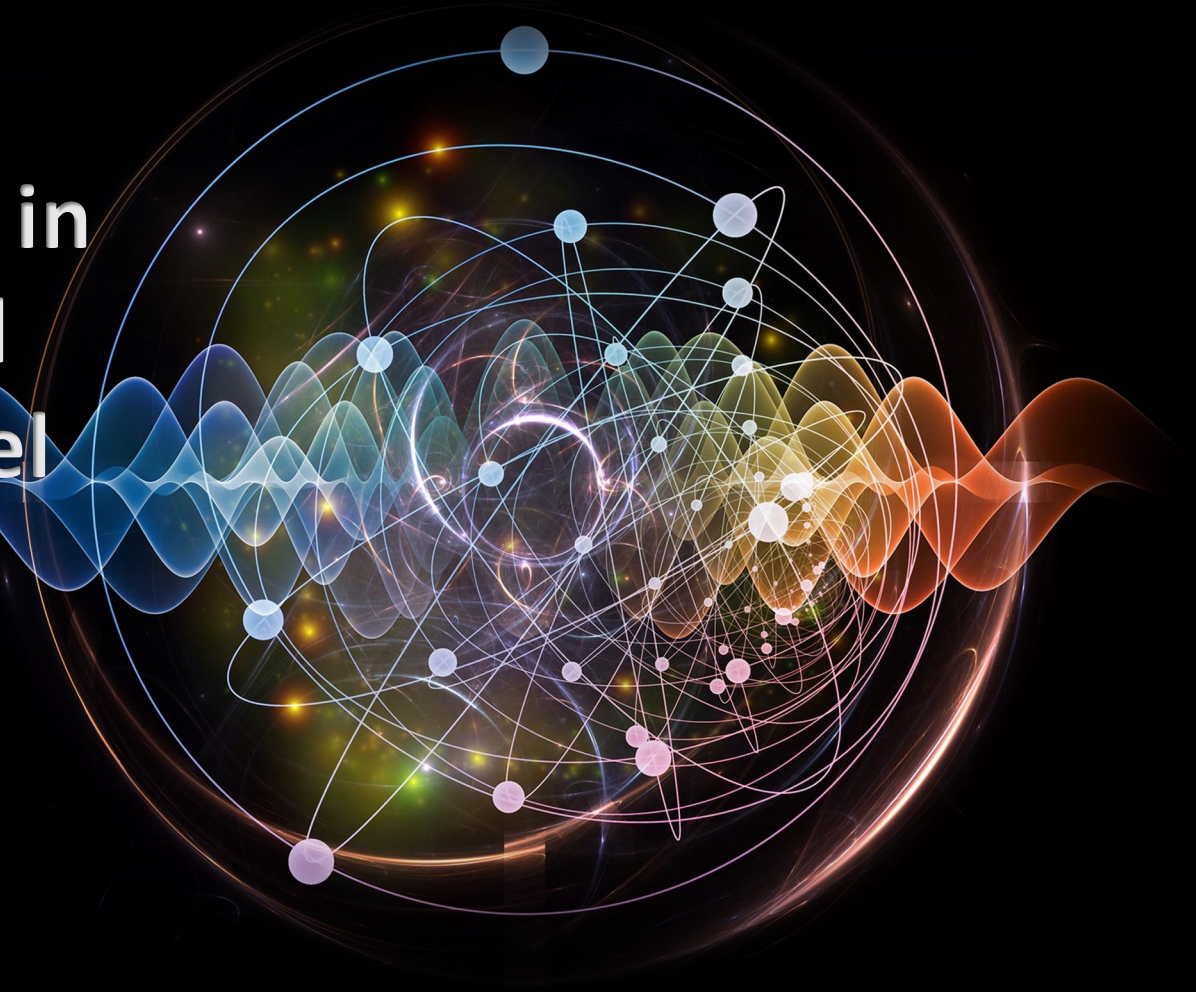


Secondary fragment production in ion beam therapy: experimental measurements for nuclear model improvement

L. Gesson, J. Gross, C. Mozzi, C. Reibel, Ch. Finck, S. Higuere, T.D. Lê, A. Sécher, M. Pullia, N. Arbor, M. Vanstalle



01. Secondary
particles in
heavy ion therapy

Secondary particles in heavy ion therapy

Cancer treatments

» First cause of death in Europe and North America



Secondary particles in heavy ion therapy

Cancer treatments

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Secondary particles in heavy ion therapy

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Secondary particles in heavy ion therapy

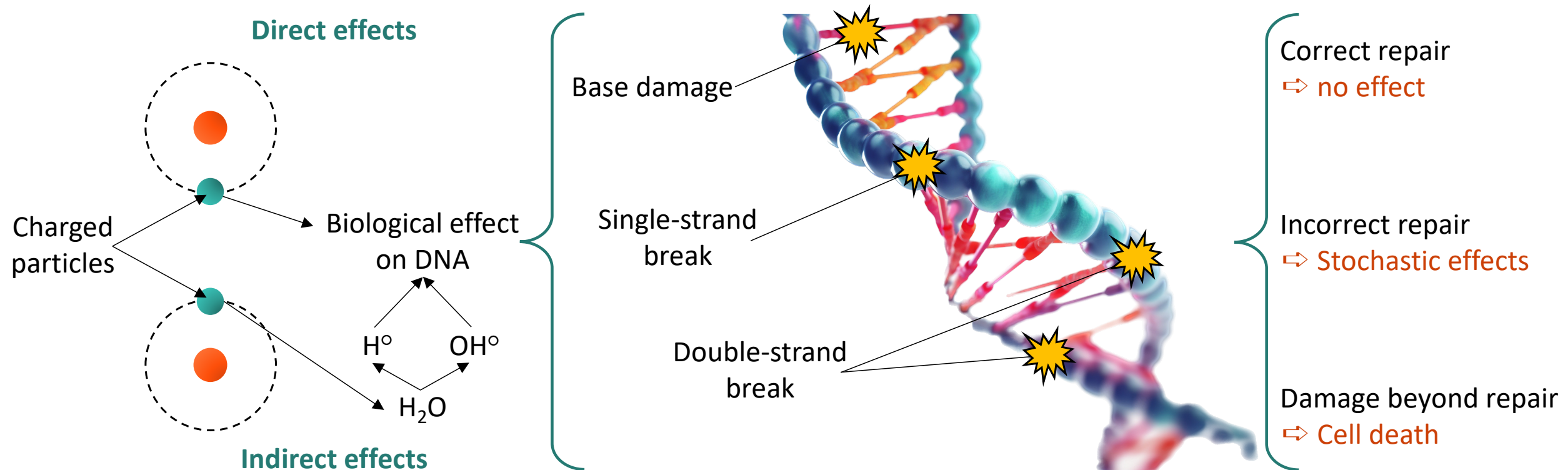
Cancer treatments

» First cause of death in Europe and North America



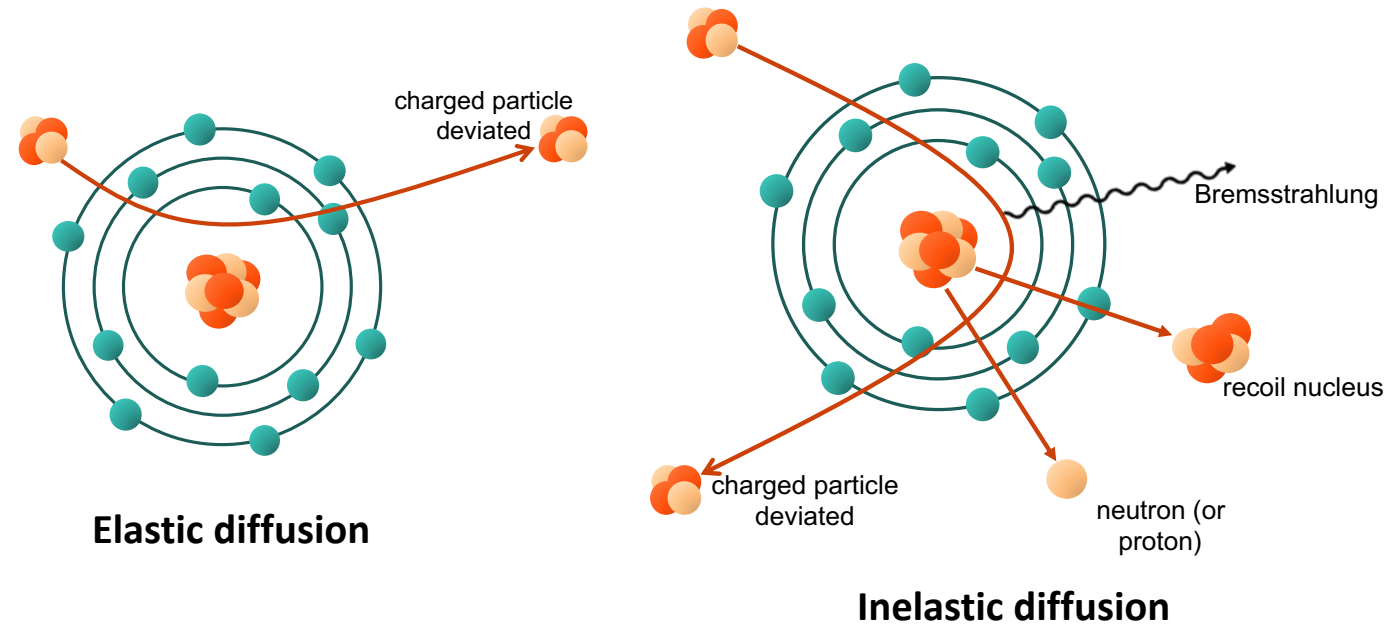
Secondary particles in heavy ion therapy

Charged particles effects



Secondary particles in heavy ion therapy

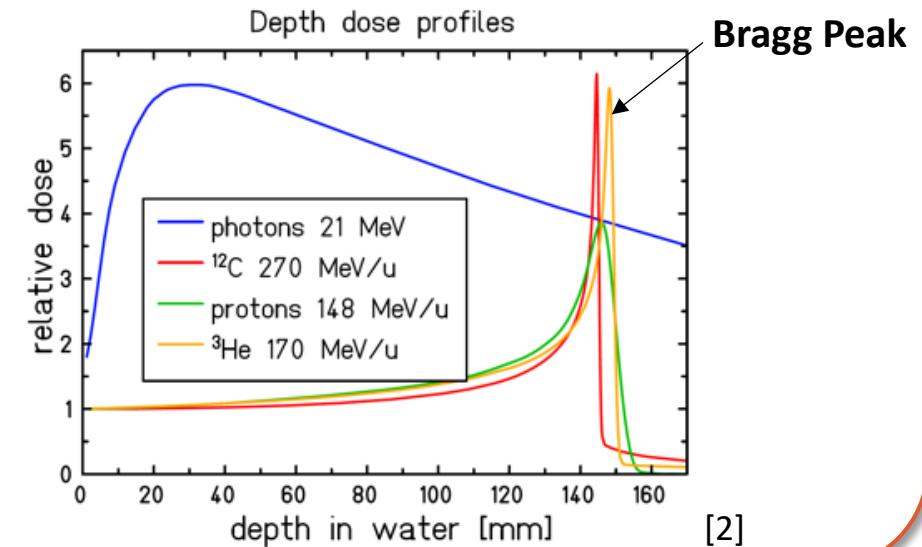
Charged particles interactions



Stopping power

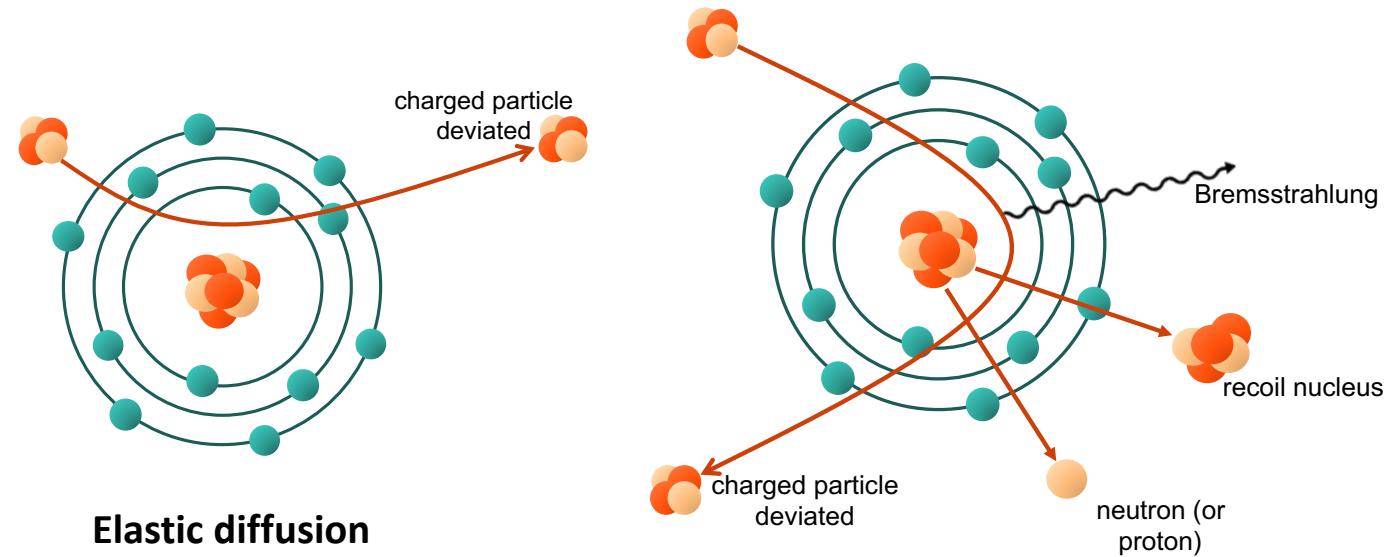
→ Slowing process dominated by inelastic collisions with target e^-

$$\rightarrow \frac{dE}{dx} = \frac{4\pi e^4 z_t z_p^2}{m_e v^2} \left[\ln \frac{2m_e v^2}{\langle I \rangle} - \ln(1 - \beta^2) - \beta^2 - \frac{c}{z_t} - \frac{\delta}{2} \right]$$



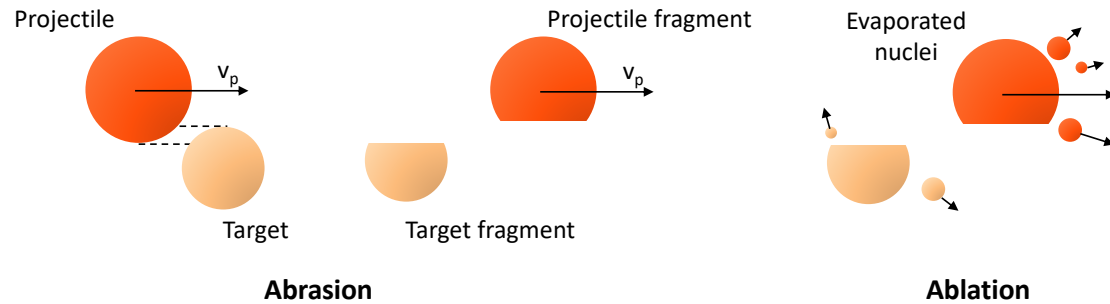
Secondary particles in heavy ion therapy

Charged particles interactions



Elastic diffusion

Inelastic diffusion



Fragmentation

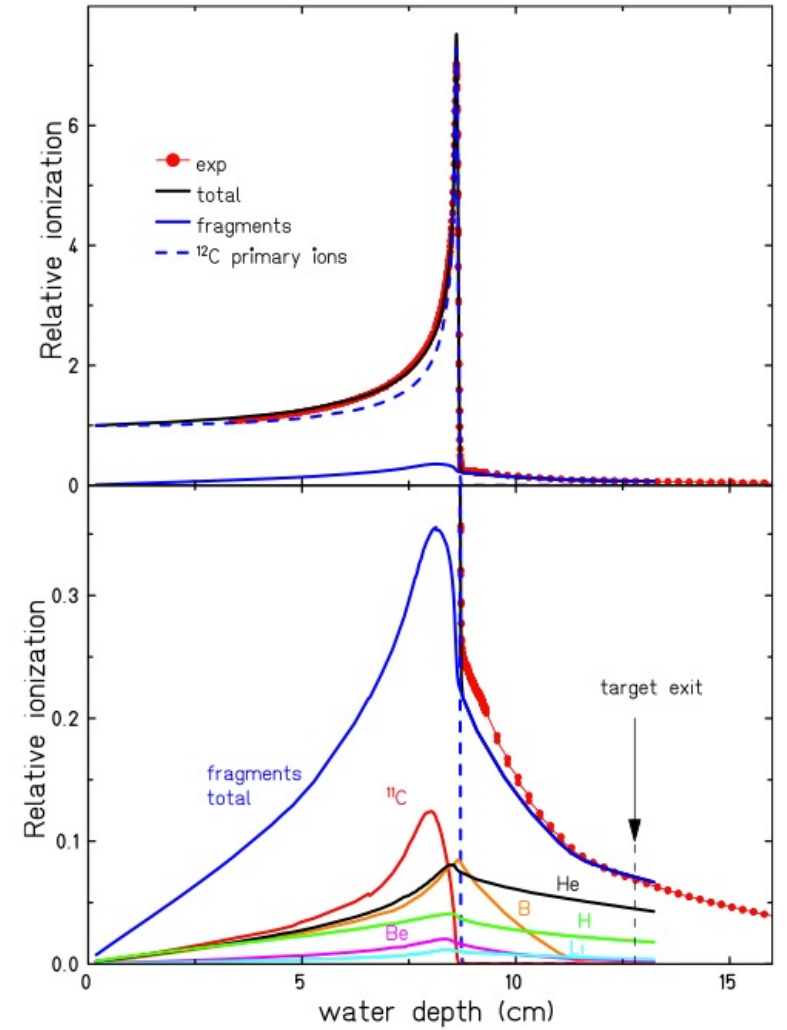


Figure - Bragg curve of a 200 MeV/u ^{12}C ion beam in water with the Monte-Carlo code PHITS [1]

Secondary particles in heavy ion therapy

Uncertainties



Secondary particles dose distribution not taken into account

- ~ 5% of total dose in Bragg peak (BP)
- dose tail after BP
- higher Linear Energy Transfer
- interact outside tumor → healthy tissues irradiation

Secondary particles in heavy ion therapy

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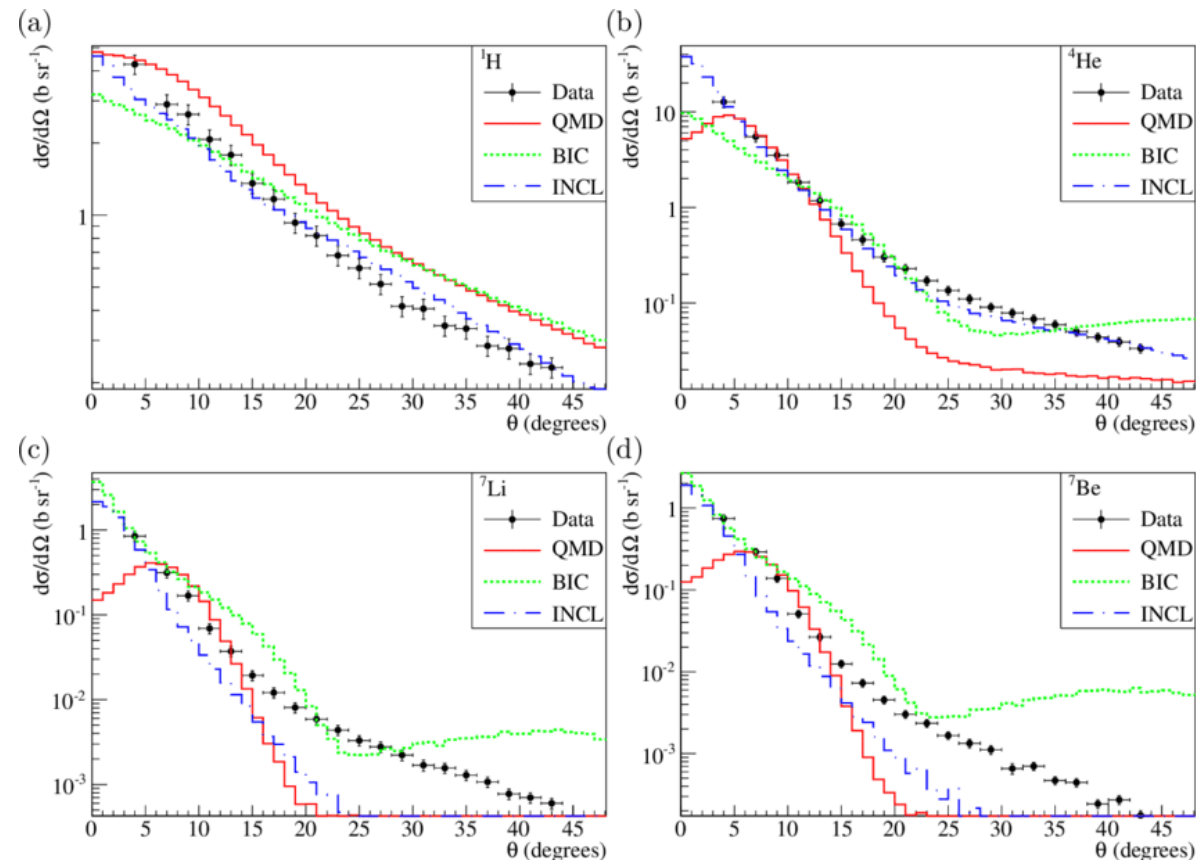


Figure - Absolute differential angular cross-sections of protons, ^4He , ^6Li , ^7Be , obtained for the carbon target. [7]

Secondary particles in heavy ion therapy

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- Incomplete cross-section data

- Discrepancies between hadronic models in MC
MC and experiment

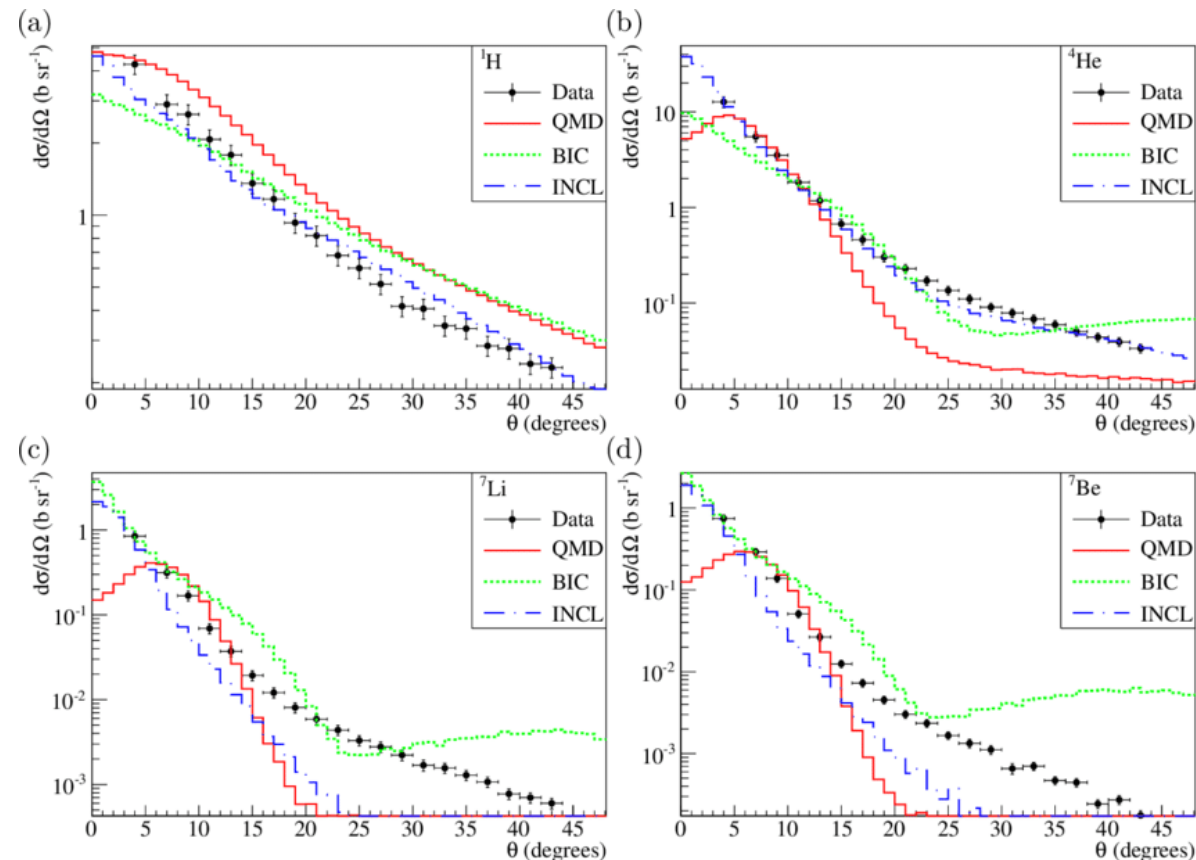


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MC and experiment

**Enhance nuclear reaction models to
better understand secondary
particles production**

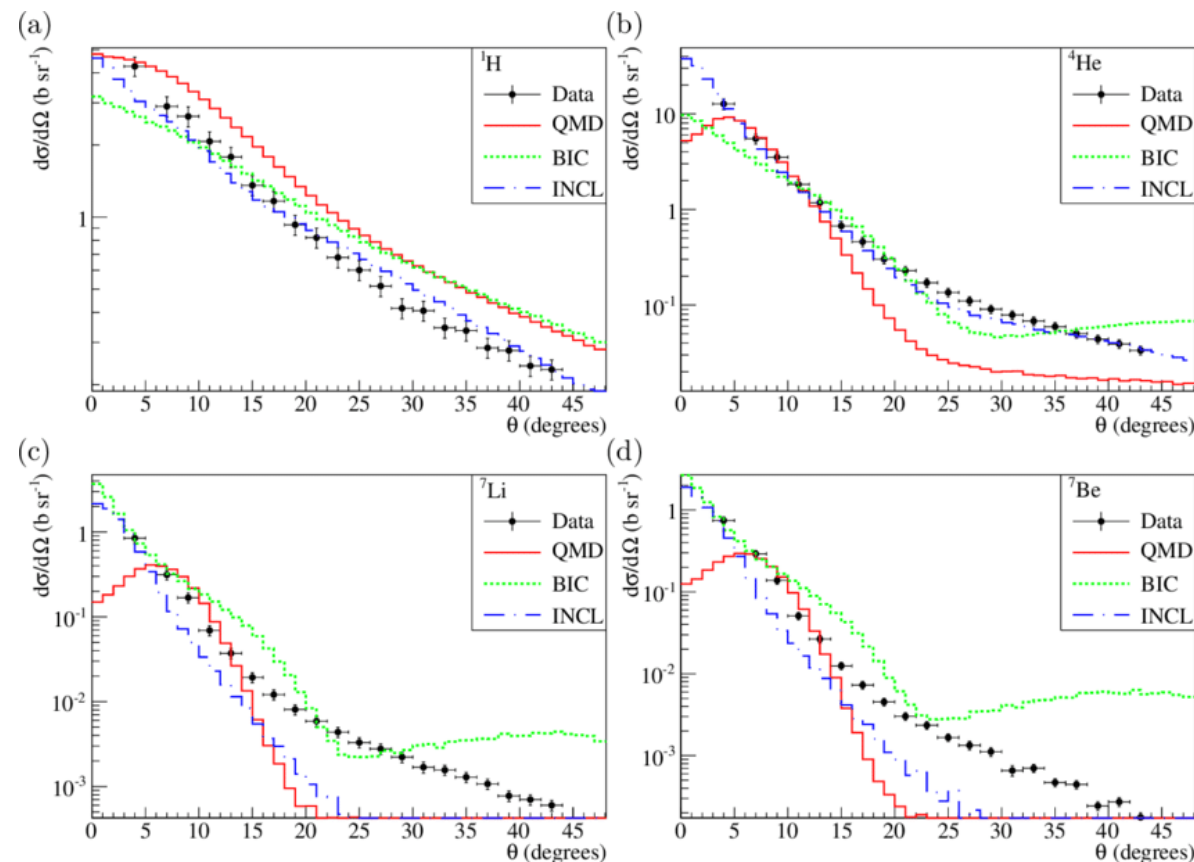


Figure - Absolute differential angular cross-sections of protons, ^4He , ^6Li , ^7Be , obtained for the carbon target. [7]

Secondary particles in heavy ion therapy

Uncertainties

Enhance nuclear reaction models to better understand secondary particles production

- Cross-sections experimental measurements (ex. FOOT collaboration experiments)
- Hadronic models theory improvement (ex. DIno deep learning algorithm)
- More “simpler” and “direct” measurements (statistics, energies, angular distribution)

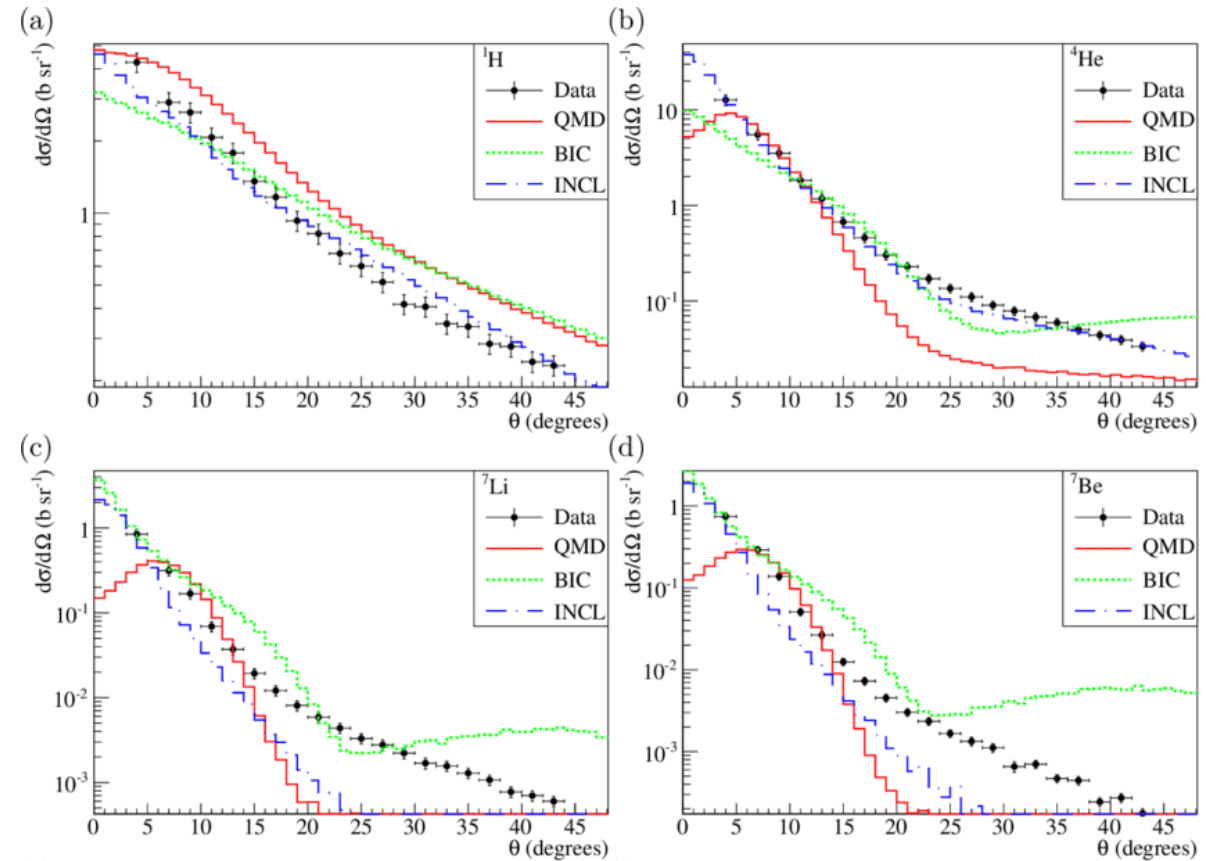


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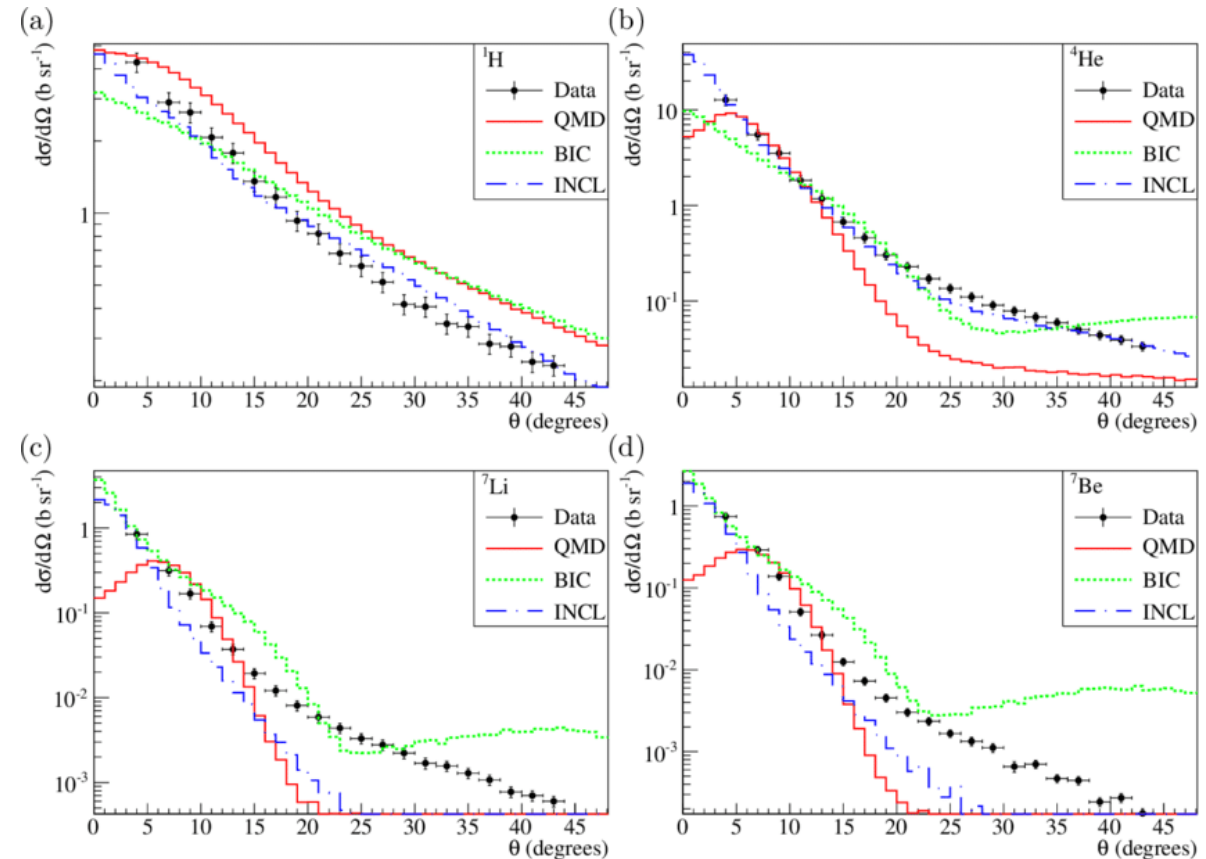


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02. CLINM – Secondary particles measurements



Secondary particles measurement

CLINM project



CLINM – Cross-Sections of Light Ion and Neutron Measurements

- Combined measurement of secondary particles and radiolysis effectiveness with radiochemistry team (IPHC)
- Secondary charged particle identification + γ + neutrons of high energy measurement

Secondary particles measurement

CLINM project

CLINM – Cross-Sections of Light Ion and Neutron Measurements

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Secondary particles measurement

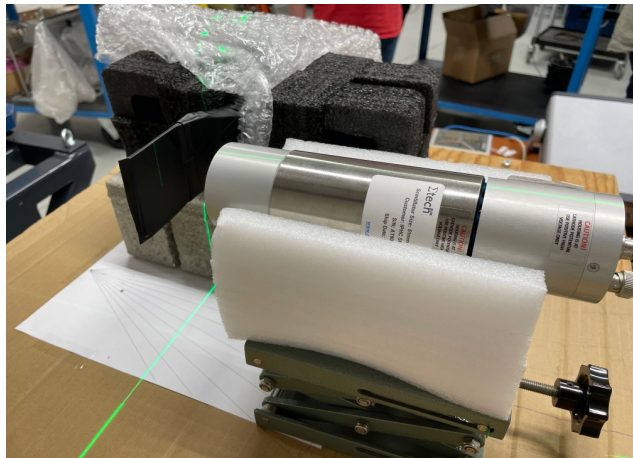
CLINM project

CLINM – Cross-Sections of Light Ion and Neutron Measurements

- Combined measurement of secondary particles and radiolysis effectiveness with radiochemistry team (IPHC)
- Secondary charged particle identification + γ + neutrons of high energy measurement

ΔE -E telescope

CeBr₃ crystal scintillator + plastic scintillator

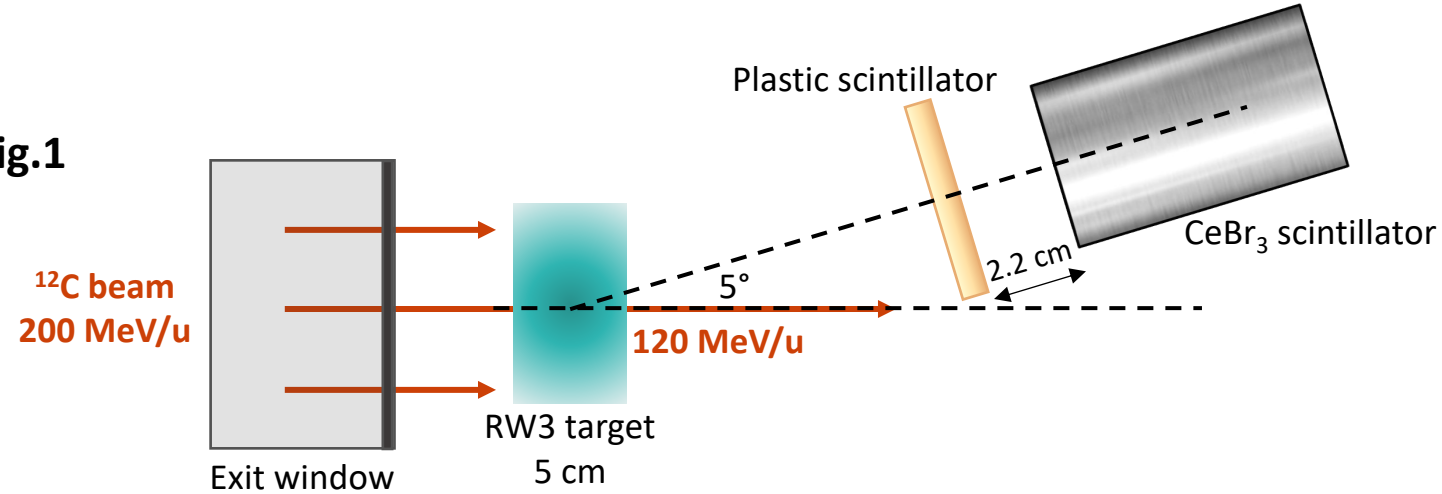


Facility	Ion type	Energy
GSI - Darmstadt	^{12}C	110 - 180 MeV/u
CNAO - Pavia	^{12}C	120 - 200 MeV/u
	^1H	80 – 200 MeV/u

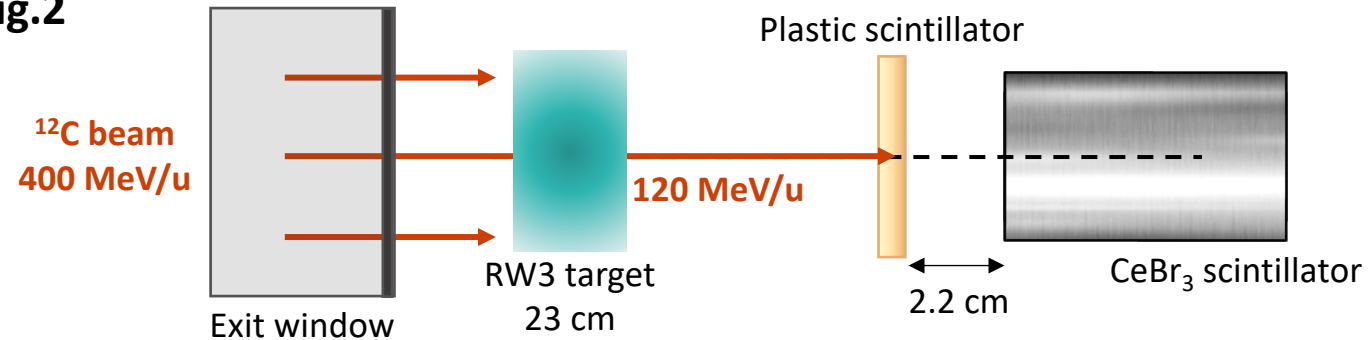
Secondary particles measurement

Experiment at CNAO

Config.1



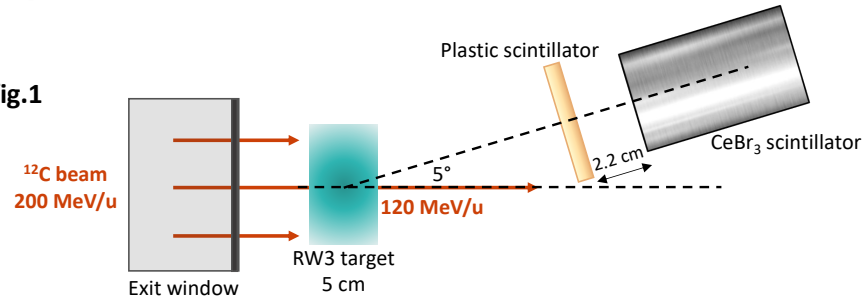
Config.2



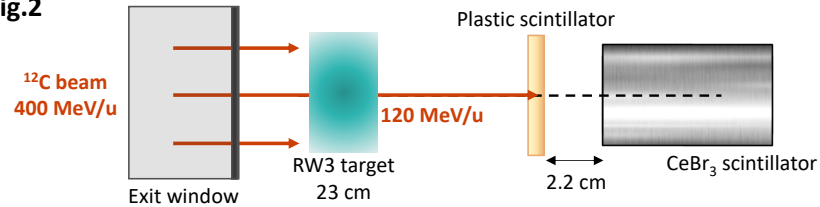
Secondary particles measurement

Experiment at CNAO

Config.1

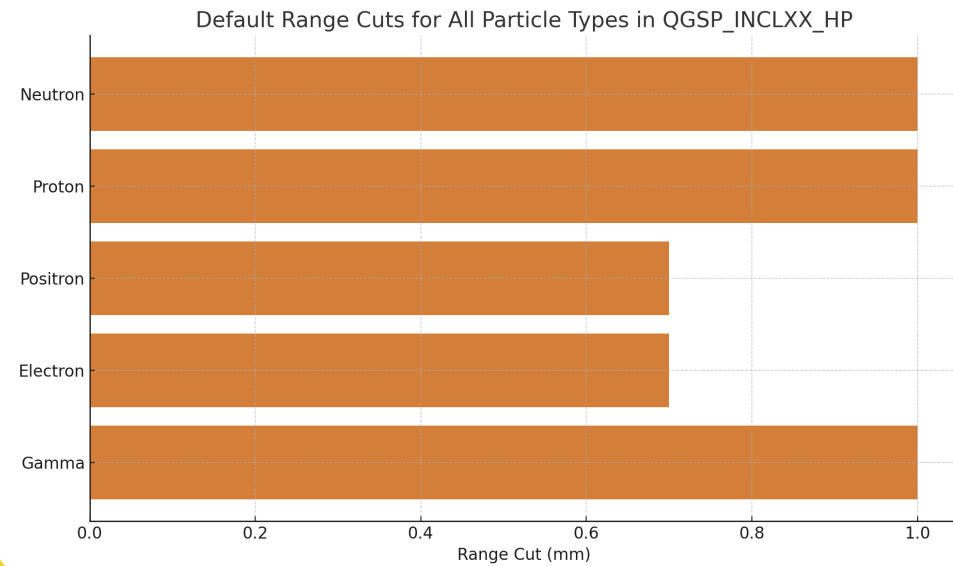


Config.2



MC Geant4 10.07 simulation

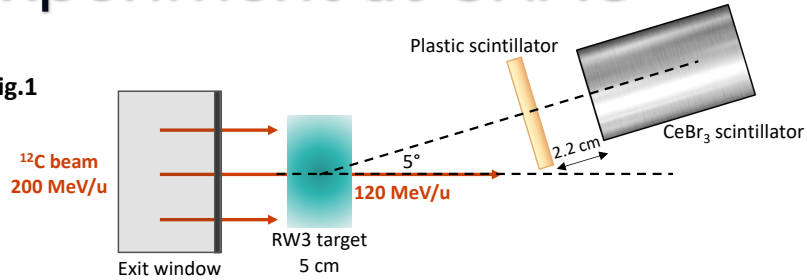
- INCL++ physic list
- Experimental setup materials, geometry detector resolutions
- Number of events : 200 000 000
- Gaussian beam energy
- Particle cuts



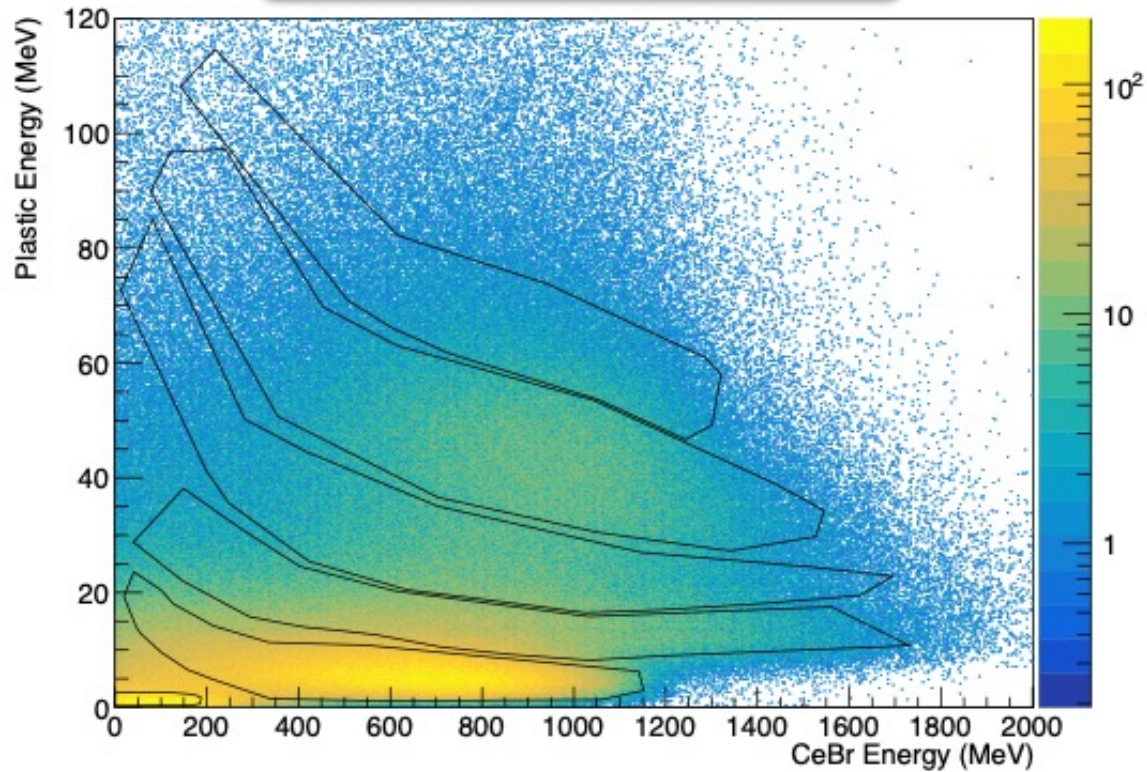
Secondary particles measurement

Experiment at CNAO

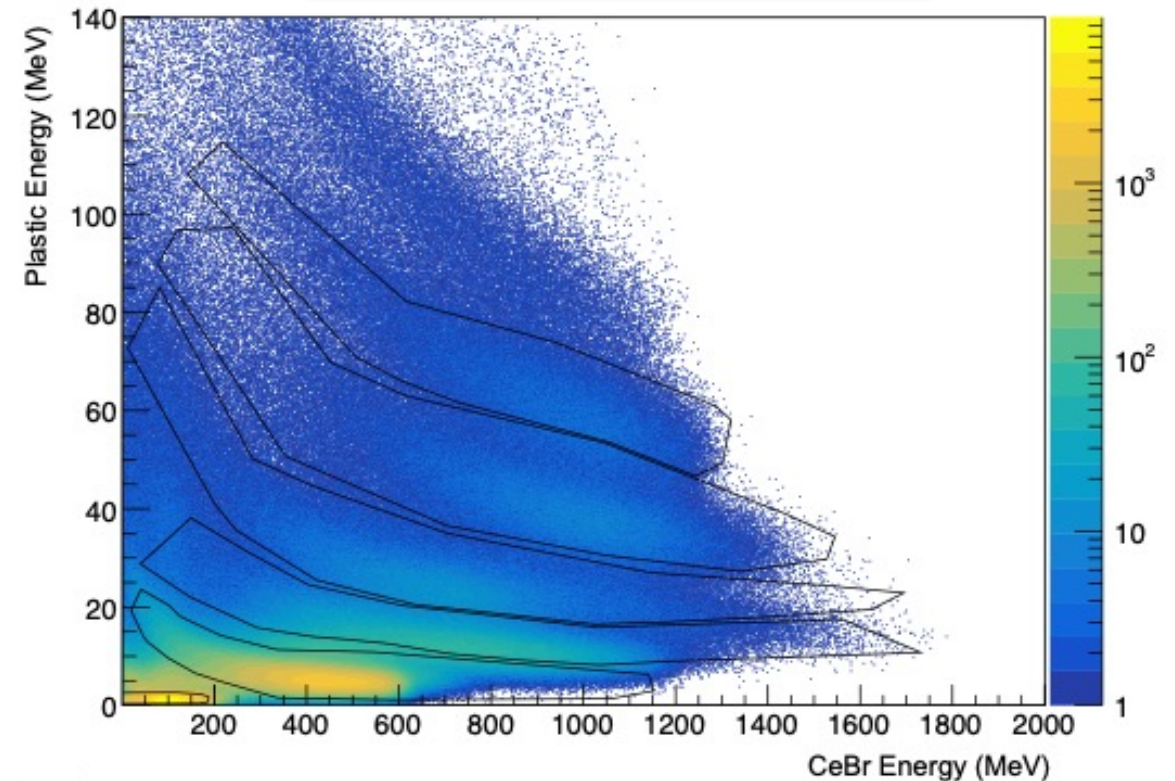
Config.1



Experimental data



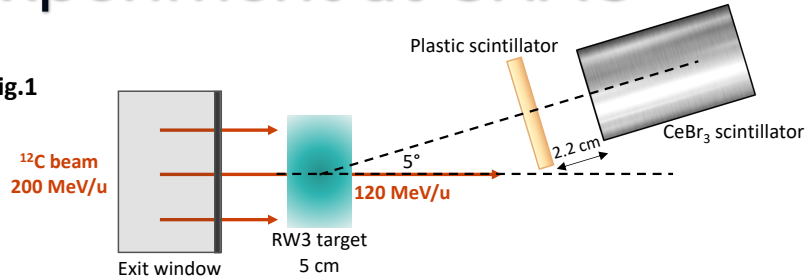
Geant 4 simulation



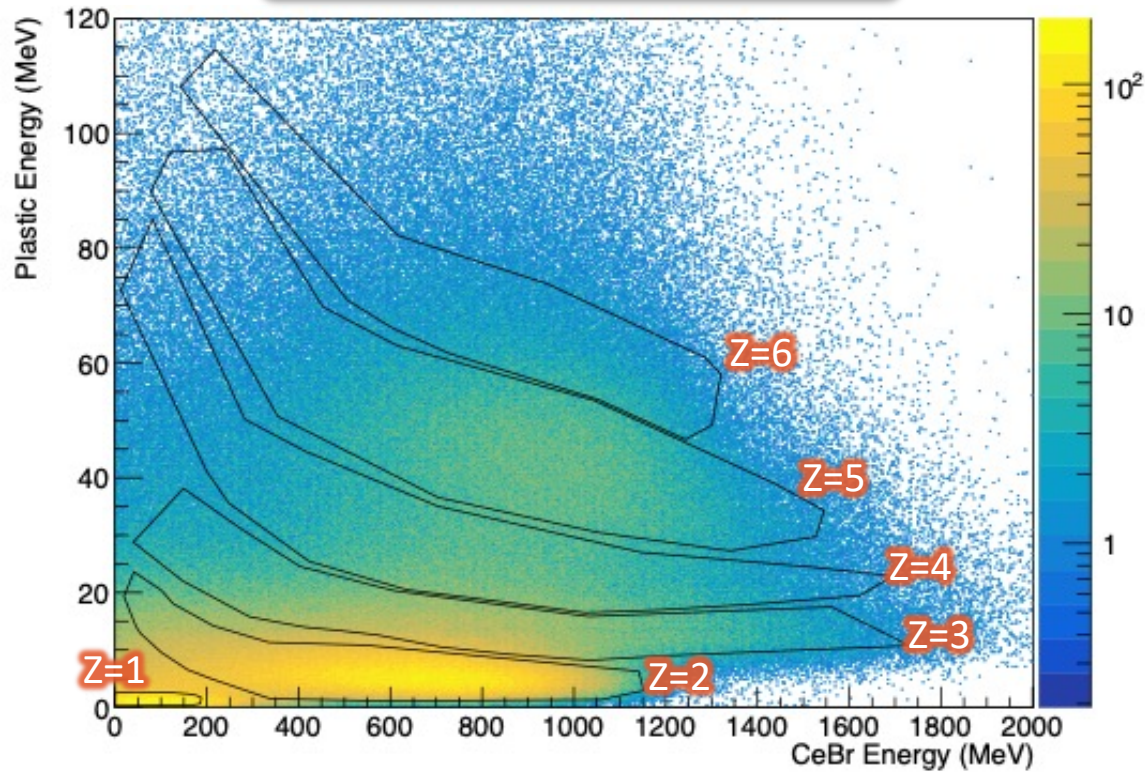
Secondary particles measurement

Experiment at CNAO

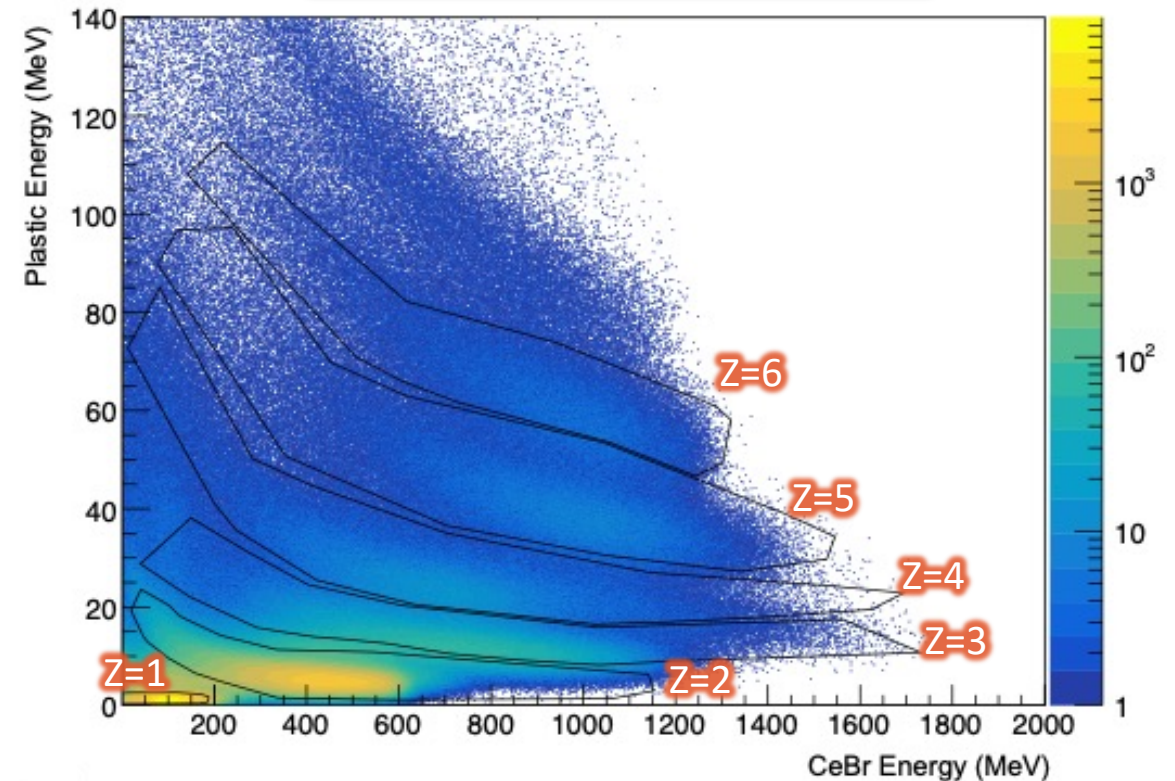
Config.1



Experimental data



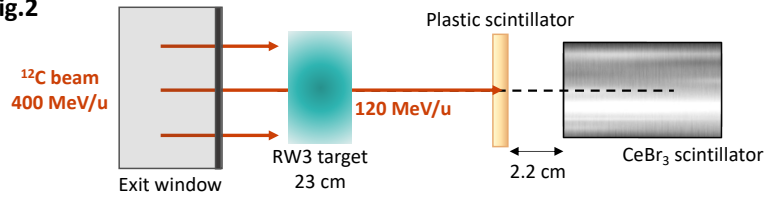
Geant 4 simulation



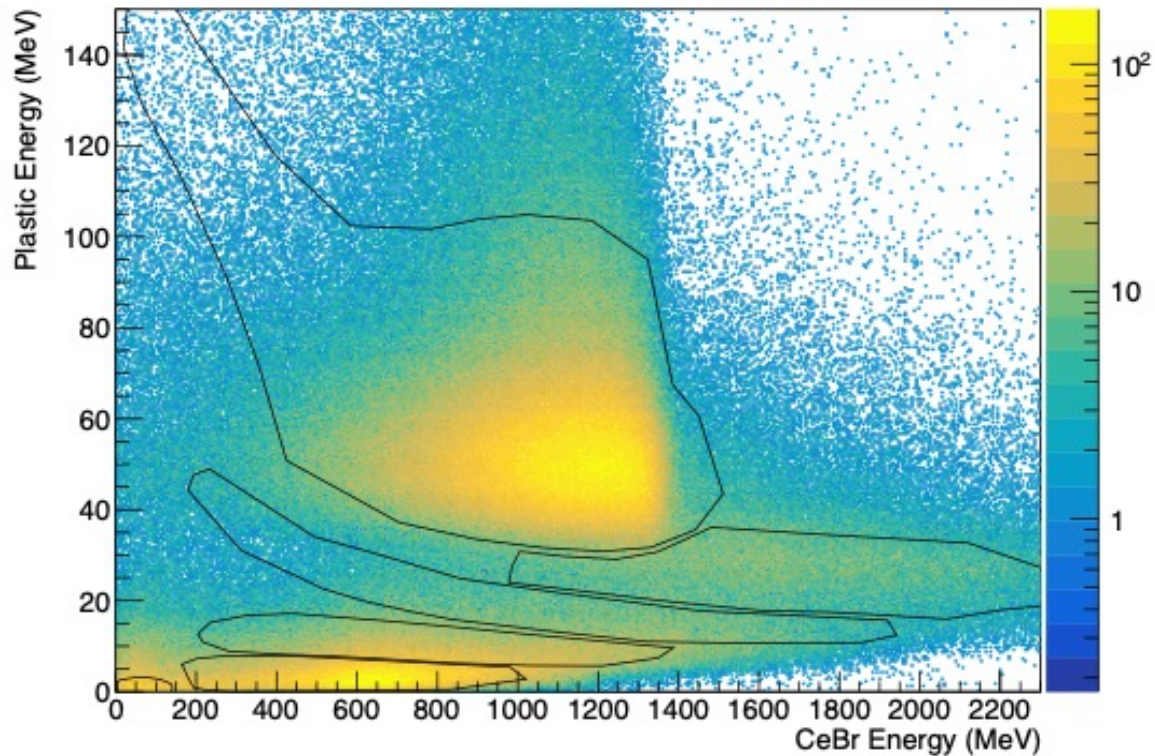
Secondary particles measurement

Experiment at CNAO

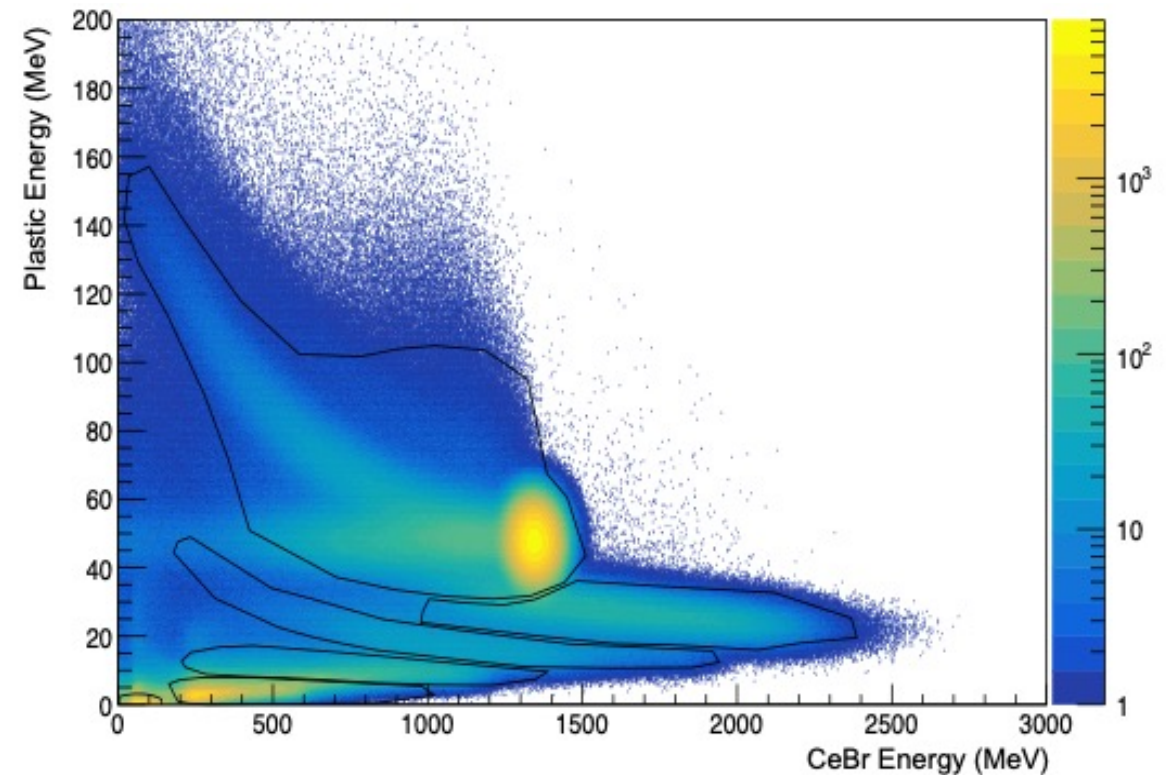
Config.2



Experimental data



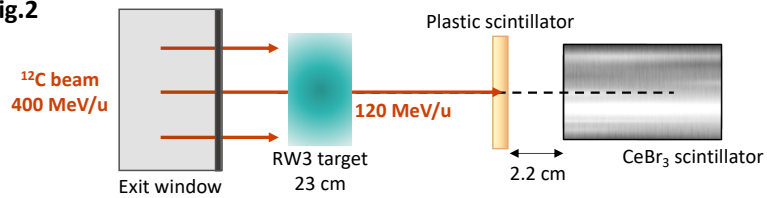
Geant 4 simulation



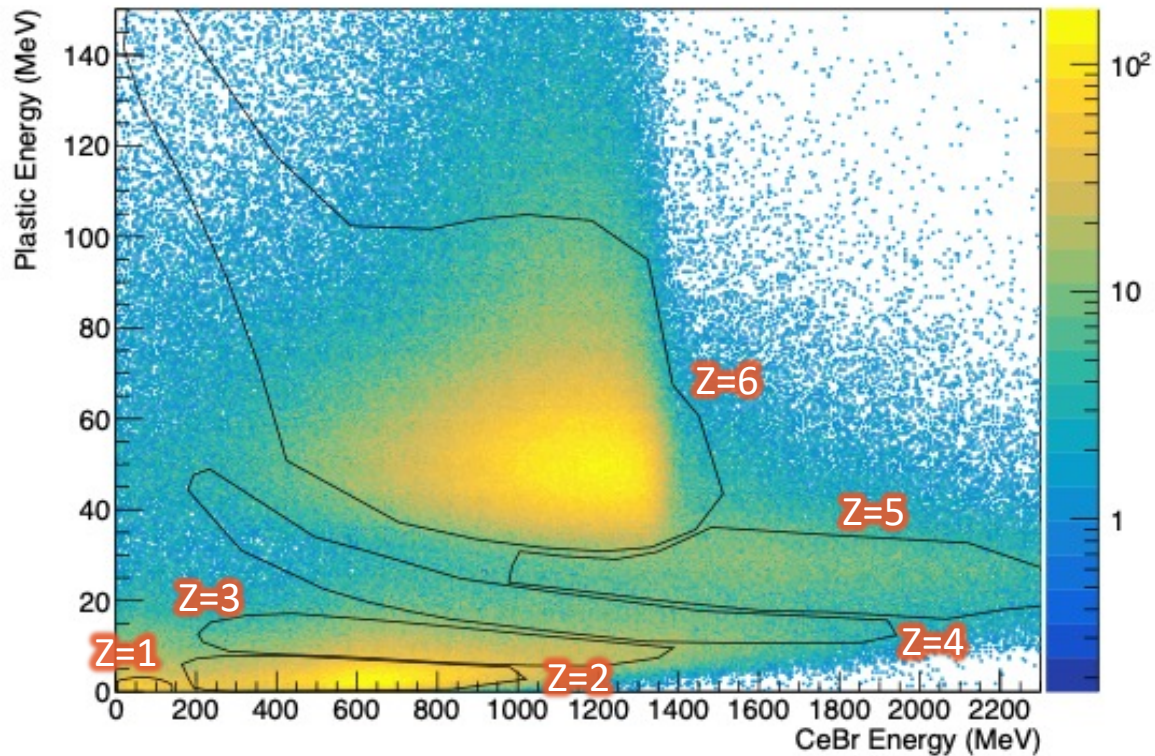
Secondary particles measurement

Experiment at CNAO

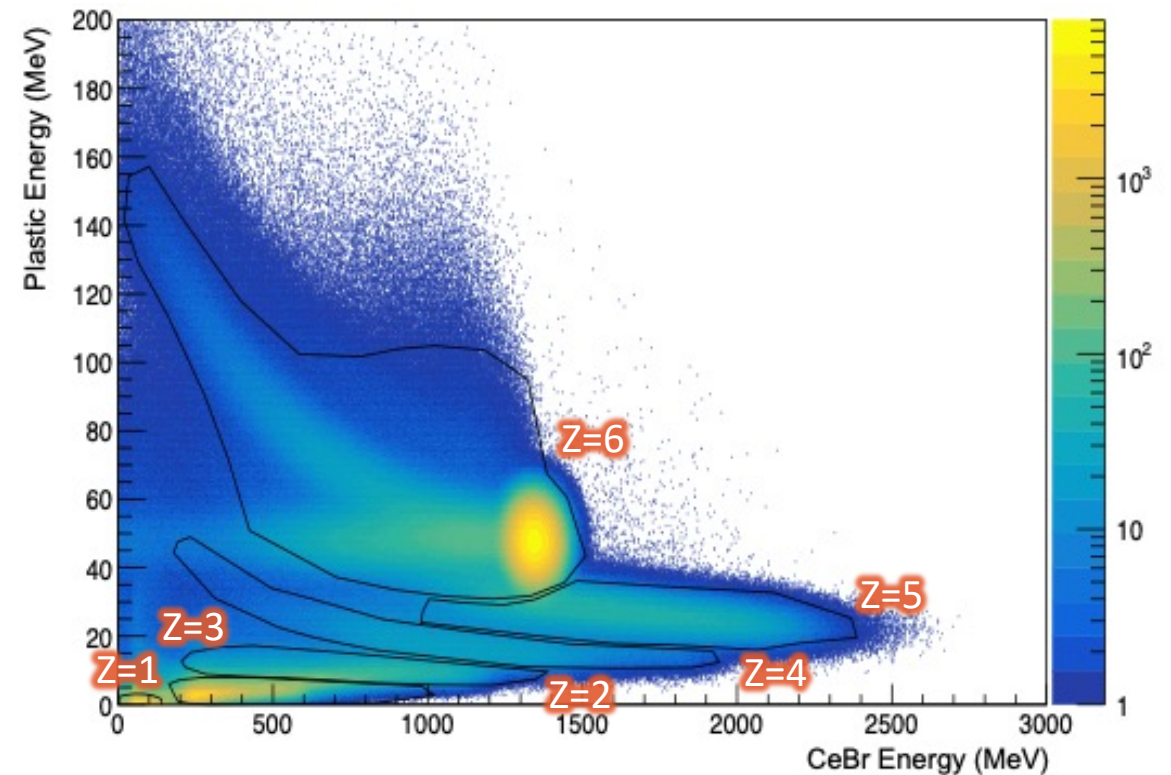
Config.2



Experimental data



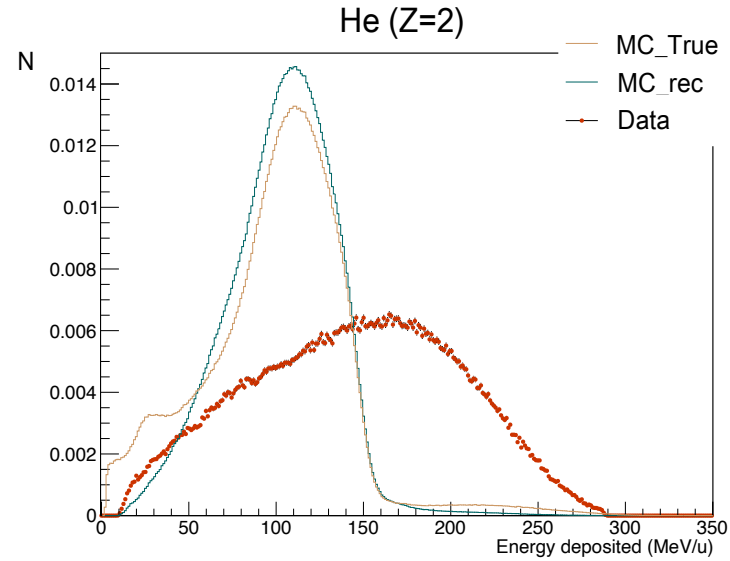
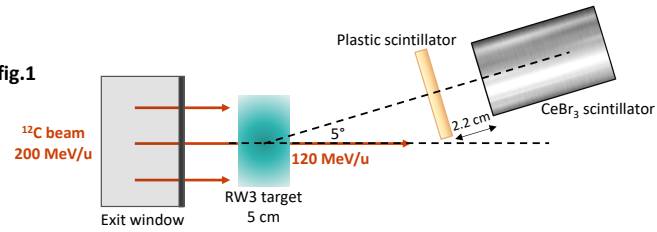
Geant 4 simulation



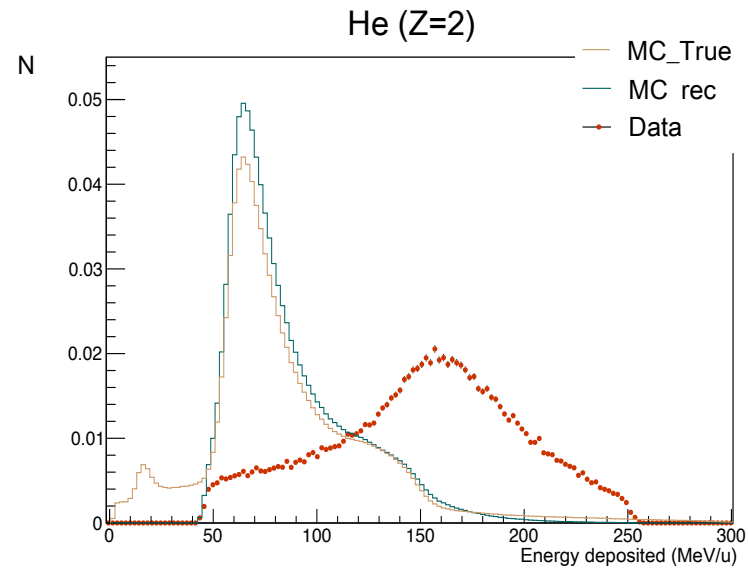
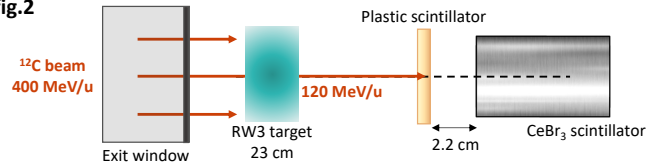
Secondary particles measurement

Experiment at CNAO

Config.1



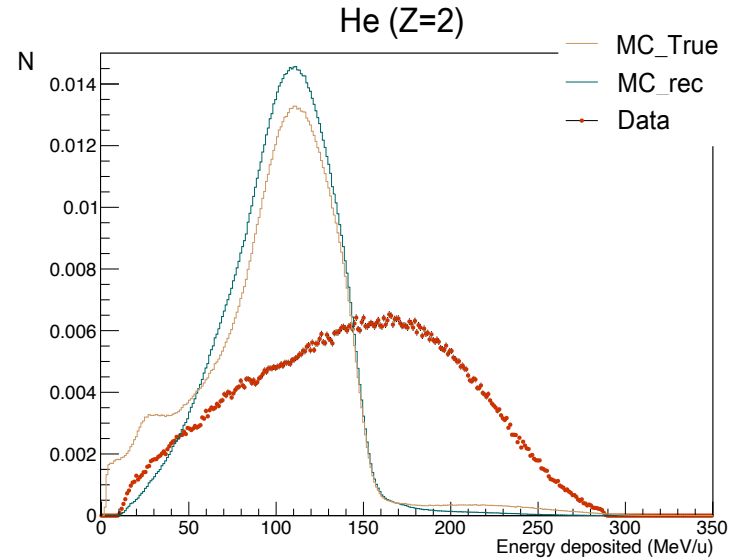
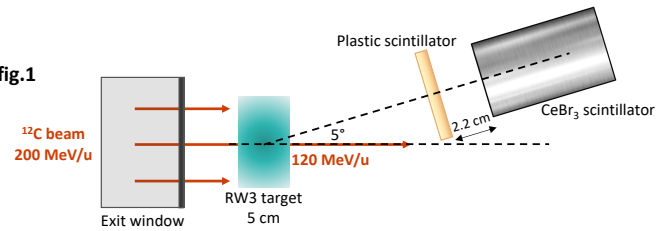
Config.2



Secondary particles measurement

Experiment at CNAO

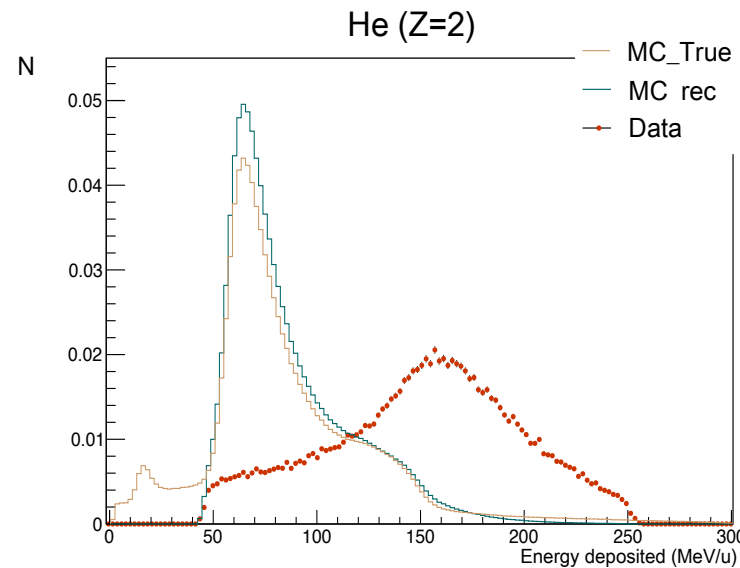
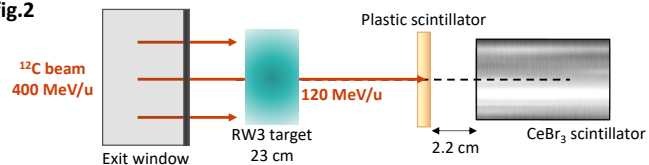
Config.1



Z=2 Helium

- Inability of Geant4 to model carbon break-up
$$^{12}\text{C} \rightarrow 3\alpha$$
$$^{12}\text{C} \rightarrow 2\alpha + \text{residuals (light nuclei)}$$
- α Pile-up in detectors

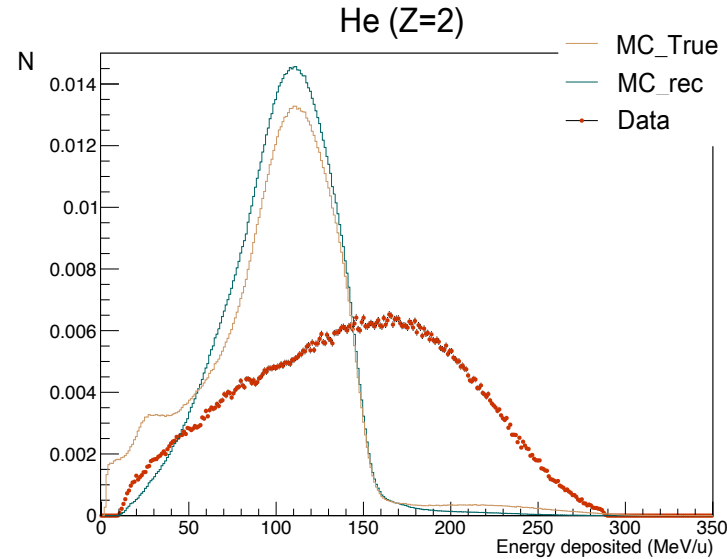
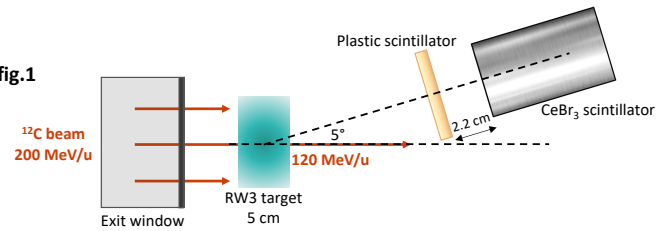
Config.2



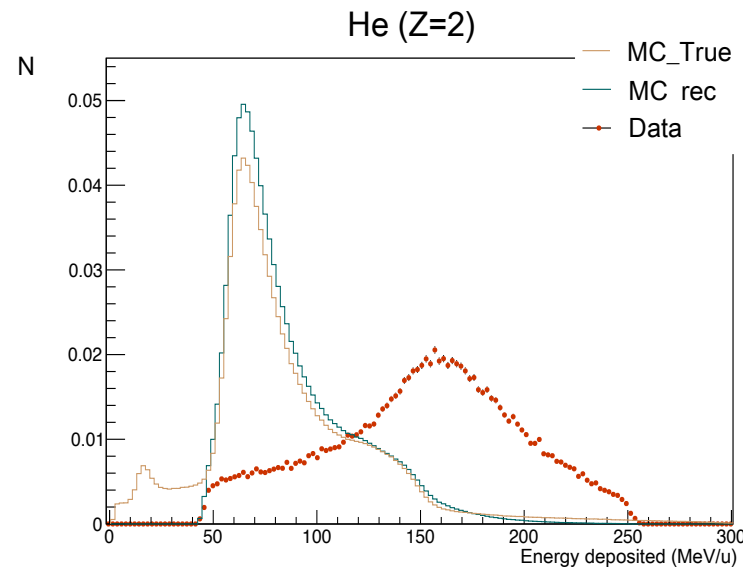
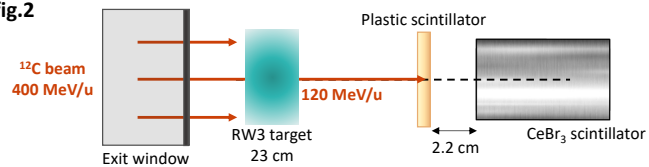
Secondary particles measurement

Experiment at CNAO

Config.1



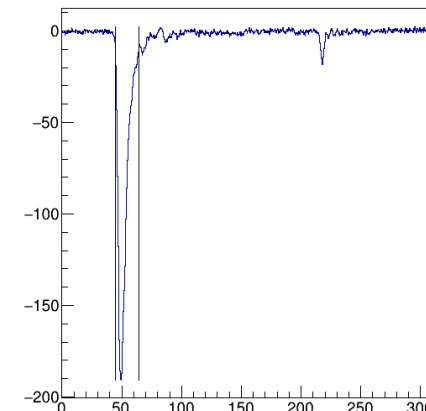
Config.2



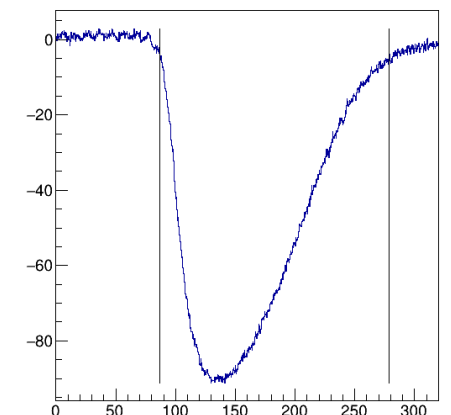
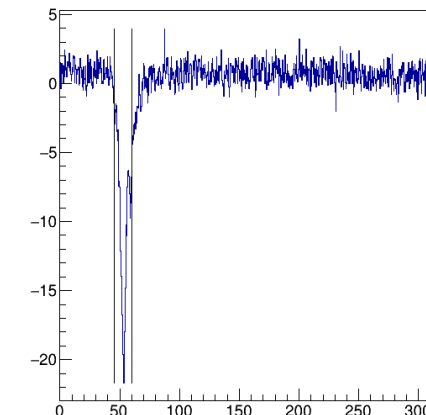
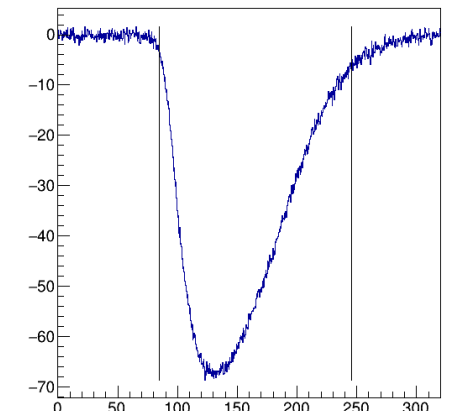
Z=2 Helium

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 $^{12}\text{C} \rightarrow 2\alpha + \text{residuals (light nuclei)}$
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Plastic



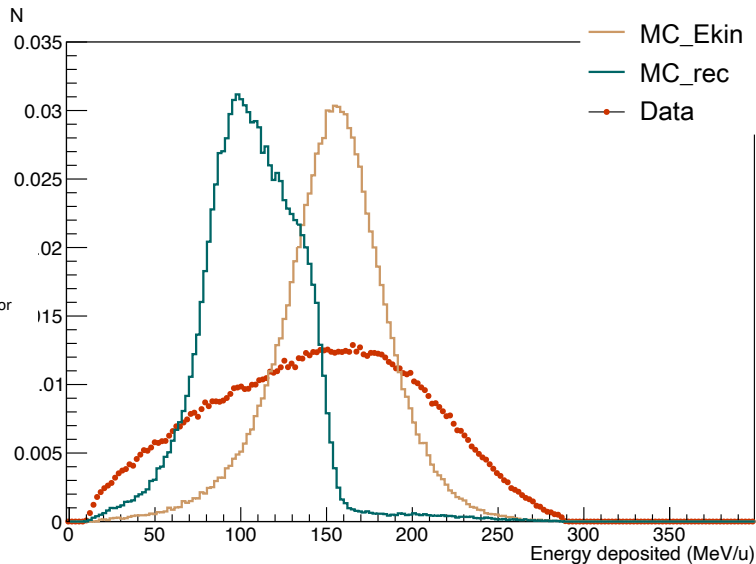
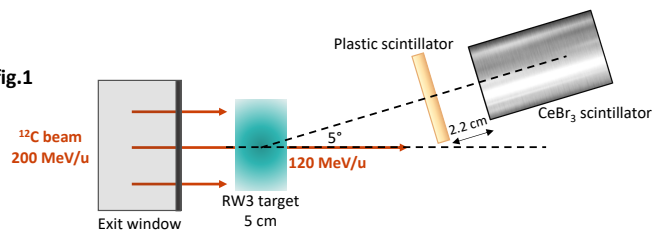
CeBr₃



Secondary particles measurement

Experiment at CNAO

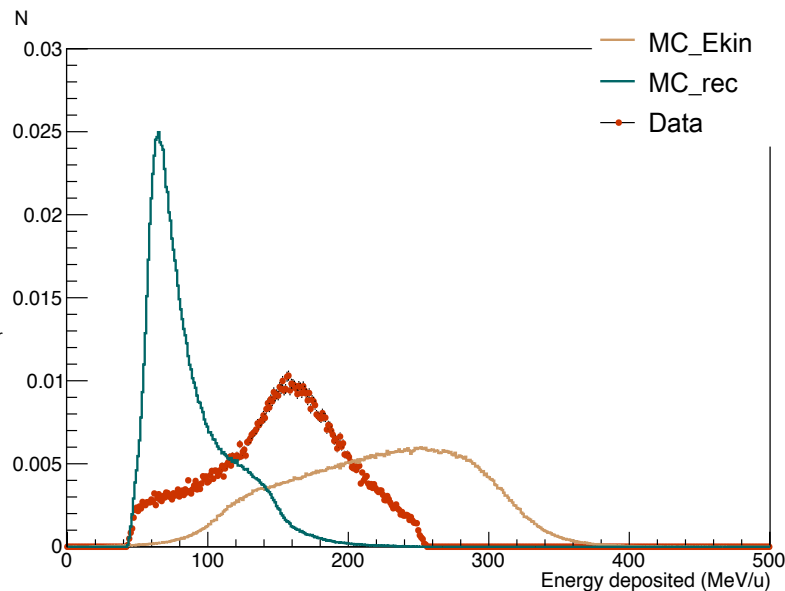
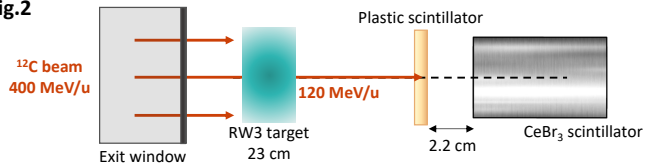
Config.1



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Config.2

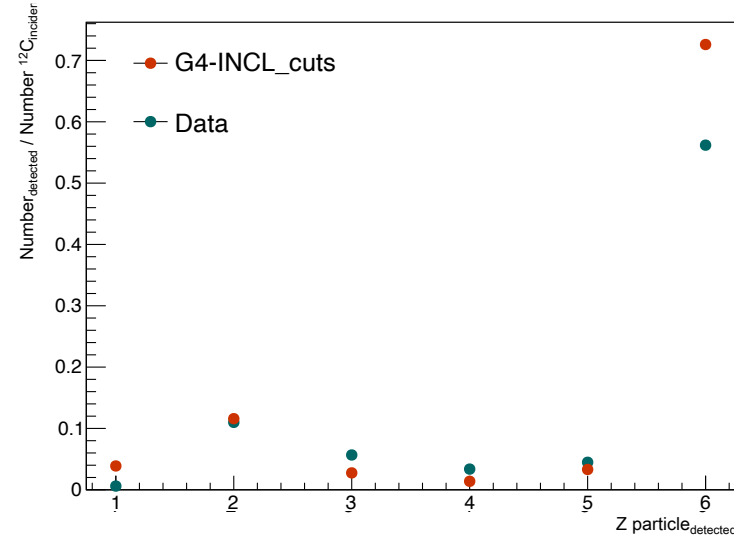
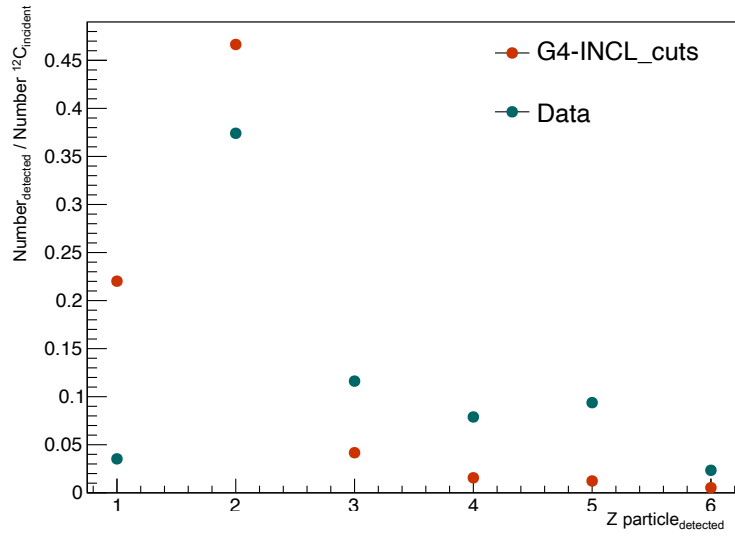


	Config. 1	Config. 2
He energy after target	130 MeV/u	260 MeV/u
He initial energy	200 MeV/u	400 MeV/u

- Each α should have half or third of initial energy
- Show the simulation inability to conserve energy during nuclear breakup process

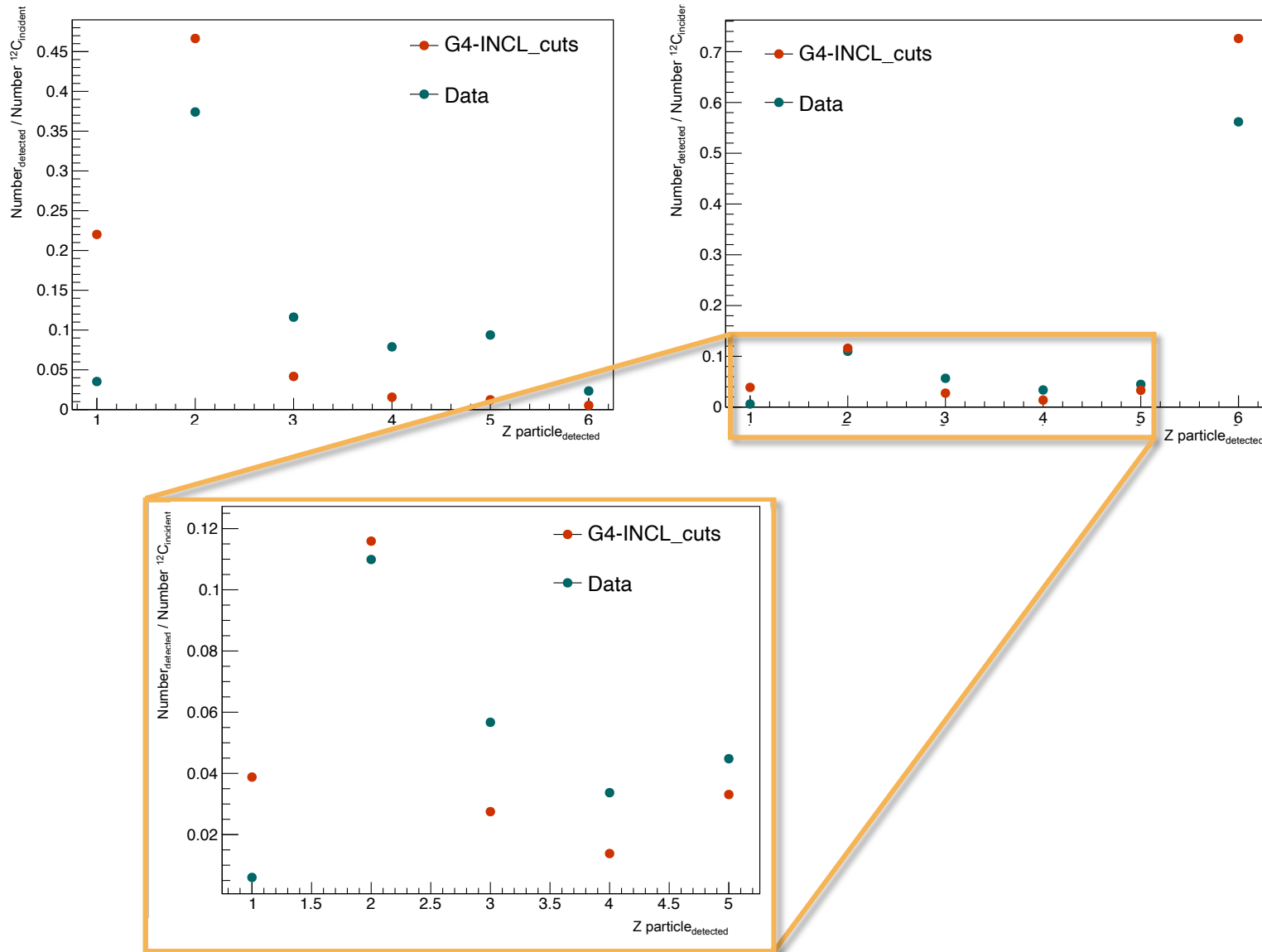
Secondary particles measurement

Yields study



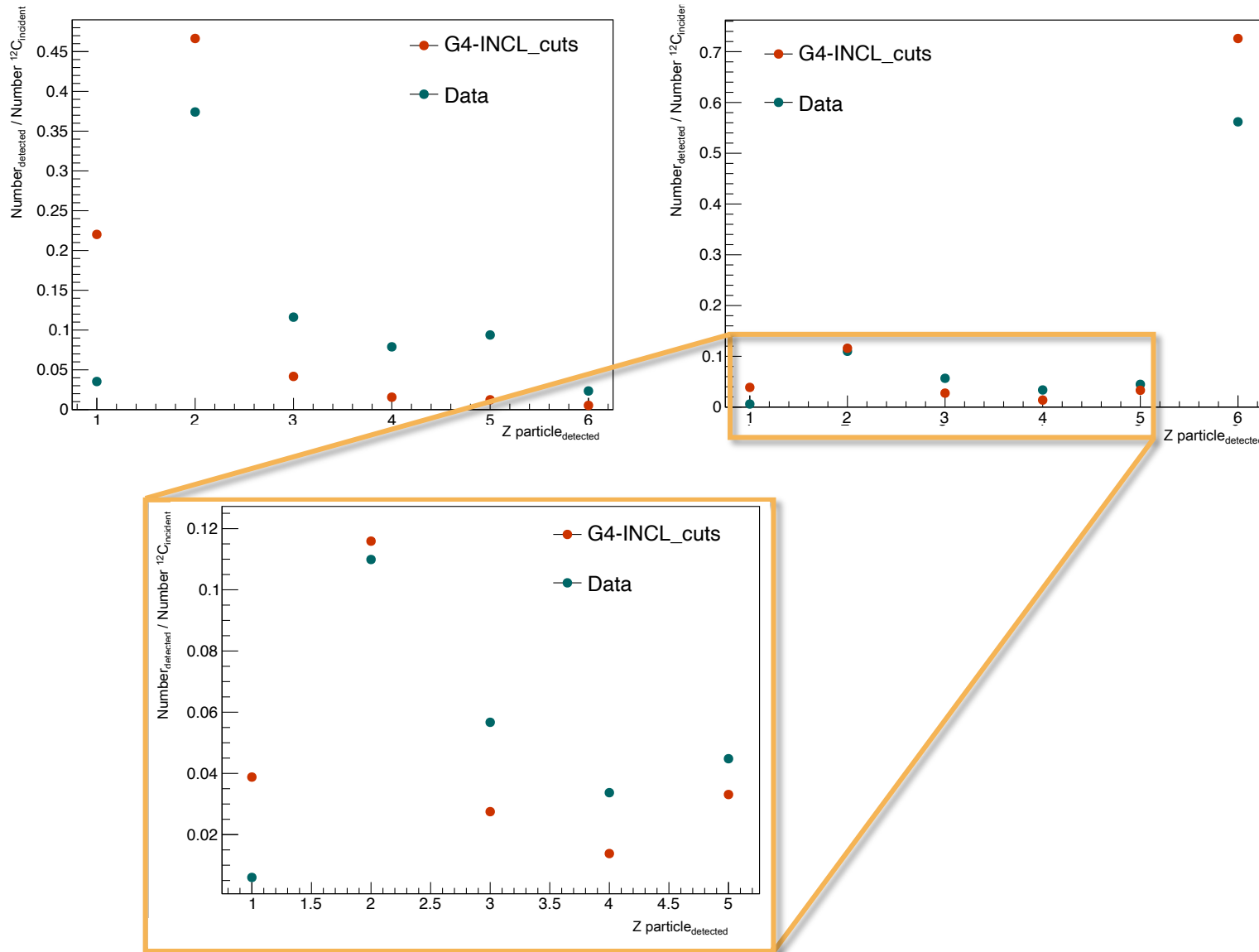
Secondary particles measurement

Yields study



Secondary particles measurement

Yields study



Relative yield

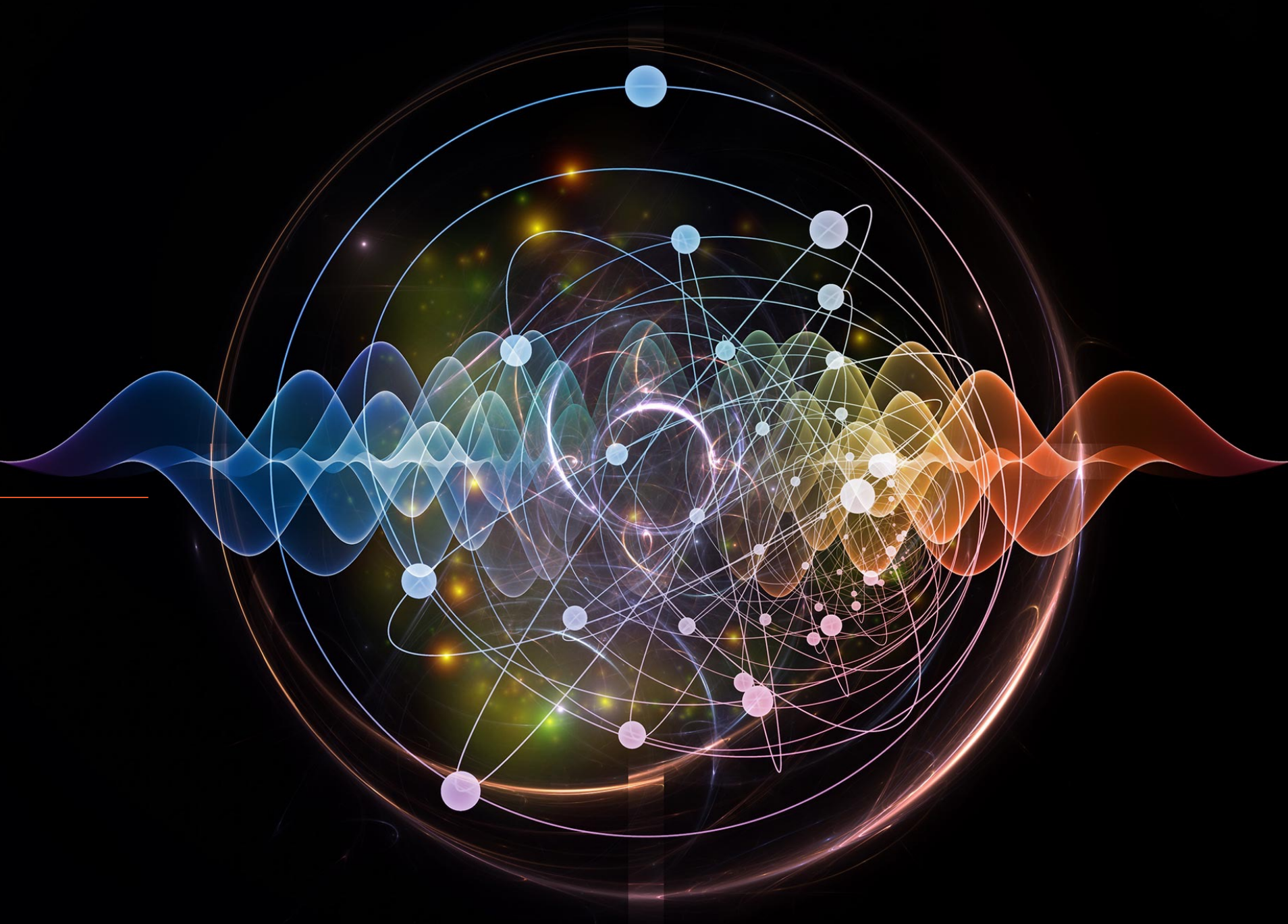
$$\Phi_Z = \frac{N_Z}{N_{\text{events}}}$$

Number of Z particle detected

Incident ¹²C ions estimated

- Z=1 and Z=2
→ overestimation by Geant4 simulation
- Z=3, Z=4 and Z=5
→ underestimation by Geant4 simulation

Conclusion



Conclusion

CNAO CLINM experiment

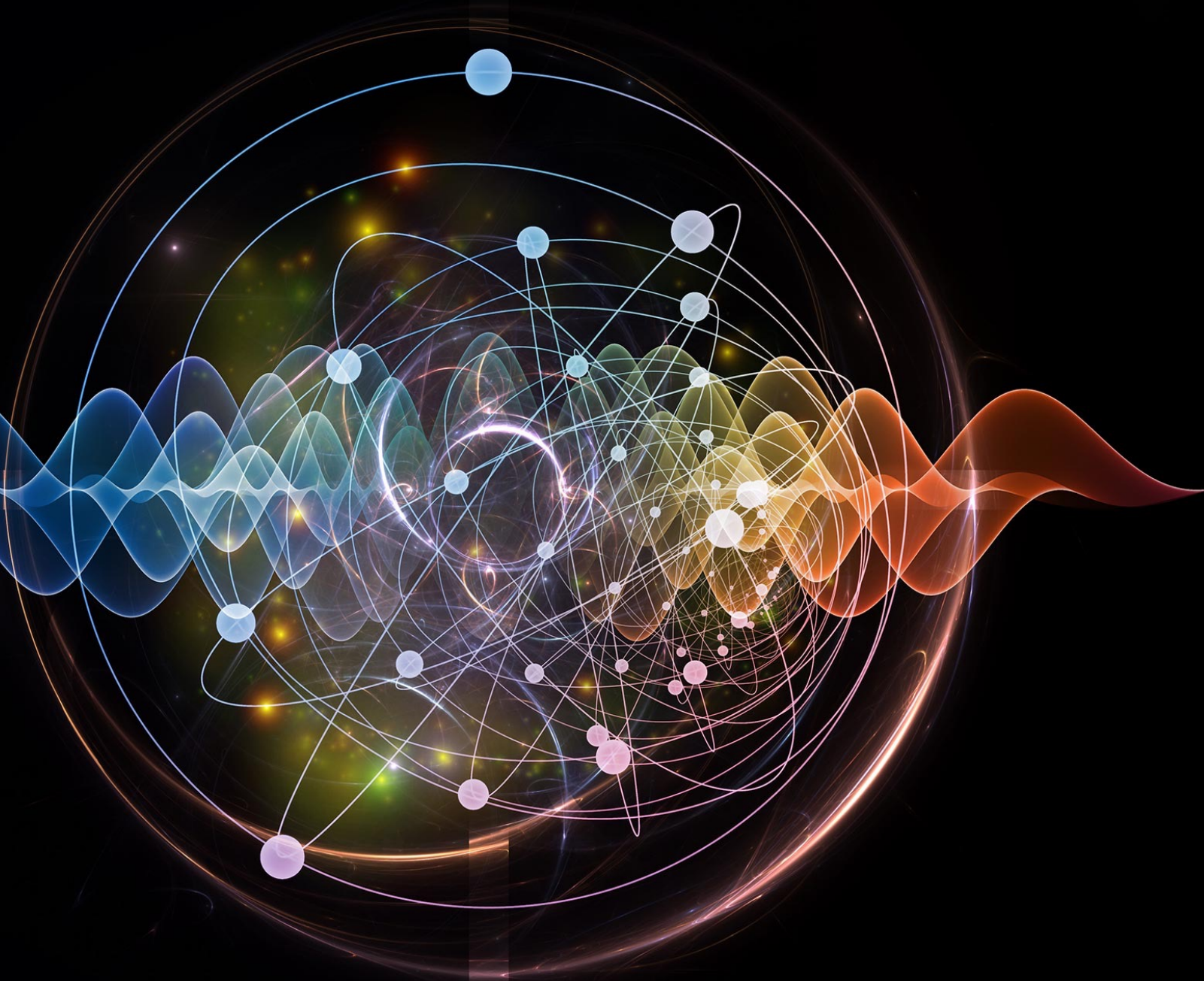
- Significant discrepancies between experimental data and Geant4 simulation
 - ↳ inaccuracies in simulation of the carbon break-up into alphas
 - ↳ underestimated secondary particle yields

Perspectives

- More experimental measurements with varying conditions → ongoing
- Implementation in Geant4 of experimental data to improve nuclear models accuracy



**Thank you for
your attention**



- [1] K. Gunzert-Marx, H. Iwase, D. Schardt, R. S. Simon, Secondary beam fragments produced by 200 mev/u 12c ions in water and their dose contributions in carbon ion radiotherapy., New Journal of Physics (July 2008). doi:0.1088/1367-2630/10/7/075003.
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URL <https://tuprints.ulb.tu-darmstadt.de/16188/1/cancers-12-03022-v2.pdf>
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URL <https://hal.in2p3.fr/in2p3-00623351>
- [5] Y.Cao, D.Tang, Y.Xiang, L.Men, C.Liu, Q.Zhou, J.Wu, L.Huo, T.Song, Y.Wang, Z.Li, R.Wei, L.Shen, J. Z. Hong, Study on the appropriate timing of postoperative adaptive radiotherapy for high-grade glioma, Cancer Manag Res. (2021).
doi:<https://doi.org/10.2147/CMAR.S300094>.
- [6] Nymus 3D animations – part of the Demcon group
- [7] Dudouet, J. & Cussol, Daniel & Durand, D. & Labalme, M.. (2013). Benchmarking GEANT4 nuclear models for carbon-therapy at 95 MeV/A. Physical Review C. 89. doi: 10.1103/PhysRevC.89.054616.
- [8] M. E. Wolf. Robust optimization in 4D treatment planning for carbon ion therapy of lung tumors. PhD thesis, Technische Universität, Darmstadt, November 2018. URL <http://tuprints.ulb.tu-darmstadt.de/8354/>
- [9] University of Iowa health care - <https://www.youtube.com/watch?v=nZ044EicYO4>
- [10] M. Kramer, et al., Treatment planning for heavy-ion radiotherapy: physical beam model and dose optimization., Phys. Med. Biol., 45(11): 528 3299 (2000). doi:10.1088/0031-9155/45/11/313.
- [11] S.M. Valle, A. Alexandrov, G. Ambrosi, S. Argirò, G. Battistoni, et al.
FOOT: a new experiment to measure nuclear fragmentation at intermediate energies, Perspectives in Science, Volume 12, 2019, 100415, ISSN 2213-0209, <https://doi.org/10.1016/j.pisc.2019.100415>.
- [12] A. Koning, D. Rochman, J.-C. Sublet, N. Dzysiuk, M. Fleming, S. van der Marck, Tendl: Complete nuclear data library for innovative nuclear science and technology, Nuclear Data Sheets 155 (2019) 1–55.
URL <https://doi.org/10.1016/j.nds.2019.01.002>

Back-up

General context

Secondary particles in heavy ion therapy

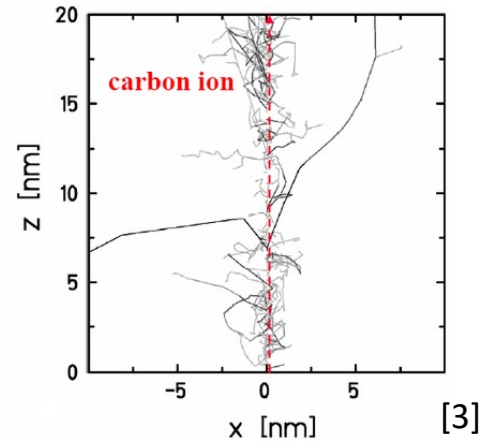
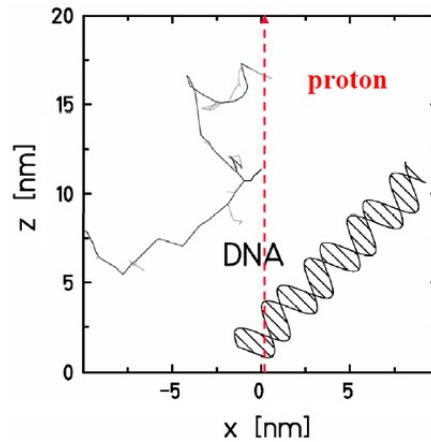
Physical aspects

Linear energy transfer (LET)

- Restricted local version of dE/dx
- Related to track length
- Dominated by ionization e^-

$$\text{LET} = \frac{dE}{dx} - \sum E_c(e_\delta)$$

↙
Total kinetic energy of electrons δ



[3]

Secondary particles in heavy ion therapy

Biological aspects

Dose → $D = \frac{dE}{dm} [\text{Gy}] \quad \text{J/kg}$

Mean energy deposited
Mass element

→ $D = \frac{\phi}{\rho} \text{LET}$ Linear energy transfer

Particle flux
Material density

Relative biological effectiveness

- Take into account radiation type
- Based on cellular survival curves

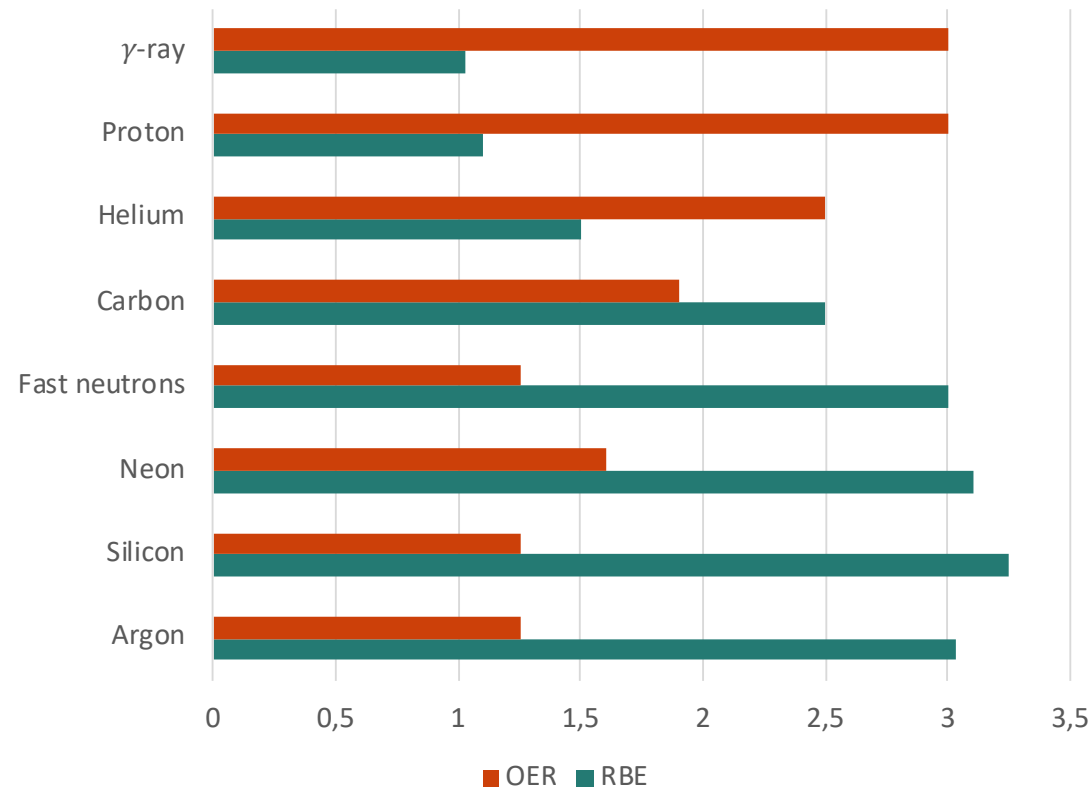
→ $\text{RBE} = \frac{D_{\text{Xray}}}{D_{\text{ion}}}$

Reference dose with X-ray therapy
Dose under investigation yielding equivalent cellular survival

Oxygen enhancement factor

- Reduced oxygen concentration in cell (hypoxic cell) reduce radiation effectiveness

→ $\text{OER} = \frac{\text{radiation dose in hypoxia}}{\text{radiation dose in air}}$



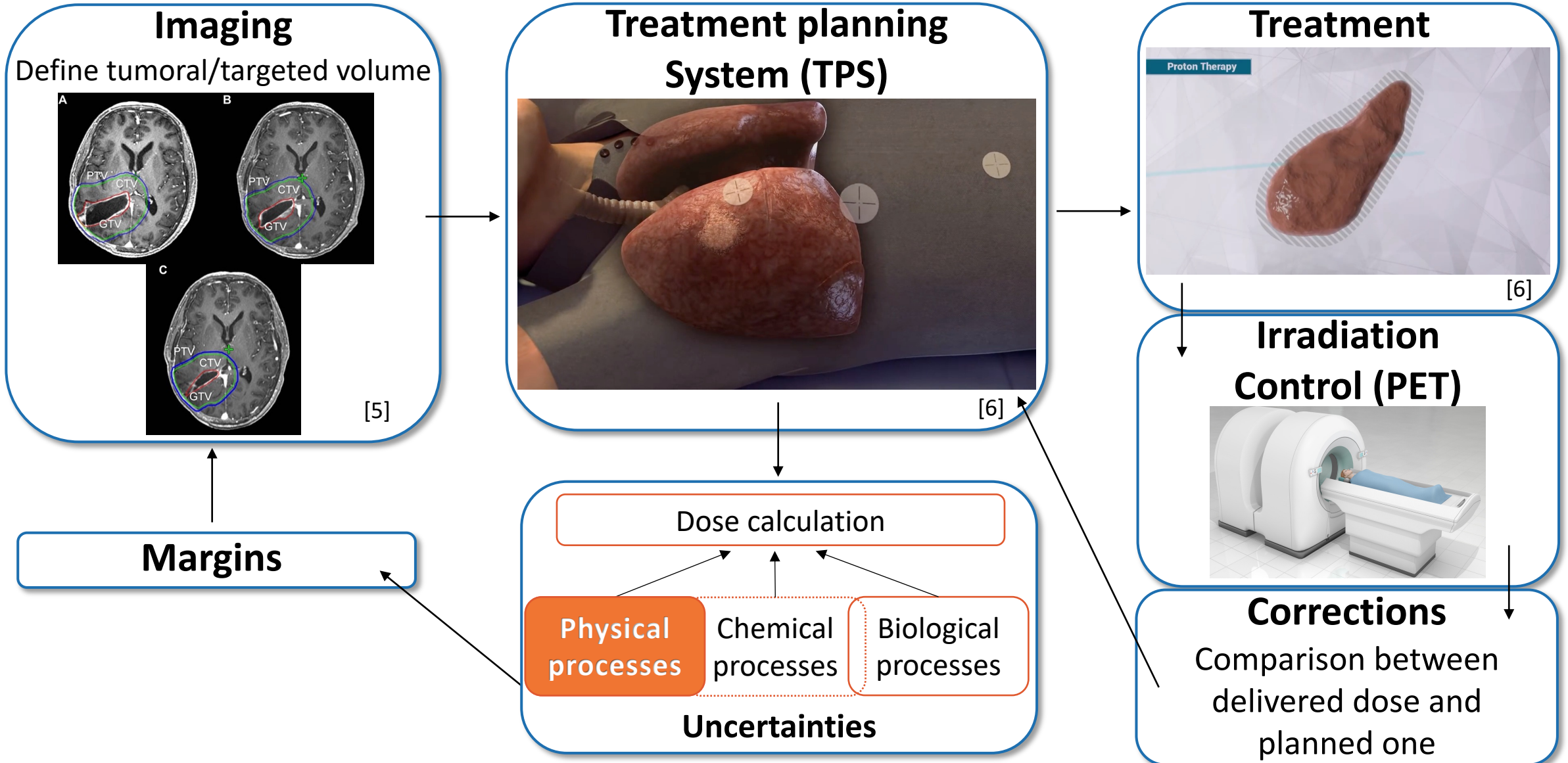
High RBE
=
Lot of damages

Low OER
=
Low resistance
of hypoxic cells

[4]

Secondary particles in heavy ion therapy

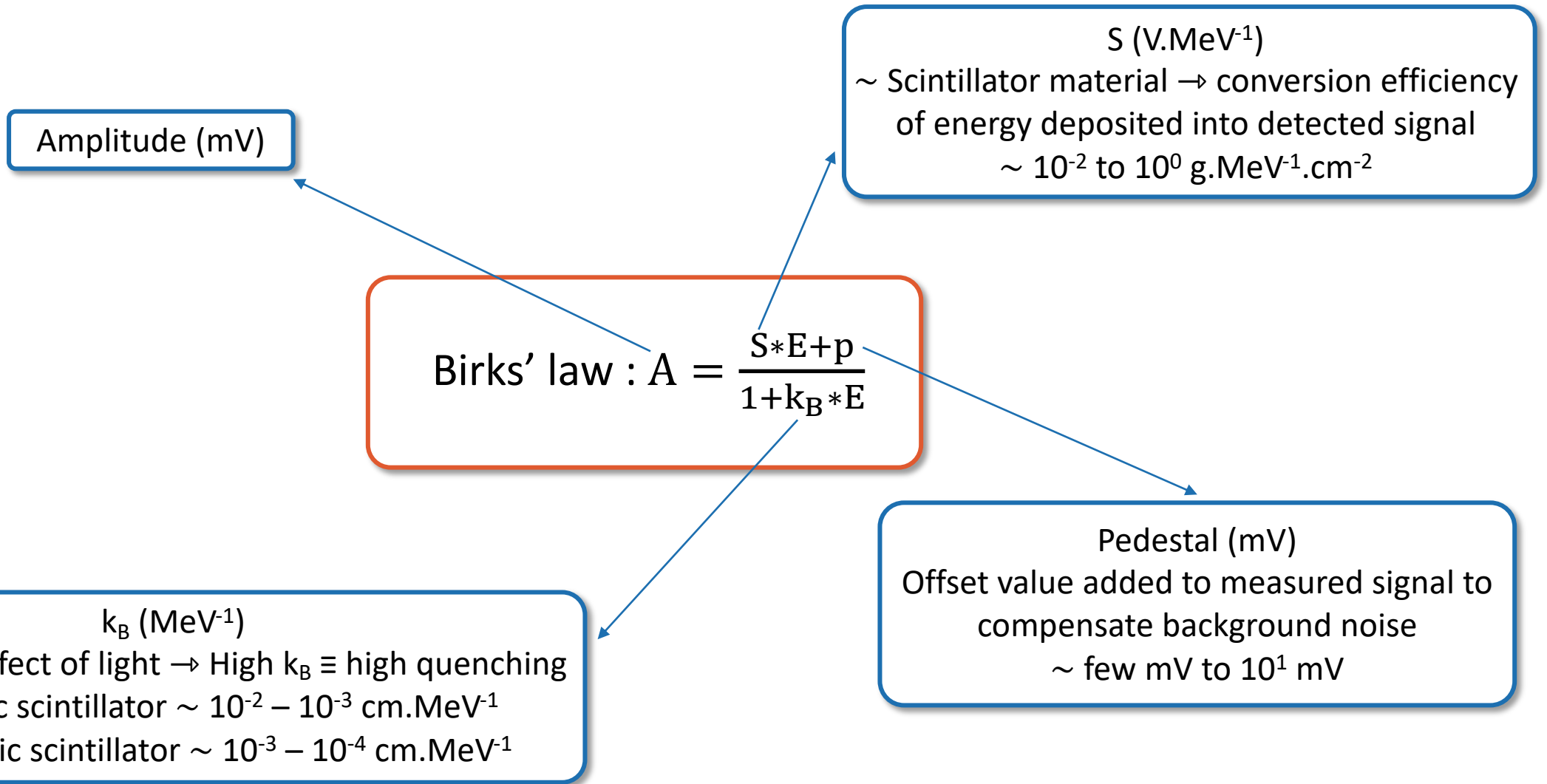
Treatment plan



Calibration

Secondary particles measurement

Calibration measurements

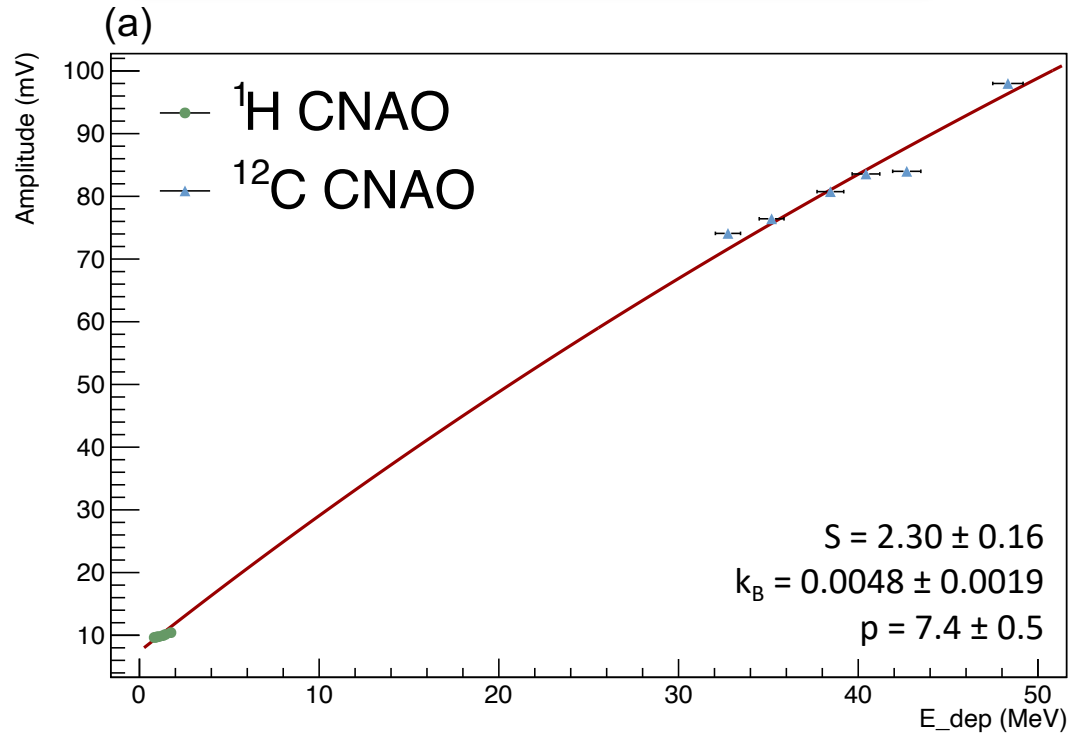


Secondary particles measurement

Plastic scintillator

Voltage applied : - 1200 V

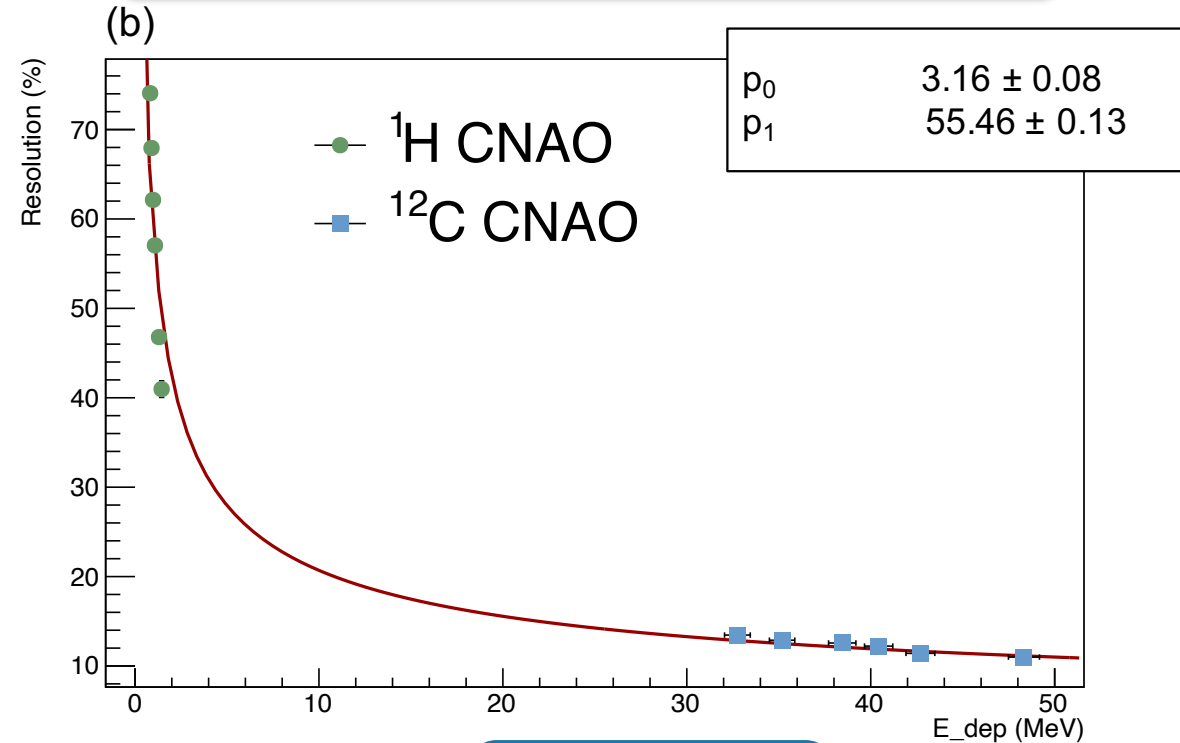
Calibration in amplitude



$$\text{Birks' law : } A = \frac{S \cdot E + p}{1 + k_B \cdot E}$$

- Birk's law respected up to 50 MeV
- Energy resolution : beam straggling effects

Energy resolution



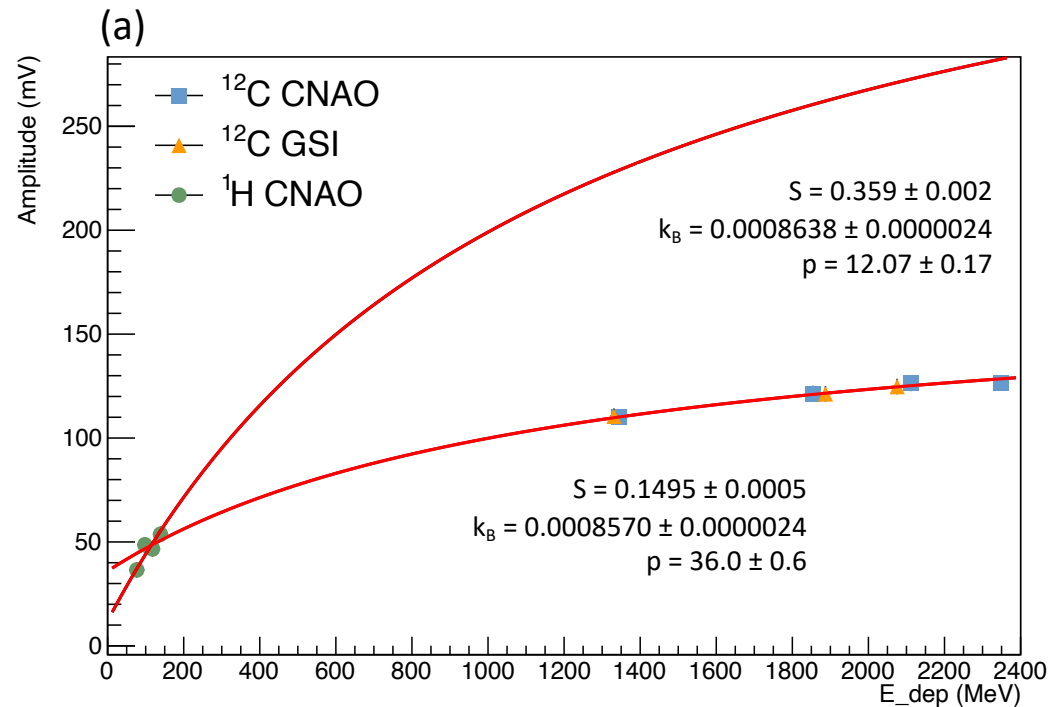
$$\text{Energy resolution : } \frac{\sigma_E}{E} = p_0 + \frac{p_1}{\sqrt{E}}$$

Secondary particles measurement

CeBr₃ scintillator

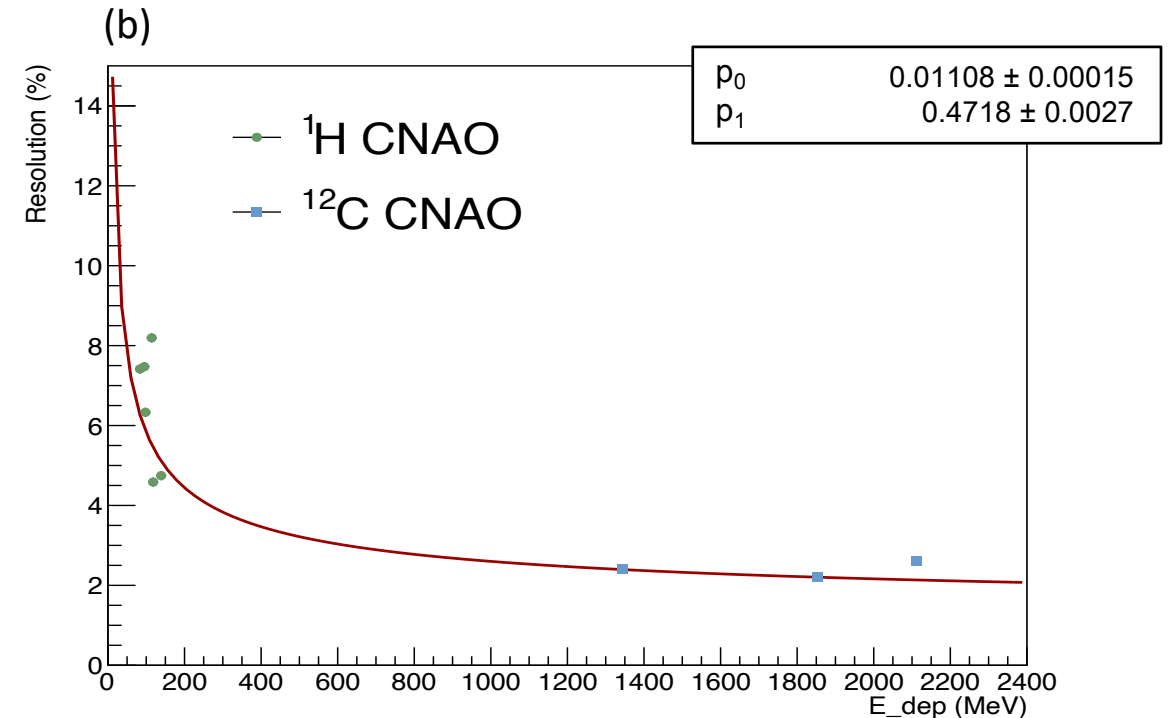
Voltage applied : + 350 V

Calibration in amplitude



$$\text{Birks' law : } A = \frac{S \cdot E + p}{1 + k_B \cdot E}$$

Energy resolution



Energy resolution :

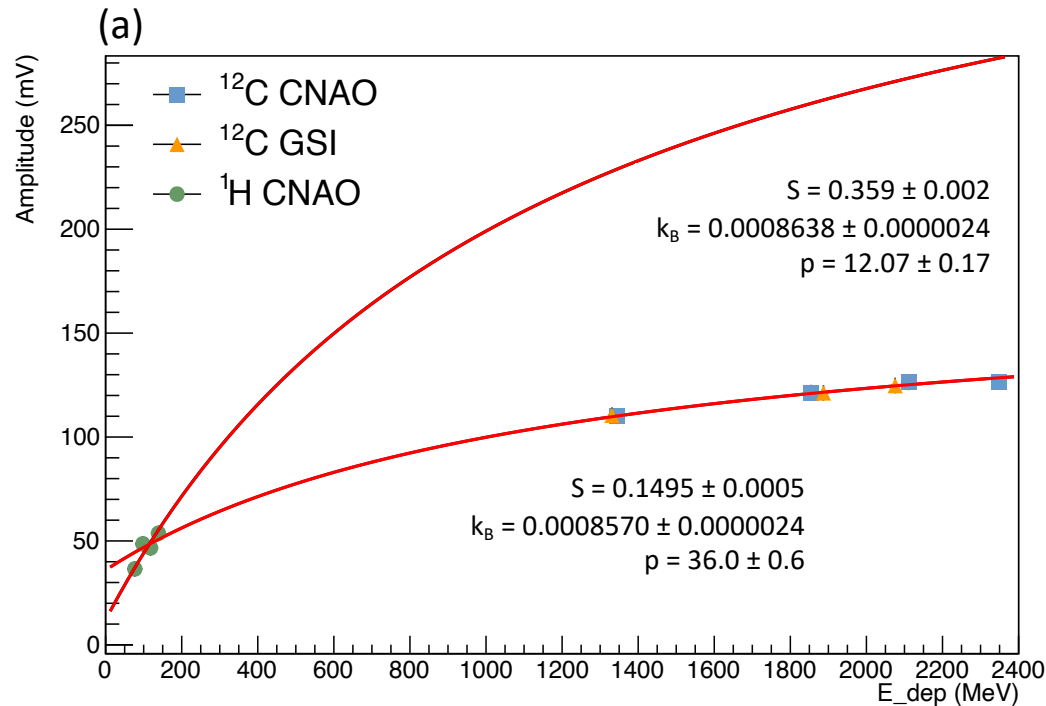
$$\frac{\sigma_E}{E} = p_0 + \frac{p_1}{\sqrt{E}}$$

Secondary particles measurement

CeBr₃ scintillator

Voltage applied : + 350 V

Calibration in amplitude



$$\text{Birks' law : } A = \frac{S \cdot E + p}{1 + k_B \cdot E}$$

- Distinct calibration functions for each ion type
- Birk constant similar for both ions
- Birk's law up to 2350 MeV

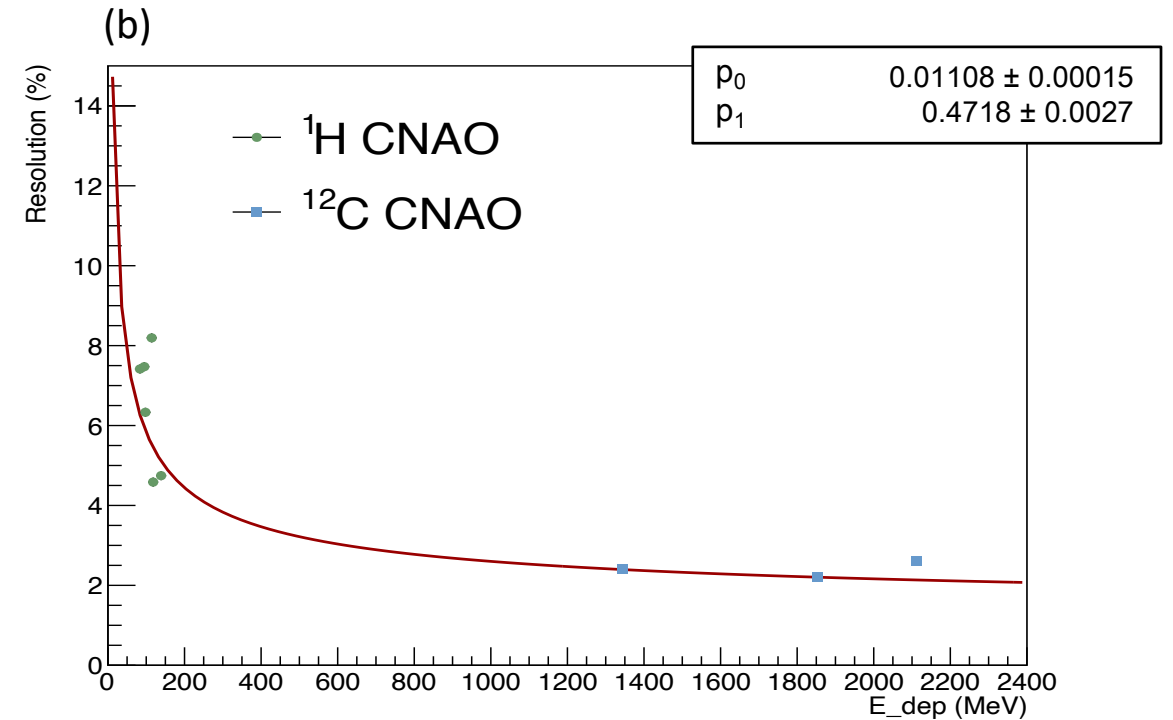
Secondary particles measurement

CeBr₃ scintillator

Voltage applied : + 350 V

- ~10 MeV energy resolution for both ion types
- Highlight scintillator precision for this ion energies

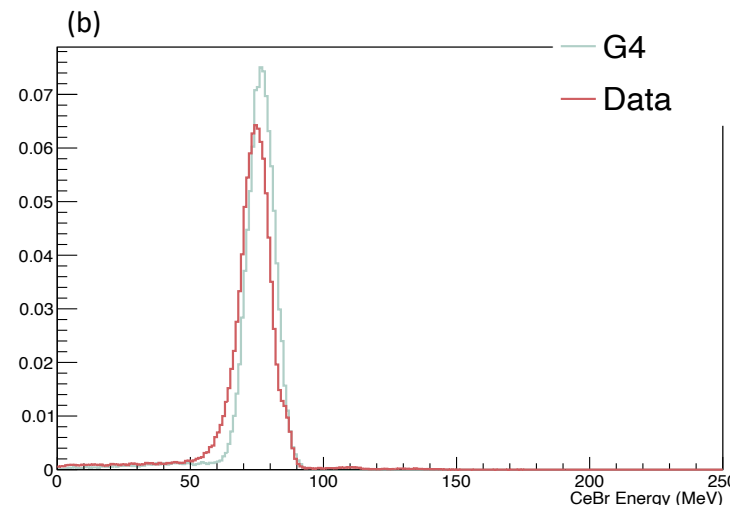
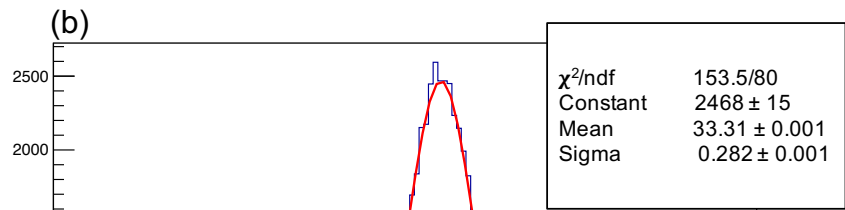
Energy resolution



Energy resolution :

$$\frac{\sigma_E}{E} = p_0 + \frac{p_1}{\sqrt{E}}$$

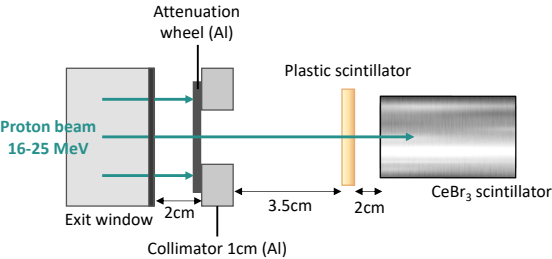
Time resolution



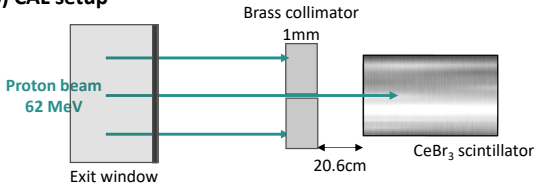
Secondary particles measurement

Calibration measurements

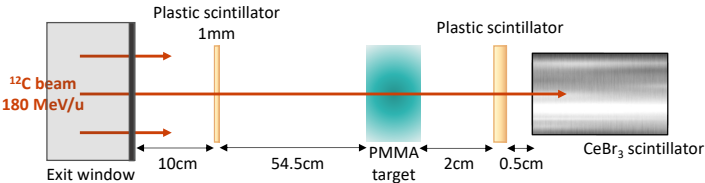
(a) Cyncé setup



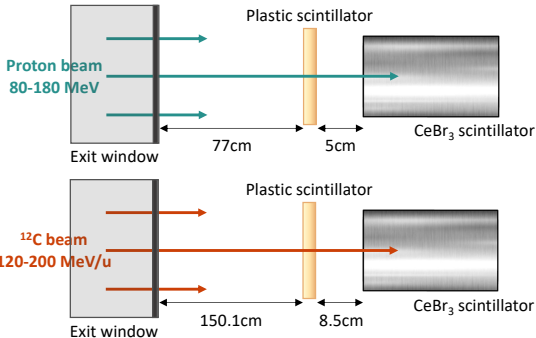
(b) CAL setup



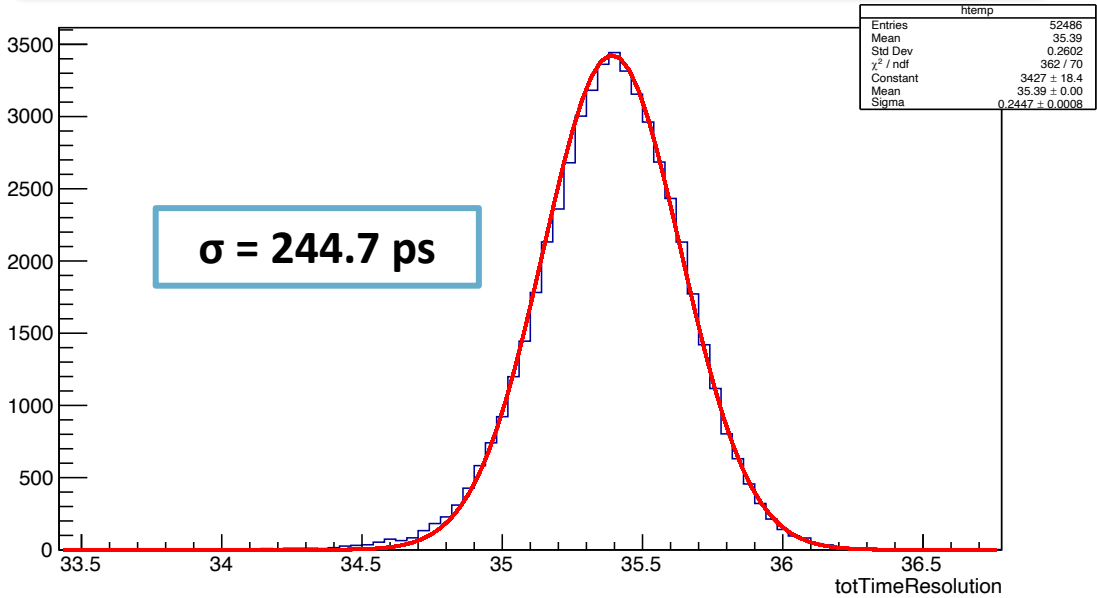
(c) GSI setup



(d) CNAO setups



Resolution in time of the coincidence detection

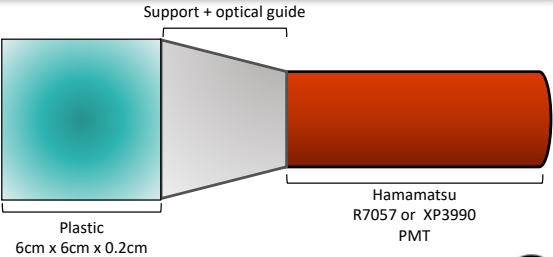


Facility	Ion type	Energy
Cyncé - Strasbourg	¹ H	16 - 25 MeV
CAL - Nice	¹ H	60 MeV
GSI - Darmstadt	¹² C	110 - 180 MeV/u
CNAO - Pavia	¹² C	120 - 200 MeV/u

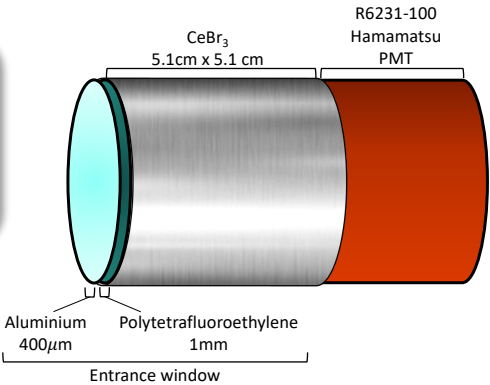
Secondary particles measurement

Detectors

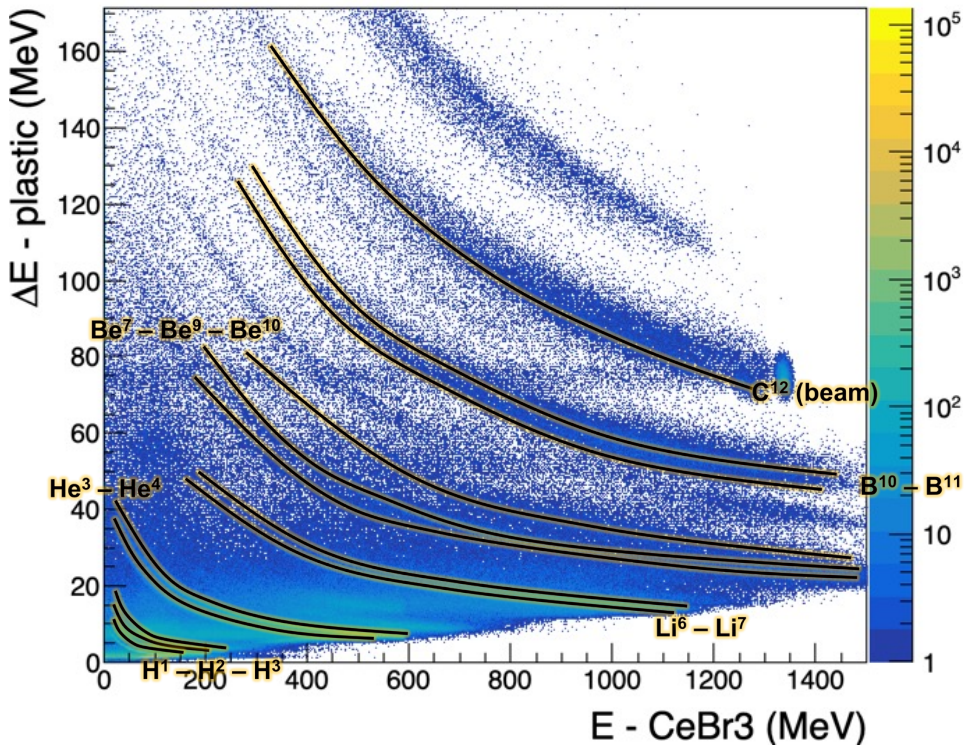
Plastic scintillator
Photomultiplier (PMT) (- 1200 V)



CeBr₃ crystal scintillator
PMT (usually + 1200 V)
+ 600 V for protons and high energy γ
+ 350 V / + 400 V for ^{12}C



ΔE -E method :

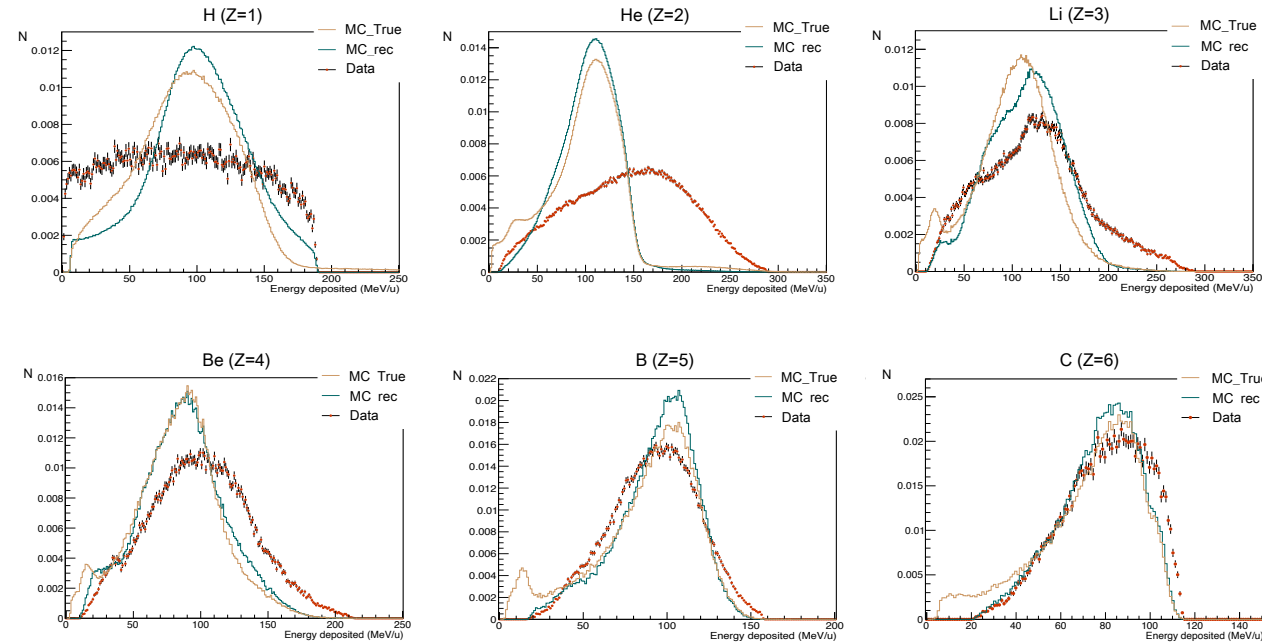


ΔE -E results from simulation with a carbon-ion beam of 200MeV, the detectors at 5° from the beam axis, and a PMMA target of 4 cm
Work done by M. Vanstalle

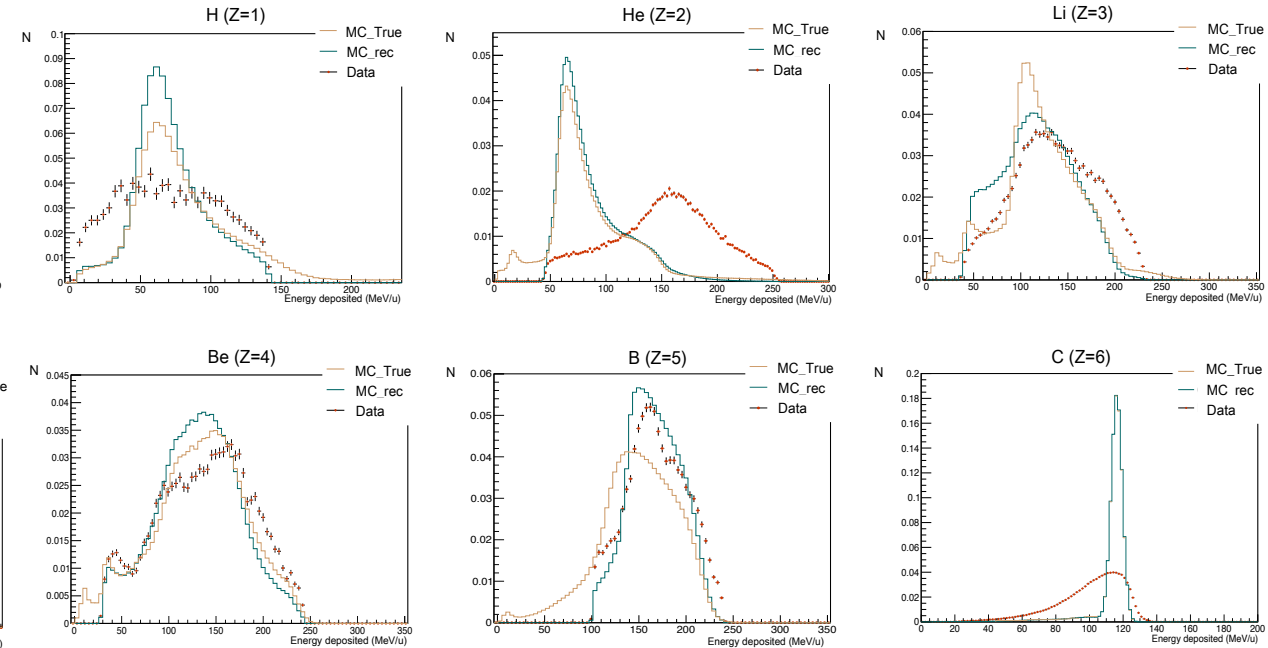
Analysis

Secondary particles measurement Experiment at CNAO

Config.1



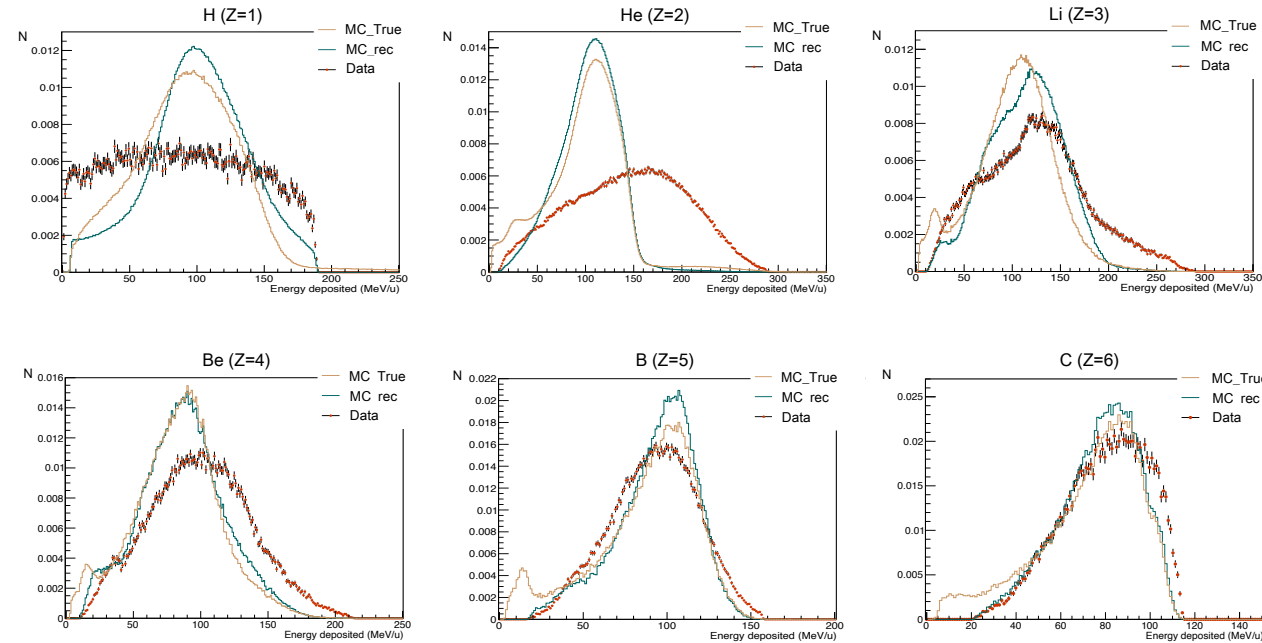
Config.2



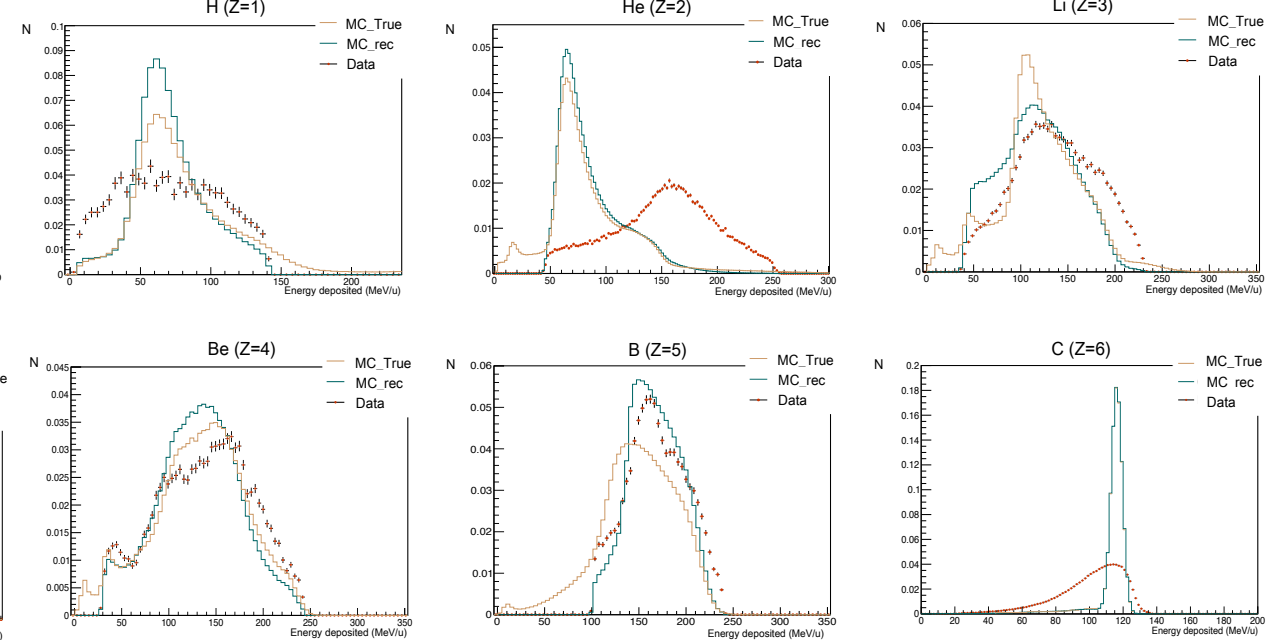
- Centered around beam energy (after target)
 - Fragments from projectile
- Data broader than MC
 - beam spread bigger than anticipated
 - further refinement in beam control needed
 - angular secondaries distributions non accurate

Secondary particles measurement Experiment at CNAO

Config.1



Config.2



- Centered around beam energy (after target)
 - Fragments from projectile
- Data broader than MC
 - beam spread bigger than anticipated
 - further refinement in beam control needed
 - angular secondaries distributions non accurate

Purity →
$$\frac{\text{Z particles correctly attributed in a cut}}{\text{total number of particle in the cut}}$$

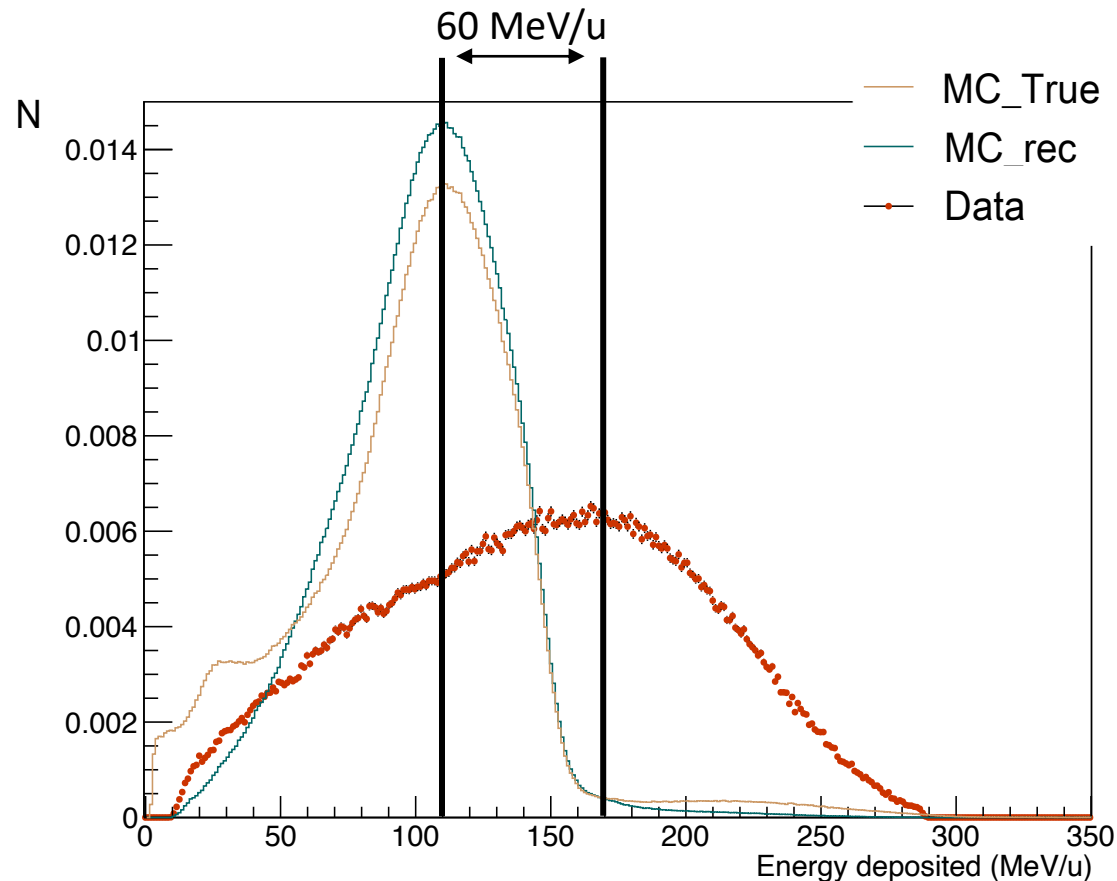
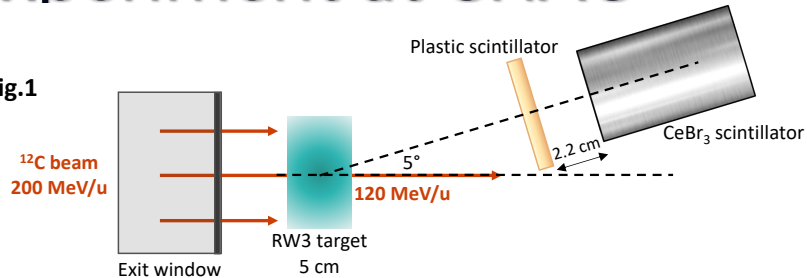
Efficiency →
$$\frac{\text{Z particles correctly attributed in a cut}}{\text{total number of Z particle detected}}$$

MC evaluated

Secondary particles measurement

Experiment at CNAO

Config.1



Z=2 Helium (MC_rec and MC_true)

- Good accordance in distribution and energy
- Underestimation of He by 6.02% in the cut

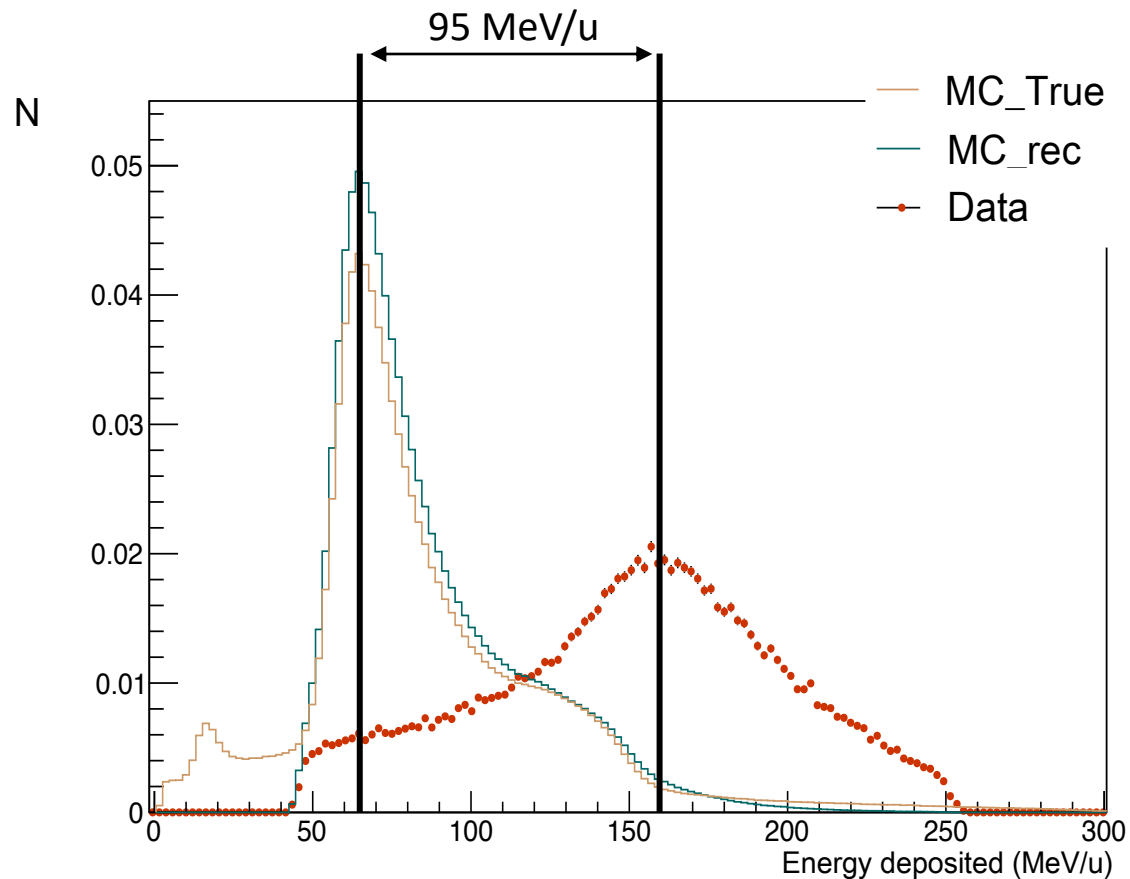
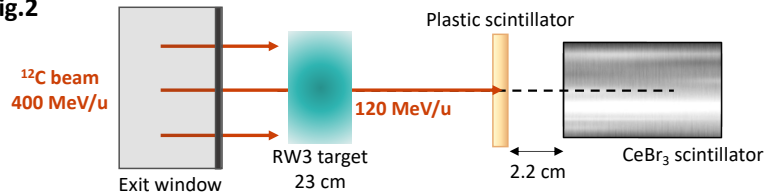
Z=2 Helium (purity and efficiency)

- High cut purity 88.01%
 - high production rate of He during C fragmentation
 - low contamination rate
- High cut efficiency 83.01%
 - include most He particles in analysis

Secondary particles measurement

Experiment at CNAO

Config.2



Z=2 Helium (MC_rec and MC_true)

- Good accordance in distribution and energy
- Underestimation of He by 7.25% in the cut

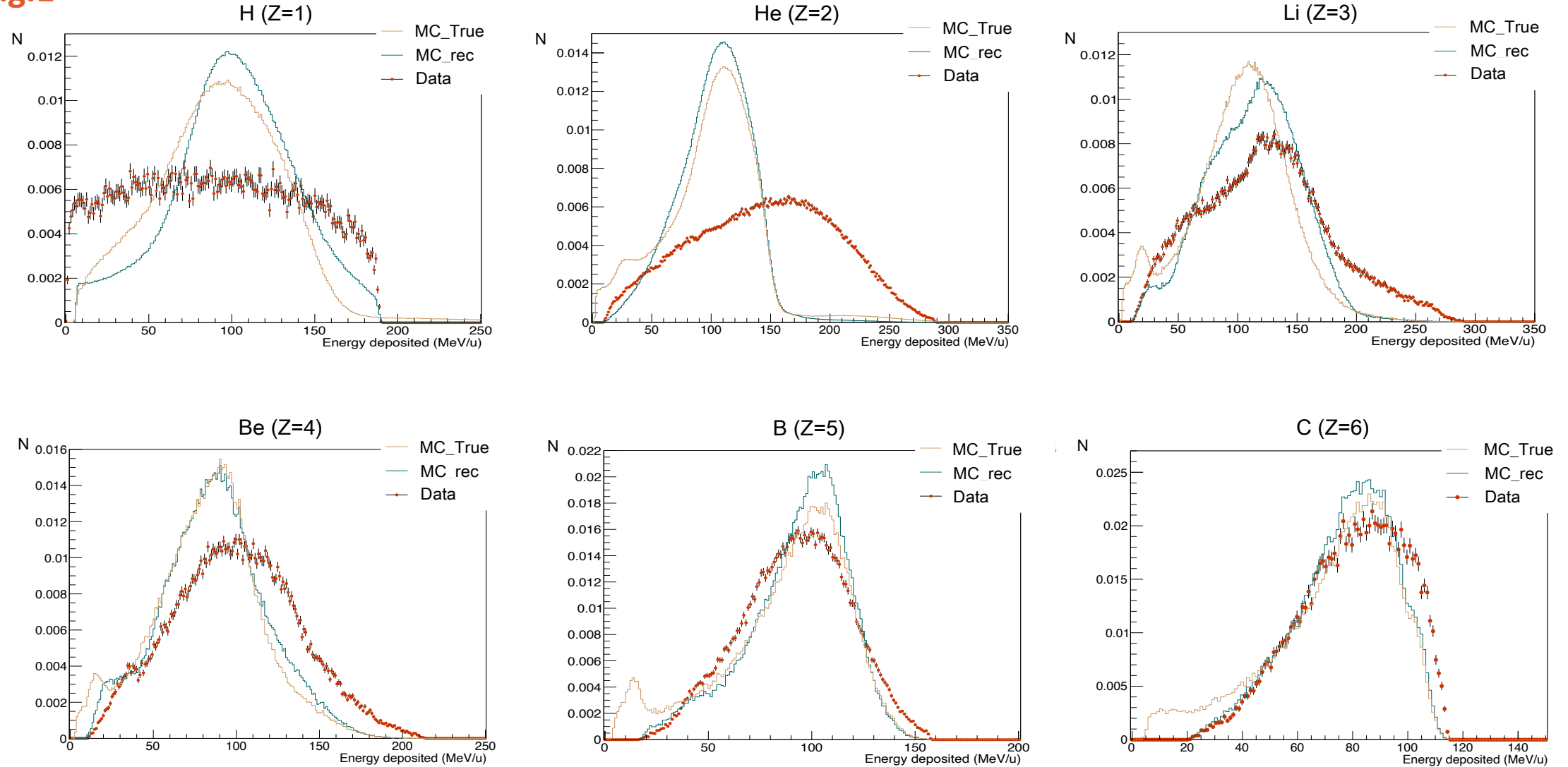
Z=2 Helium (purity and efficiency)

- High cut purity 85.11 %
 - high production rate of He during C fragmentation
 - low contamination rate
- High cut efficiency 79.36 %
 - include most He particles in analysis

Secondary particles measurement

Experiment at CNAO

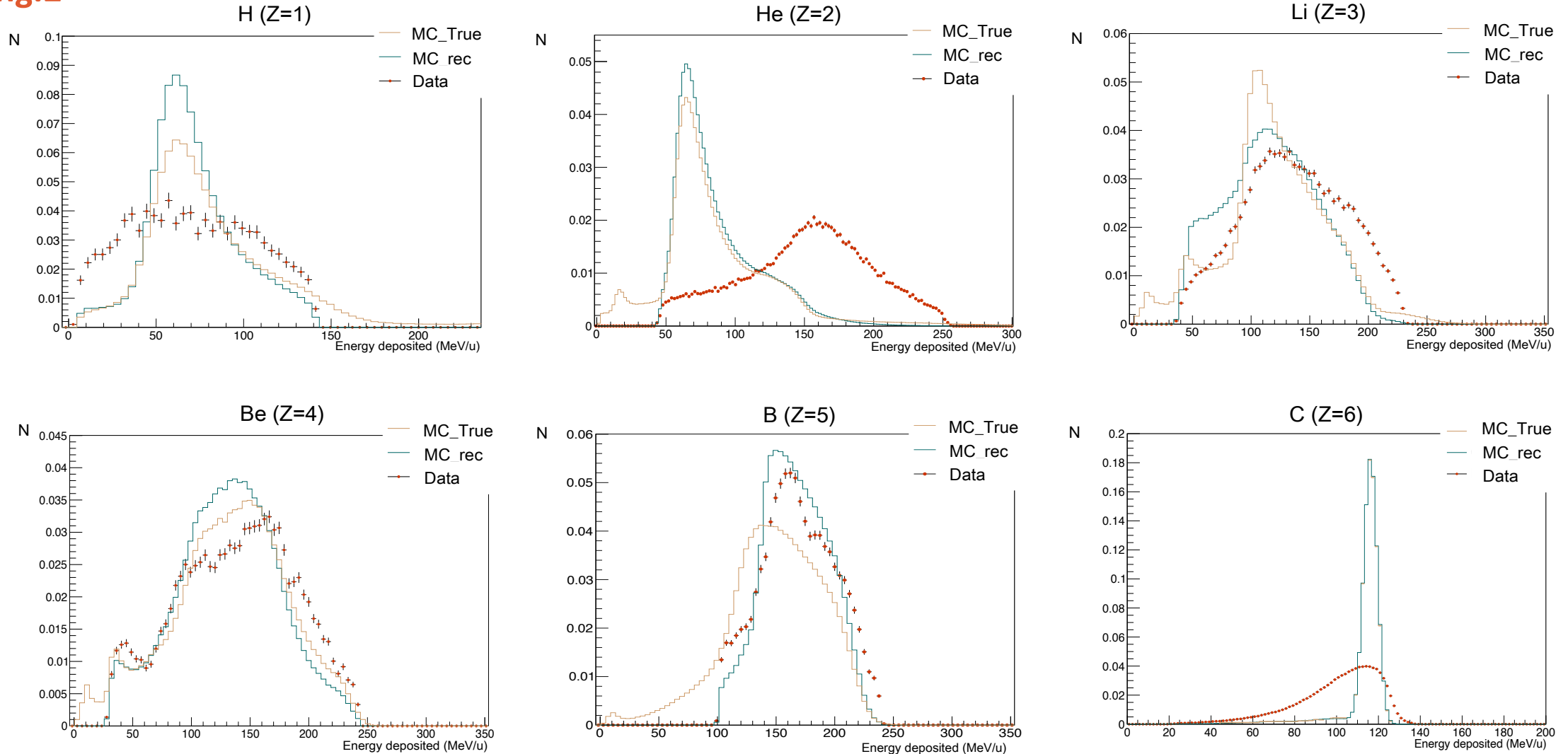
Config.1



Secondary particles measurement

Experiment at CNAO

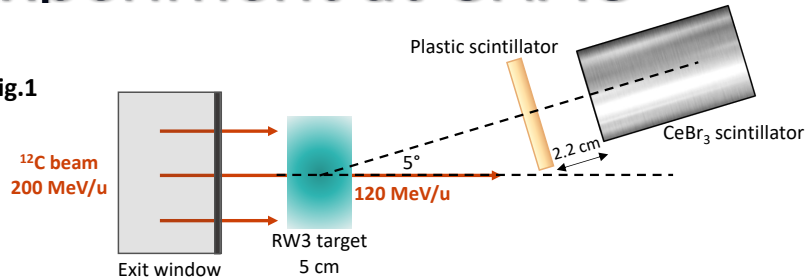
Config.2



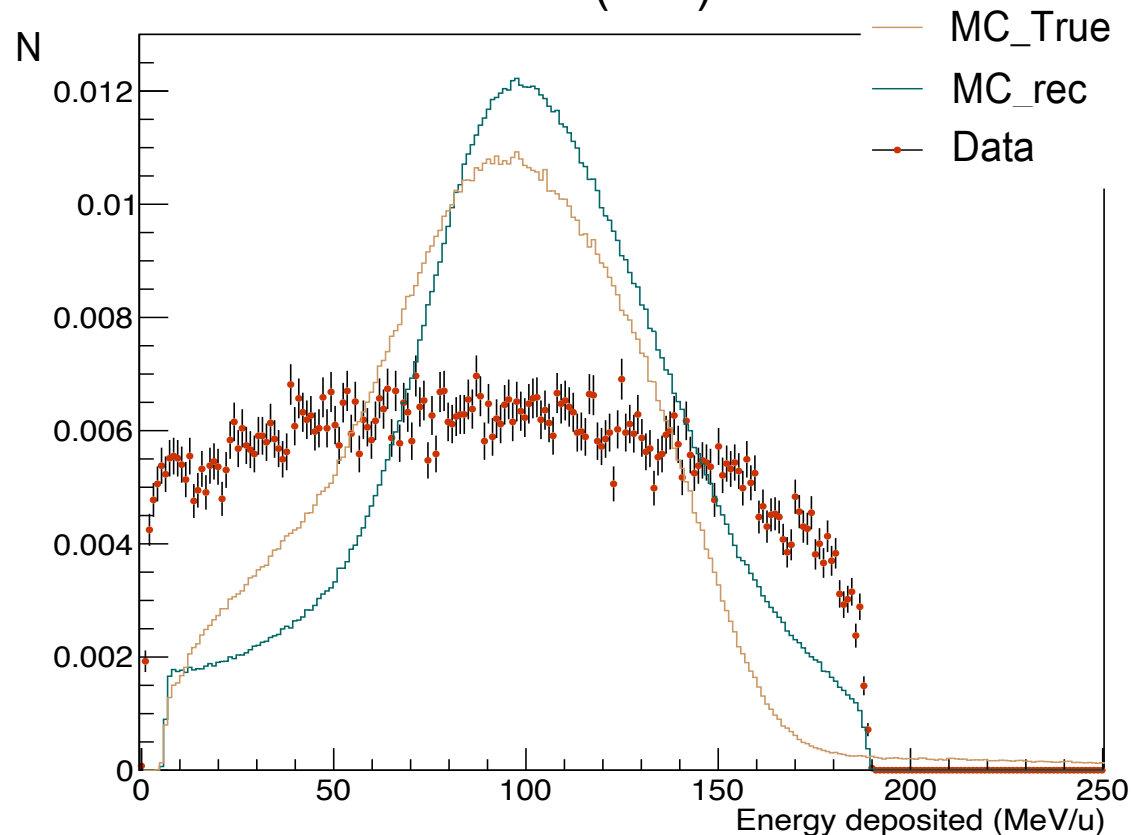
Secondary particles measurement

Experiment at CNAO

Config.1



H (Z=1)



Z=1 Hydrogen (MC_rec and exp data)

- Strong correspondance in energy between
- Resolution constraint at low energy
- Proton scattering and beam spread

Z=1 Hydrogen (MC_rec and MC_true)

- Overall agreement
- Minor distribution and energy shift 5MeV/u
- Overestimation of H by 39.31% in the cut

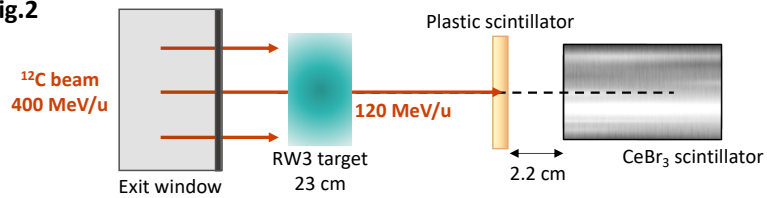
Z=1 Hydrogen (purity and efficiency)

- Cut purity 45.52%
 - mostly He mistakenly classified as H
 - protons isolation challenging with this setup
- Cut efficiency 75.01%
 - most H included in the analysis

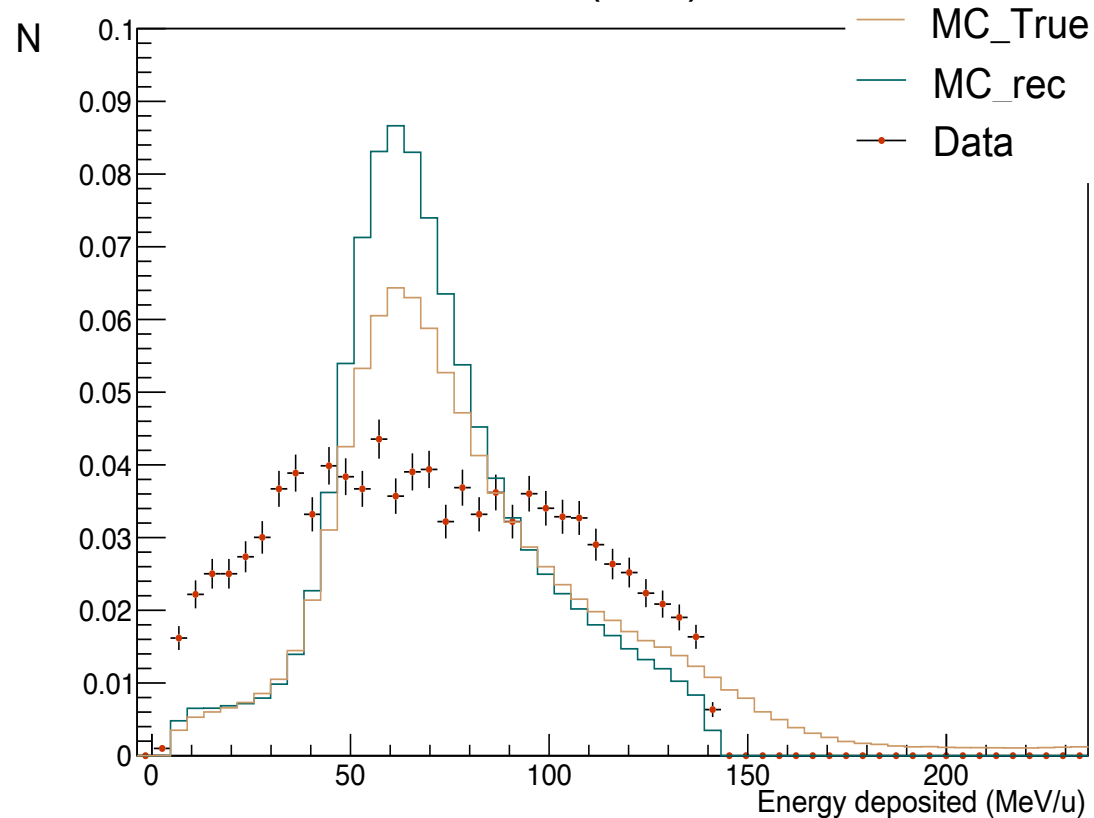
Secondary particles measurement

Experiment at CNAO

Config.2



H (Z=1)



Z=1 Hydrogen (MC_rec and exp data)

- Both centered at 70MeV/u
- Resolution constraint at low energy
- Proton scattering and beam spread

Z=1 Hydrogen (MC_rec and MC_true)

- Overall agreement
- Overestimation of H by 55.09% in the cut

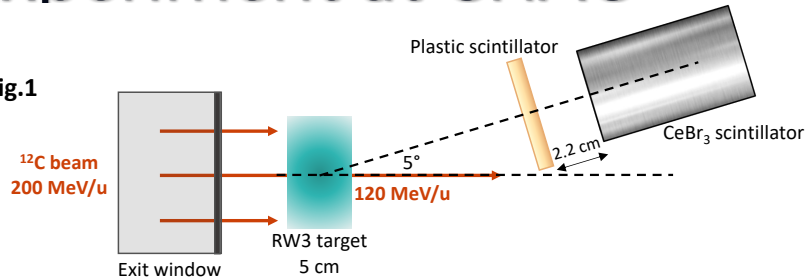
Z=1 Hydrogen (purity and efficiency)

- Cut purity 36.54%
 - mostly He mistakenly classified as H
 - protons isolation challenging with this setup
- Cut efficiency 78.88%
 - most H included in the analysis

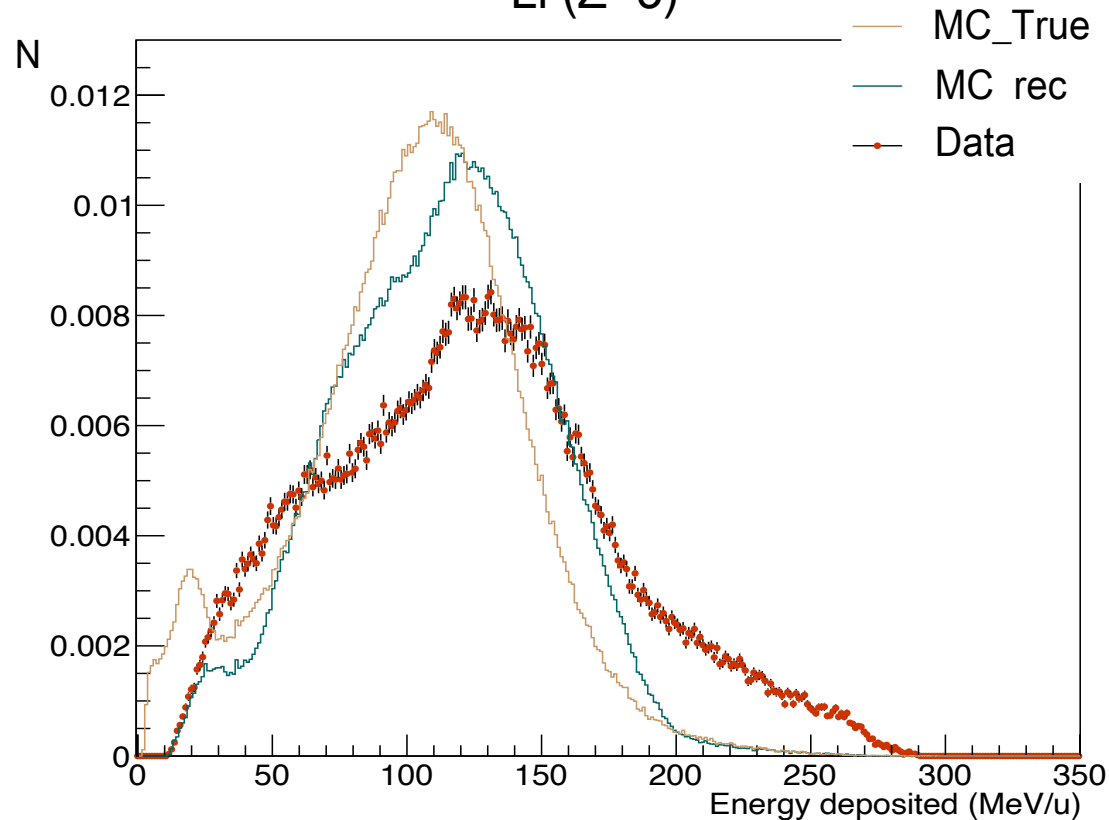
Secondary particles measurement

Experiment at CNAO

Config.1



Li (Z=3)



Z=3 Lithium (MC_rec and exp data)

- Isolation and identification difficult (statistical presence of He)
- Agreement in energy apart resolution

Z=3 Lithium (MC_rec and MC_true)

- Overall agreement
- Minor distribution and energy shift 10 MeV/u
- Overestimation of Li by 15.31% in the cut

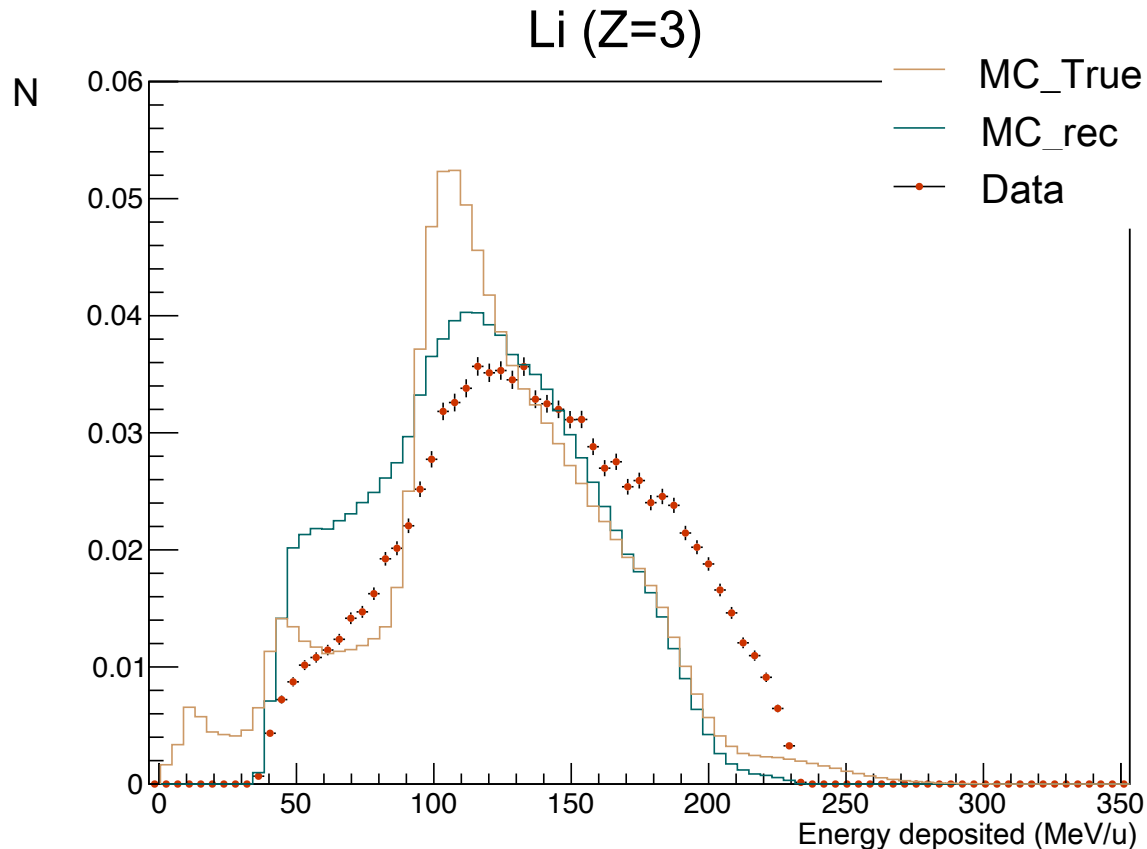
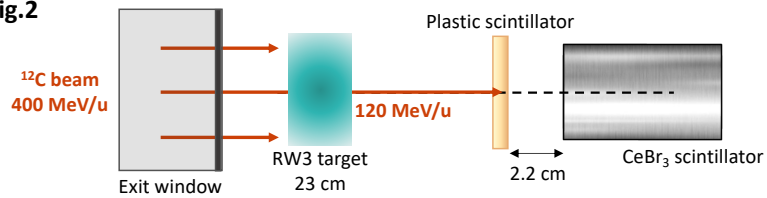
Z=3 Lithium (purity and efficiency)

- Cut purity 53.27%
 - overlap in the energy loss with He and Be
- Cut efficiency 62.90%
 - significant fraction of Li excluded
 - confirm overlap

Secondary particles measurement

Experiment at CNAO

Config.2



Z=3 Lithium (MC_rec and exp data)

- Isolation and identification difficult (statistical presence of He even more important)
- Small shift in energy of 10 MeV/u

Z=3 Lithium (MC_rec and MC_true)

- Overall agreement
- Minor distribution and energy shift 10 MeV/u
- Overestimation of Li by 6.75% in the cut

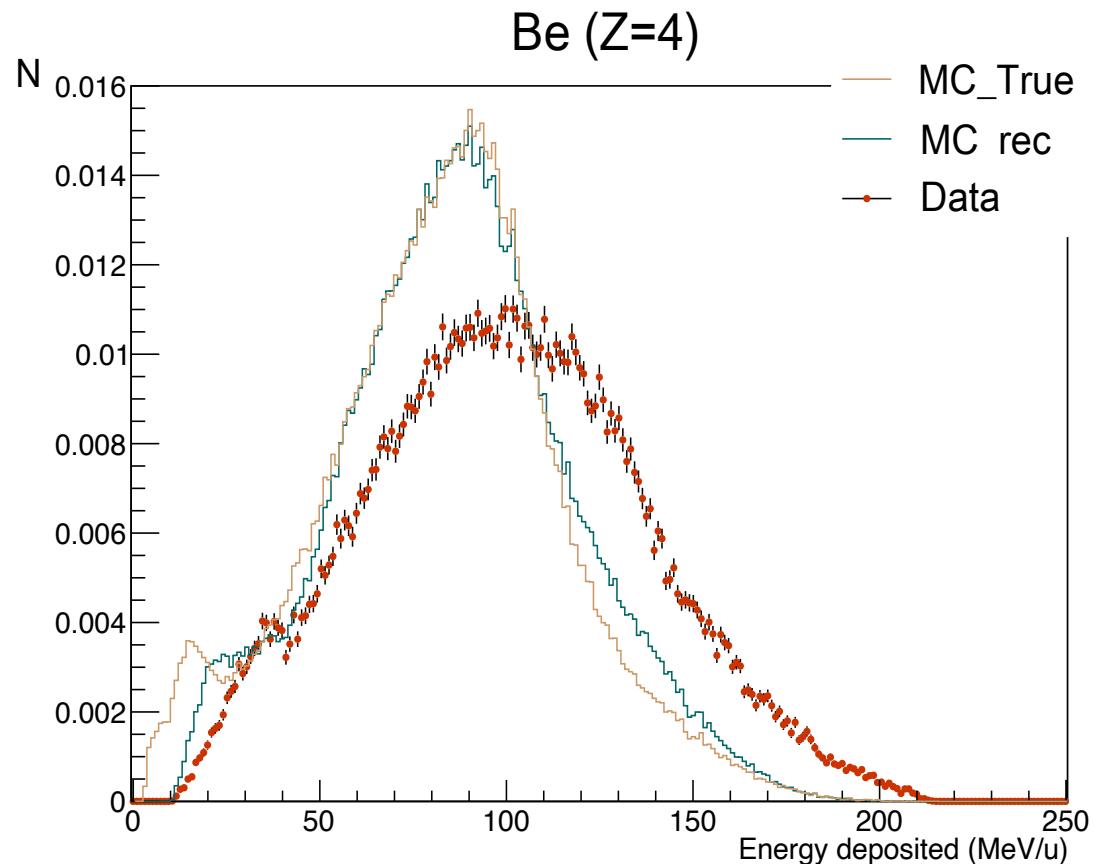
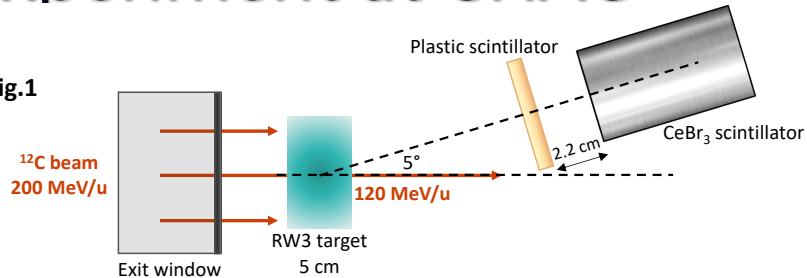
Z=3 Lithium (purity and efficiency)

- Cut purity 58.18%
 - overlap in the energy loss with He and Be
- Cut efficiency 62.39%
 - significant fraction of Li excluded
 - confirm overlap

Secondary particles measurement

Experiment at CNAO

Config.1



Z=4 Beryllium (MC_rec and exp data)

- Energy shift of 10 MeV/u
- Better accurate resolution reproduction

Z=4 Beryllium (MC_rec and MC_true)

- Good agreement in distribution and energy
- Slight underestimation of Be of 4.65% in the cut

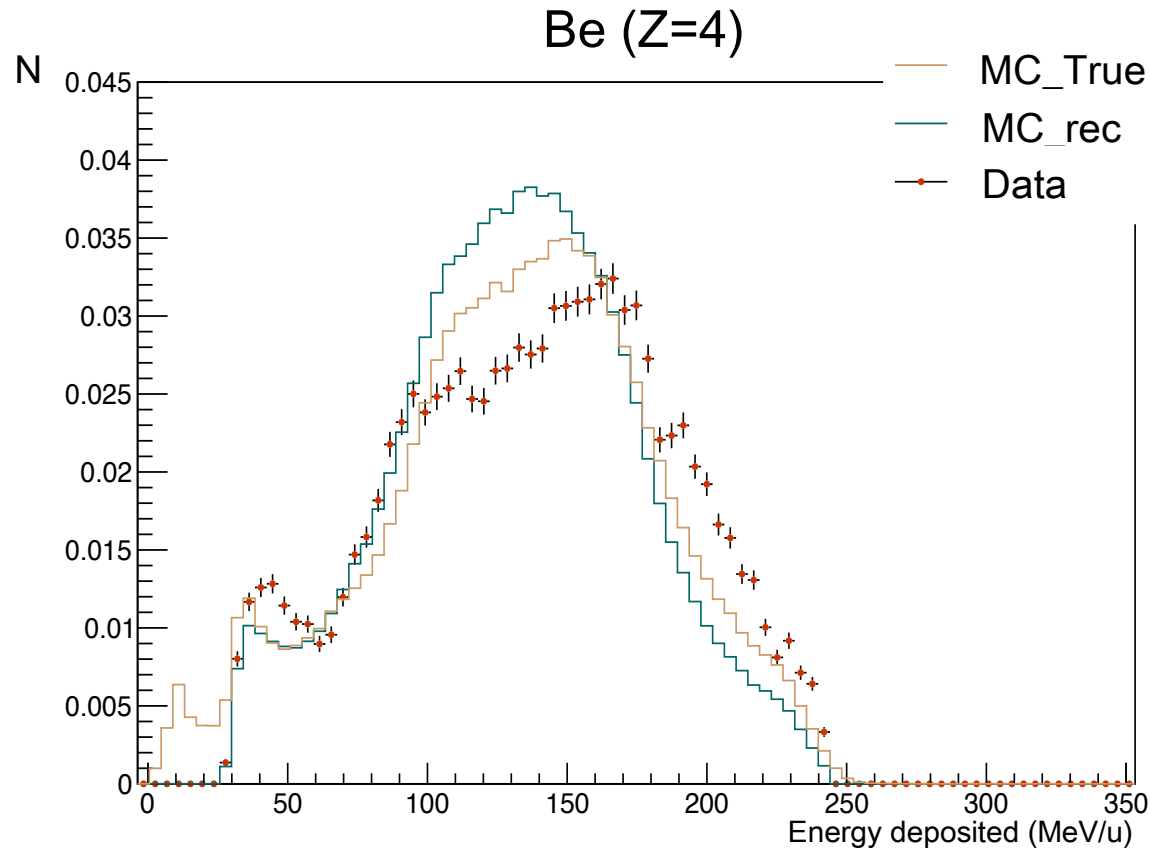
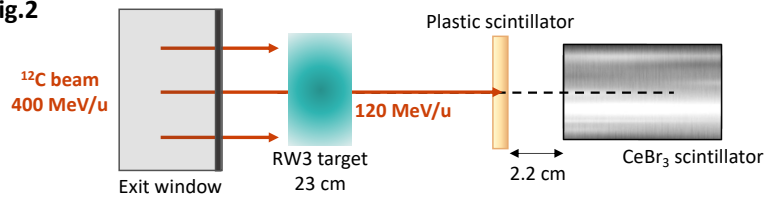
Z=4 Beryllium (purity and efficiency)

- High cut purity 77.92%
 - effective discrimination criteria
- Cut efficiency of 74.46%
 - reasonable balance between capturing most particles and maintaining purity

Secondary particles measurement

Experiment at CNAO

Config.2



Z=4 Beryllium (MC_rec and exp data)

- Energy shift of 25MeV/u
- Better accurate resolution reproduction

Z=4 Beryllium (MC_rec and MC_true)

- Good agreement in distribution and energy
- Slight underestimation of Be of 13.09% in the cut

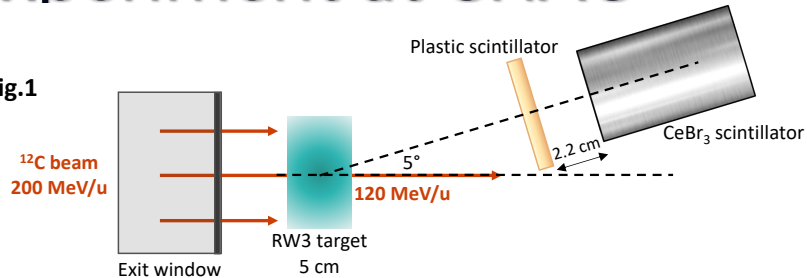
Z=4 Beryllium (purity and efficiency)

- High cut purity 69.96%
 - effective discrimination criteria
- Cut efficiency of 61.86%
 - reasonable balance between capturing most particles and maintaining purity

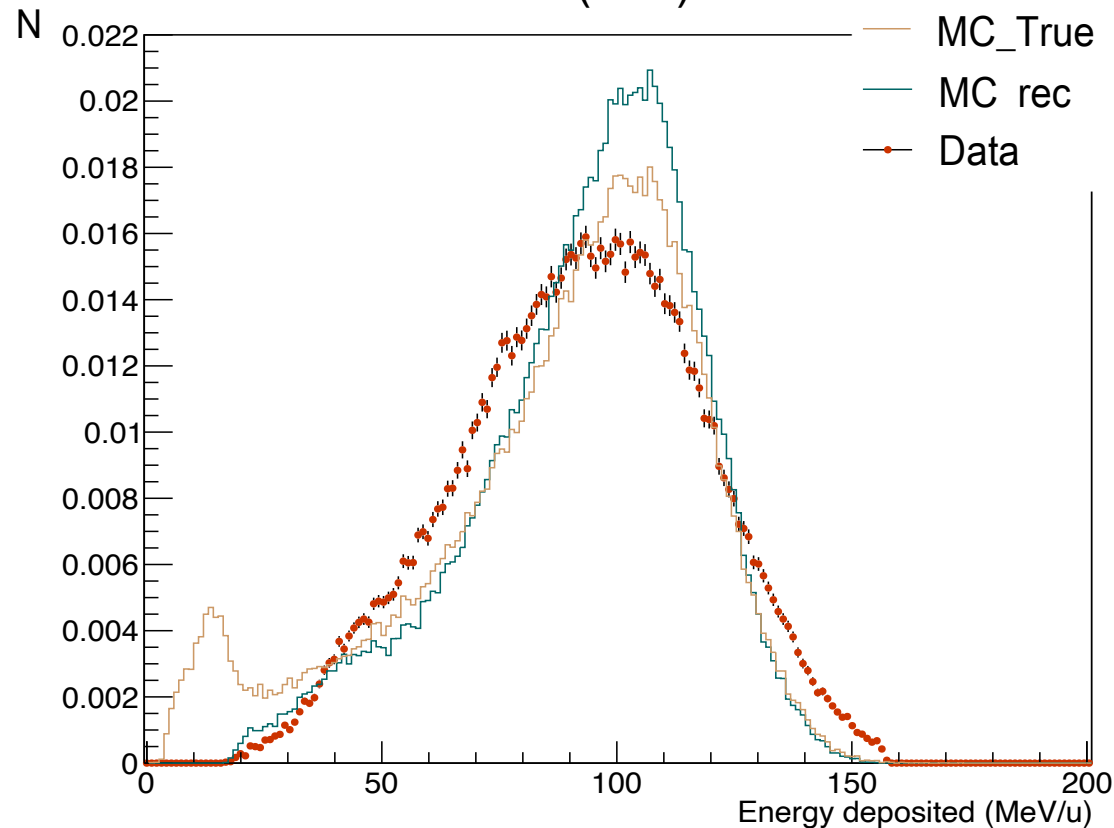
Secondary particles measurement

Experiment at CNAO

Config.1



B (Z=5)



Z=5 Boron (MC_rec and exp data)

- Slight energy deviation less than 10 MeV/u
- Improved reproduction of calculated resolution

Z=5 Boron (MC_rec and MC_true)

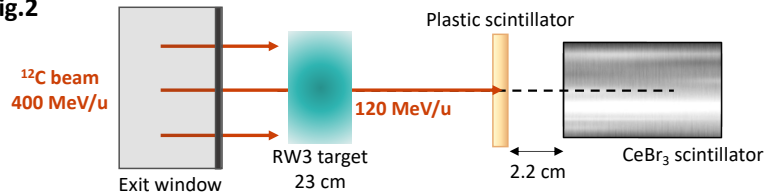
- Consistent agreement in distribution and energy
- Marginal underestimation of 0.67% in the cut

Z=5 Boron (purity and efficiency)

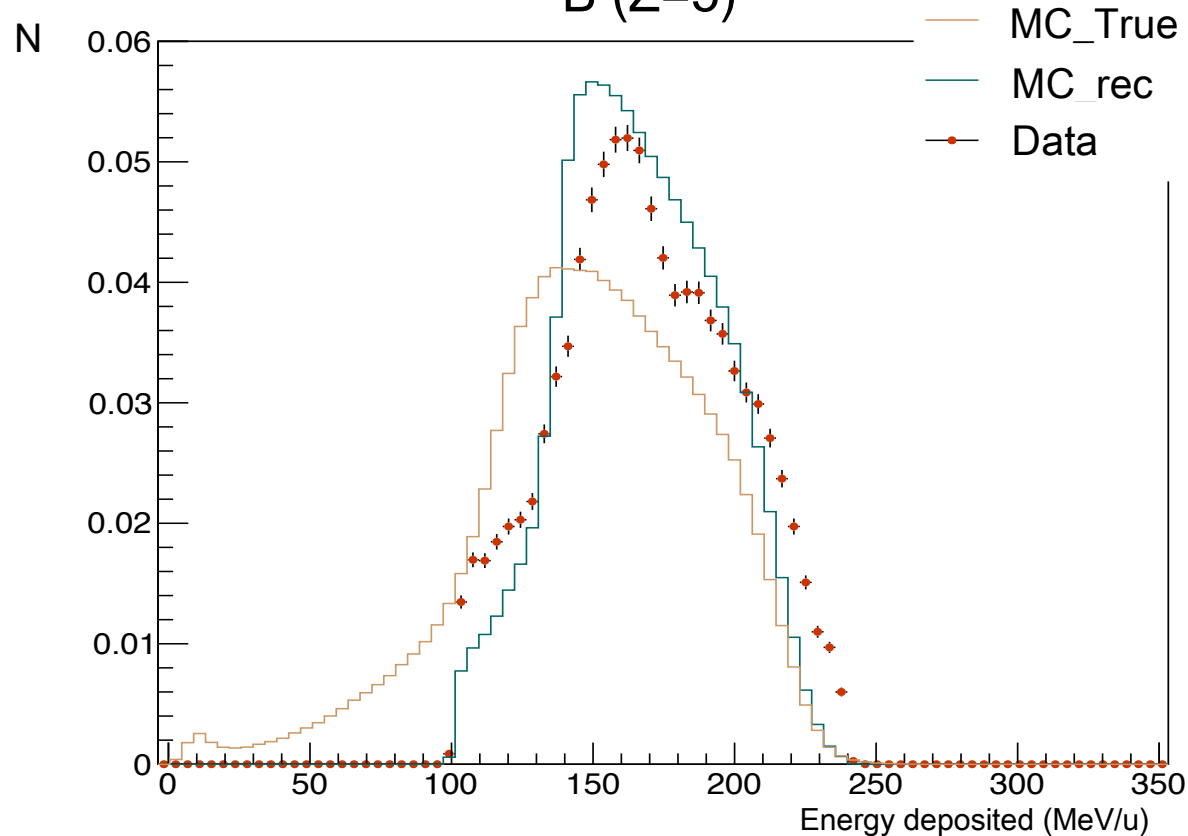
- High cut purity 80.05%
 - high purity at the higher energy setting
 - effective discrimination criteria
- Cut efficiency of 79.66%
 - reasonable balance between capturing most particles and maintaining purity

Secondary particles measurement Experiment at CNAO

Config.2



B (Z=5)



Z=5 Boron (MC_rec and exp data)

- Slight energy deviation of 10MeV/u
- Improved reproduction of calculated resolution

Z=5 Boron (MC_rec and MC_true)

- Consistent agreement in distribution and energy
- Small energy shift of 10MeV/u
- Marginal underestimation of 4.05% in the cut

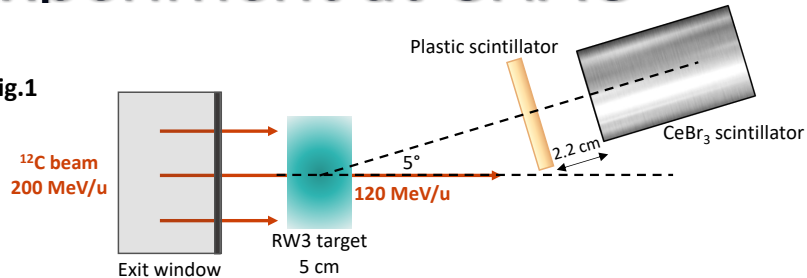
Z=5 Boron (purity and efficiency)

- High cut purity 92.16%
 - high purity at the higher energy setting
 - effective discrimination criteria
- Cut efficiency of 65.58%
 - reasonable balance between capturing most particles and maintaining purity

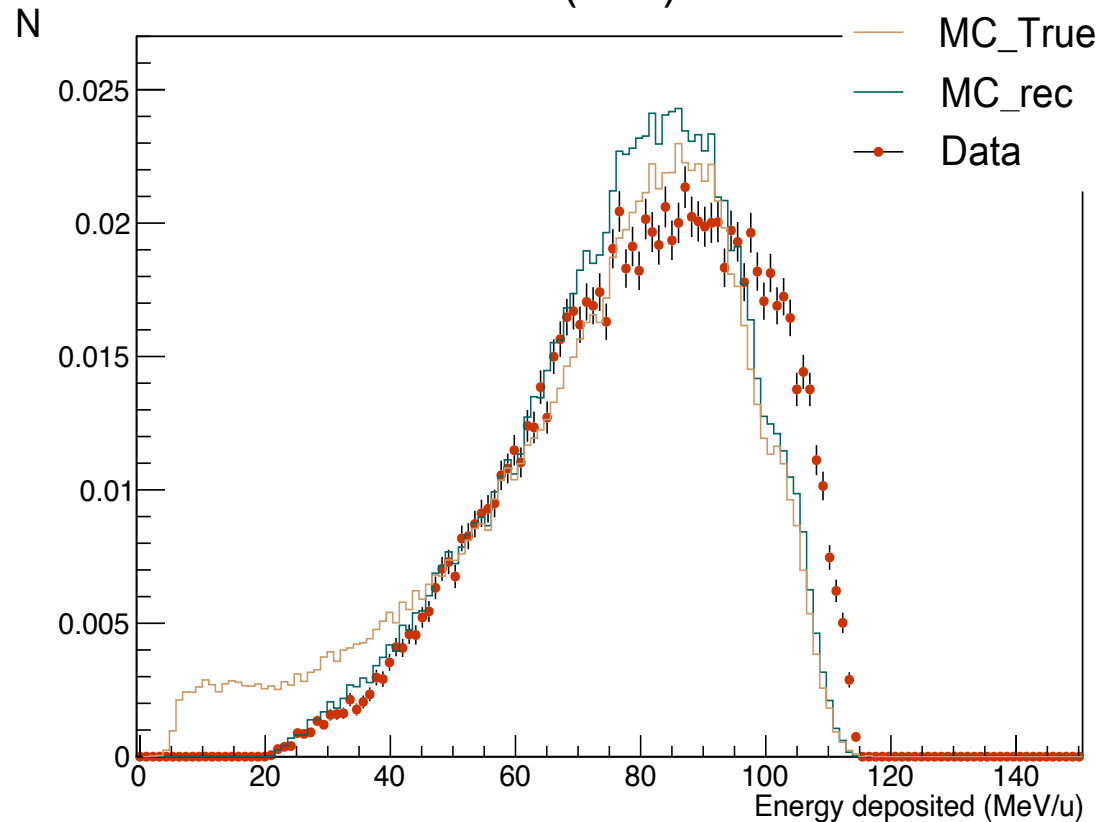
Secondary particles measurement

Experiment at CNAO

Config.1



C (Z=6)



Z=6 Carbon (MC_rec and exp data)

- Slight energy shift less than 5MeV/u
- Close reproduction of calculated resolution

Z=6 Carbon (MC_rec and MC_true)

- Consistent agreement in distribution and energy
- Significant underestimation of 59.84% in the cut

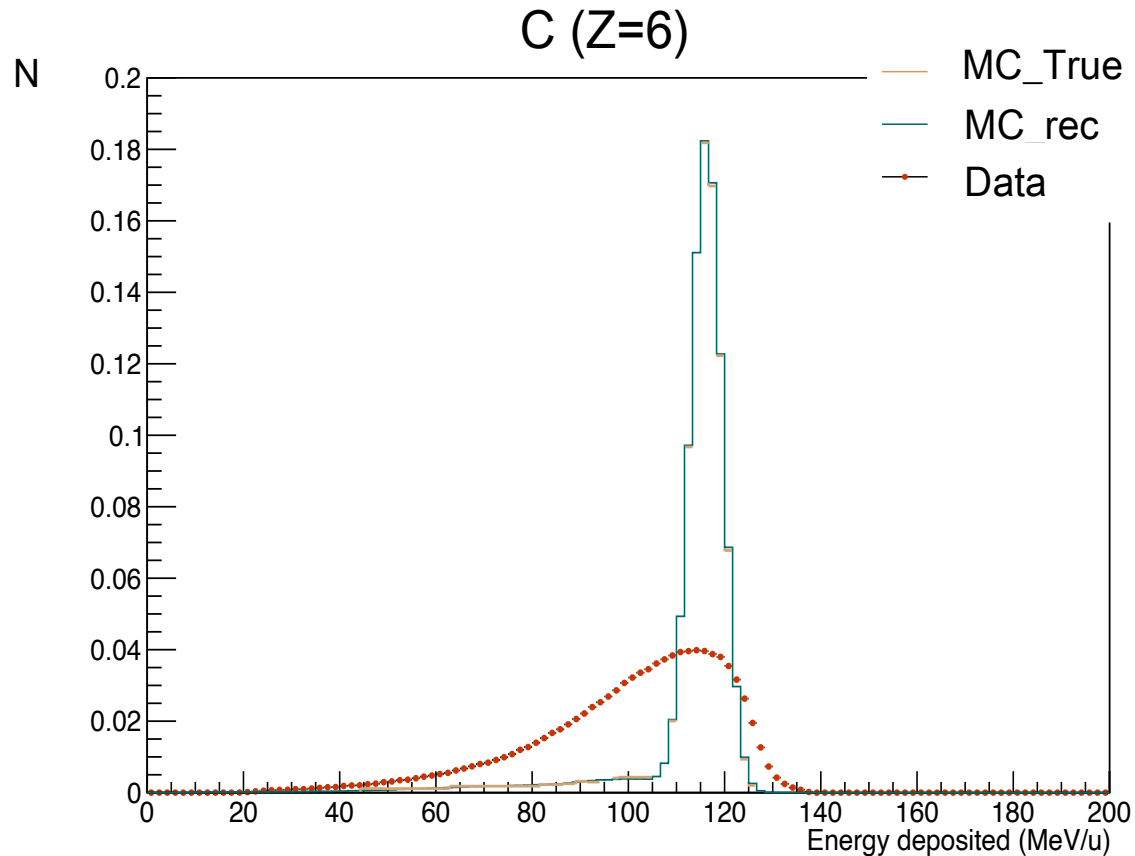
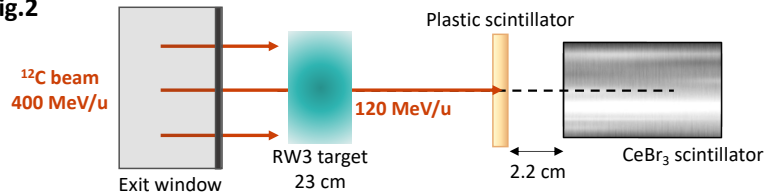
Z=6 Carbon (purity and efficiency)

- Highest cut purity 94.56%
 - good identification fidelity
- Cut efficiency 59.16%

Secondary particles measurement

Experiment at CNAO

Config.2



Z=6 Carbon (MC_rec and exp data)

- Slight energy shift less than 5MeV/u

Z=6 Carbon (MC_rec and MC_true)

- Consistent agreement in distribution and energy
- Insignificant underestimation of 0.24% in the cut

Z=6 Carbon (purity and efficiency)

- Highest cut purity 99.48%
 - good identification fidelity
 - isolation with great precision when aligned with the beam
- Cut efficiency 98.71%

Secondary particles measurement

Errors evaluation

Secondaries	200MeV/u on 5cm target, with detectors at 5°		400MeV/u on a 23cm target, with detectors at 0°	
	Cut purity	Cut efficiency	Cut purity	Cut efficiency
Z=1 (H)	$45.52 \pm 0.03 \%$	$75.01 \pm 0.03 \%$	$36.54 \pm 0.03 \%$	$78.88 \pm 0.04 \%$
Z=2 (He)	$88.01 \pm 0.01 \%$	$83.01 \pm 0.01 \%$	$85.11 \pm 0.01 \%$	$79.36 \pm 0.02 \%$
Z=3 (Li)	$53.27 \pm 0.06 \%$	$62.90 \pm 0.07 \%$	$58.18 \pm 0.04 \%$	$62.39 \pm 0.04 \%$
Z=4 (Be)	$77.92 \pm 0.09 \%$	$74.46 \pm 0.09 \%$	$69.96 \pm 0.05 \%$	$61.86 \pm 0.05 \%$
Z=5 (B)	$80.05 \pm 0.09 \%$	$79.52 \pm 0.10 \%$	$92.16 \pm 0.02 \%$	$65.58 \pm 0.03 \%$
Z=6 (C)	$94.56 \pm 0.08 \%$	$59.16 \pm 0.14 \%$	$99.48 \pm 0.01 \%$	$98.71 \pm 0.01 \%$

- Cut parameters highly effective for some Z (He and C)
- But variability in performance across different Z and experimental setups
- For H and Li further refinement of detectors resolution needed
 - adjusting ΔE -E thresholds to reduce overlap
 - adding detectors
 - use better resolution detector than plastic like silicium