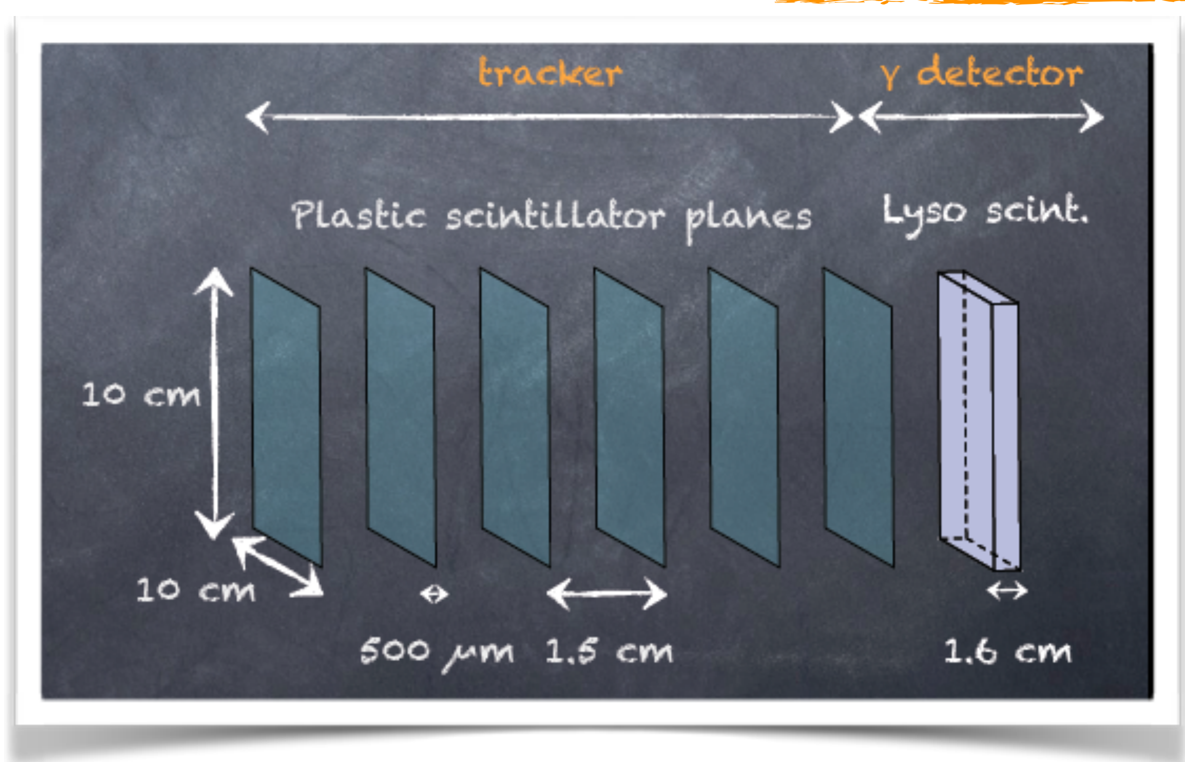
- Several secondaries could be used:
- β+ emitters
  - main are:
    - ^{11}C ($T_{1/2}$=20 min)
    - ^{10}C ($T_{1/2}$=20 sec)
    - ^{15}O ($T_{1/2}$=120 sec)
- prompt γ
- charged light fragments
- neutrons?



Dose Profiler

- Online monitor using secondaries rate
- To be deployed in the CNAO treatment center
- simultaneously measure the rate of:
    - charged particles with multilayer for track reconstruction
    - single photons with compton camera

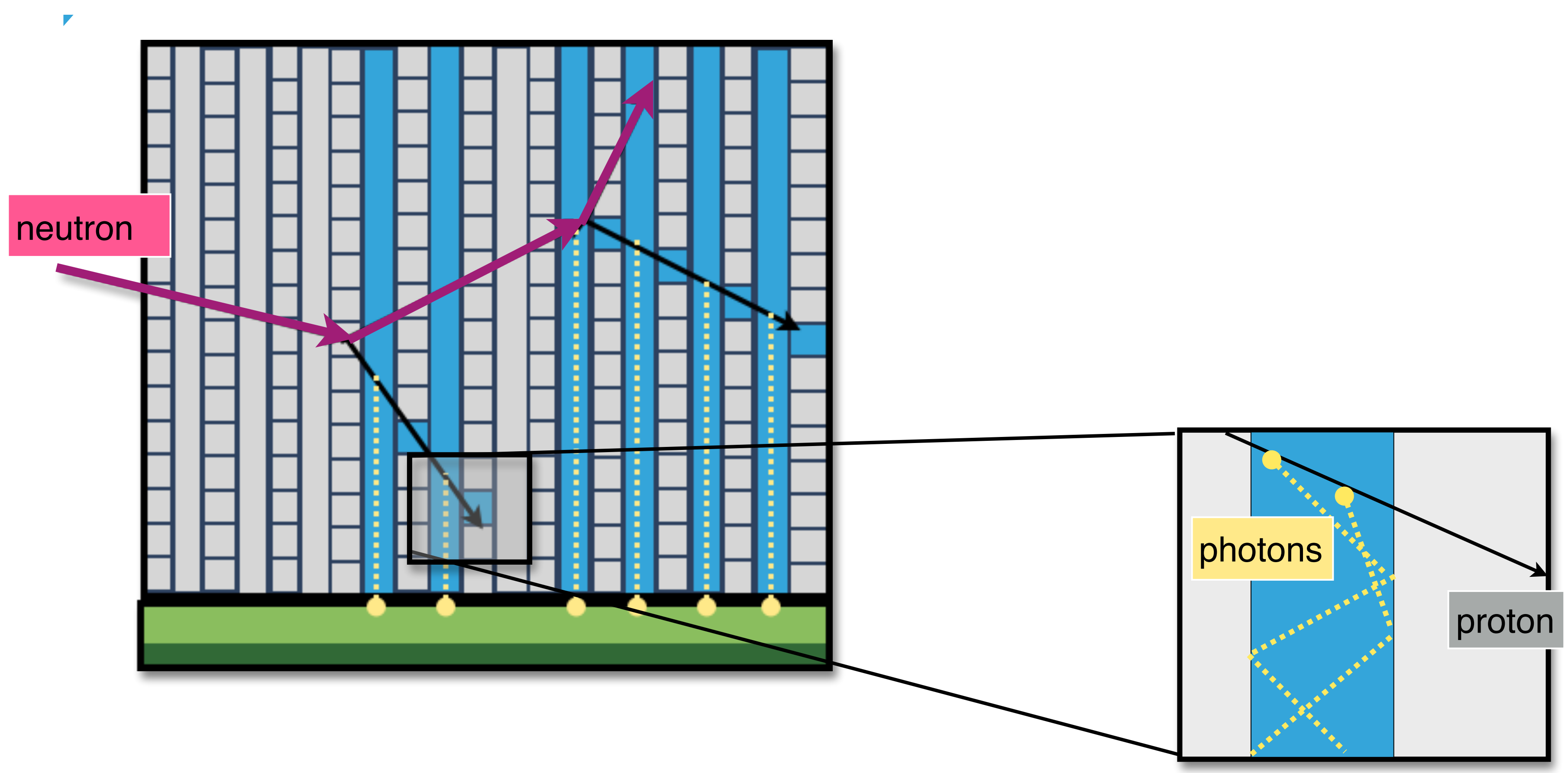




MONDO

MOnitor for Neutron Dose for hadrOntherapy

- Fast (100 MeV - E_{beam}) neutron tracker
- Using double elastic scattering

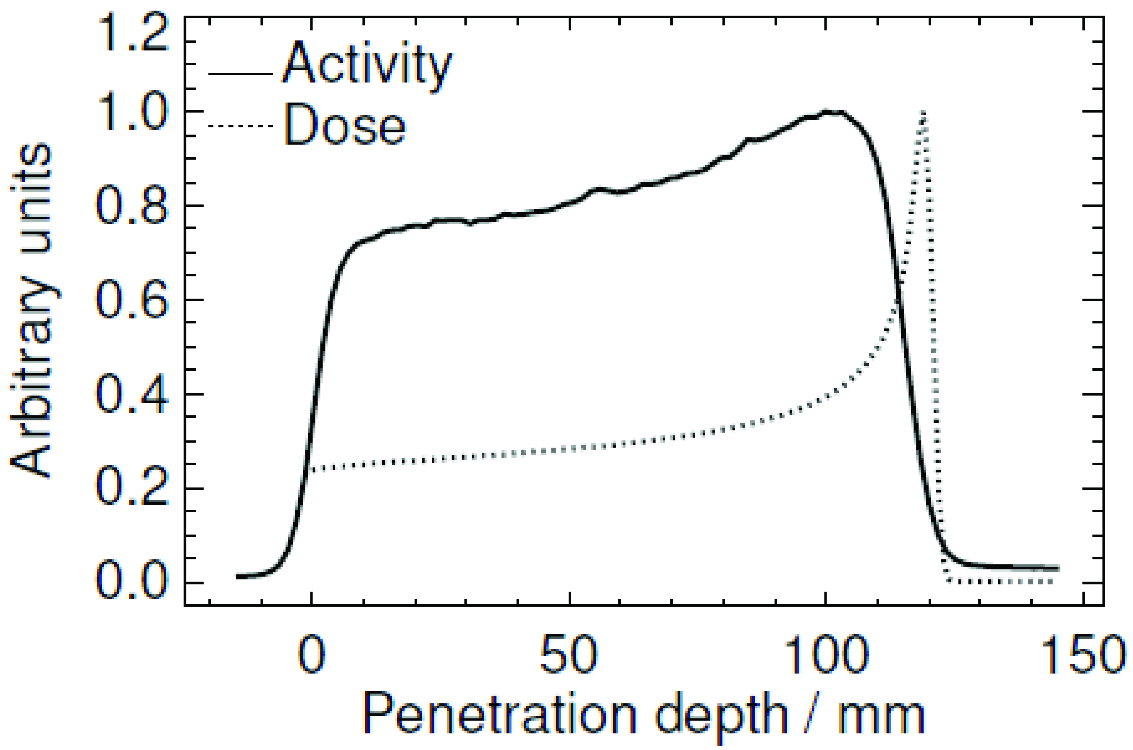


Correlation between activity and dose

- Nuclear interaction are below threshold before the BP

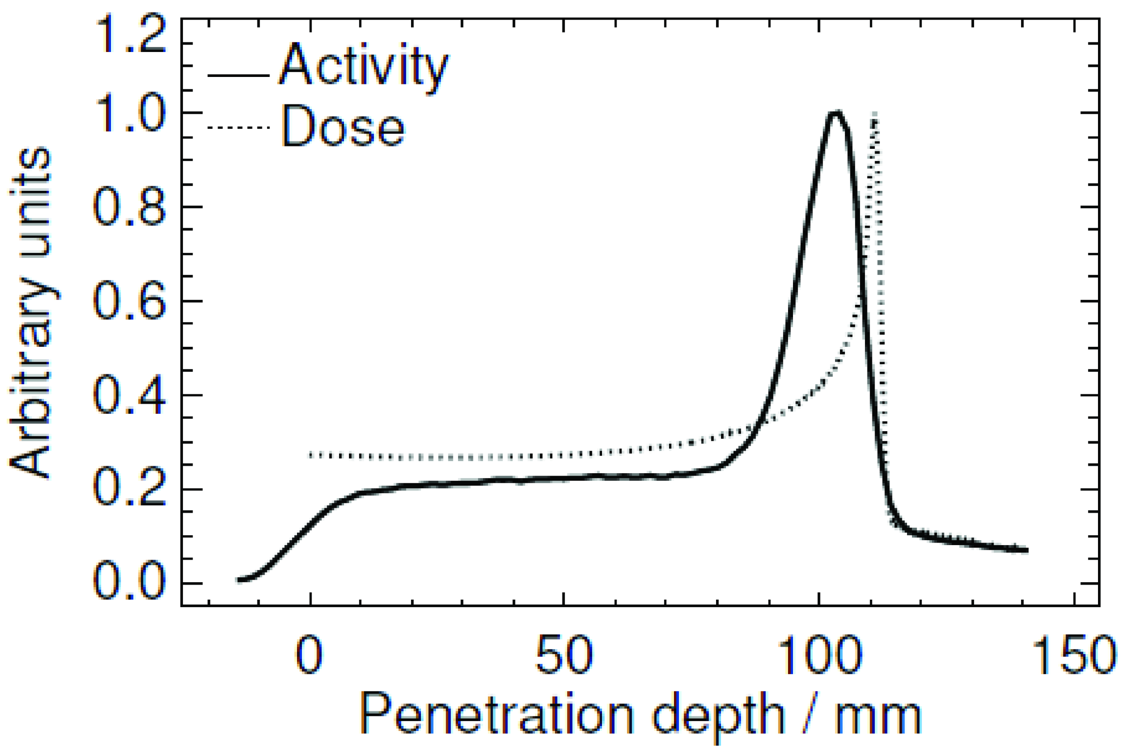
MC needed

protons at 140 MeV



Target fragmentation

^{12}C at 259.5 MeV/u



Projectile and target fragmentation

plots from: K. Parodi Ph.D. thesis (2004)

Beam monitoring

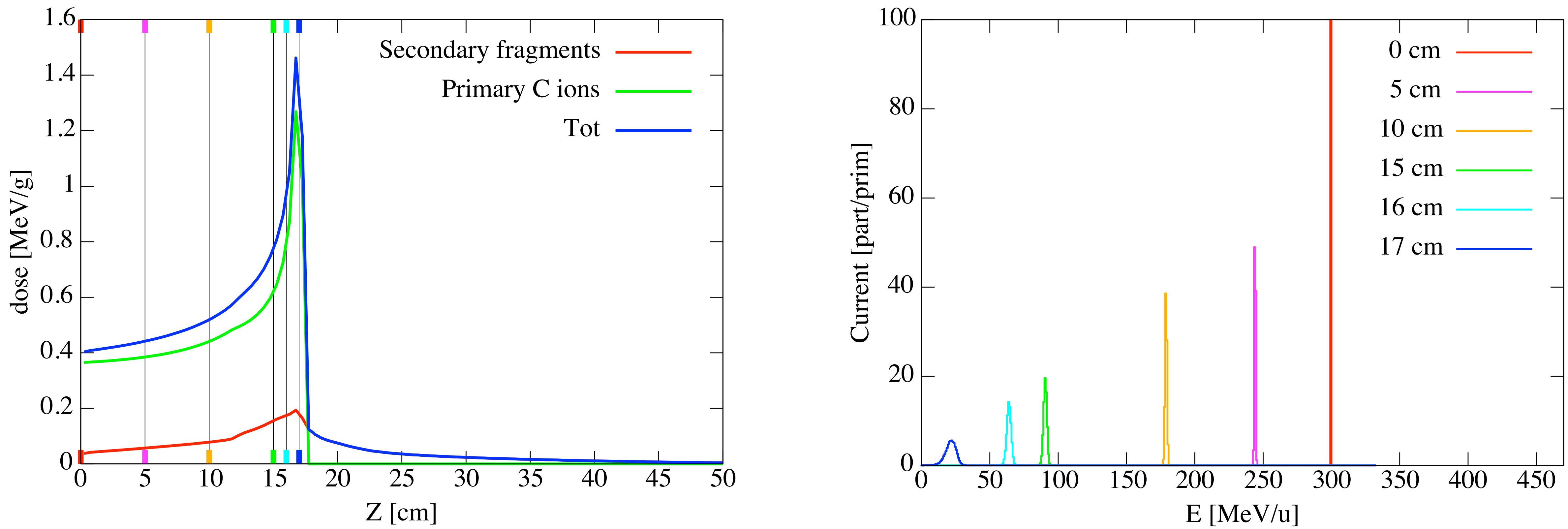
Therapy beam	^{1}H	^{3}He	^{7}Li	^{12}C	^{16}O	Nuclear medicine
Activity density / Bq cm^{-3} Gy^{-1}	6600	5300	3060	1600	1030	$10^4 – 10^5$ Bq cm^{-3}

- Activities 2/3 orders of magnitude smaller than diagnostic

- High efficiently detector needed

Experimental methods

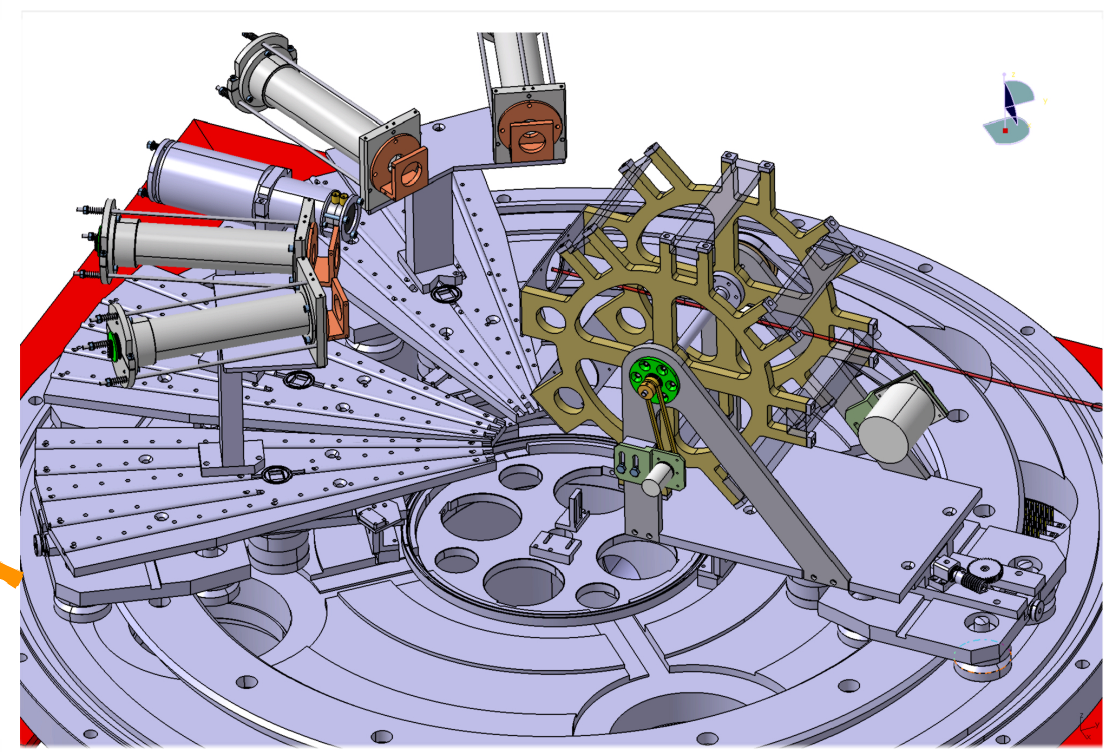
The Energy in the Bragg peak region

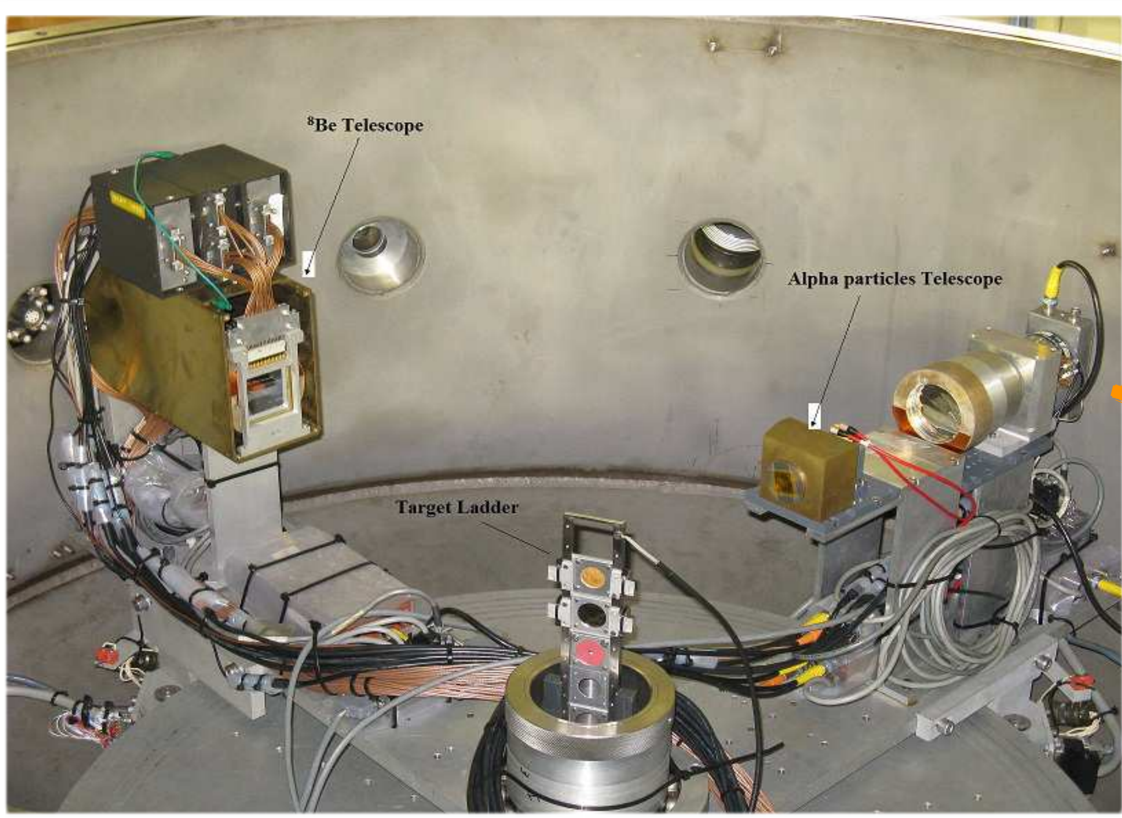


- A C beam with 300 MeV/u (typical therapy energy) close to the Bragg peak has roughly 1/10 of the Energy

Fragmentation experiments

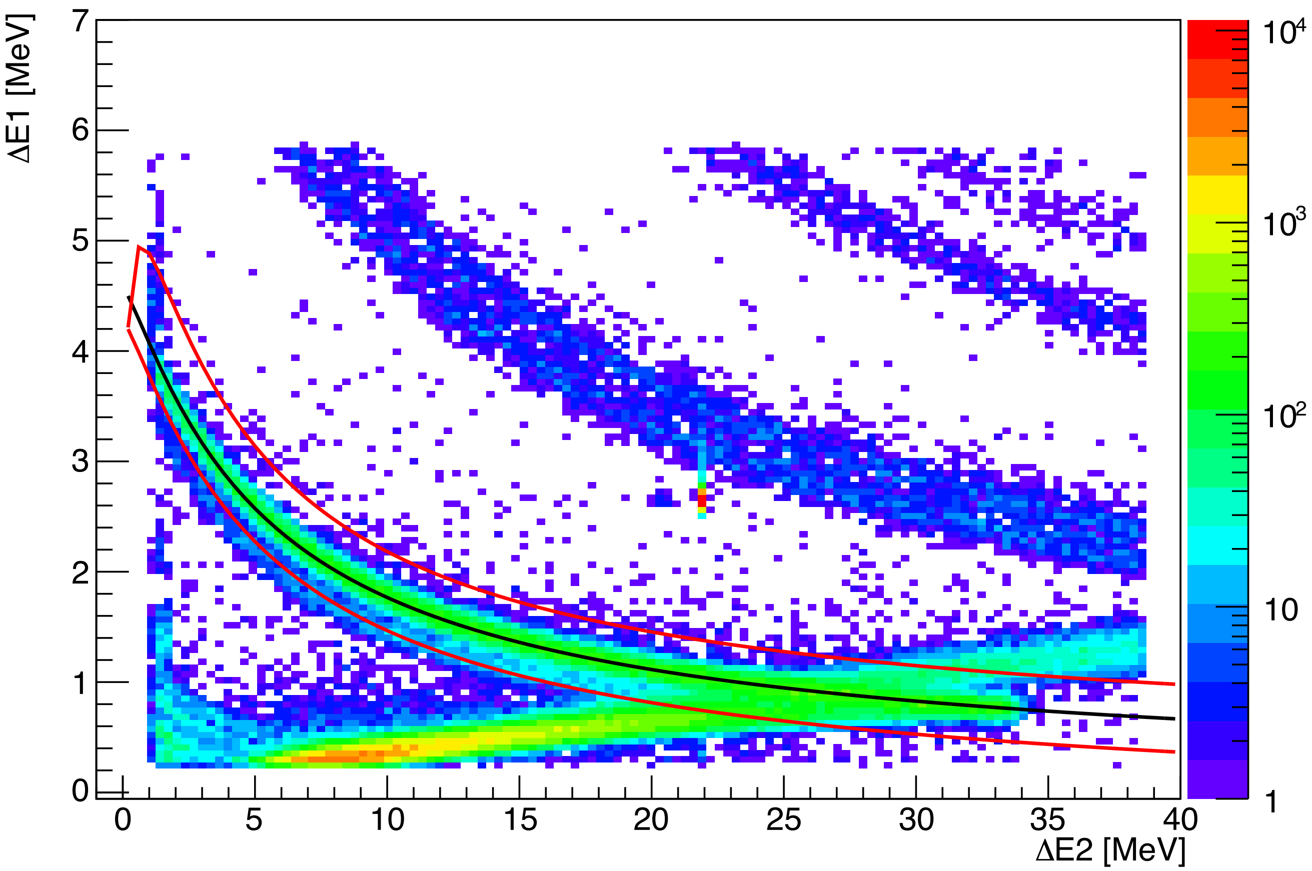
E600 experiment at Ganil
^{12}C at 95 MeV/u on thick PMMA targets

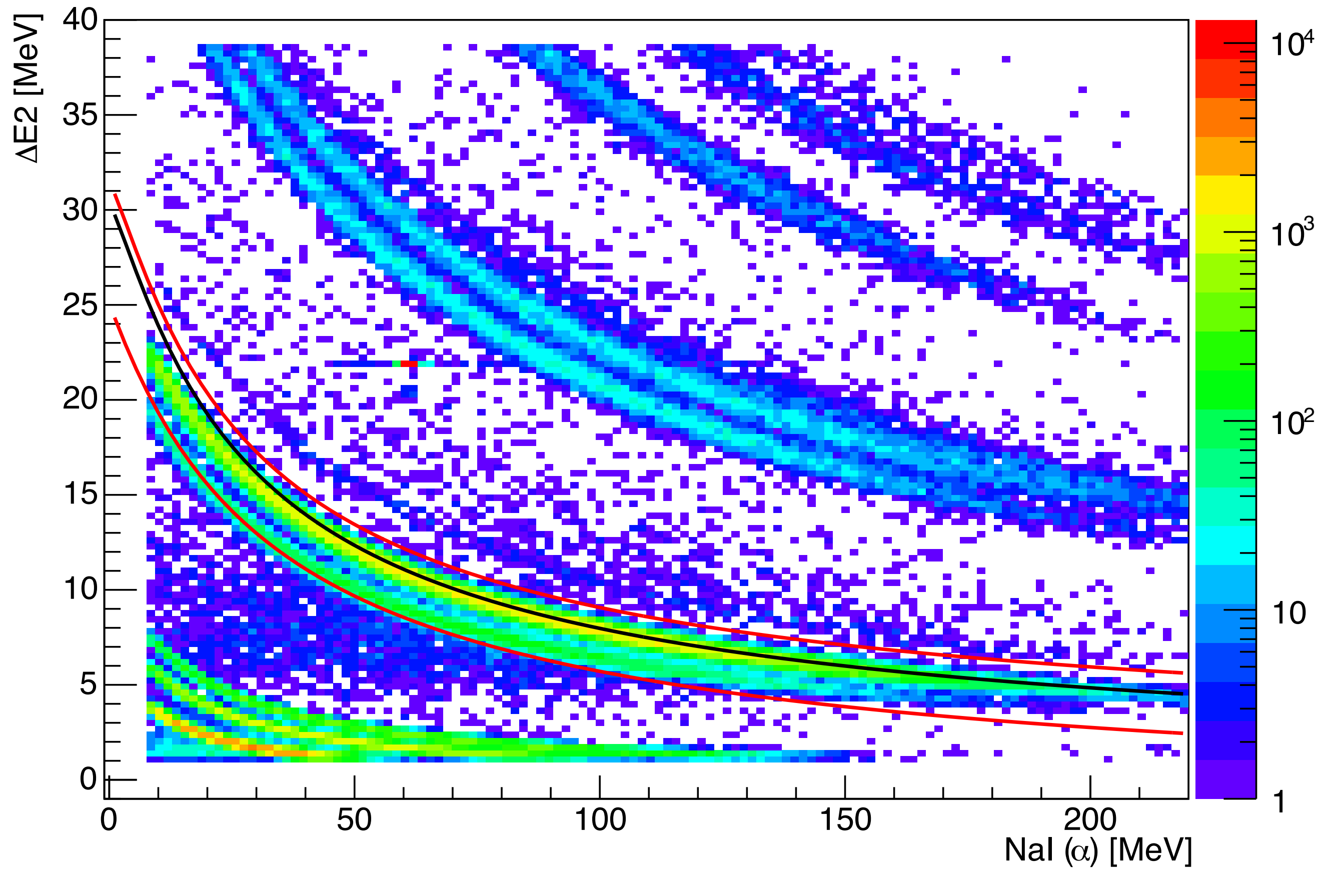


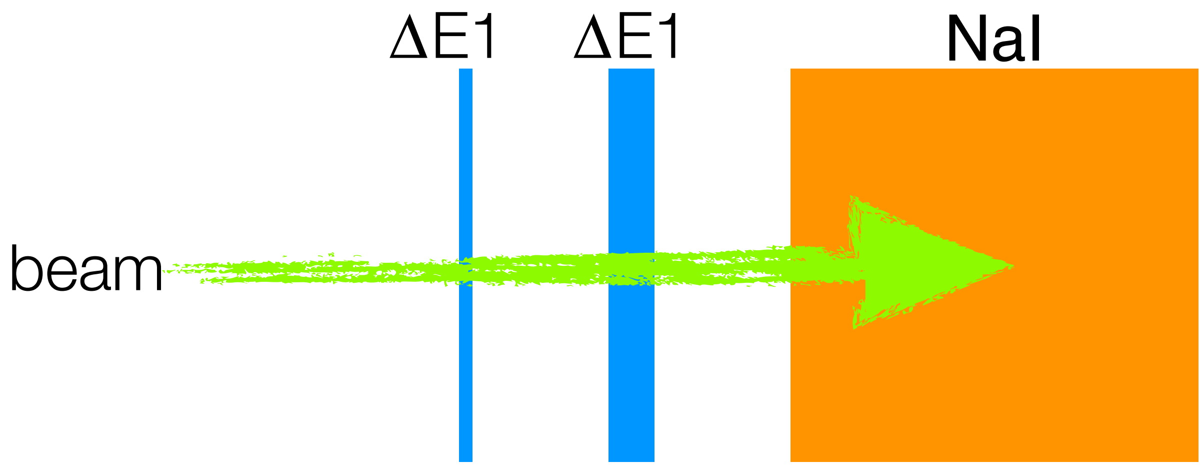


iThemba experiment
^{12}C at 33 MeV/u on thin targets

Particle identification

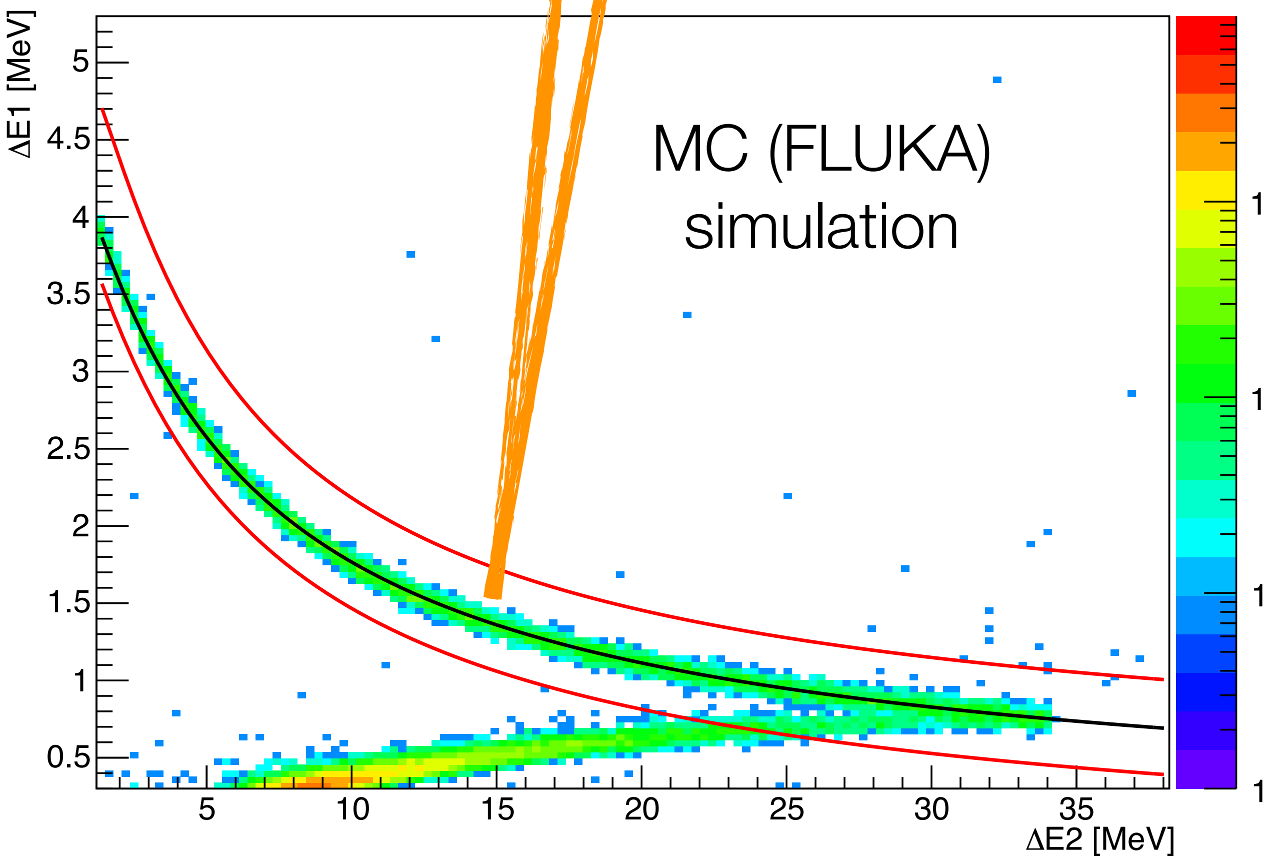


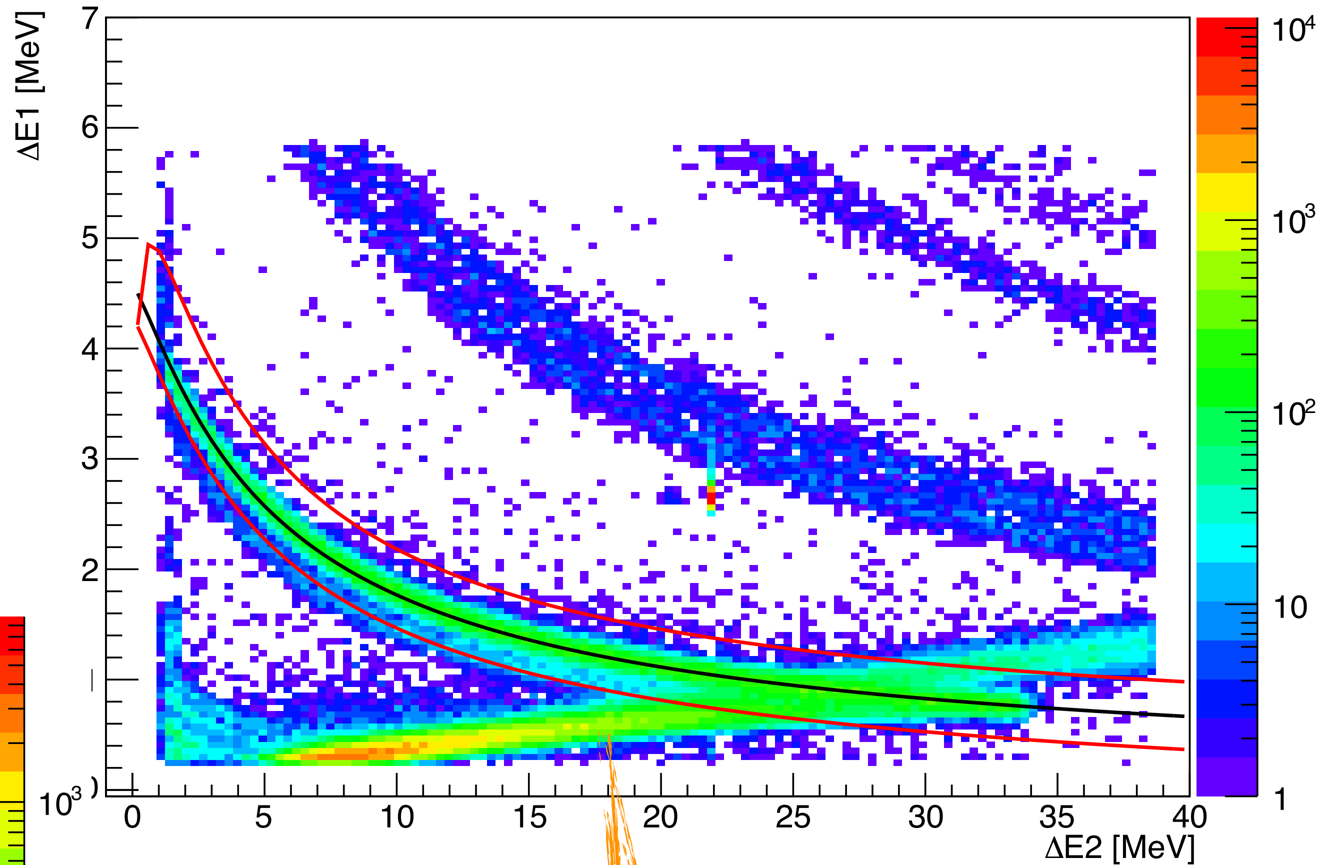




Particle identification

α stopped in the ΔE2 detector

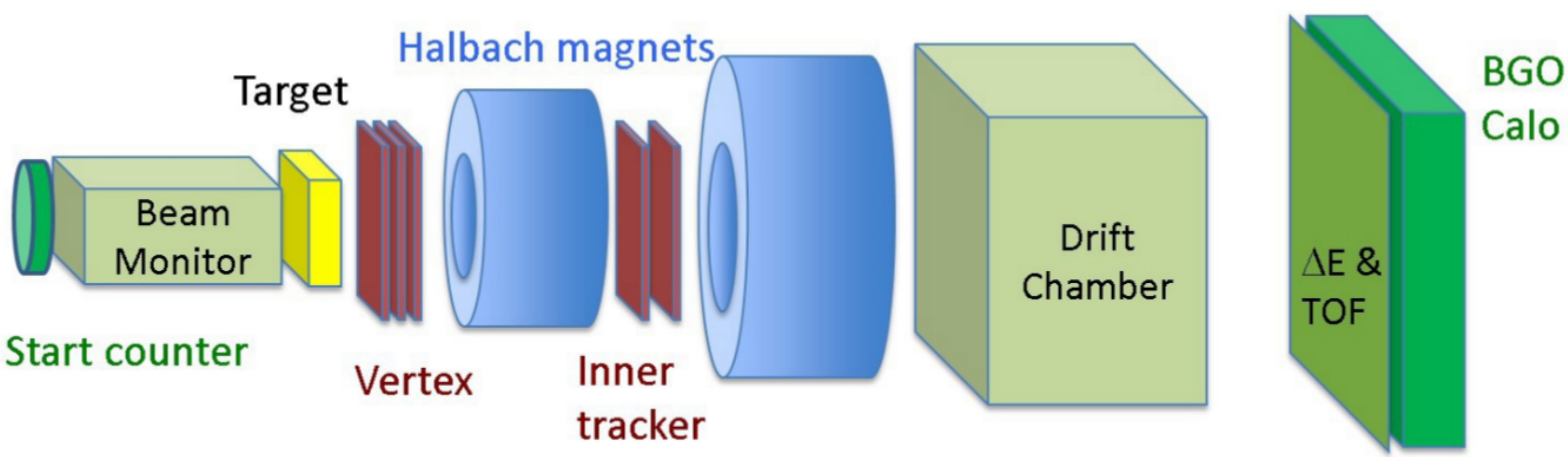




α passing through ΔE2 detector

FOOT FragmentatiOn Of Target

- Will measure p->H,C,O fragment production at 100-200 MeV
- The elastic interaction and the forward Z=1 fragment production (p,d,t) are quite well known.
- Large uncertainty on large angle Z=1,2 fragments
- Missing data on heavy fragments



Shooting the patient on the beam!

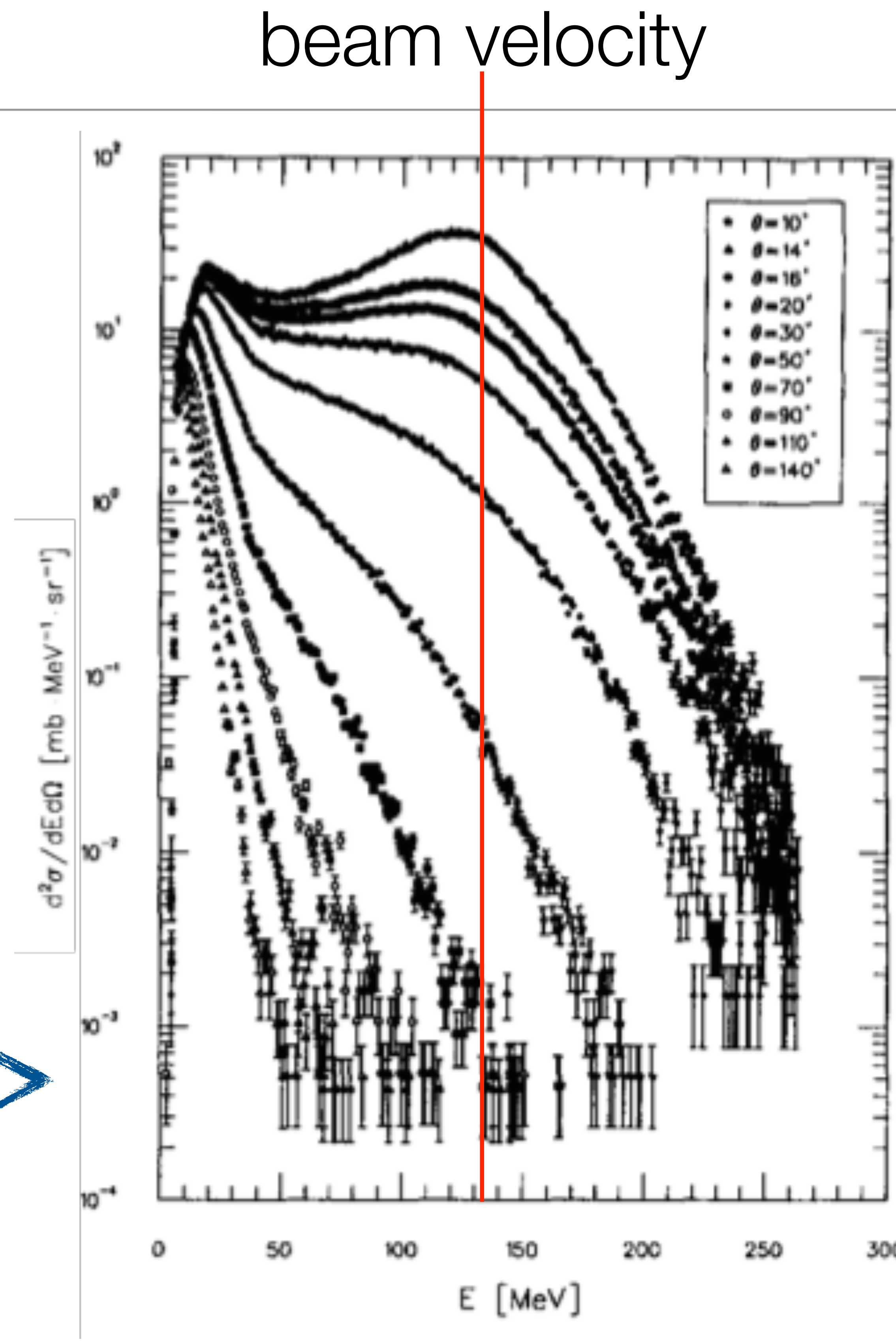
Shooting a proton with a given b (for instance Ekin=200 MeV b=0.6) on a patient (i.e. at 98% a H,C,O nucleus) at rest gives little detection opportunity...
let's shoot a b=0.6 patient (i.e. O,C beam) on a proton at rest and measure how it fragments

- Very low energy → short range fragments
- Inverse kinematic strategy:
- Use as beams the ions that are the constituents of the patient (mainly ^{16}O, ^{12}C) with Ekin/nucl in the 100-200MeV.
- Use twin targets made of C and polyethylene $(C_2H_4)n$ and obtain the H target result from difference
- Apply the reverse boost with the well known β of the beam
- The fragment direction must be well measured in the Lab frame to obtain the correct energy in the Patient frame

α fragments

- Many experiments showed that low mass projectiles produce a large number of α
- Mostly emitted in the forward direction
- Broad peak with a mean energy corresponding to beam velocity

double differential α spectra for ^{12}C on ^{93}Nb at 33 MeV/u

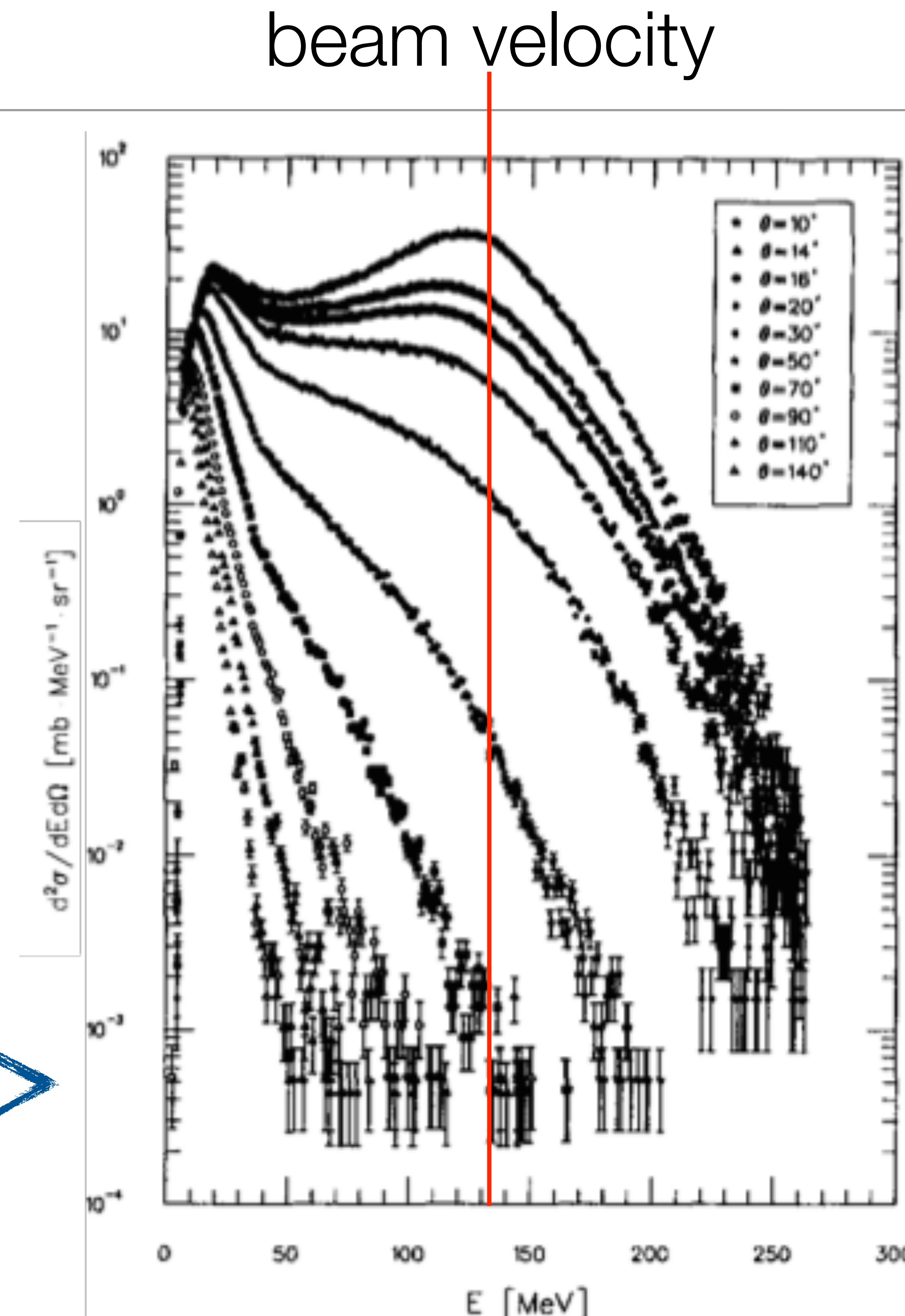


plot from: E. Gadioli et al. "Alpha particle emission in the interaction of C-12 with Co-59 and Nb-93 at incident energies of 300 and 400 MeV," Nuclear Physics A, vol. 654, no. 3, pp. 523–540, 1999.

α fragments

- A large fraction of these a's is produced in the reaction: $^{12}C \rightarrow {}^{8}Be + {}^{4}He$
- ^{8}Be decays almost immediately in two ^{4}He
- Therefore the ^{4}He could be produced when one of the two fragments fuses with the target or in quasi-elastic break-up

double differential α spectra for ^{12}C on ^{93}Nb at 33 MeV/u



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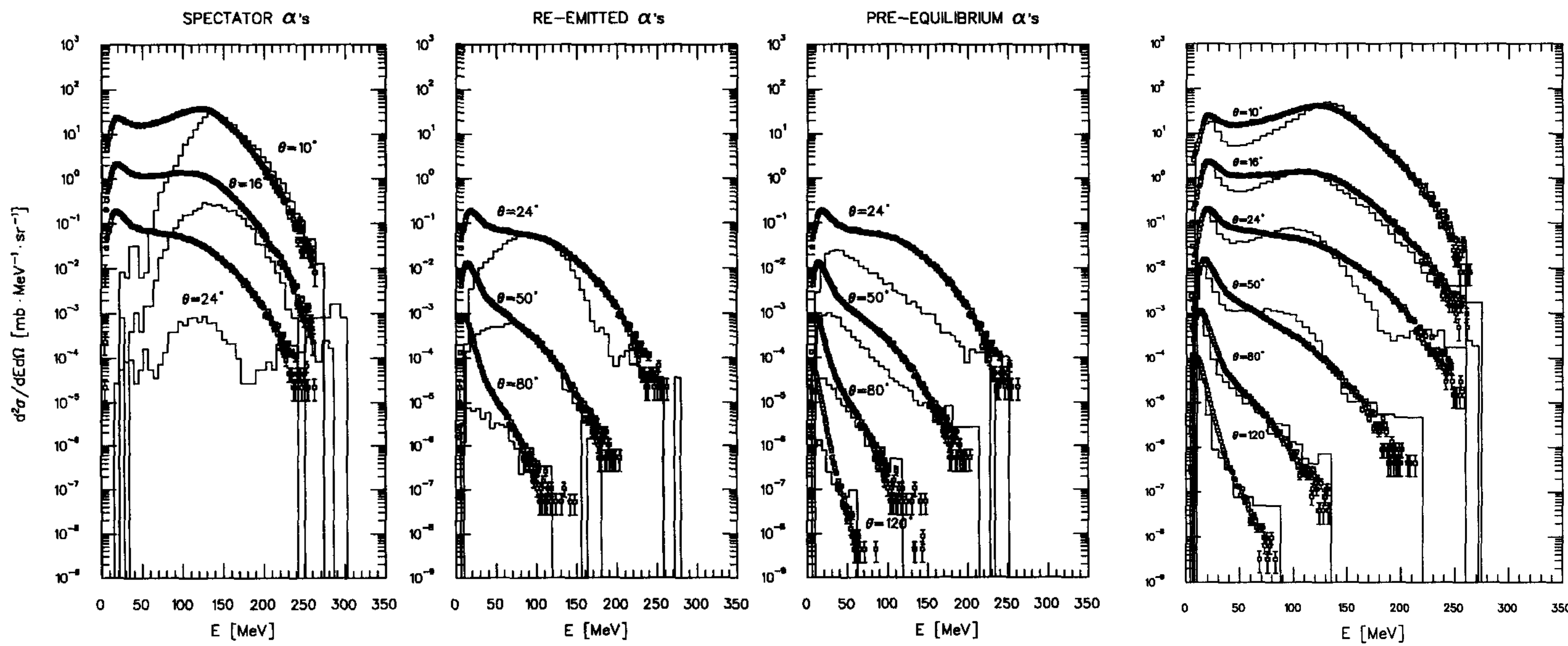
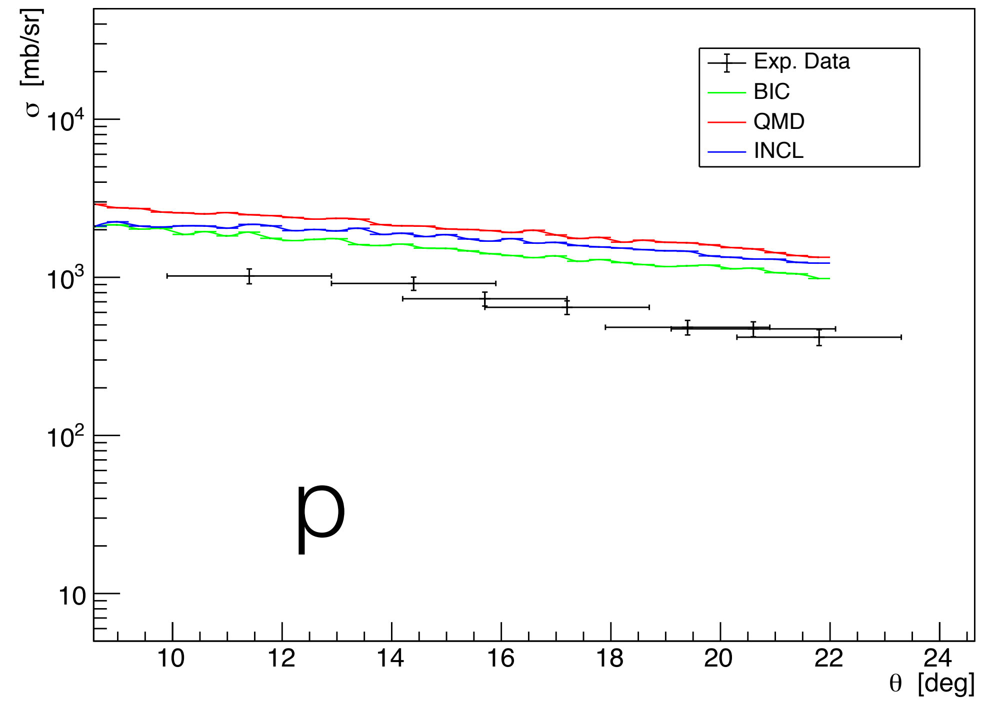
Contribution to α spectra



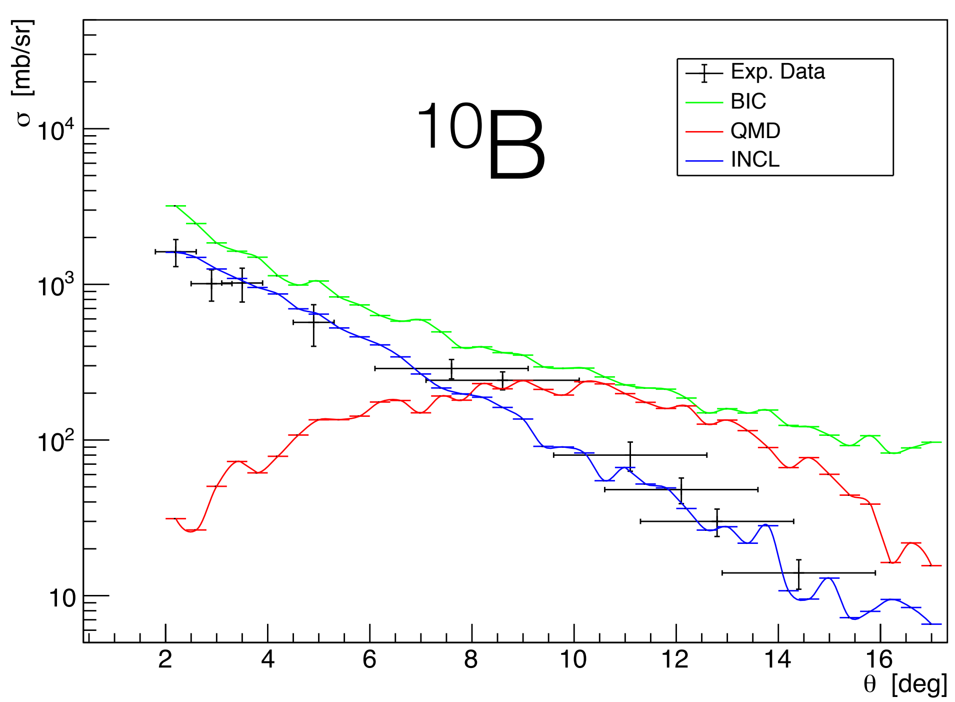
Angular distributions

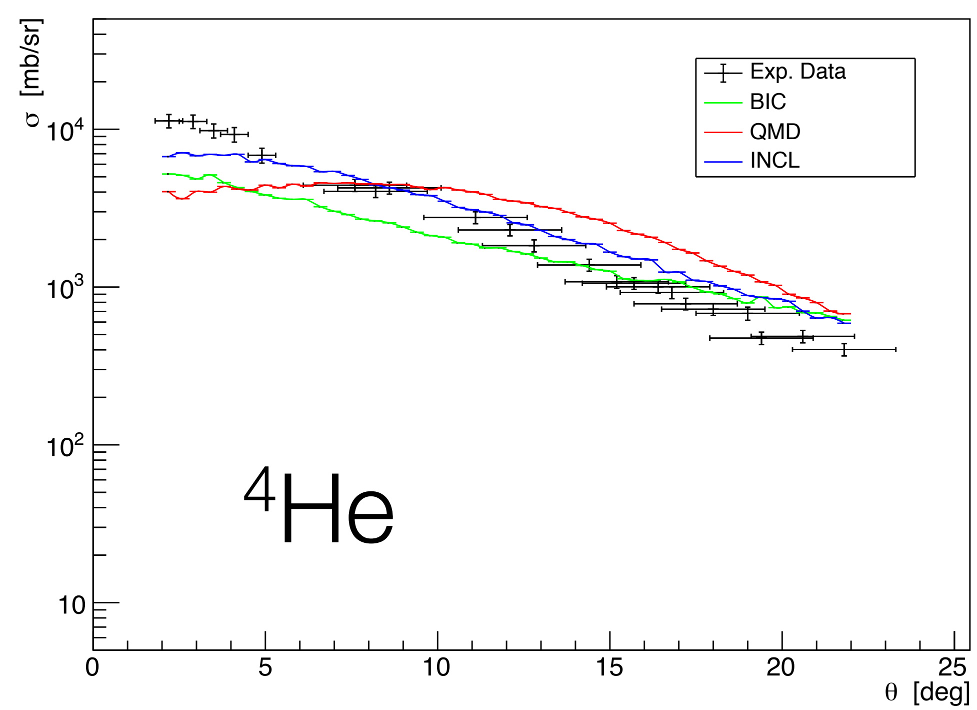
- Heavy fragments are mainly emitted in the beam direction
- p are more isotropic

differential spectra
for ^{12}C on ^{nat}C thin target at 62 MeV/u

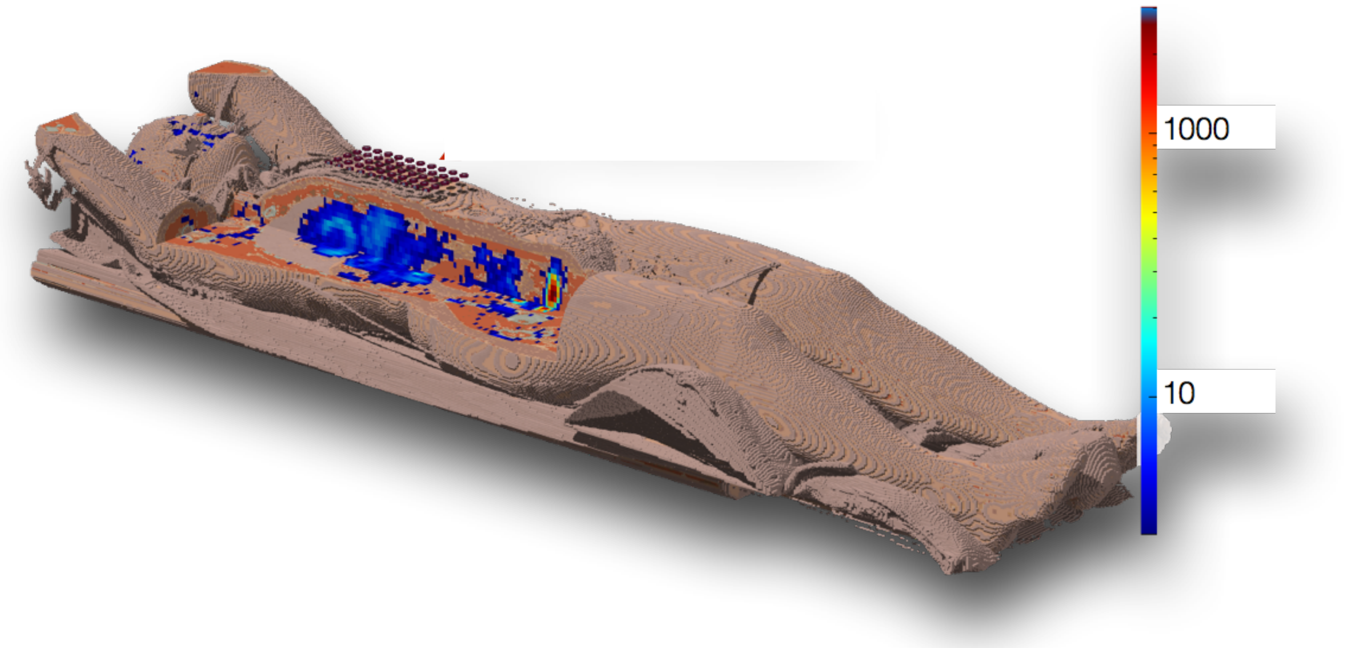


[exp. data from De Napoli et al. Phys. Med. Biol., vol. 57, no. 22, pp. 7651–7671, Nov. 2012]



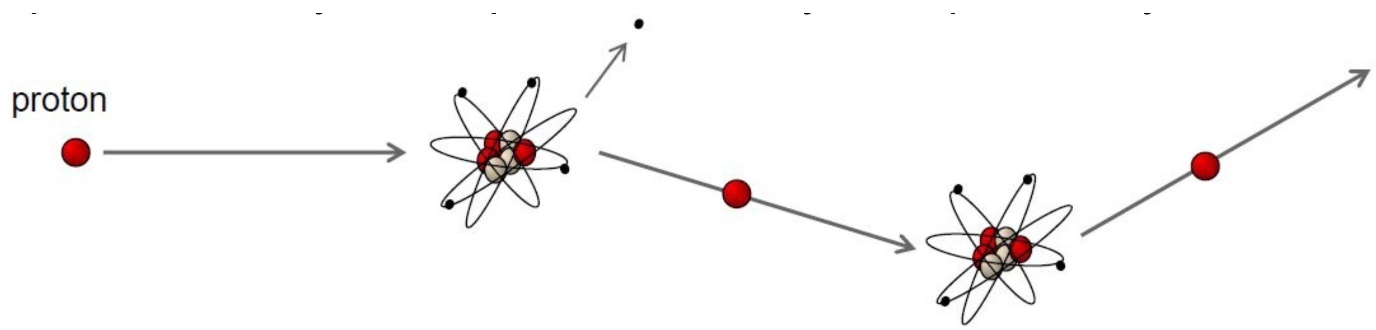


Monte Carlo methods



MC for hadrontherapy

- Each particle is tracked and its interactions are sampled from probability distributions
- Energy losses, scattering and nuclear interactions are modeled



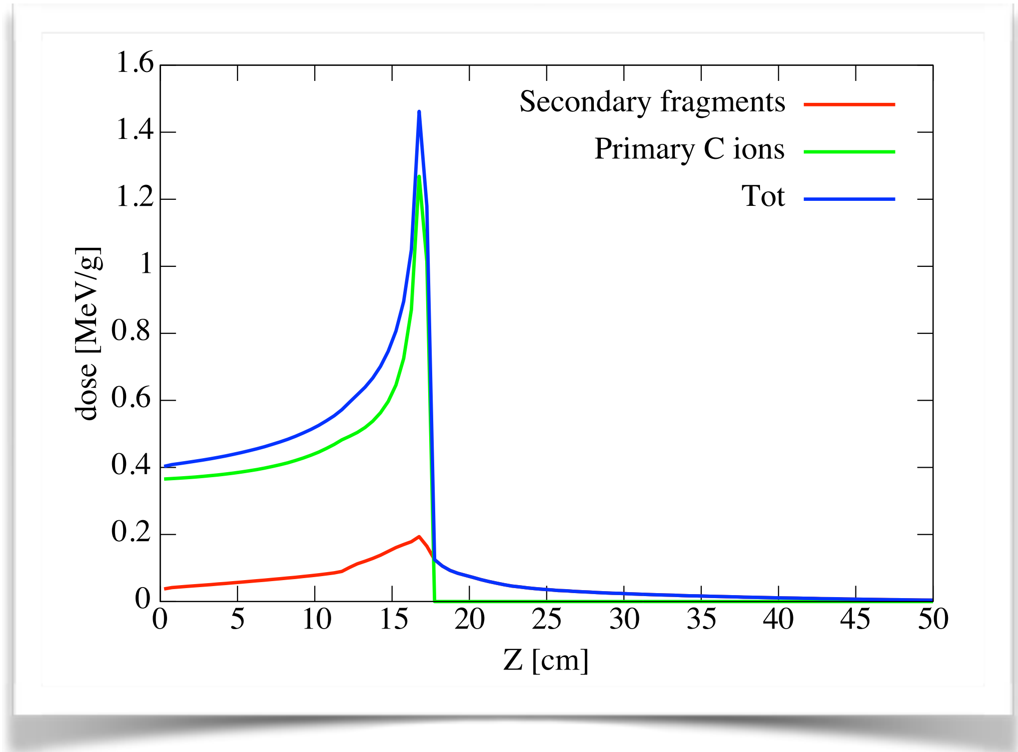
- Chemical composition of tissues (no water equivalent approach)
- Include effects of heterogeneities

“Monte Carlo dose calculation is considered to be the most accurate method to compute doses in radiation therapy.”

AAPM Task Report by Chetty et al. 2007, Med. Phys.

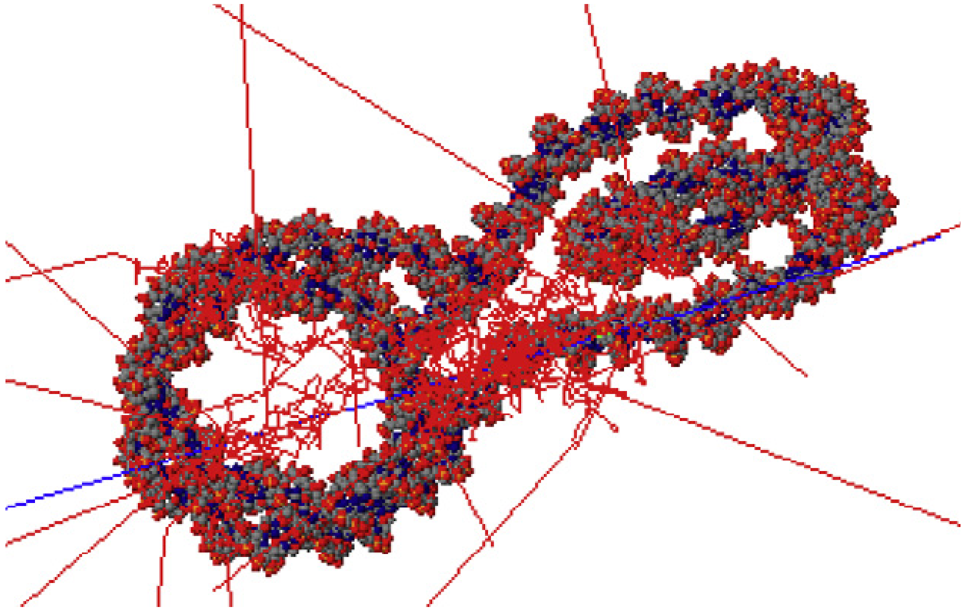
Fluka

- A general purpose tool for calculations of particle transport and interactions in matter
- Already successfully used in hadron therapy at CNAO, HIT and Massachusetts General Hospital for Treatment Planning commissioning, verification and β+ activity prediction



Geant4

- Geant4 is a comprehensive Monte Carlo (MC) toolkit that describes the passage and the interactions of particles through matter
- It has a dedicated package for modeling early biological damage induced by ionizing radiation at the DNA scale (Geant4-DNA)



atomistic view of a dinucleosome irradiated by a single 100 keV proton

Image from M. A. Bernal et al Physica Medica, vol. 31, no. 8, pp. 861–874, Dec. 2015.

Geant4 models for the entrance channel

- **Binary Intra-nuclear Cascade (BIC)** “participating” particles, are tracked in the nucleus. The interactions are between them and an individual nucleon of the nucleus.

- **Quantum Molecular Dynamics (QMD)** all the nucleons are considered as “participants”, scattering between them is included

- **Liège Intranuclear Cascade (INCL++)** The nucleons are modeled as a free Fermi gas in a static potential well. The particles are assumed to propagate along straight-line trajectories until an interaction

Geant4 models for the exit channel

- **Evaporation Model** associates the probability that a nucleus with A nucleons emits one of them, remaining with A-1 nucleons, to the probability that the produced nucleus, with A-1 nucleon, captures the nucleon in object

- **Generalized Evaporation Model (GEM)** same approach of the previous one, but it takes into account the emission of fragments heavier than α particles and uses a more accurate level density function, based on the Fermi gas model

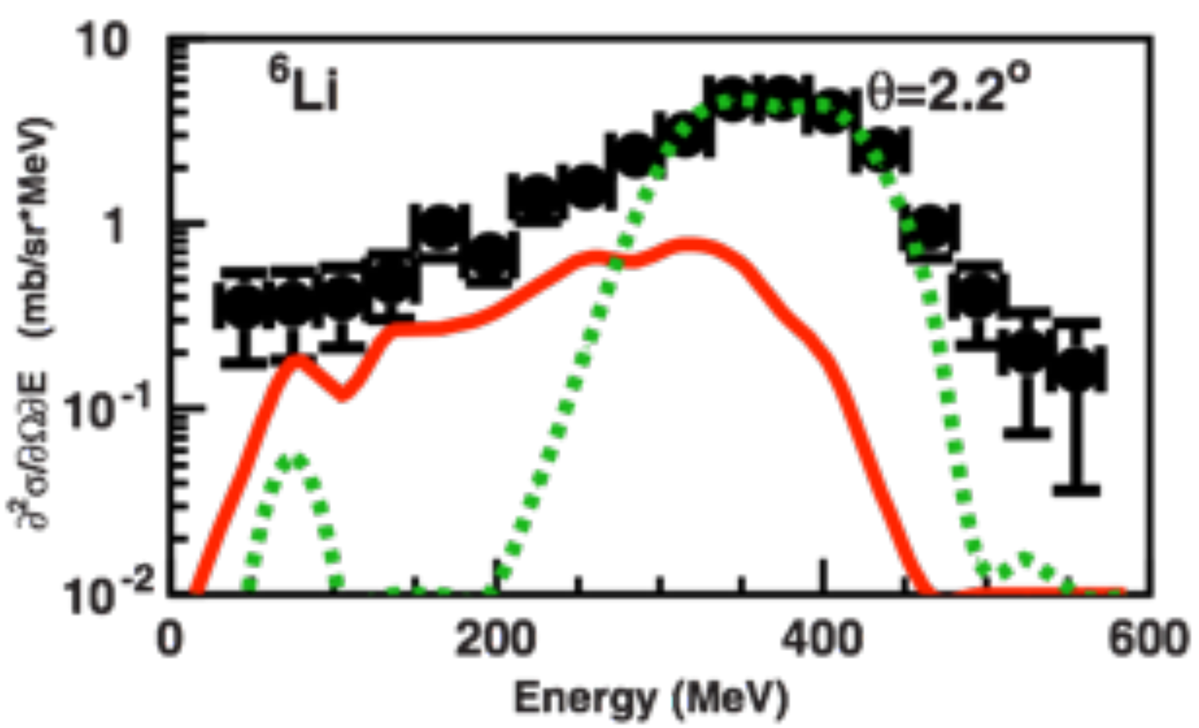
- **Fermi Break-up** considers the decay of an excited light (Z<9 and A<17) nucleus into several stable fragments. The break-up probabilities for each decay channel are calculated by considering the n-body phase space distribution

Problems in Geant4 below 100 MeV/A

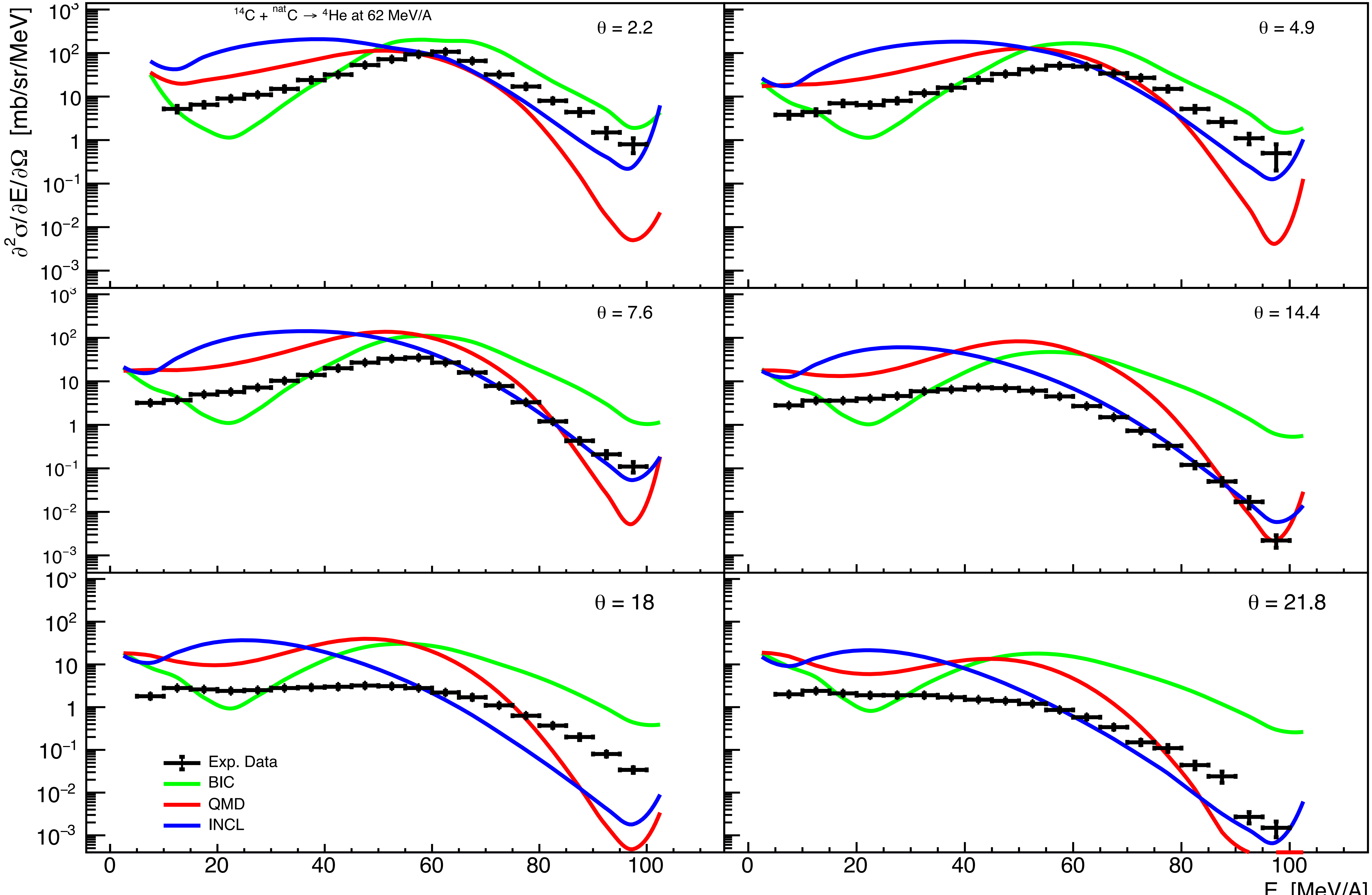
- Braunn et al. have shown discrepancies up to one order of magnitude in ^{12}C fragmentation at 95 MeV/A on thick PMMA target
- De Napoli et al. showed discrepancy specially on angular distribution of the secondaries emitted in the interaction of on 62 MeV/A ^{12}C thin carbon target
- Dudouet et al. found similar results with a 95 MeV/A ^{12}C beam on H, C, O, Al and Ti targets

- **Exp. data**
- **BIC**
- **G4QMD**

[Plot from De Napoli et al. Phys. Med. Biol., vol. 57, no. 22, pp. 7651–7671, Nov. 2012]



Cross section of the ^{6}Li production at 2.2 degree in a ^{12}C on ^{12}C reaction at 62 MeV/A.



[exp. data from De Napoli et al. Phys. Med. Biol., vol. 57, no. 22, pp. 7651–7671, Nov. 2012]

double differential spectra of ^{4}He production for ^{12}C on ^{nat}C at 62 MeV/u

GeNIALE

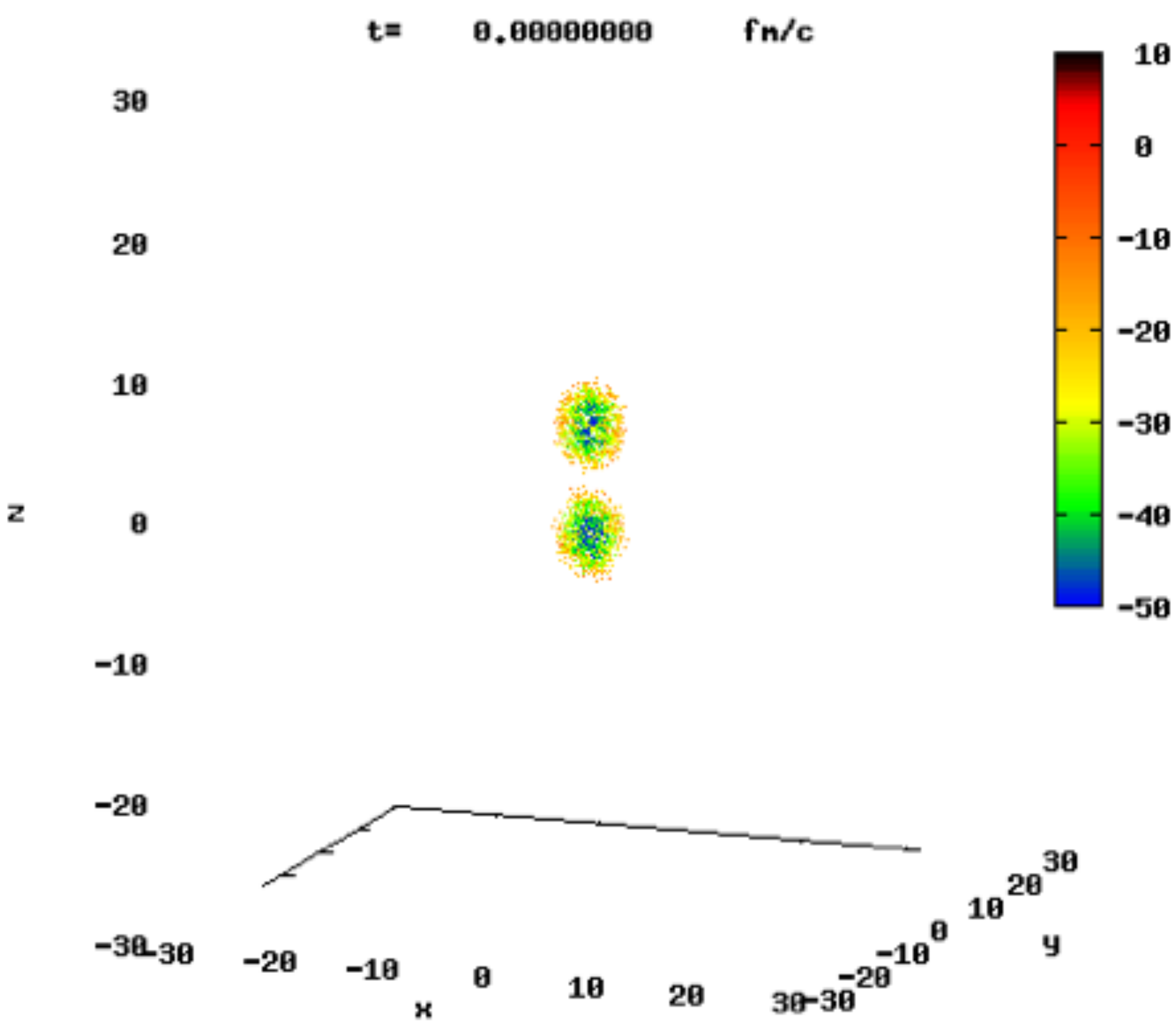
Geant Nucleat Interaction At Low Energy

- Benchmark and **improve** the capacity of Geant4 to simulate **nuclear fragmentation** in the energy range **below 100 MeV/A**
- Implementing in Geant4 a new model for the **first stage of the interaction** between a hadron -or a nucleus- and a target nucleus
- Such a model will be coupled with the models already existing in Geant4 for the second stage, and with the Geant4 framework in general

Suitable models

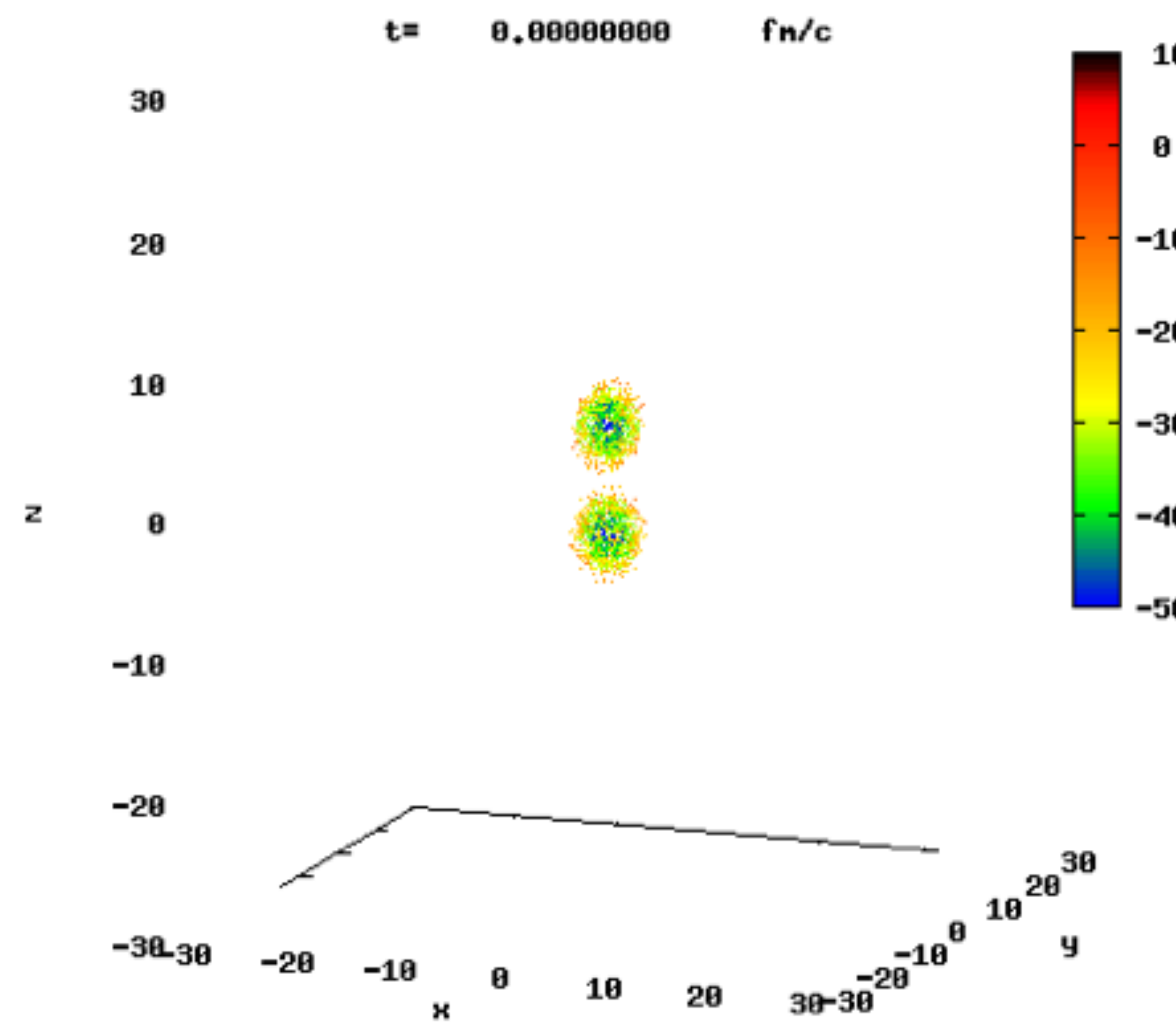
- **Boltzmann-Uehling-Uhlenbeck (BUU)**
  - describes the time evolution of the density distribution
- **Boltzmann-Langevin (BL)**
  - BUU plus fluctuations in the nucleon-nucleon collisions
- **Antisymmetrized Molecular Dynamics (AMD)**
  - reproduce the molecular dynamics in the nuclear field

Blob and Twingo



Blob

100 test particles per nucleon
^{12}C on ^{12}C at 62 MeV/n



Twingo

FRED

- MC TPS with GPU

Hardware and Performance

		Threads	primary/s	$\mu s/primary$
CPU[a]	full-MC *	1	0.75 k	1340
	FRED	1	15 k	68
	FRED	16	50 k	20
	FRED	32	80 k	12.5
GPU	FRED	1 GPU[1]	500 k	2
	FRED	2 GPU[2]	2000 k	0.5
	FRED	4 GPU[3]	20000 k	0.05

Table A1: Computing times for different hardware architectures.

[a] motherboard with two Intel® Xeon E5-2687 8-Core CPU at 3,1GHz

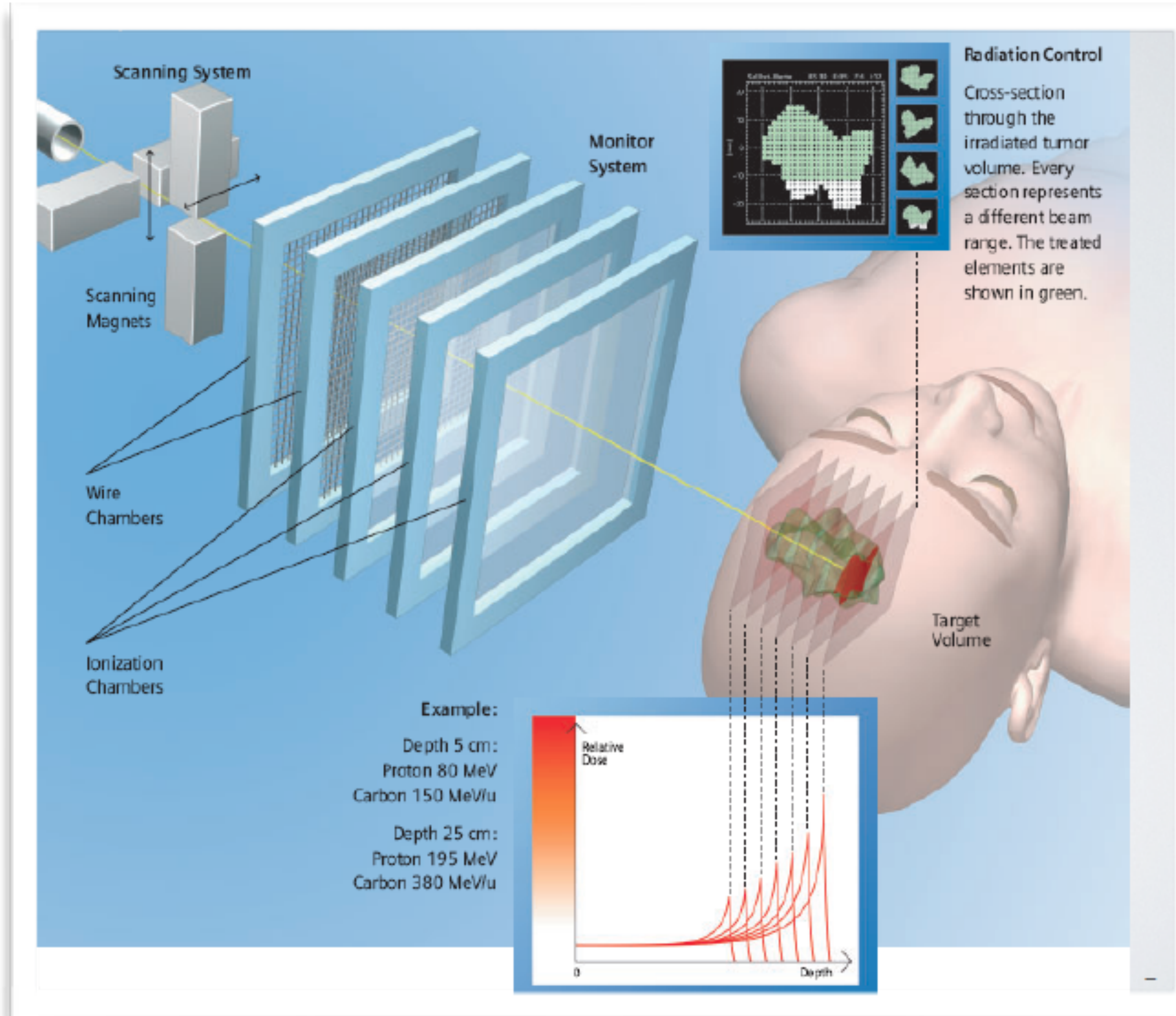
[1] LAPTOP: Apple® MacBook Pro with one AMD® Radeon R9 M370X.

[2] DESKTOP: Apple® Mac Pro with two AMD® FirePro D300.

[3] WORKSTATION: Linux box with four NVIDIA® GTX 980.

* FLUKA or Geant4

6



Suitable models

- **Boltzmann-Uehling-Uhlenbeck (BUU)** model
  - describes the time evolution of the density distribution
  - involves the implementation of an effective attractive mean-field nuclear interaction
  - mean-field is self-consistent, depends on the density
  - includes two-bodies correlations through nucleon-nucleon collisions

Suitable models

- **The Boltzmann-Langevin (BL)** model
  - an enhancement of the BUU
  - adds some fluctuations in the dynamics treating the nucleon-nucleon collisions as a stochastic process

Suitable models

- **Antisymmetrized Molecular Dynamics (AMD)** or **Fermionic Molecular Dynamics (FMD)**.
    - stochastic models
    - try to reproduce the molecular dynamics in the nuclear field
    - the many-body state is represented as an anti-symmetrized product of single particle gaussian wave packets
    - better description of fermionic systems with respect to QMD
    - different correlations with respect to BL because of the gaussian wave packet (there is a greater localization of the nucleons)

Missing LET

- When a projectile of mass M_P with kinetic energy T_P hits a target with mass M_T the Energy conservations laws is:

$$M_P c^2 + T_P + M_T c^2 = \sum_{Fi} M_{Fi} c^2 + T_{Fi}$$

- Defining:

$$Q = M_P c^2 + M_T c^2 - \sum_{Fi} M_{Fi} c^2$$

- So that:

$$\sum_{Fi} T_{Fi} = T_P + Q$$

Missing LET

- For small nuclei (< Iron) Q is negative
- The sum of kinetic energies is smaller
- The total LET is smaller than the initial kinetic energy of the projectile