A Monte Carlo study of target fragmentation in Protontherapy

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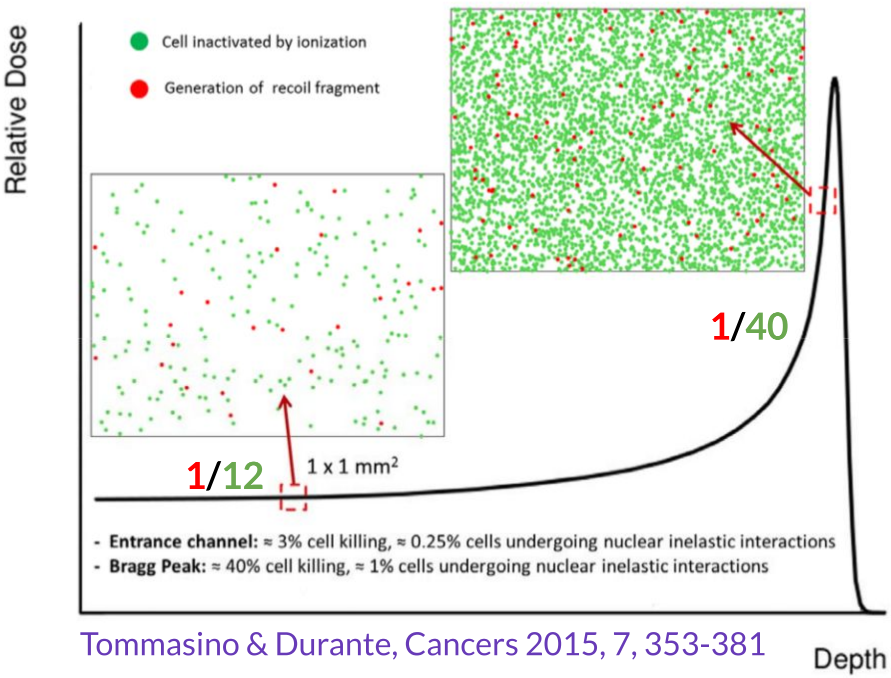
Target Fragmentation

In Protontherapy, secondary particles are produced through primary beam interactions with the patient's body. The fragments created have:

- Low kinetic energy fragments ➪ small range
- High Z ➪ high cell killing effectiveness (dE/dx increase with Z)
- High LET ➪ increase of RBE
- Higher production cross section in the entrance channel ➪ relevant for healthy tissue



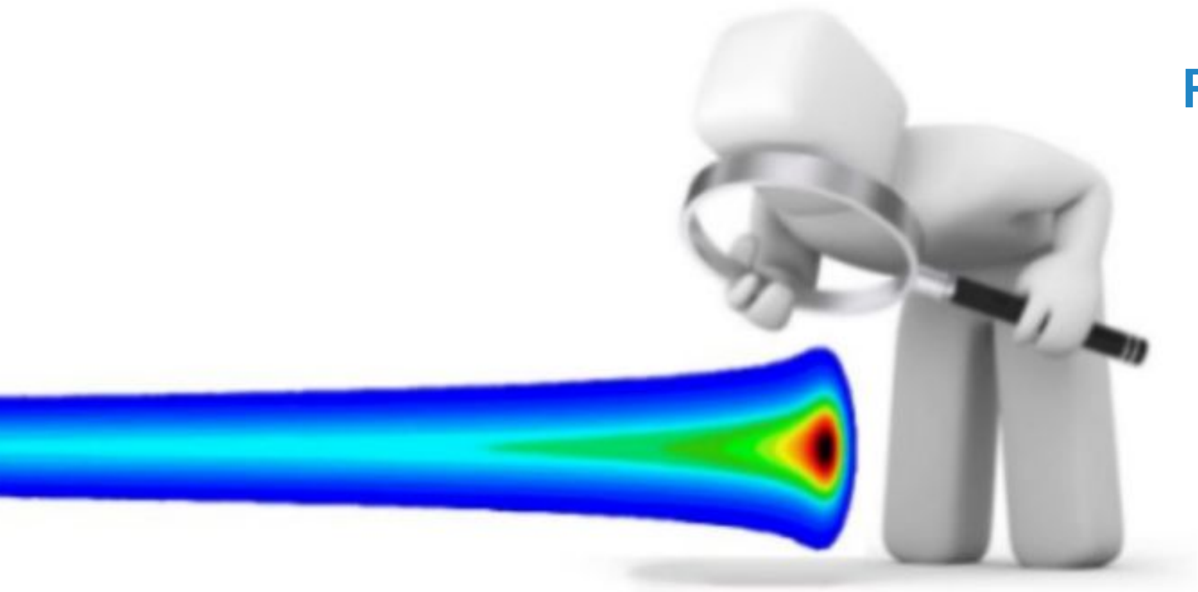
Tommasino & Durante, Cancers 2015, 7, 353-381

The inclusion of target fragmentation processes can be important for the accurate evaluation of the dose in the treatment.

MC study of target fragmentation

Target fragmentation is not implemented in commercial TPSs.

Monte Carlo simulations were employed to estimate the effect of target fragmentation in Protontherapy.



Fragments characterization:

- **Production Cross Section**
- **Range**
- **Fluence**
- **MoVe IT**

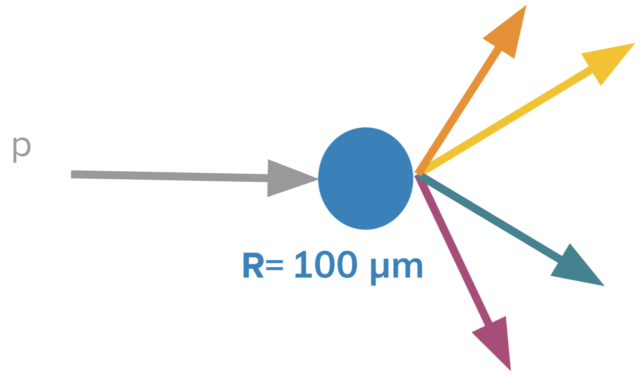
Production
Cross Section

Energy spectra

The energy distribution of main fragments produced by proton beam in water have been simulated with FLUKA.

Simulation setup

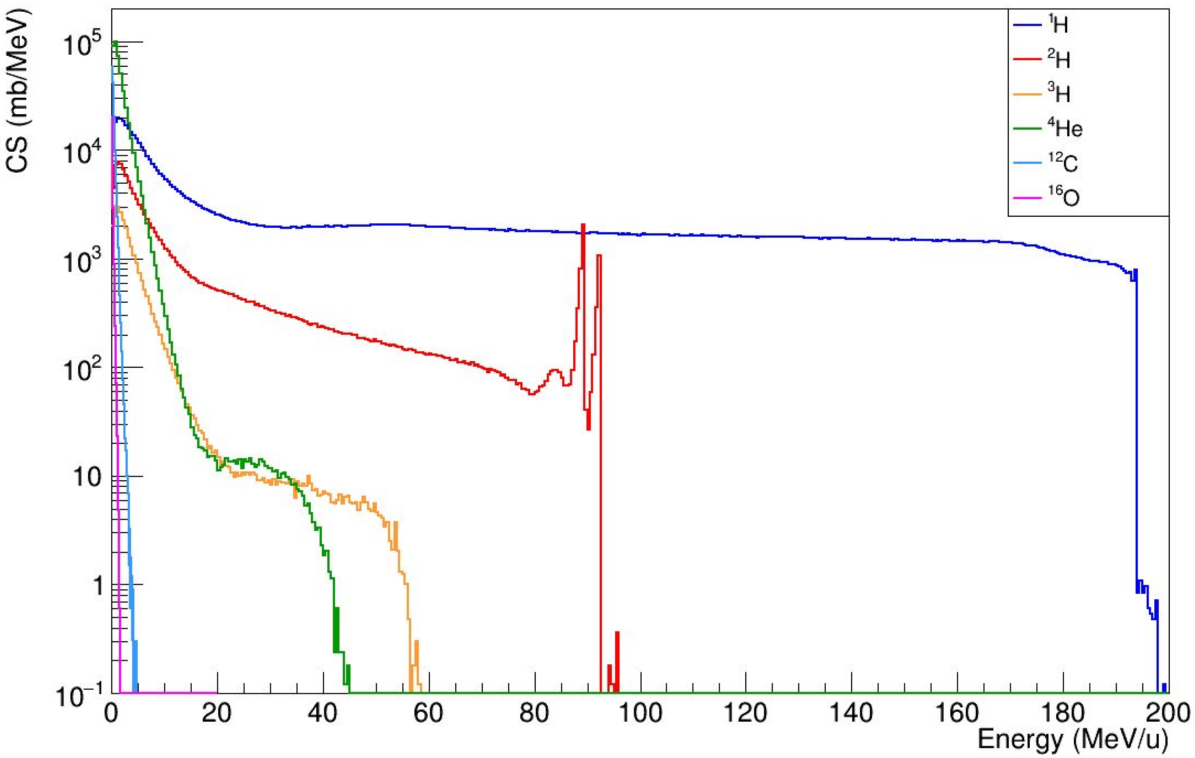
p beam on water target



The energy distribution of main fragments produced by proton beam in water have been analyzed, considering initial kinetic energy **Ep=50, 100, 150, 200 and 250 MeV.**

Energy distribution of fragments

Production CS of inelastic interaction induced by proton beam of 200 MeV in water.



	E_{MAX} (MeV/u)	E_{mean} (MeV/u)
^1H	200	65.4
^2H	95	16.7
^3H	58	3.9
^4He	45	1.7
^{12}C	4.7	0.4
^{16}O	1.7	0.1

Range

Range of fragments

Target fragments can have **high charge** (i.e. high biological effectiveness) and **low residual range**. This means that they will deposit all their energy close to their generation point.

Tommasino & Durante, Cancers 2015, 7, 353-381

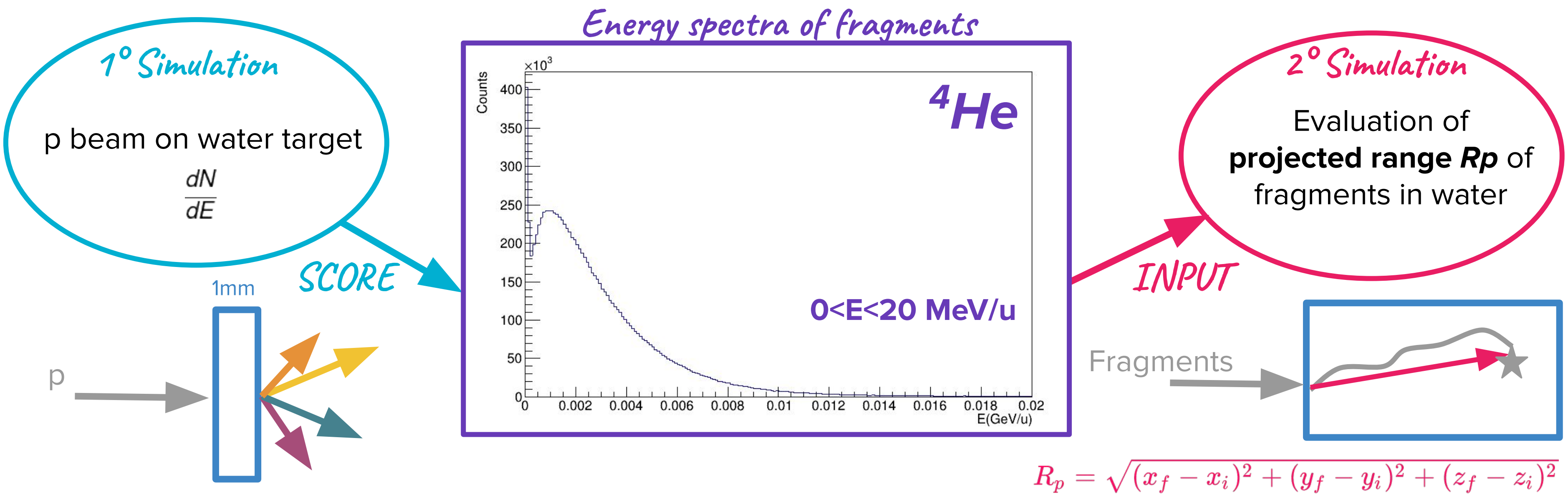
Fragment	E (MeV)	LET (keV/μm)	Range (μm)
^{15}O	1.0	983	2.3
^{15}N	1.0	925	2.5
^{14}N	2.0	1137	3.6
^{13}C	3.0	951	5.4
^{12}C	3.8	912	6.2
^{11}C	4.6	878	7.0
^{10}B	5.4	643	9.9
^{8}Be	6.4	400	15.7
^{6}Li	6.8	215	26.7
^{4}He	6.0	77	48.5
^{3}He	4.7	89	38.8
^{2}H	2.5	14	68.9

- Not experimental data
- Average energies of fragments are evaluated using Goldhaber formula
- Range has been estimated starting from average energy

The energy and residual range of target fragments produced in water have been studied using FLUKA MC code.

Simulation setup

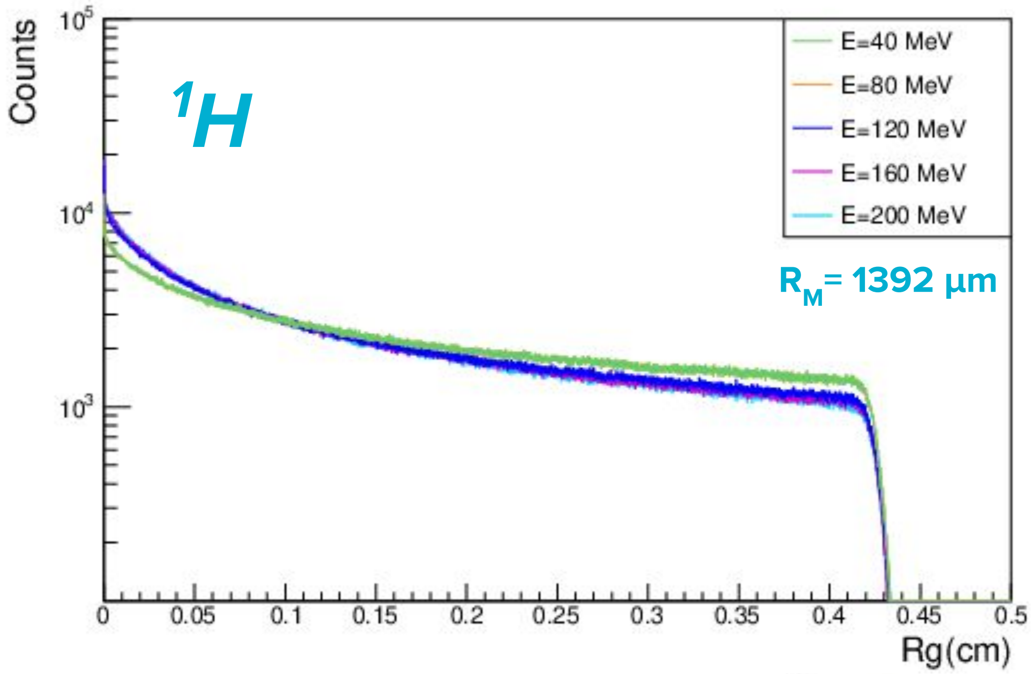
The energy spectrum and range distribution of fragments have been simulated with FLUKA:



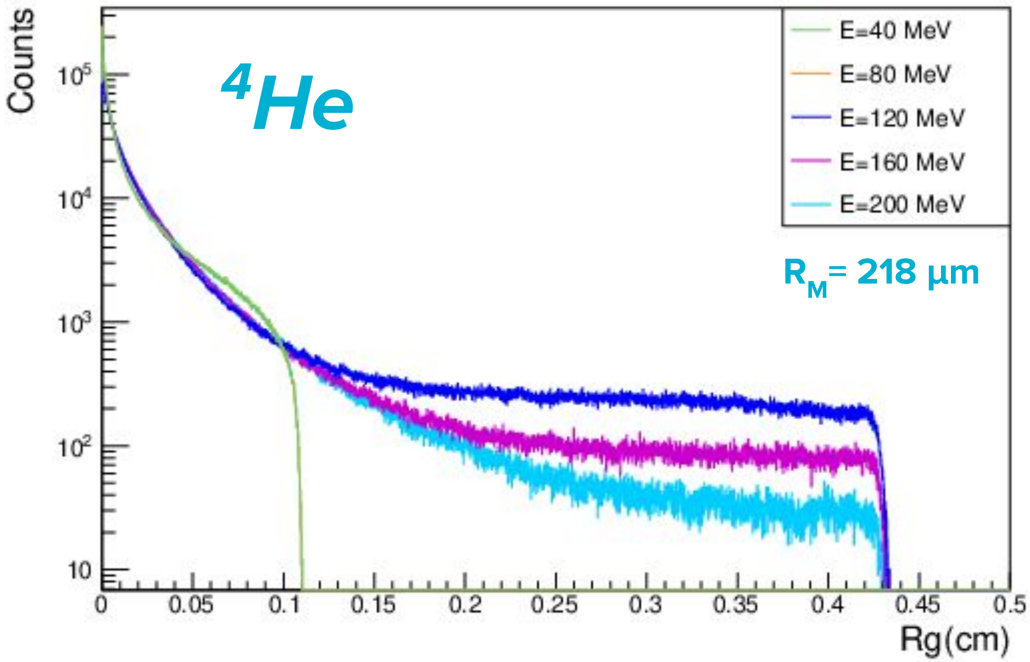
$$R_p = \sqrt{(x_f - x_i)^2 + (y_f - y_i)^2 + (z_f - z_i)^2}$$

Ep=40,80,120,160,200 MeV/u.

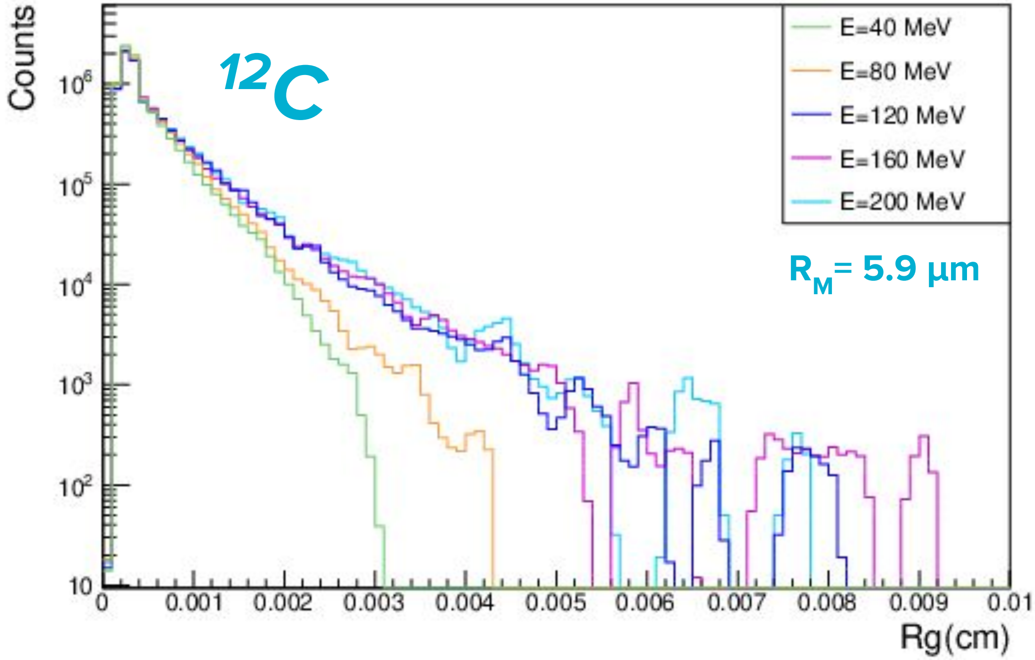
Range distribution of fragments



Rg = range
R_M = mean range



Range distribution of fragments



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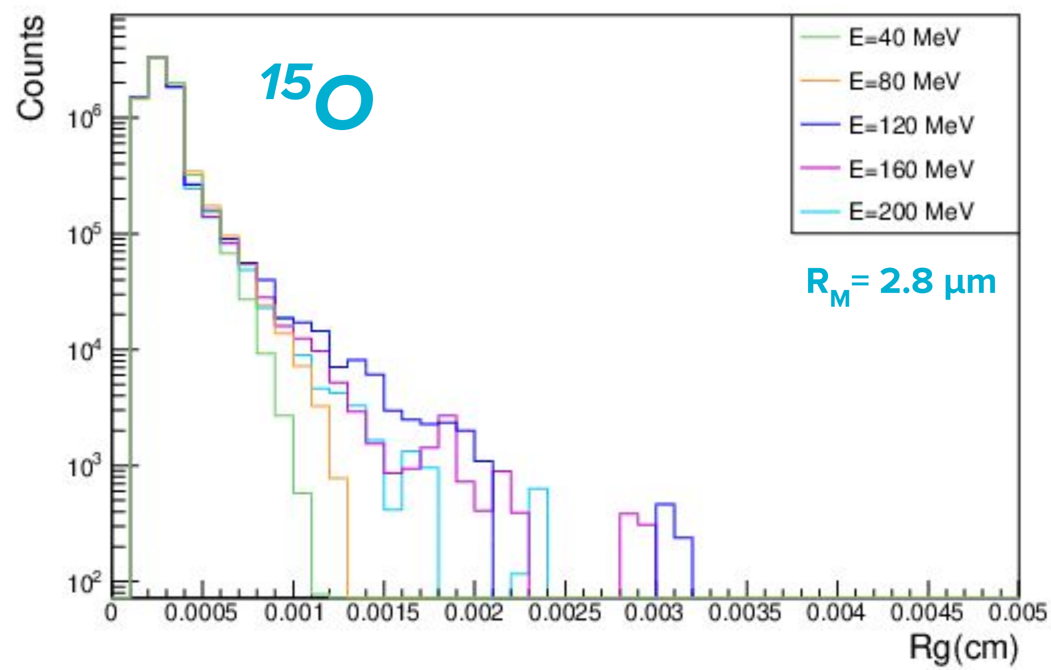


Range of fragments

Starting from the energy distribution of fragments, **the range distribution** has been evaluated.

For heavier fragments: the mean range obtained from the distribution is similar to the value reported in Cancers.

For low Z fragments: difference between average range in analytical formula and MC distribution.

→ **MC more complete description of physical processes ➪ Range is more reliable**

CONCLUSION

Low Z fragments R > cell nucleus

Heavier fragments R < cell nucleus
Colocalization effects?

FLUKA — Tommasino & Durante

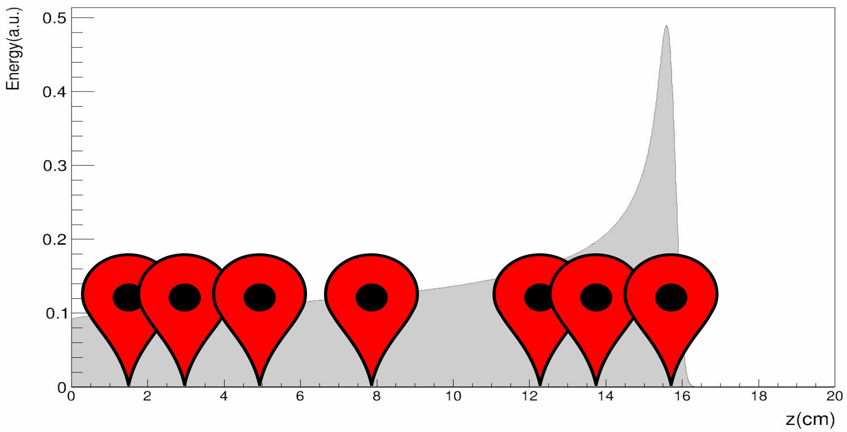
Fragment	$R_p(\mu m)$	$R_{TD}(\mu m)$
^{1}H	1392	-
^{2}H	2117	68.9
^{3}H	1383	-
^{3}He	465.7	38.8
^{4}He	218.3	48.5
^{6}He	229.3	-
^{6}Li	75.7	26.7
^{7}Li	74.1	-
^{7}Be	42.6	-
^{9}Be	26.1	-
^{9}B	24.4	-
^{10}B	14.5	9.9
^{11}B	11.2	-
^{10}C	9.9	-
^{11}C	8.1	7
^{12}C	5.9	6.2
^{13}N	4.4	-
^{14}N	4.1	3.6
^{15}O	2.8	2.3
^{16}O	3.5	-

Fragments fluence

Fragments Fluence

To include the impact of fragmentation in the TPS (TRIP98) and estimate the biological effect of fragments, their production in water has been calculated with FLUKA.

Fragments fluence as a function of energy evaluated at different depth



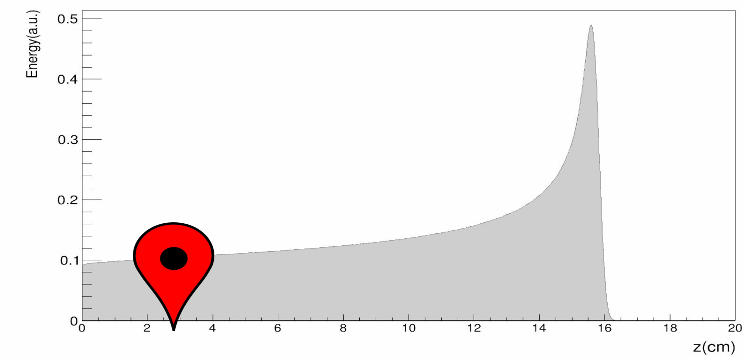
Source:
proton beam E=150 MeV

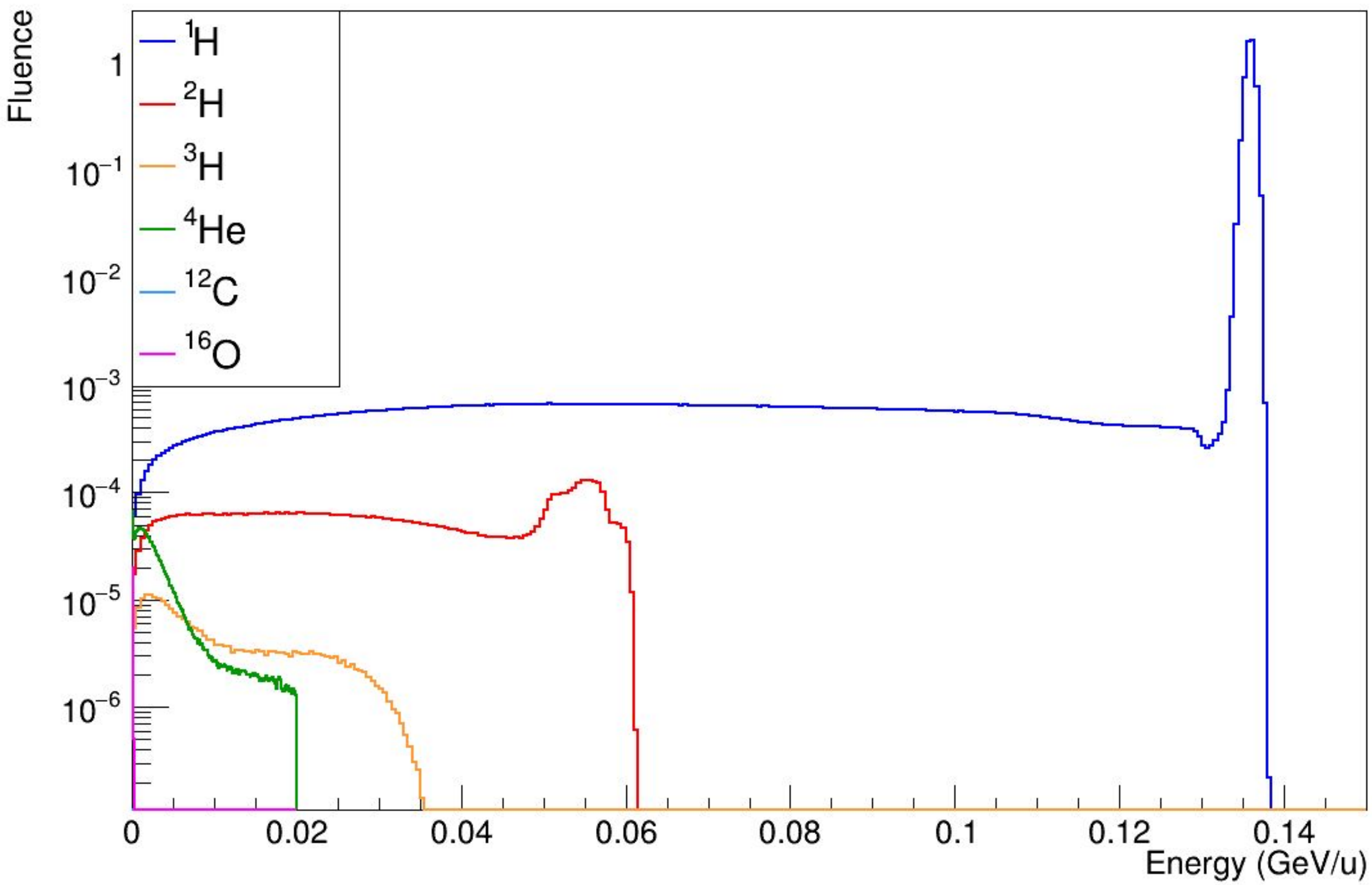
Geometry & Material:
parallelepiped of WATER

Scored quantity:
Fluence of charged particles as a function of energy

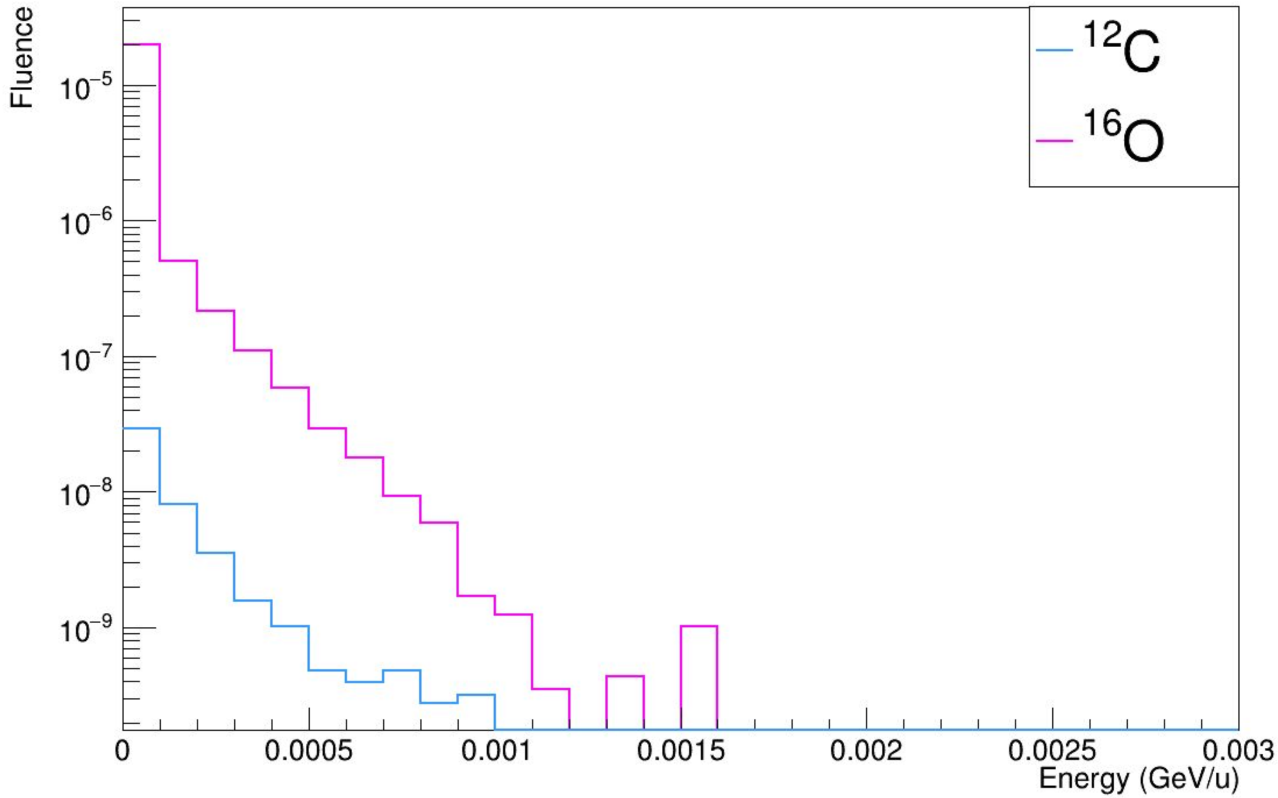
Statistics: 10^9 primaries

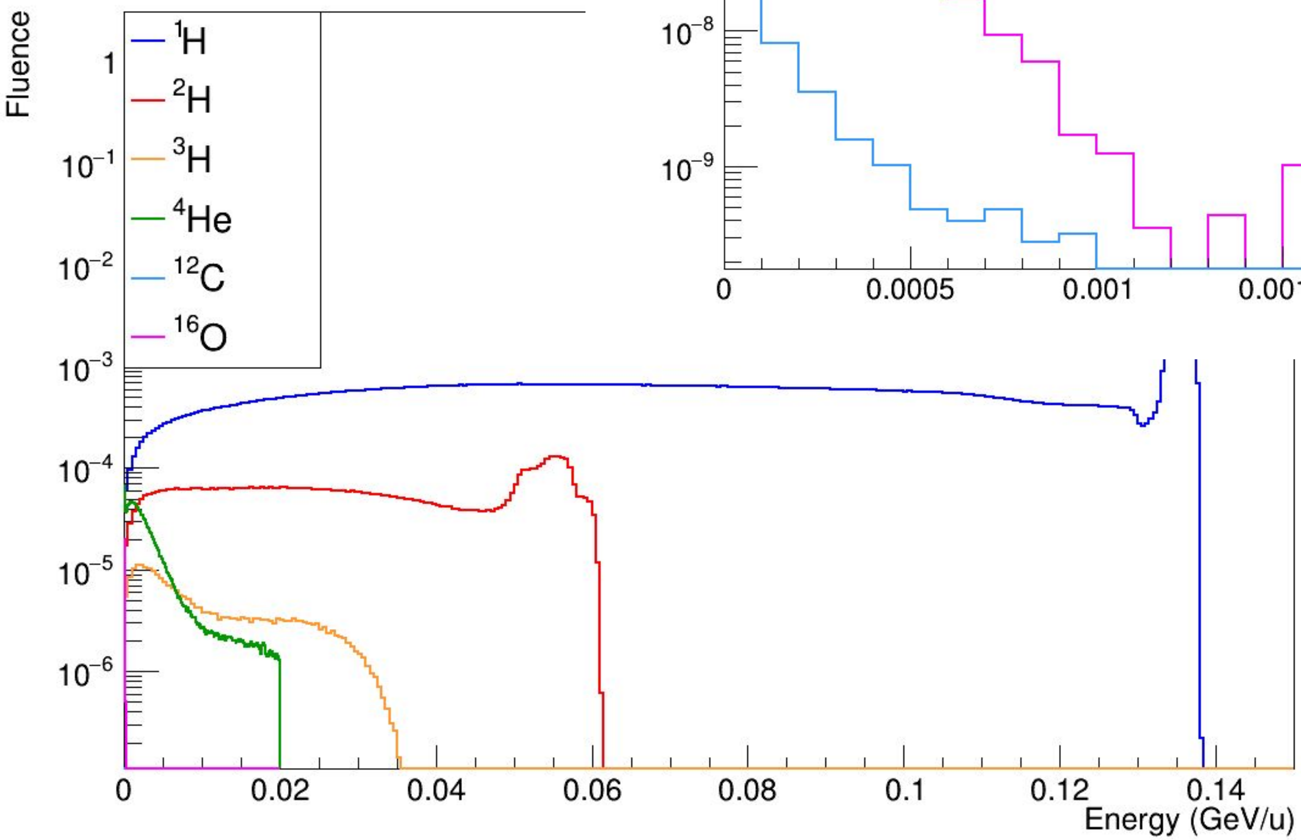
Fragments Fluence



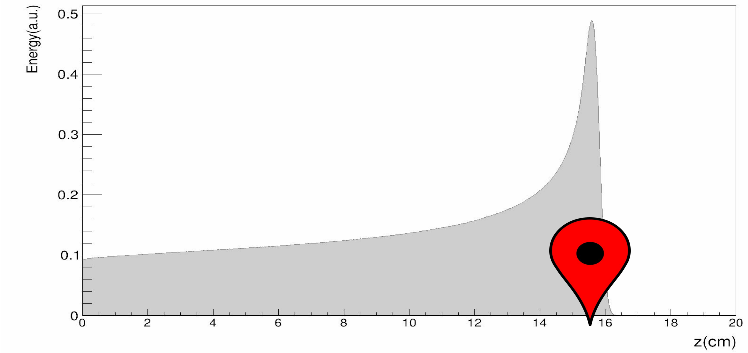


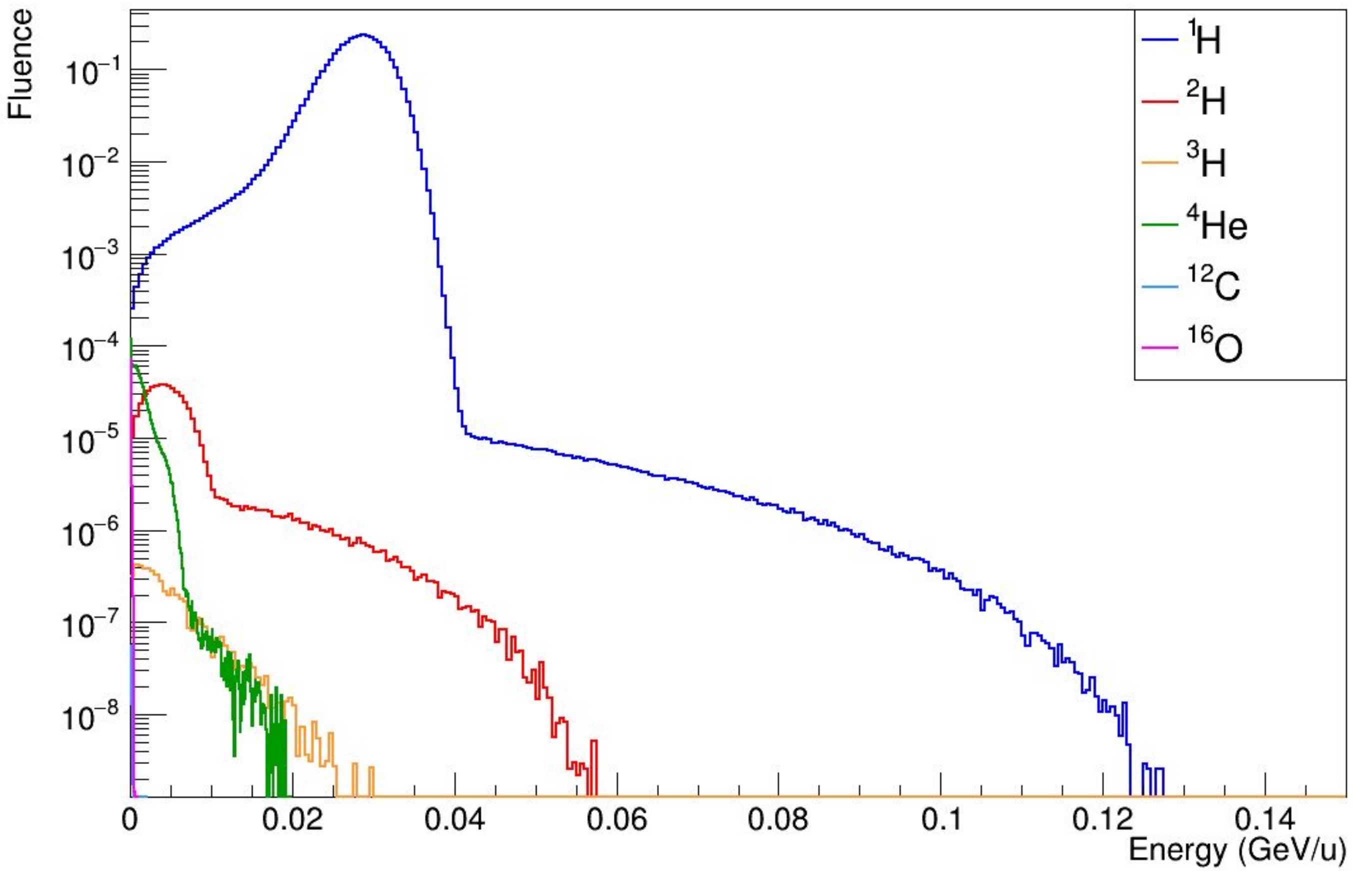
Fragments Fluence



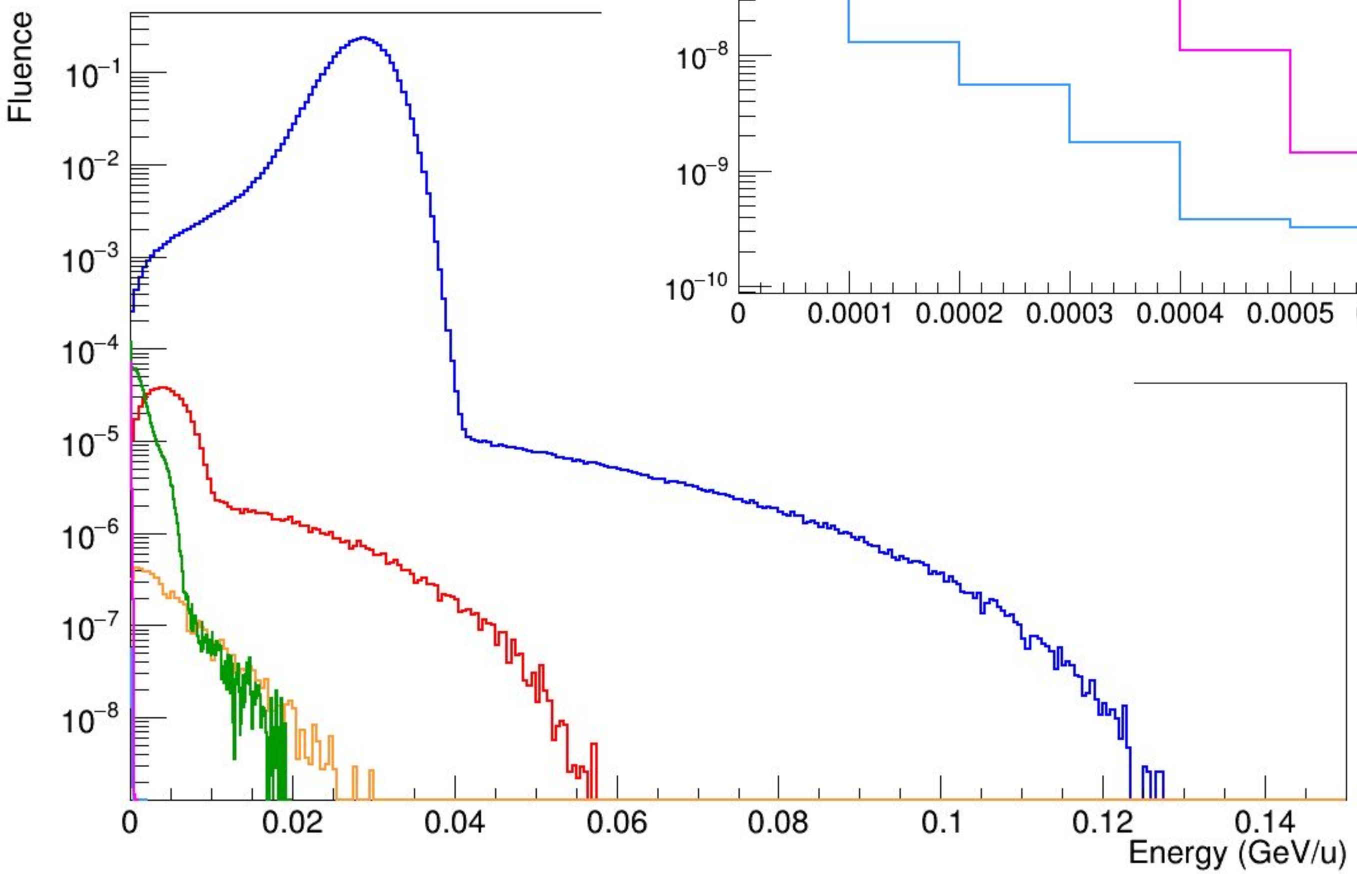


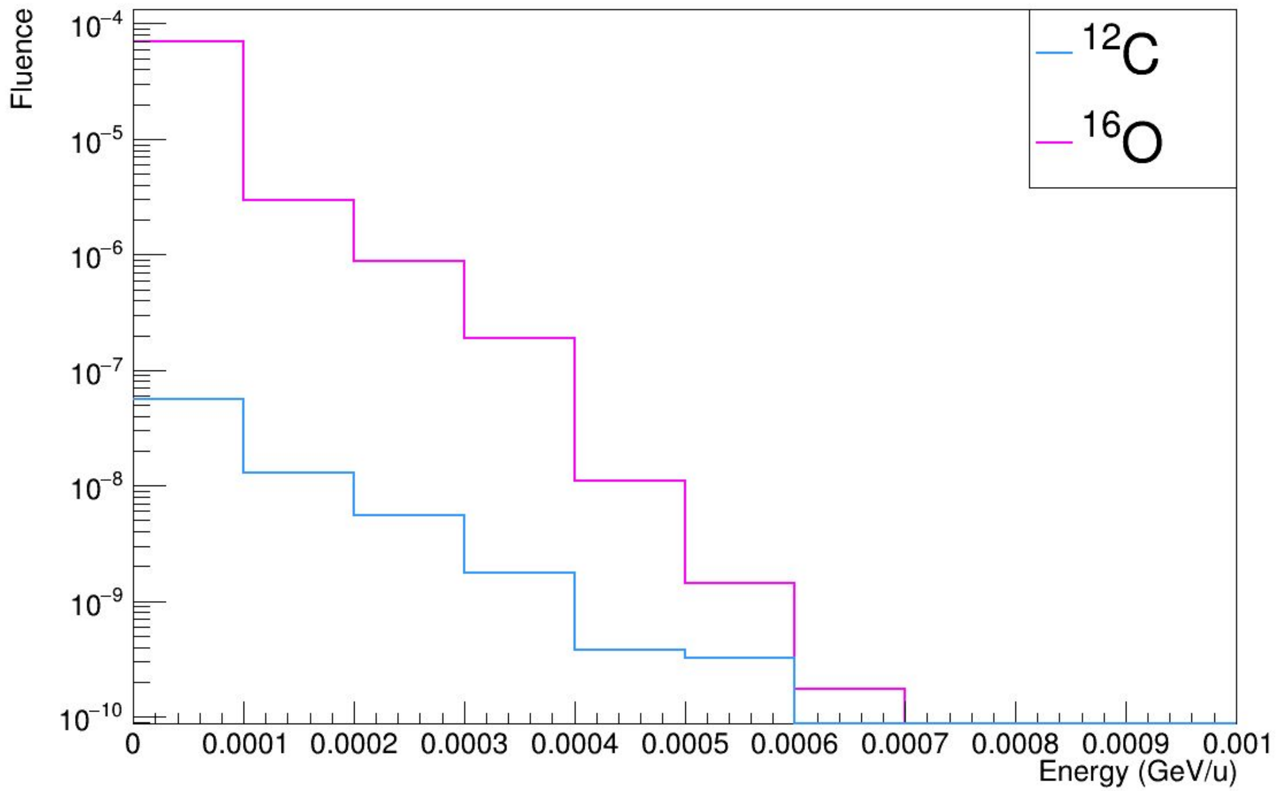
Fragments Fluence





Fragments Fluence





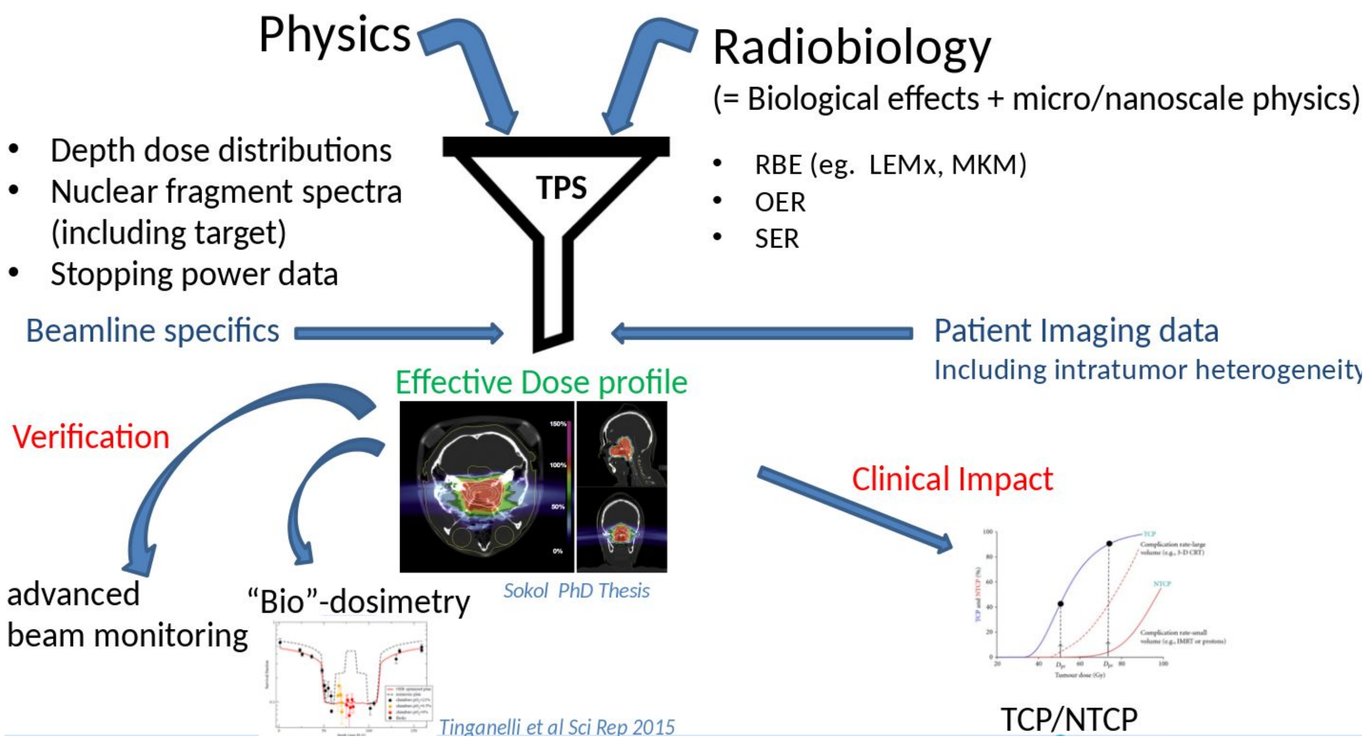
MoVe IT

Modeling and **Ve**rification for **I**on beam **T**reatment planning

MoVe IT

The main effects that will be explored in MoVe-IT project are:

- **biological impact of target nuclei fragmentation**
- **relative biological effectiveness (RBE)**
- **intra-tumor heterogeneity**



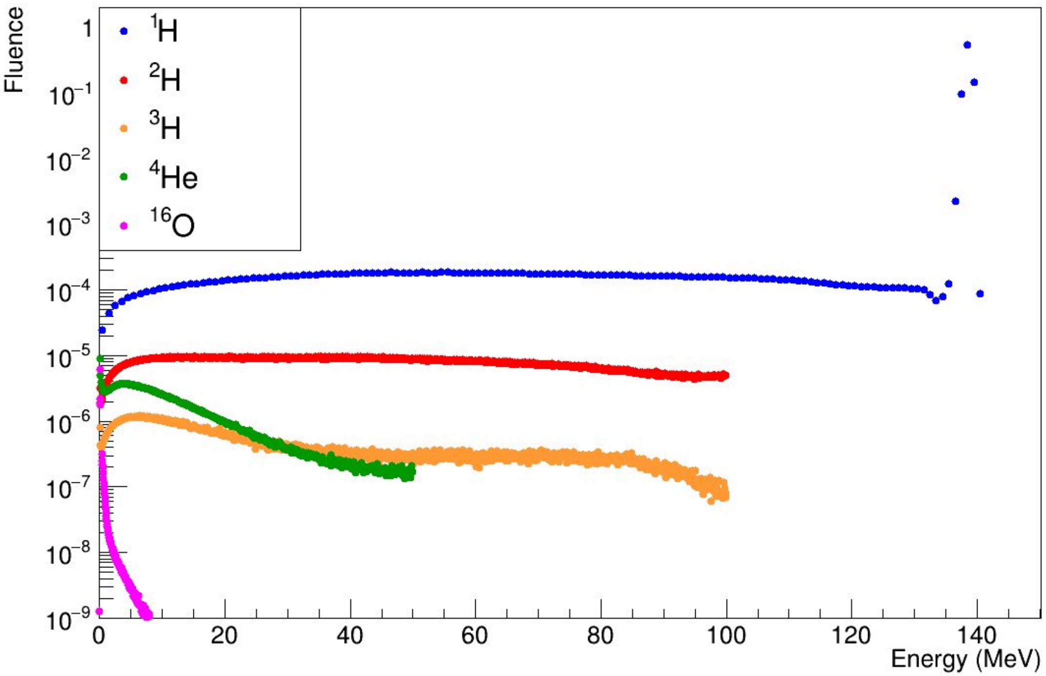
Target fragmentation

In order to describe the target fragmentation and estimate the biological effect of fragments, **MoVe IT propose an approach based on a RBE modellization:**

Fragments fluence	RBE	Biological dose
describe the physical dose including the contribution of each **single fragment produced by a proton in water**	evaluate the total RBE by using a **mixed field approach** to weights all the single fragments contributions	**import the results in TRiP98 TPS and test the biological dose** differences respect to the default calculations

Fragments Fluence

The fluence spectra have been obtained performing Monte Carlo simulations as separate single beams, scoring the fluence of all the produced particles.



Fluence of main fragments produced by proton beam of 150 MeV after 2 cm in water.

Fluence Database

$(E_k, E_f, A, Z, z_{depth})$

The mixed field model

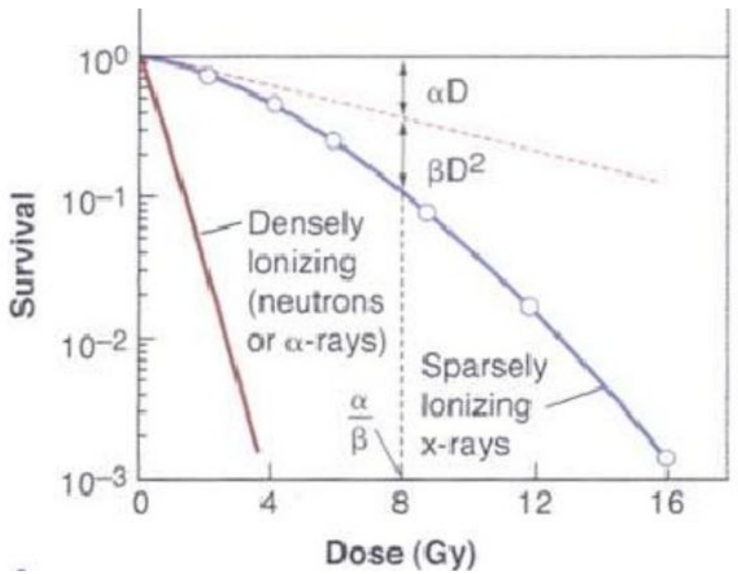
Primary proton's fragments are considered as secondary particles; each single spectra of those fragments is evaluated separately, considering its impact on the RBE.

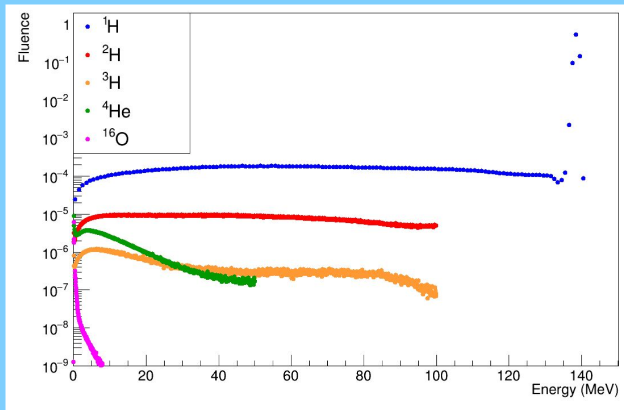
The total RBE is evaluated by using **Zeider & Rossi formula for mixed field irradiation** and **LEM IV model:**

$$\alpha = \frac{\sum_i \alpha_i D_i}{\sum_i D_i}$$

$$\sqrt{\beta} = \frac{\sum_i \sqrt{\beta}_i D_i}{\sum_i D_i}$$

$$S(D) = \exp -(\alpha D + \beta D^2)$$





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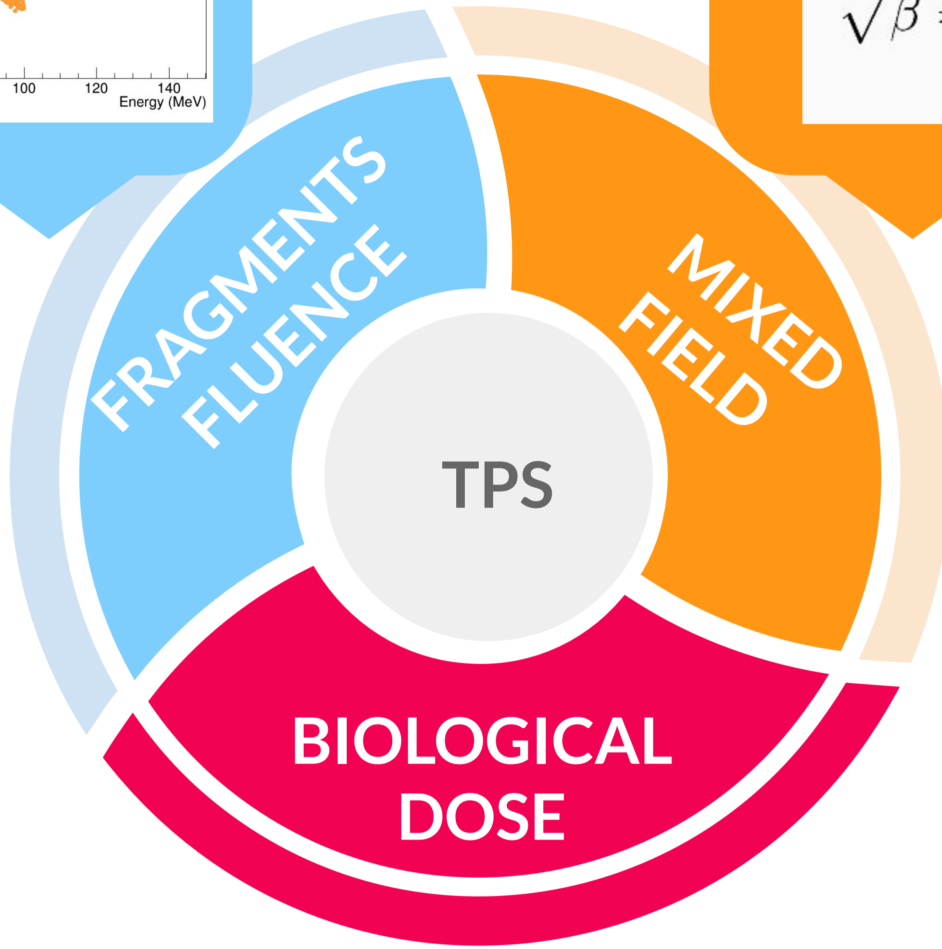


Biological dose comparison

Preliminary comparison between default TRiP98 data vs new TOPAS-base data

Tissue comparison:

Synthetic tissues obtained from LEM-IV model and characterized by α/β = 2Gy to represent a normal tissue.

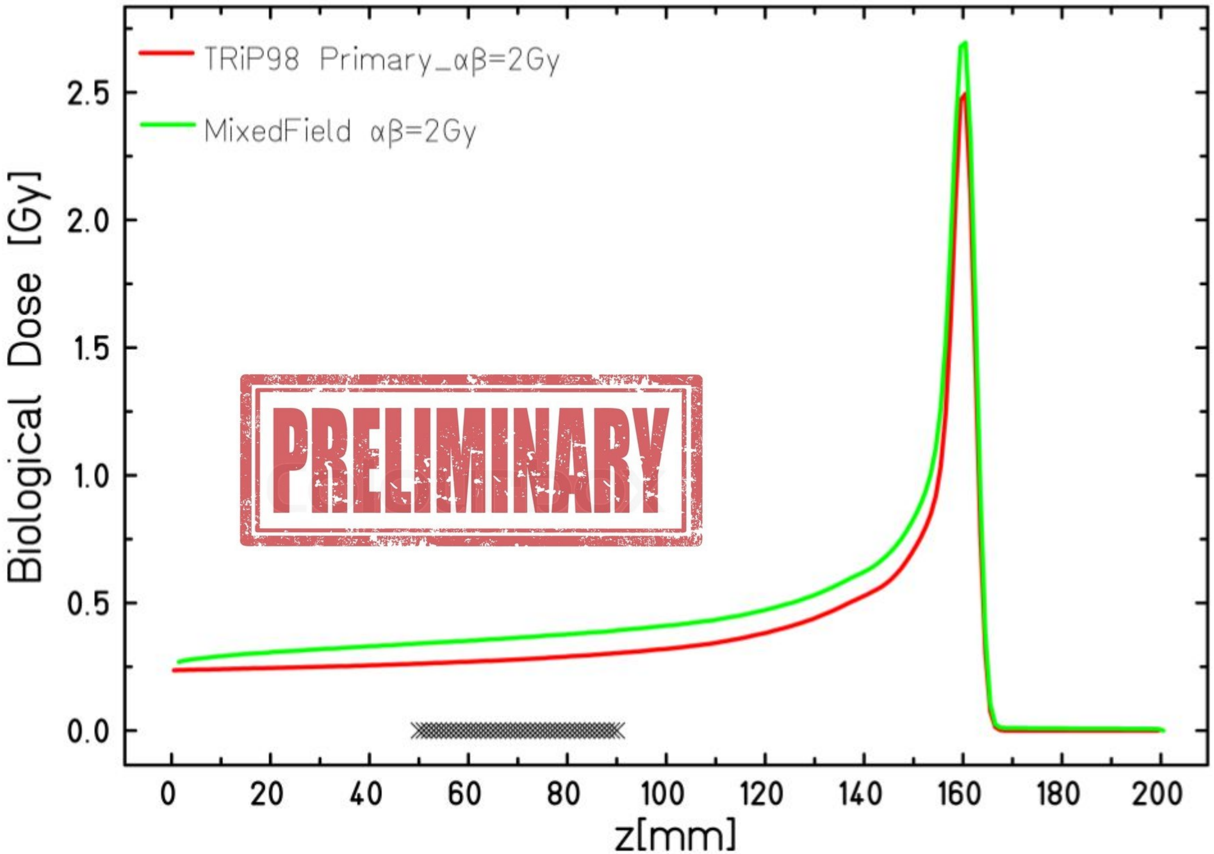
Particles contribution comparison:

- only primaries (Z=1 primary)
- only protons (primary and secondaries) (Z=1)
- All produced fragments

Biological dose comparison

Comparison between default TRiP98 data vs mixed field with TOPAS-base data

Courtesy of E. Bellinzona



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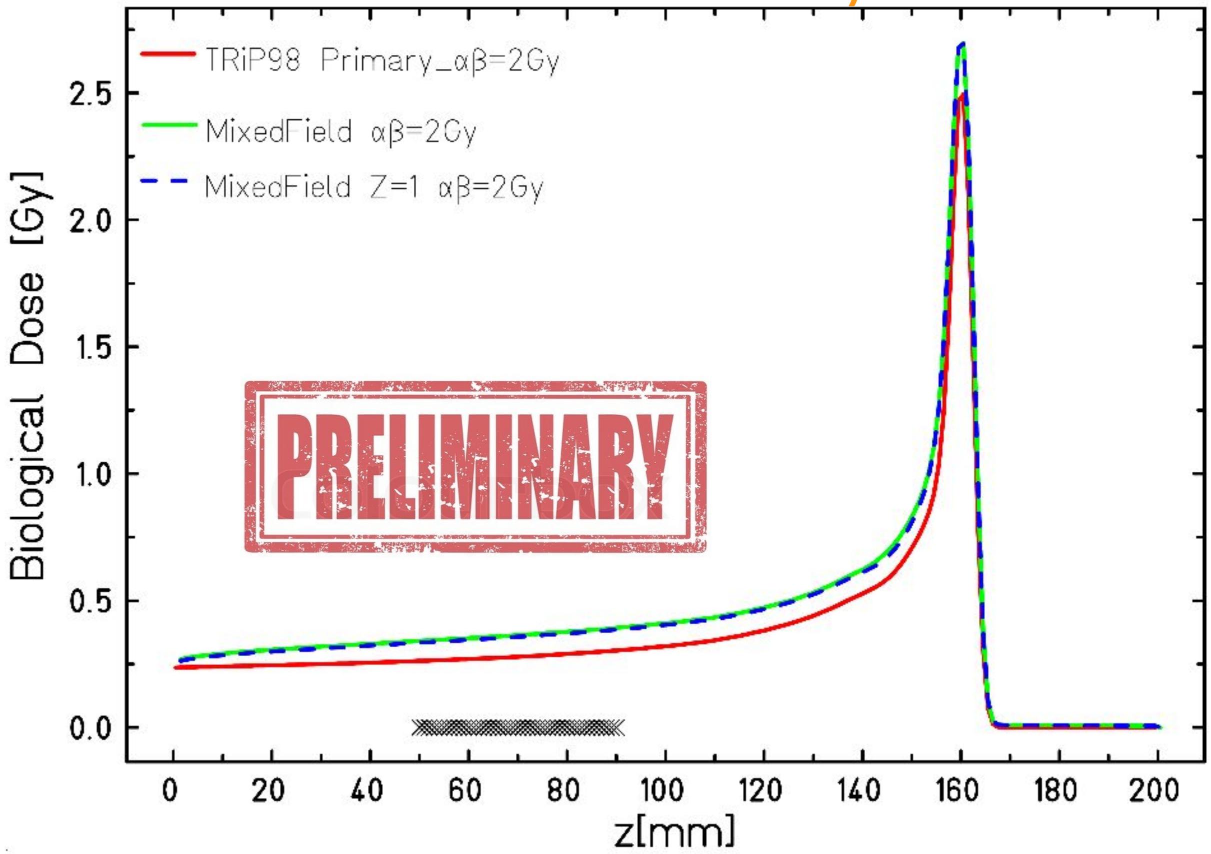

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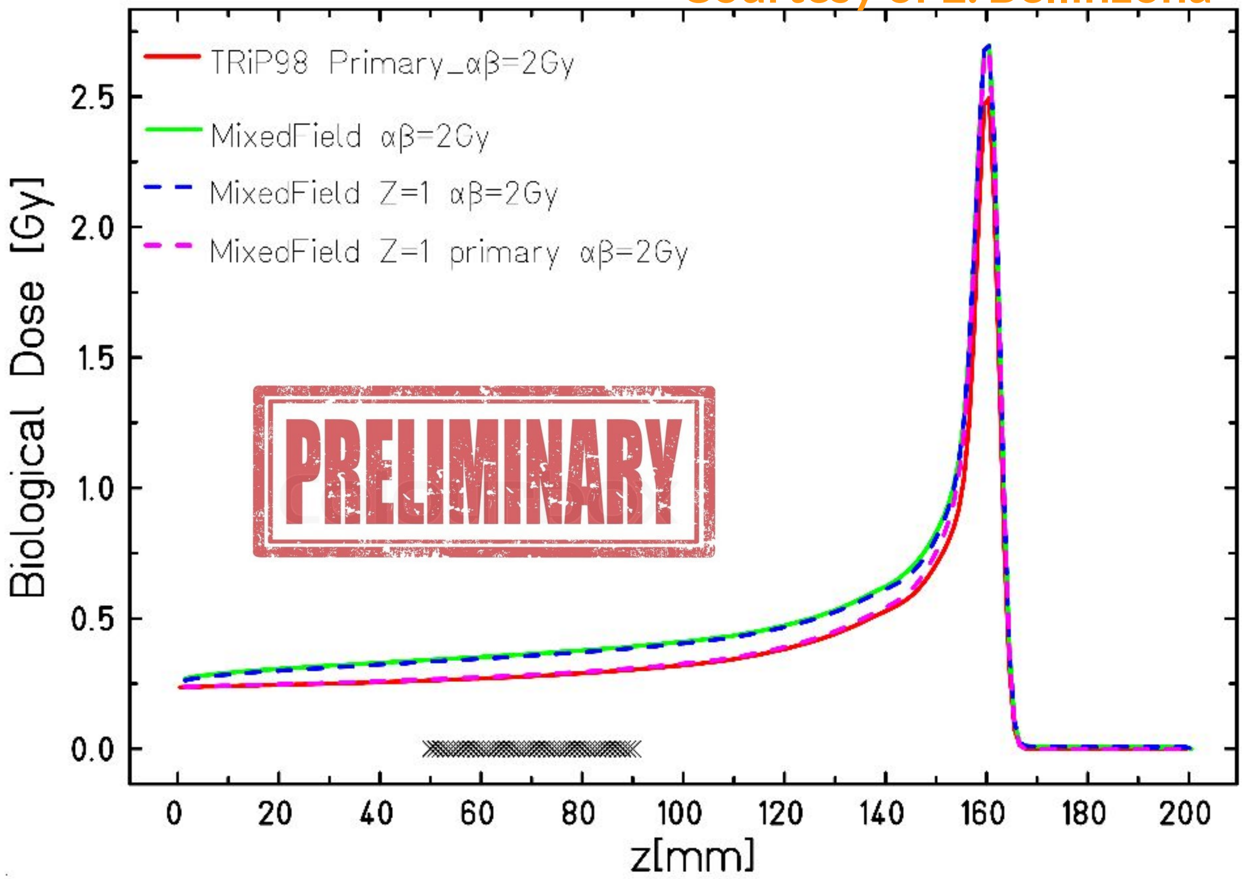
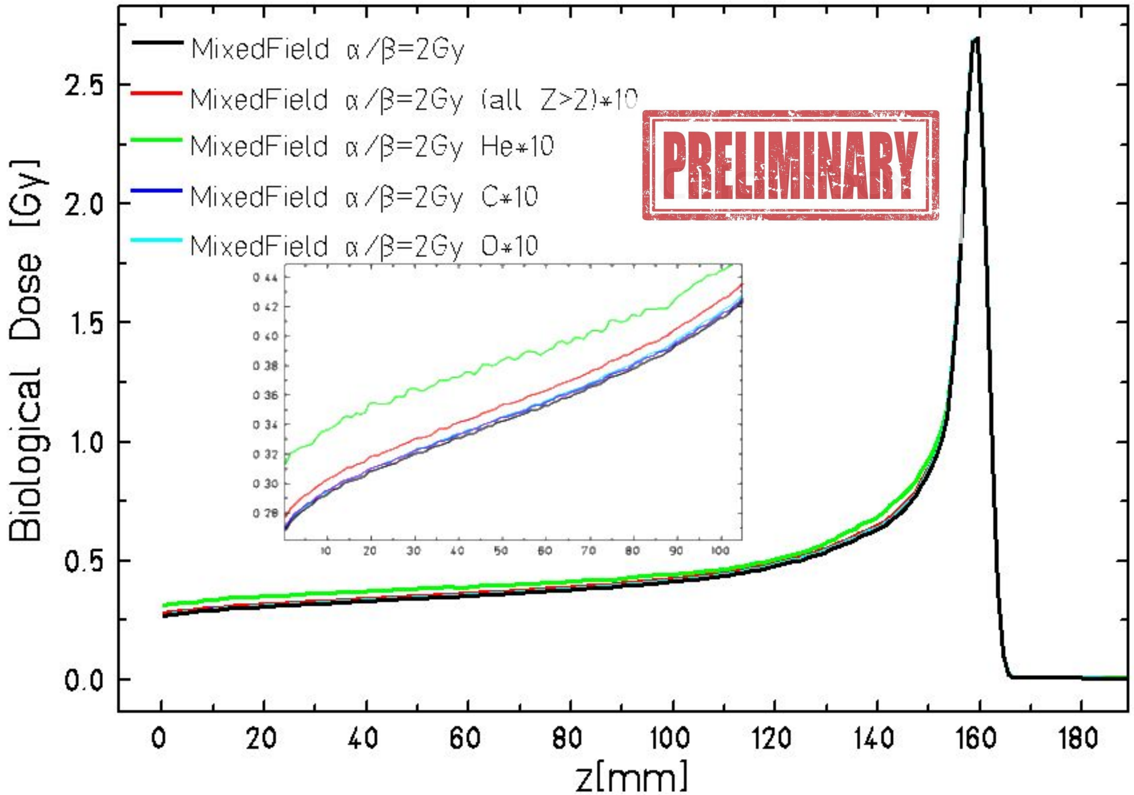


Fragment impact

The fluence contribution of main fragments has been enhanced (by a factor 10) to analyse the dependence of species contribution on the biological dose.

Courtesy of E. Bellinzona



MoVe IT Future perspective

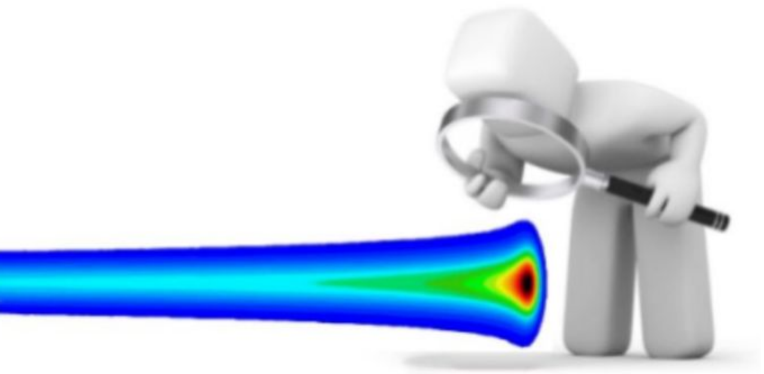
- Creation of fragments fluence database ($\mathbf{E_k}$, $\mathbf{E_f}$, **A, Z,** $\mathbf{z_{depth}}$)
- Results validation with different MC simulations (FLUKA, GEANT4, TOPAS)
- Biological dose evaluation of SOPB with TRIP98, starting from MC databases, in water at two depths (entrance and distal region)

WAITING FOR FOOT EXPERIMENTAL DATA

(see poster #8:
FOOT FragmentatiOn Of Target)

Conclusions

Target fragmentation has been studied using ***FLUKA MC code.***



- The energy spectra of fragments: **0<E<20 MeV/u**
  LOW ENERGY and **HIGH Z**
  → ***ENHANCED RBE***
- The range of fragments is of the order of 10-100 μm **SMALL RANGE**
  → Relevant for normal tissues in the entrance region

MoVe IT

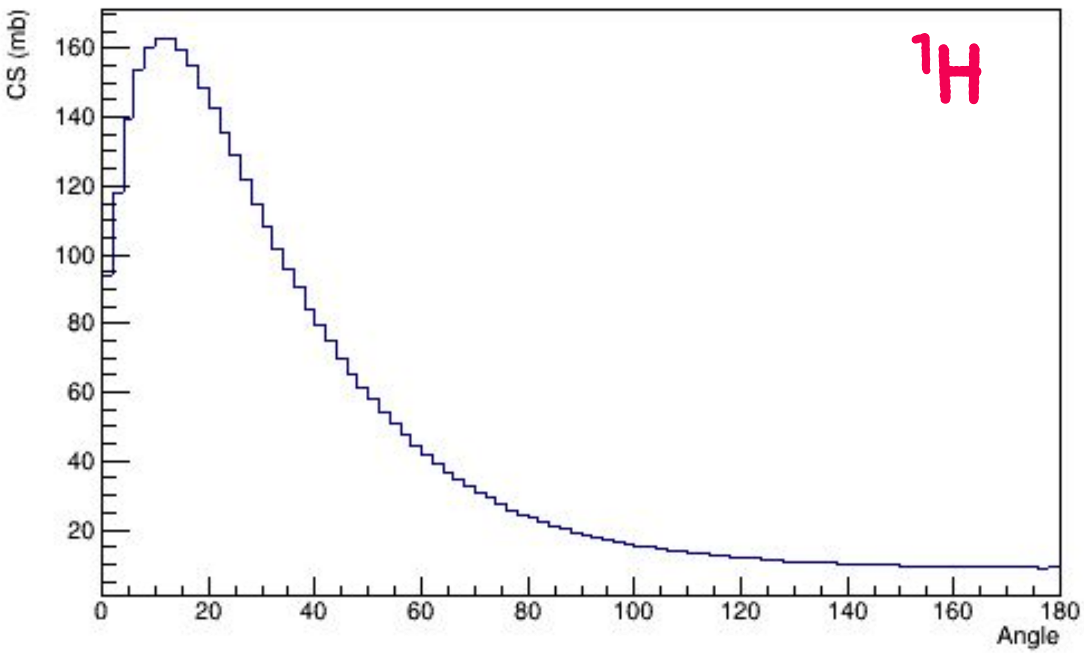
Starting from these preliminary results, the next step is the creation of the fragments database (fluence, energy, Z, A) for the inclusion of target fragmentation in the TPS.

THANK YOU!

BACKUP SLIDE

Angular distribution of fragments

Production CS of inelastic interaction induced by proton beam of 200 MeV in water.



Angular distribution of fragments

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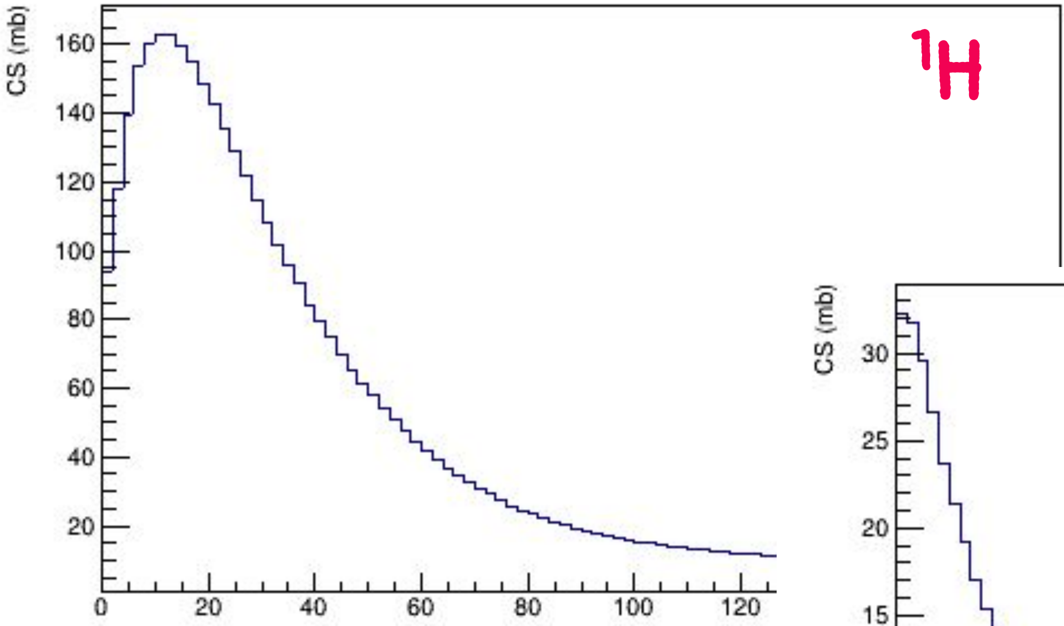
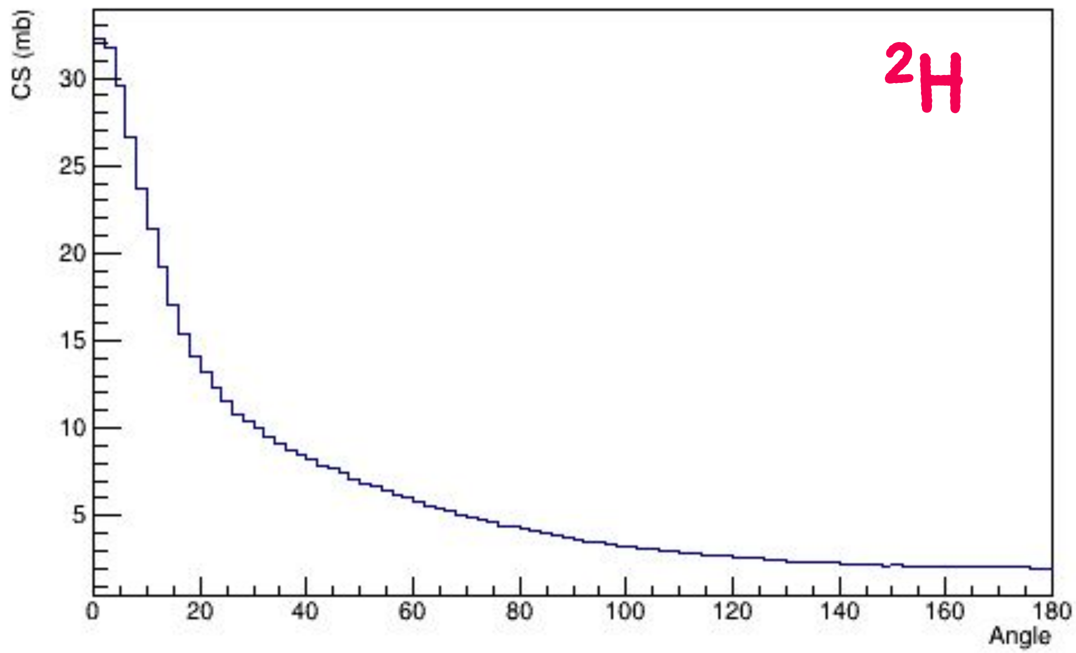


The emission of Hydrogen fragments is focused forward.



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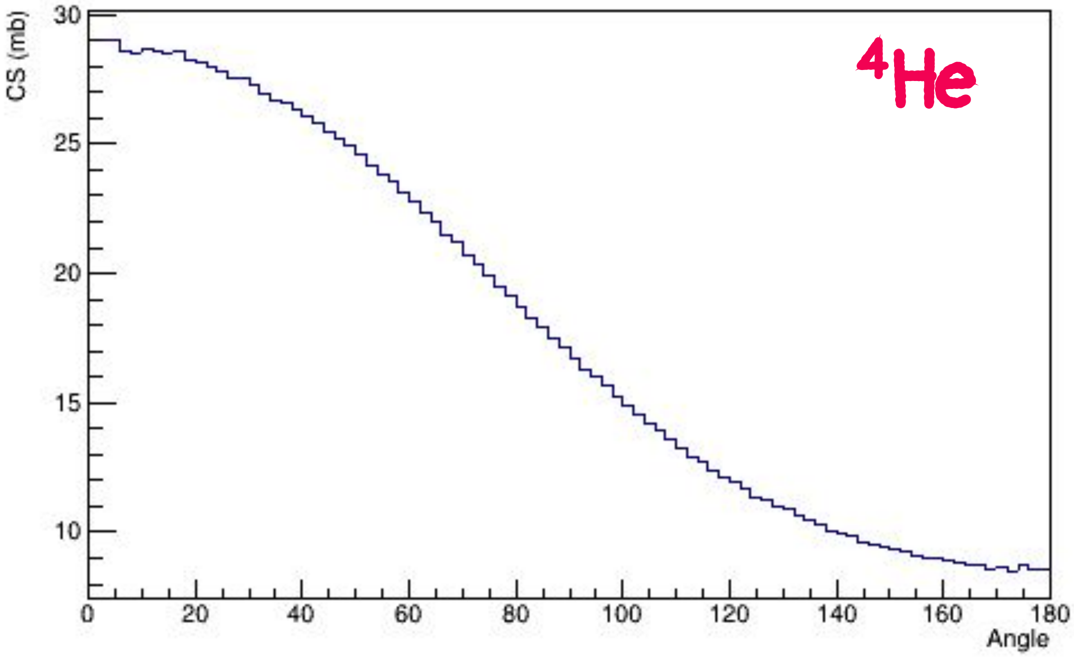

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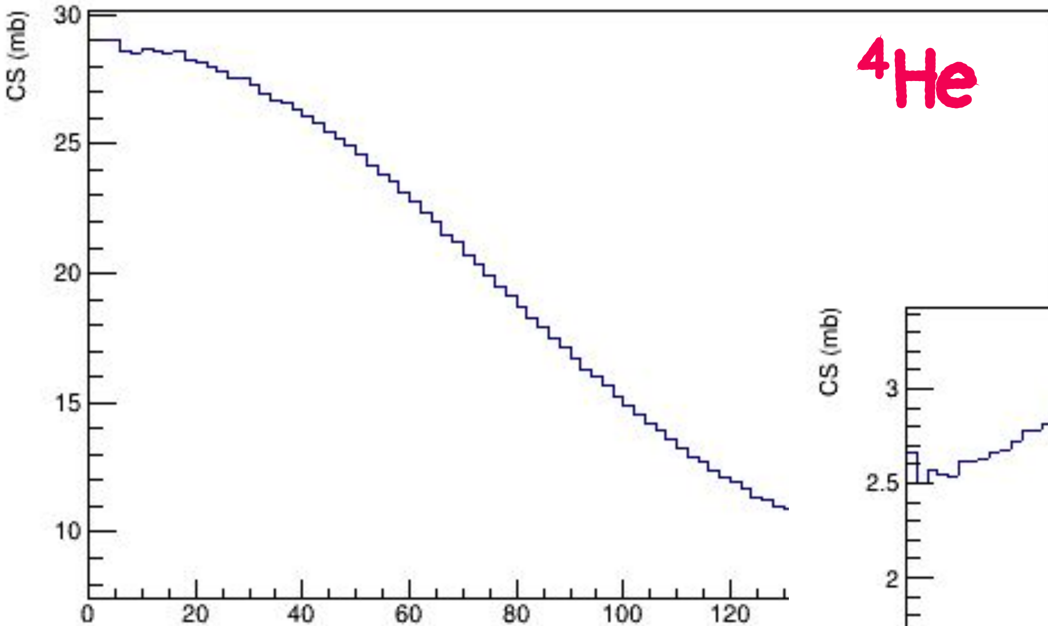
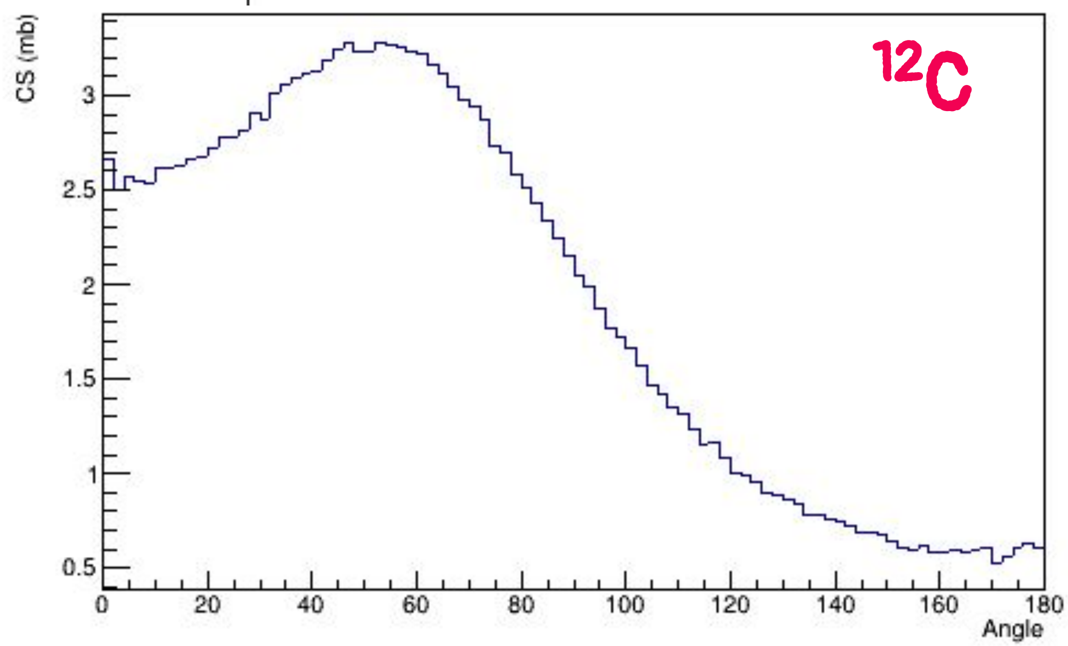


For heavy fragments, the angular distribution present a mean value of 60 degree.



Range of fragments

The range distribution of main fragments produced by proton beam in water have been analyzed, considering different energies **Ep=40,80,120,160,200 MeV/u.**

The energy spectra of fragments are in a range **0<E<20 MeV/u.**

Starting from the energy distribution of fragments, **the range distribution** has been evaluated.

For heavier fragments: the mean range obtained from the distribution is similar to the value reported in Cancers.

For low Z fragments: difference between average range in analytical formula and MC distribution.

FLUKA → R_p column; **Tommasino & Durante** → R_{TD} column

Fragment	$R_p(\mu m)$	$R_{TD}(\mu m)$
^{1}H	1392	-
^{2}H	2117	68.9
^{3}H	1383	-
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^{10}C	9.9	-
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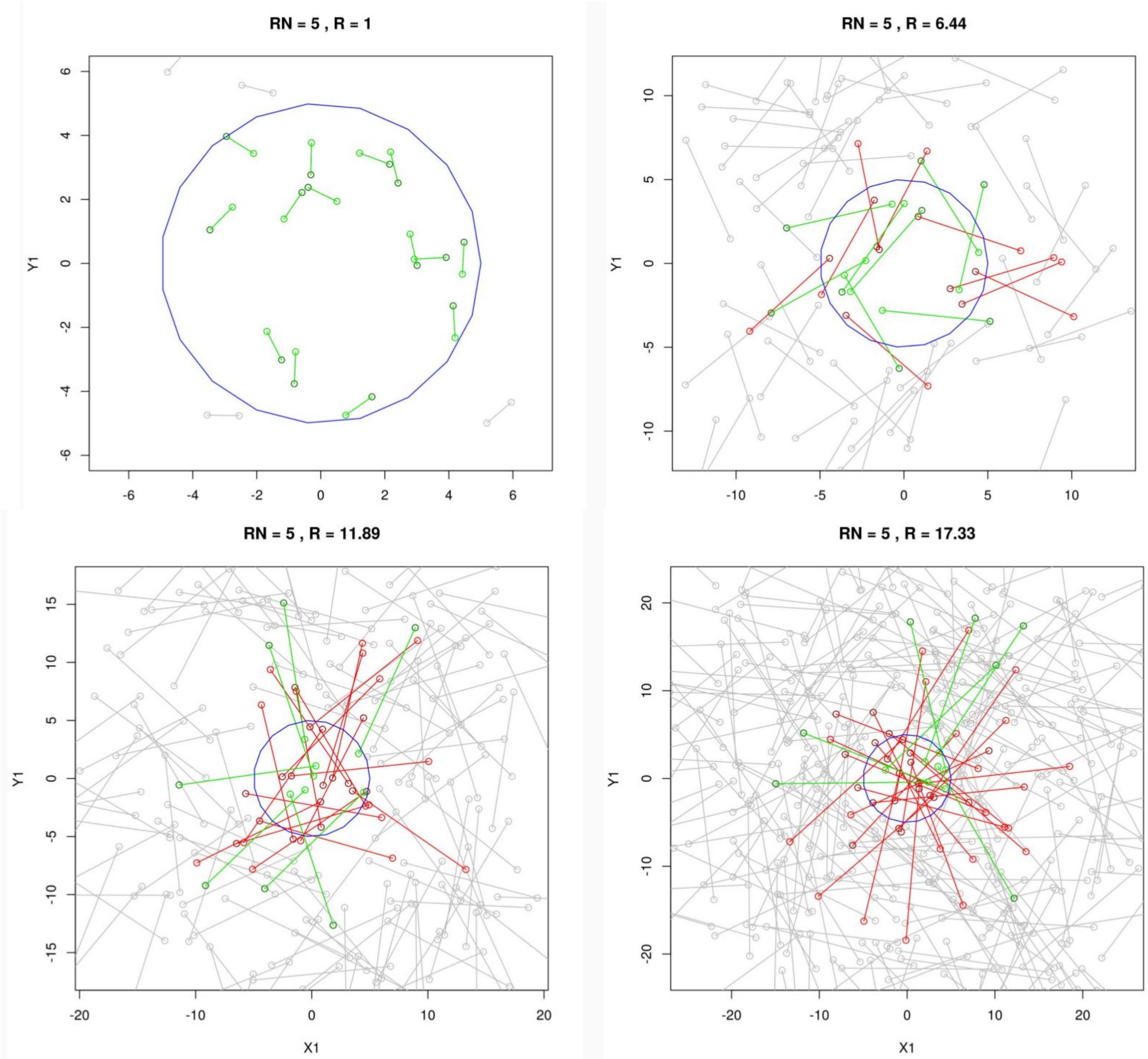
^{13}N	4.4	-
^{14}N	4.1	3.6
^{15}O	2.8	2.3
^{16}O	3.5	-

→ **MC more complete description of physical processes**

→ **Range is more reliable**

Fragments Range

Courtesy of A. Attili



Fragments Range

Courtesy of A. Attili

SRIM evaluation of projected range as a function of energy:

Low Z fragments
R> cell nucleus

Heavier fragments
R< cell nucleus
Colocalization effects