Recent developments of FLUKA for hadron therapy

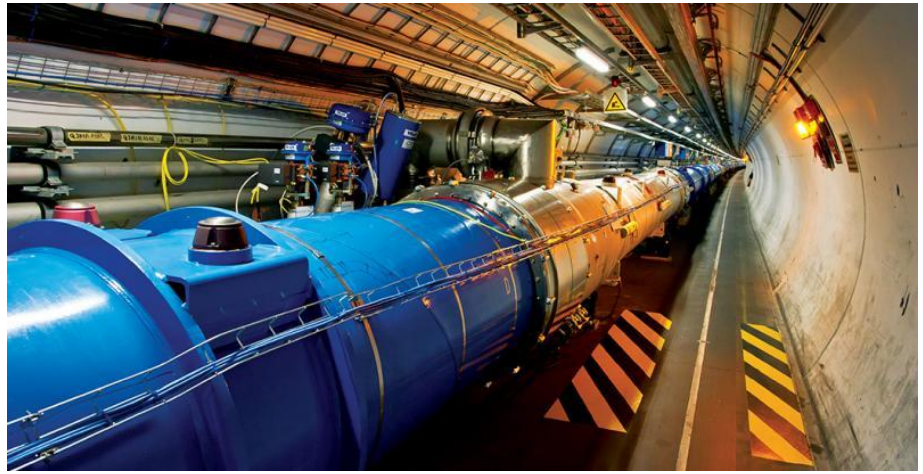
Giulia Aricò (CERN), Francesca Ballarini (University and INFN of Pavia), Judith Besuglow (HIT), Mario Carante (INFN of Pavia), Felix Horst (GSI and THM), Wioletta Kozlowska (CERN), Giuseppe Magro (CNAO), Andrea Mairani (HIT and CNAO), Stuart Mein (HIT), Christoph Schuy (GSI), Uli Weber (GSI) and Alfredo Ferrari (CERN)

Outline

- **Introduction to FLUKA**
- Nuclear reaction cross sections in FLUKA for helium ions
- Radiobiological studies in FLUKA for hadron therapy

FLUKA

- a fully integrated particle physics Monte Carlo code
- simulations of particle transport and interactions with matter
- widely used in physics for :
  - particle accelerator and detector design
  - shielding
  - dosimetry
  - calorimetry
  - activation
  - medical applications ⇨ **Hadron therapy**



LHC at CERN

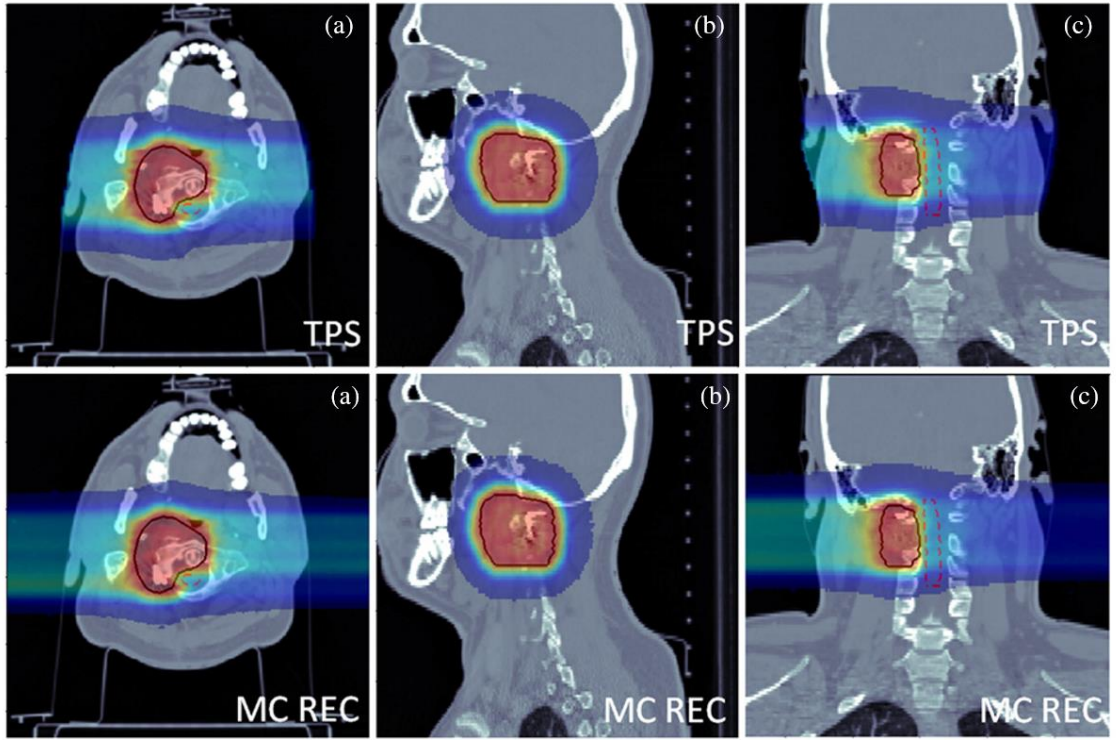
https://home.cern/topics/large-hadron-collider

Medical applications

At CNAO (Italy), HIT and MIT (Germany), cancer patients are treated with protons and carbon ions.

In those facilities FLUKA is used:

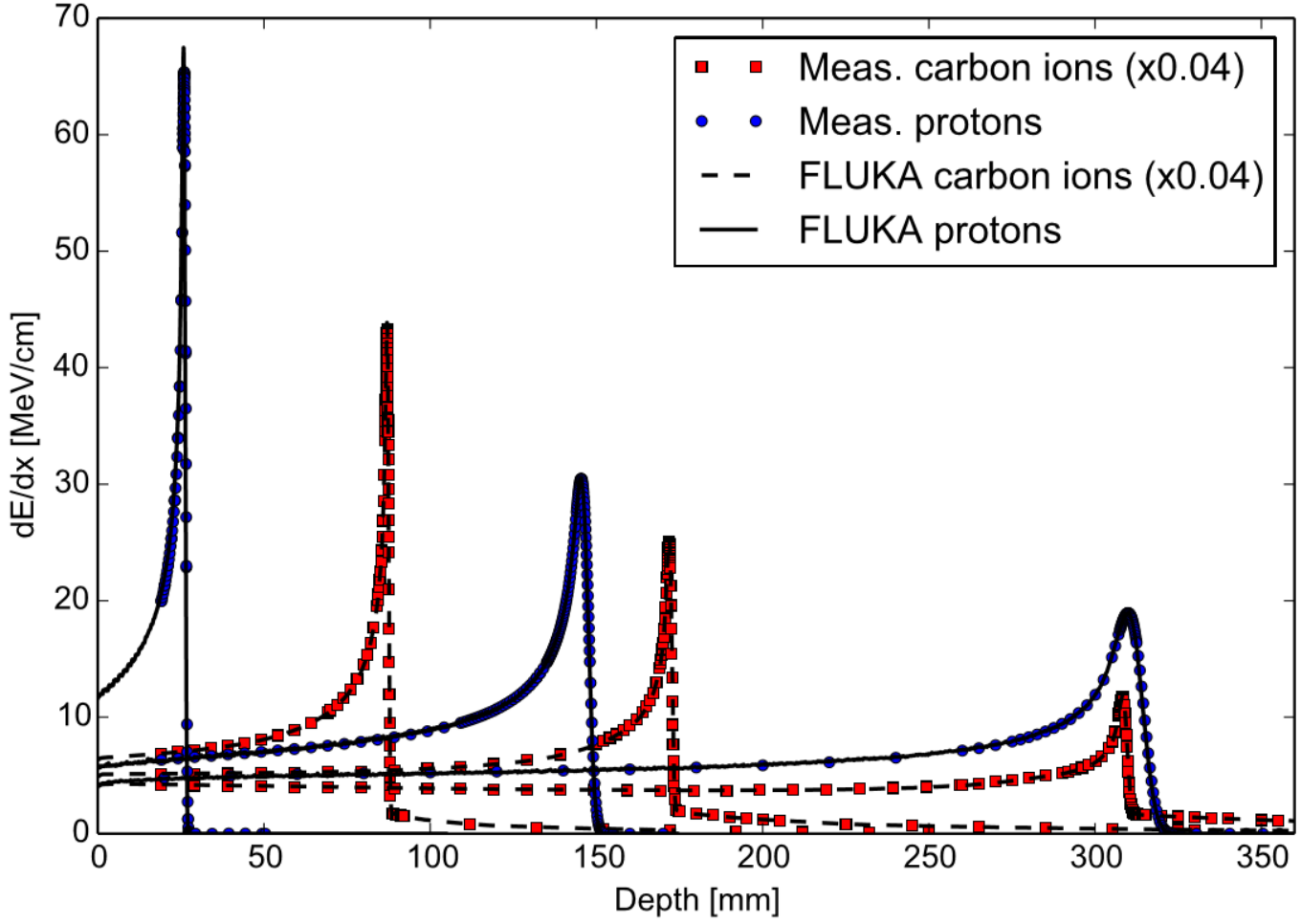
- to **generate input data** for the treatment planning systems,
- to **validate the dose calculations**.



Mairani A *et al* PMB **58** (2013) 2471-2490

Medical applications

Single Bragg Peaks



Data acquired at HIT:

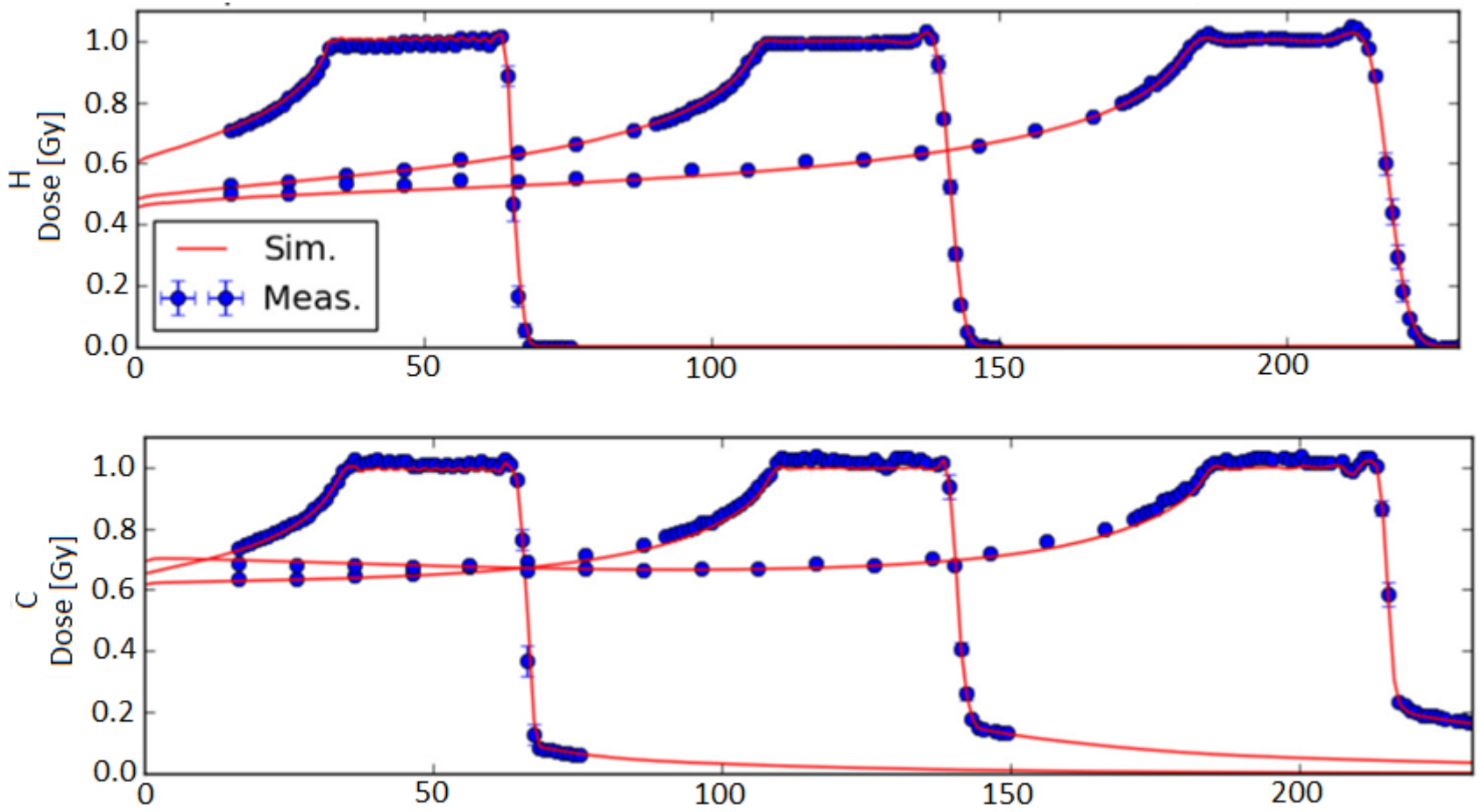
Ep = 54.10 MeV
142.66 MeV
221.05 MeV

EC = 200.28 MeV/u
299.94 MeV/u
430.10 MeV/u

Battistoni G *et al* (2016) Front Oncol 6:116

Medical applications

Spread out Bragg Peaks



Tessonnier T *et al*
PMB.**62**(2017) 6579-6594

Overview

- Introduction to FLUKA
- **Nuclear reaction cross sections in FLUKA for helium ions**
- Radiobiological studies in FLUKA for hadron therapy

Helium ion therapy

The interest on helium ions is growing fast in the last years.

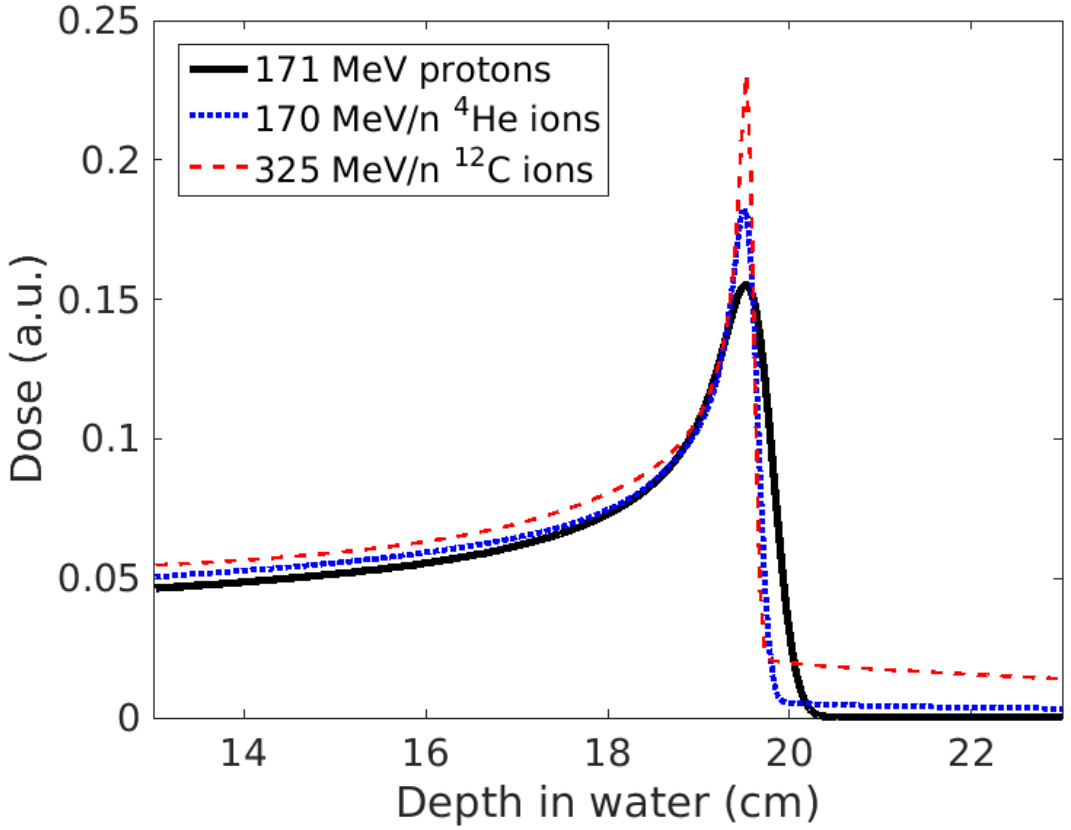
The Heidelberg Ion-Beam Therapy center (HIT, Germany) is planning to use helium ion beams for radiotherapy in the near future.

Helium ions vs protons:

- ✓ Less scattering
- ✓ Wider penumbra
- X Higher costs

Helium ions vs carbon ions:

- ❑ Lower RBE
- ✓ Less fragmentation tail
- ✓ Lower costs



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- ✓ Less fragmentation tail
- ✓ Lower costs

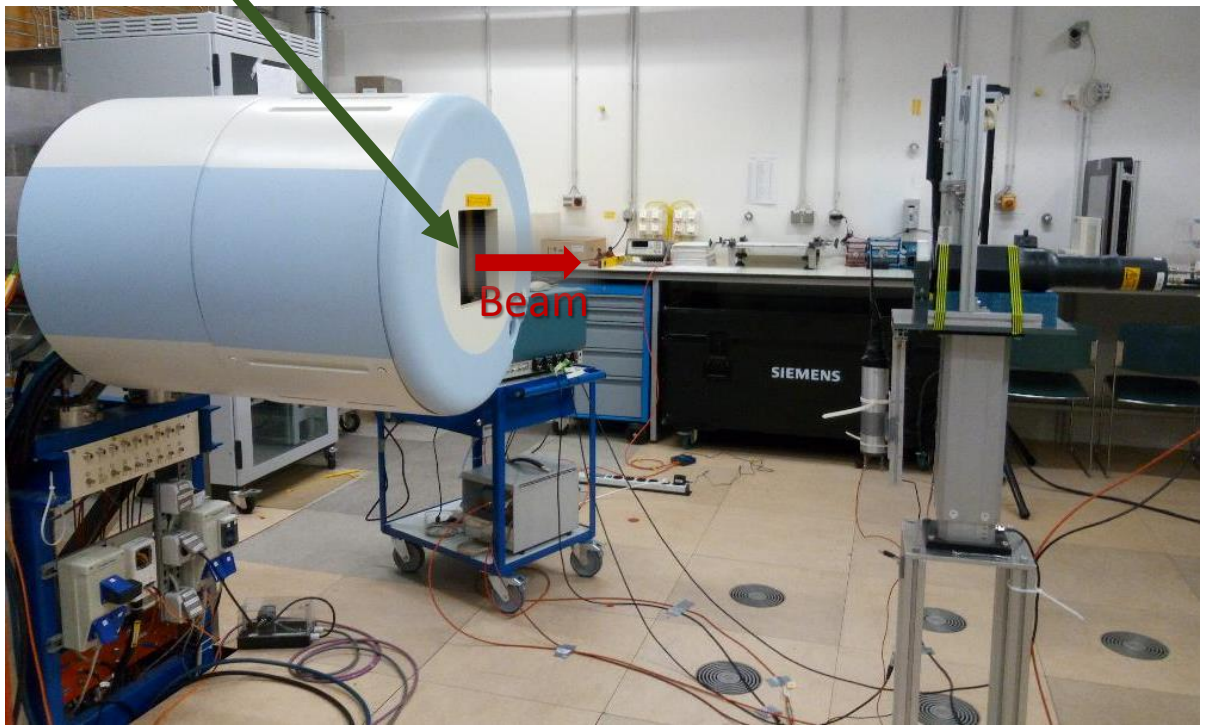
AIM:

Improvements of the **nuclear reaction model** in FLUKA for helium ions

Experimental setup

Incident beam : He ions

Exp. setup mounted @ HIT

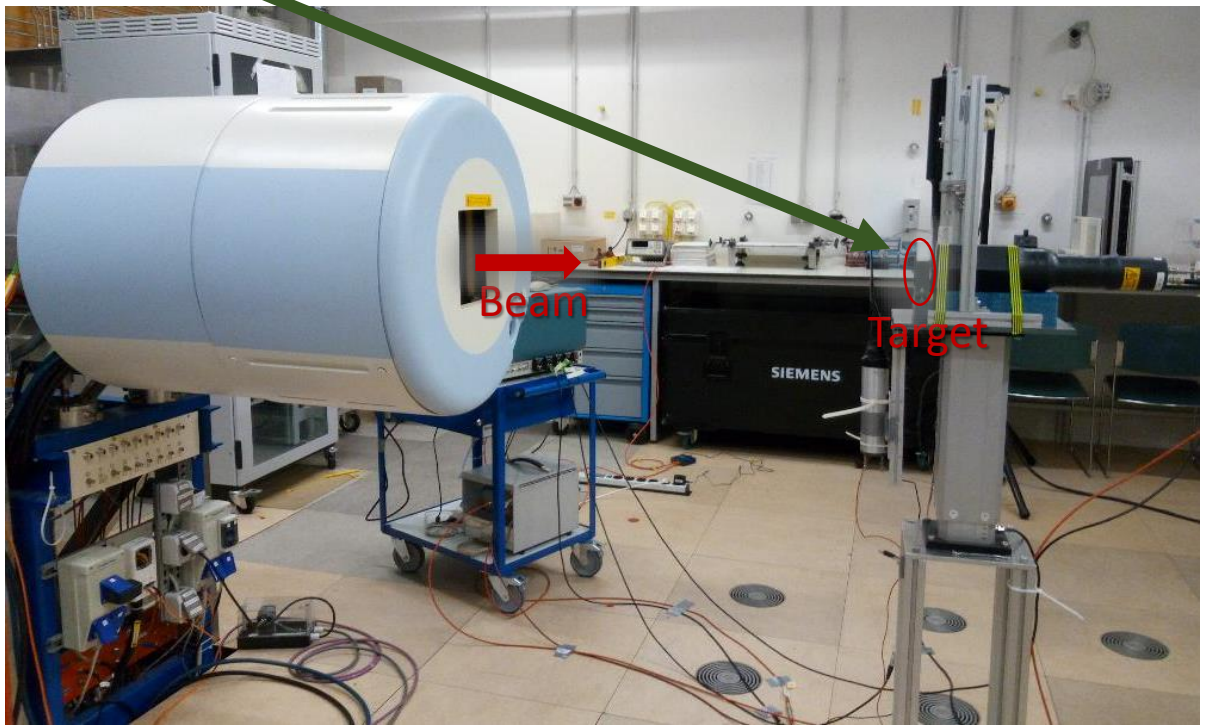


Experimental setup

Incident beam : He ions

Target : thin graphite, silicon, silicon dioxide

Exp. setup mounted @ HIT



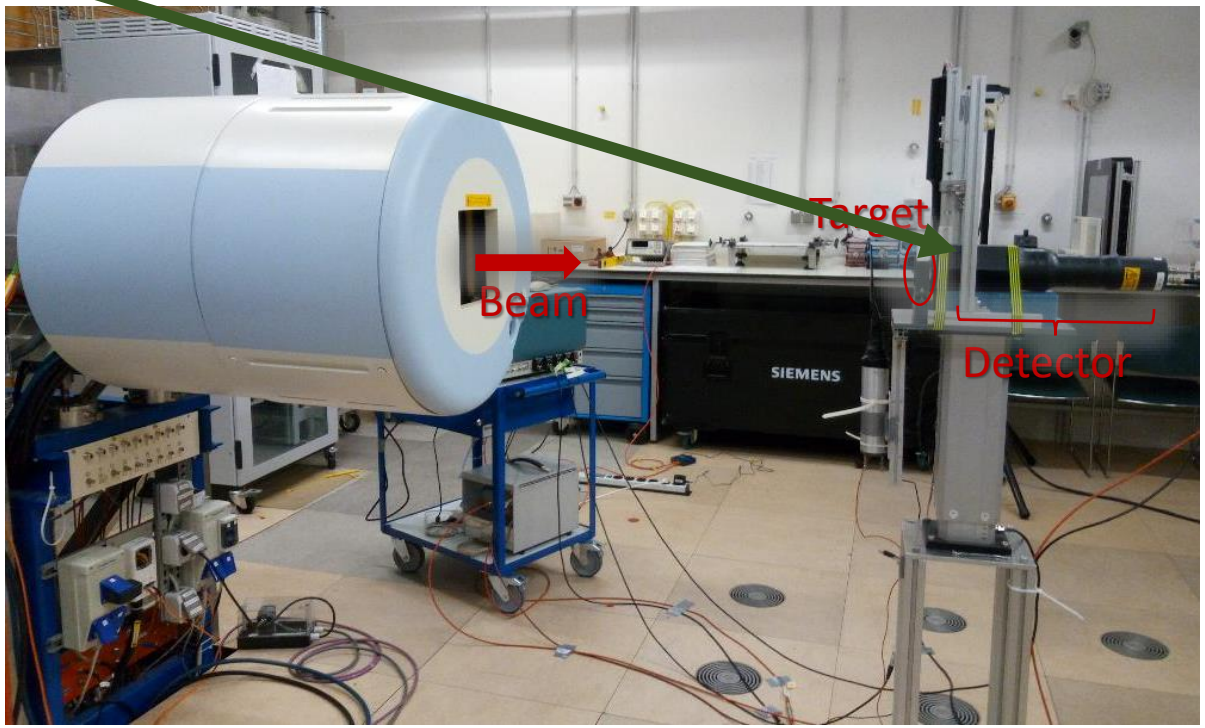
Experimental setup

Incident beam : He ions

Target : thin graphite, silicon, silicon dioxide

Detector : $\Delta E/E$ telescope (provided by GSI)

Exp. setup mounted @ HIT



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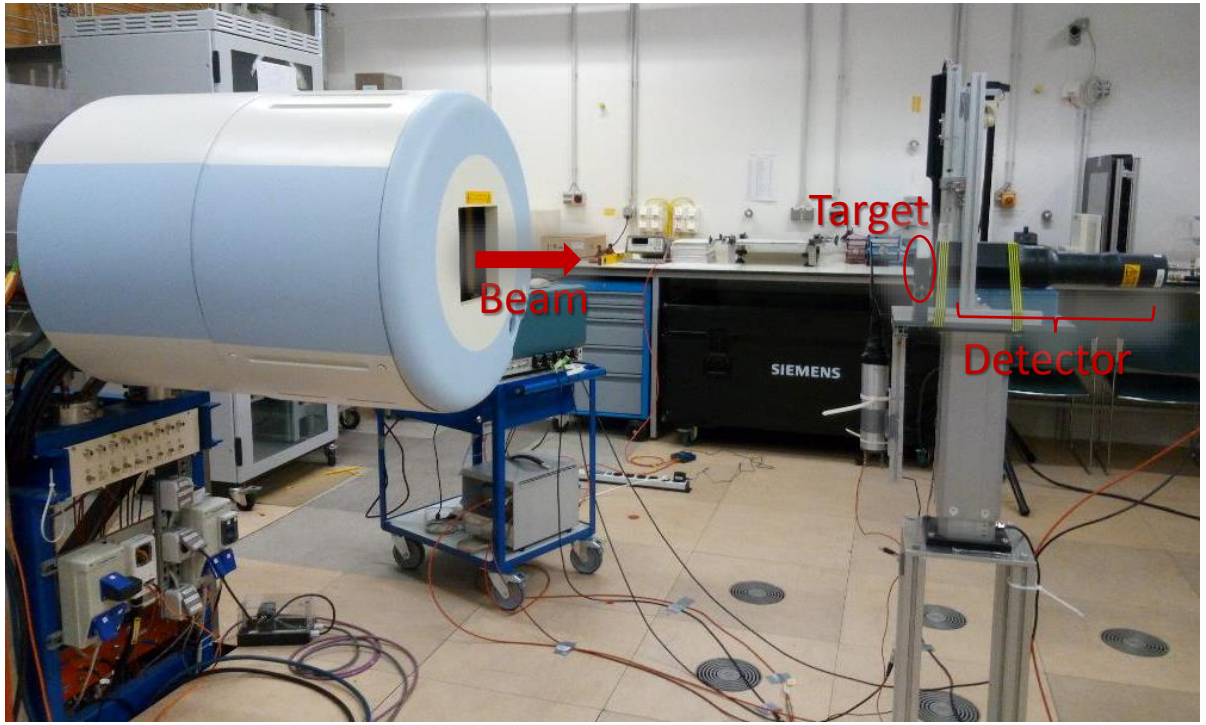


Experimental measurements:

mass changing cross sections ($\sigma_{\Delta A}$)

charge changing cross sections ($\sigma_{\Delta Z}$)

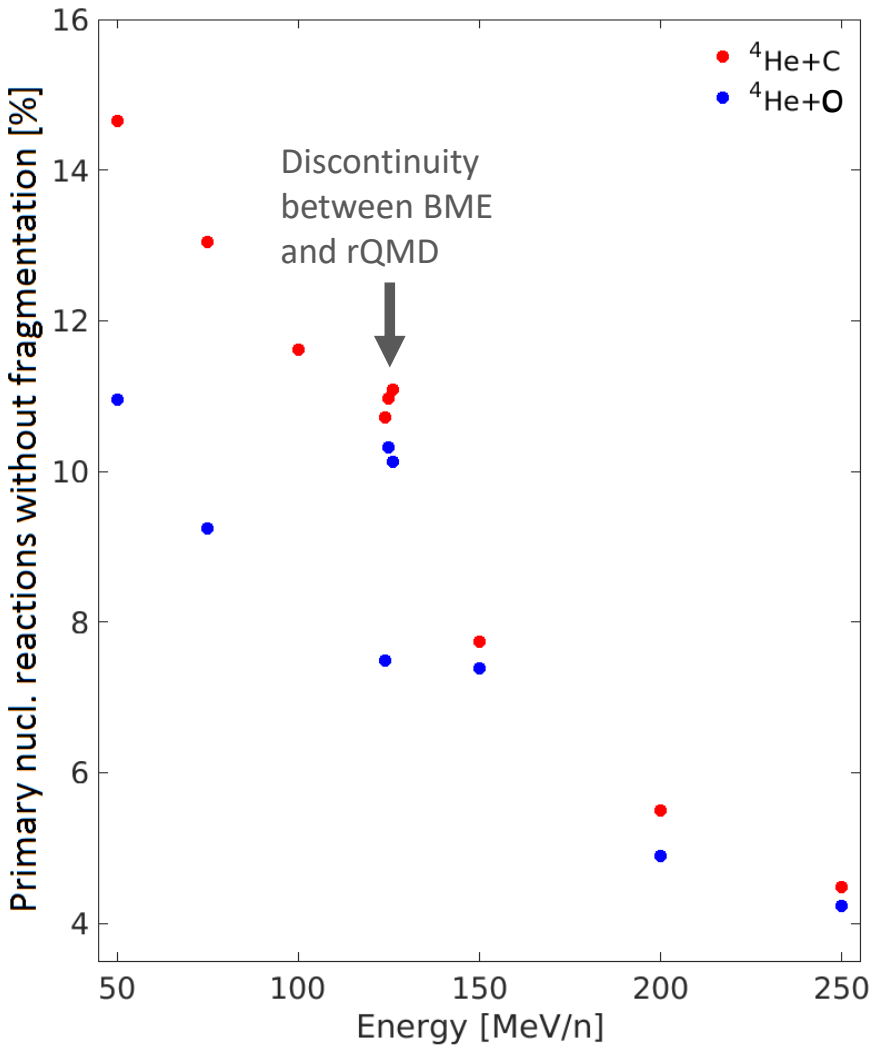
$^4He + T \rightarrow X + R$

Note:

Primary helium ions that interact in the target without undergoing fragmentation are not measured in the experiments

$^4He + T \rightarrow {}^4He + T^*$

Results



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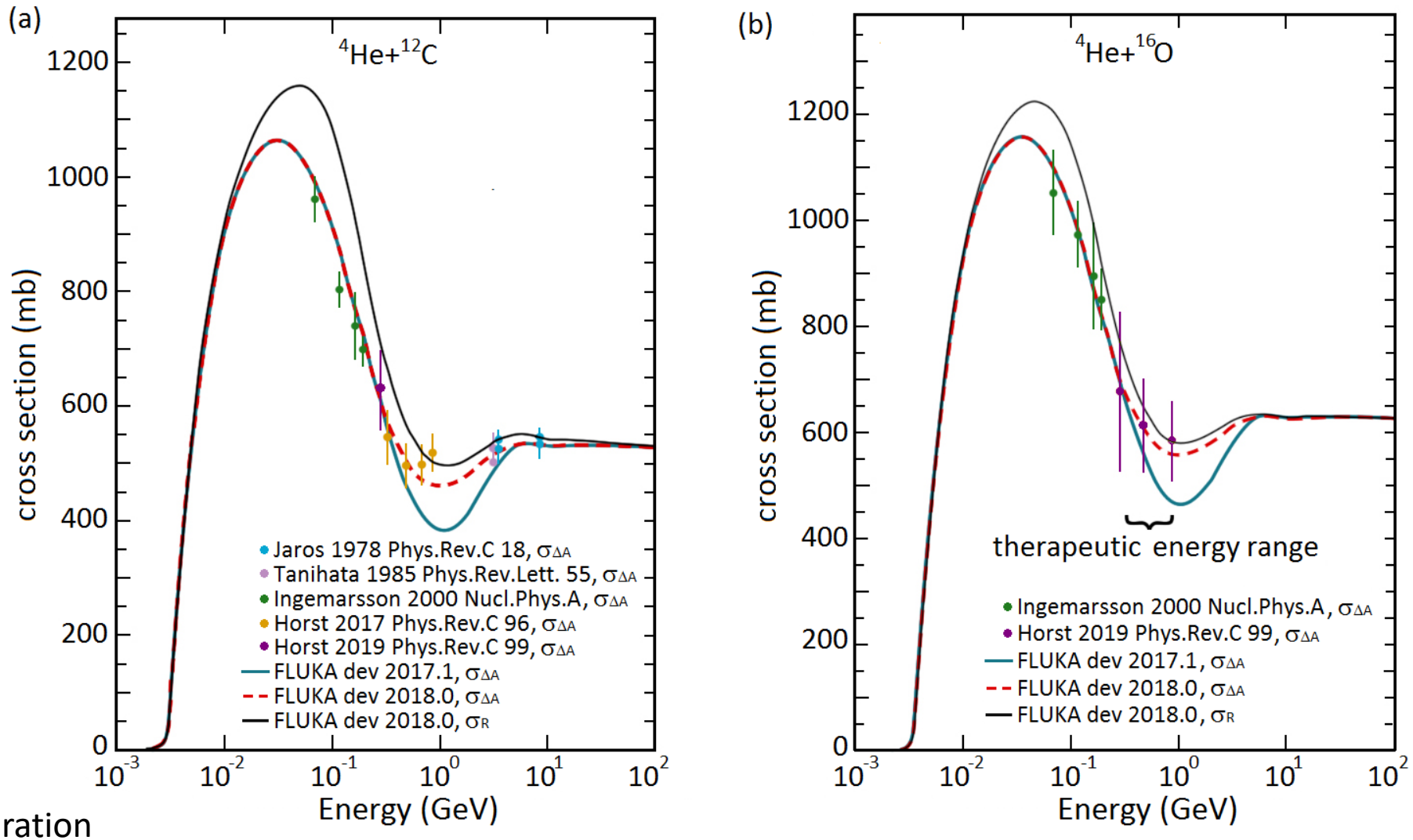
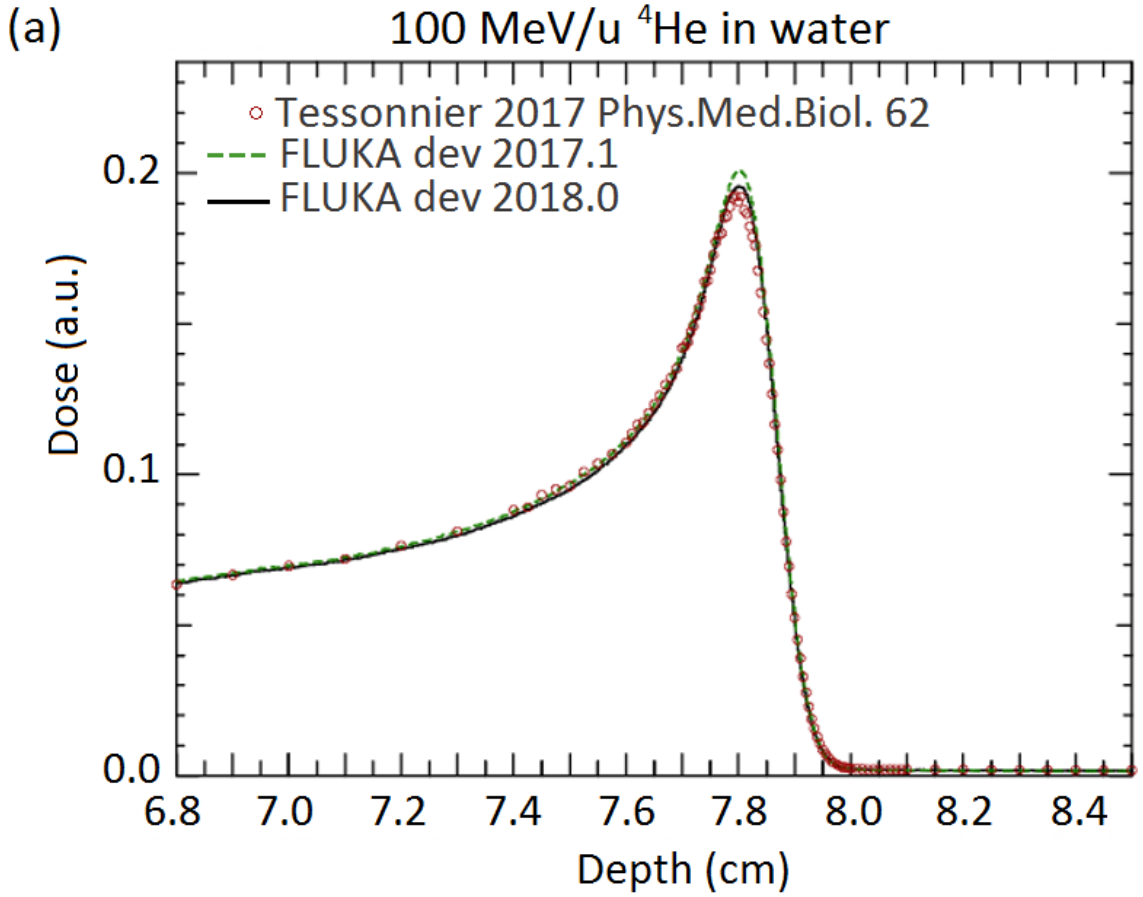
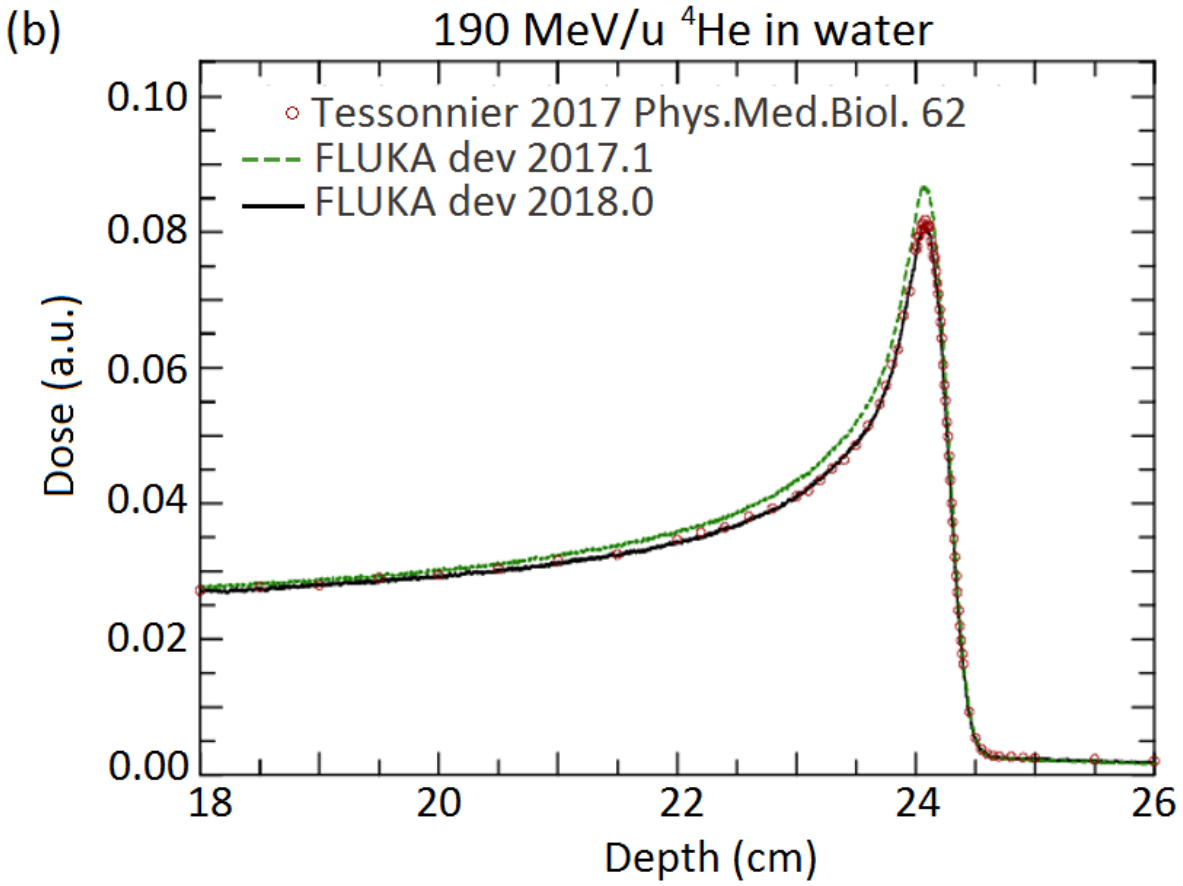


Article in preparation

Results





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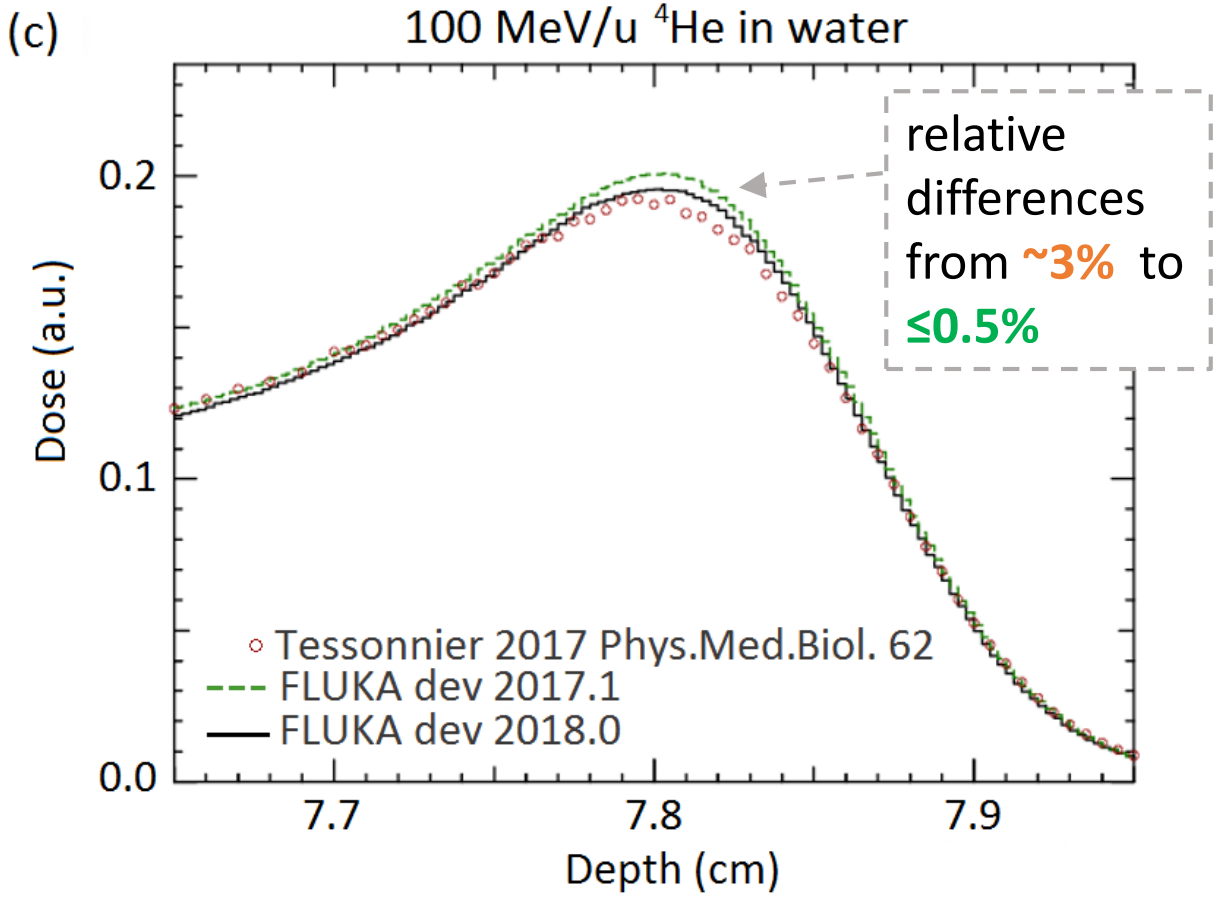
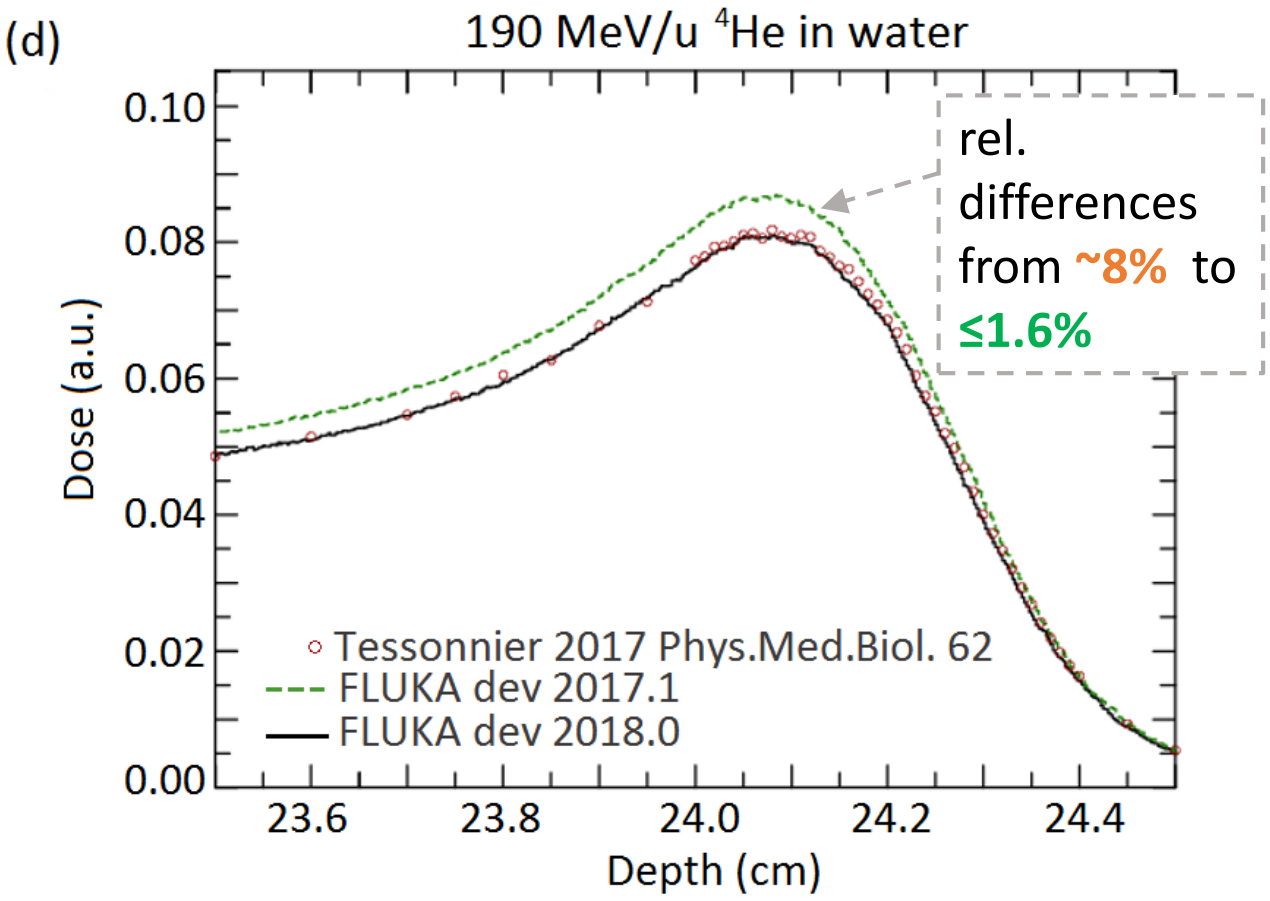
Results





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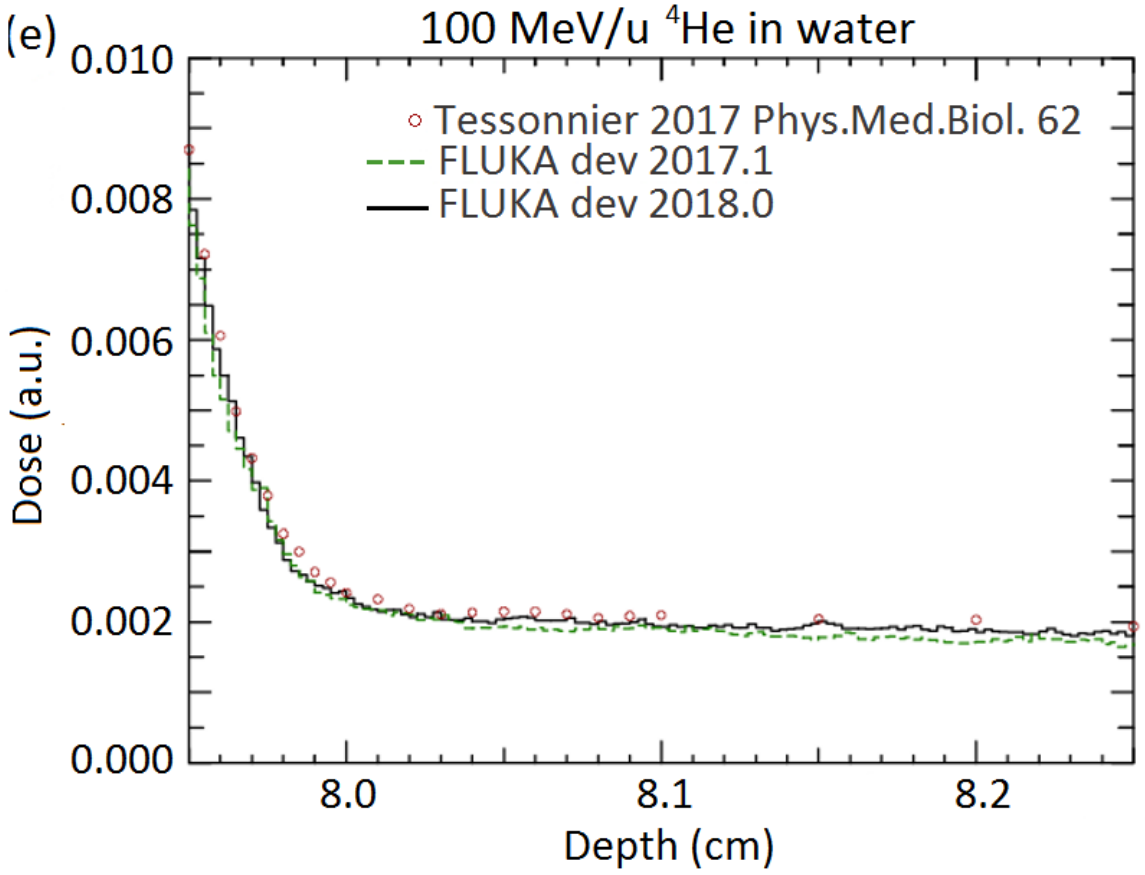
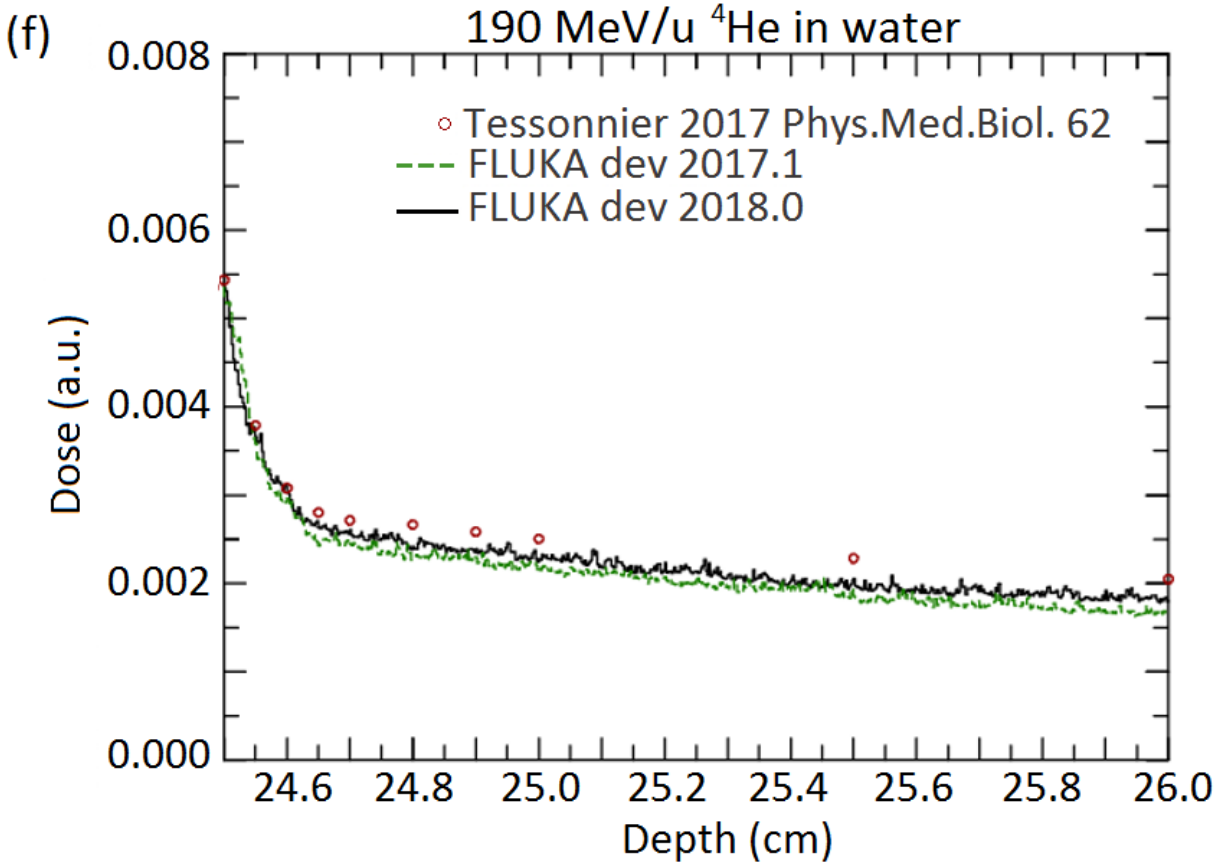
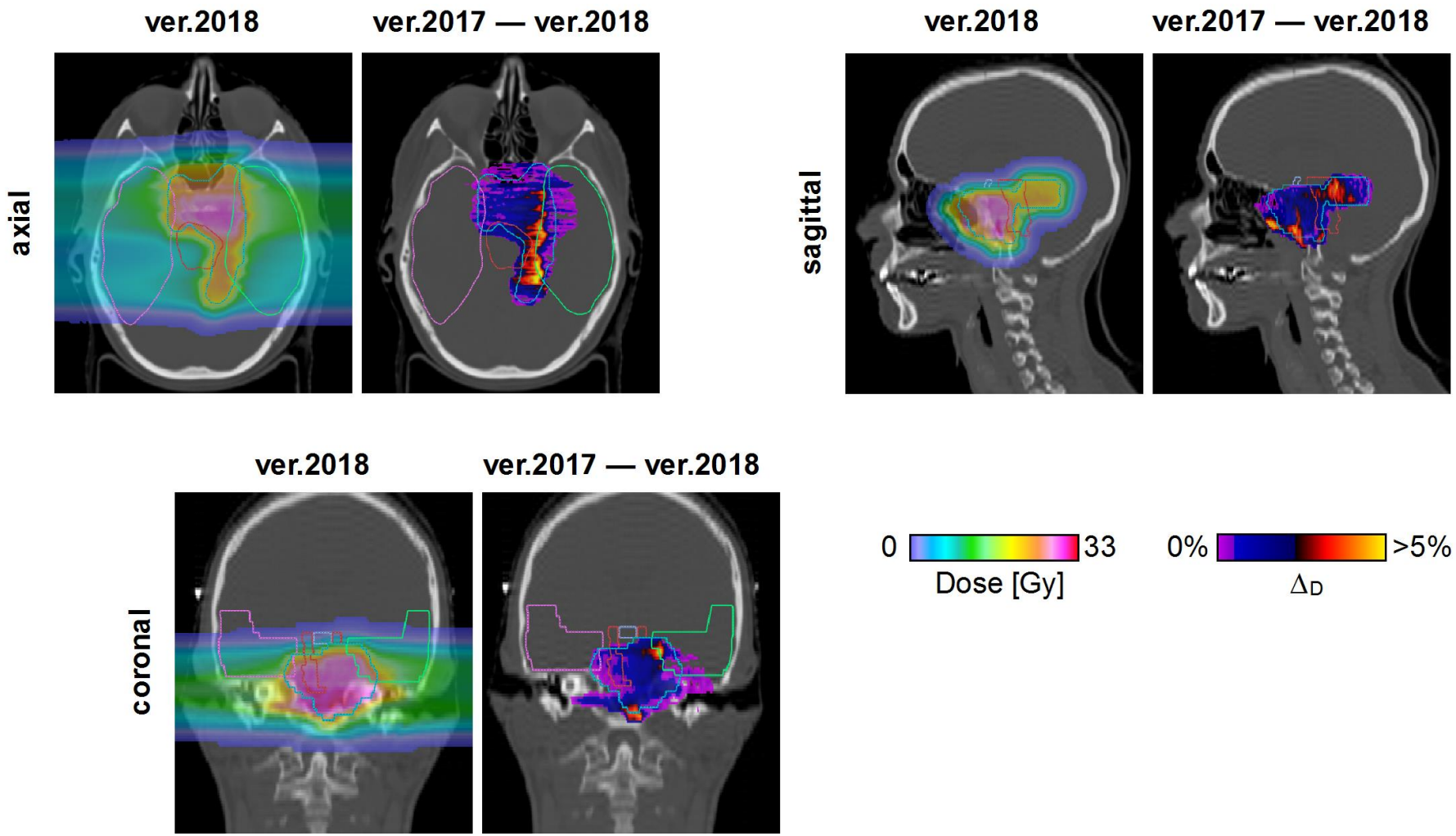
Results





Article in preparation

Results



Article in preparation

Summary and Conclusions

In some cases, helium ion therapy can be a viable alternative to proton and carbon ion therapy.

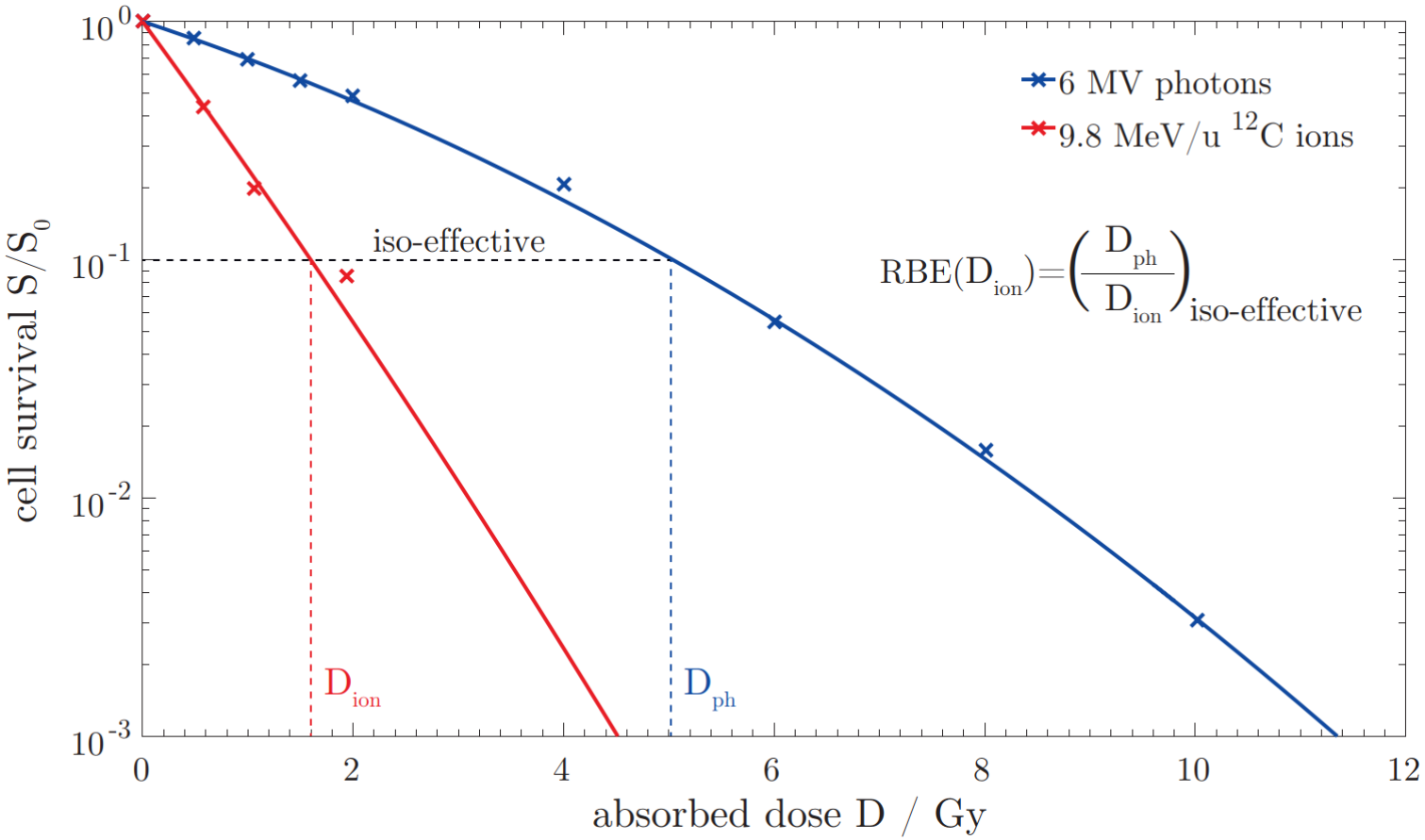
- Prior to the use of helium ions for clinical applications, their physical and biological properties have to be well known.
- New experimental data in the therapeutic energy range were used to benchmark the FLUKA nuclear reaction cross sections.
- An additional renormalization factor was considered to calculate the total reaction cross section from the fragmentation cross section (measured in the experiments).

➢ Improvements in the FLUKA nuclear reaction cross sections were needed for more accurate dose calculations.

Overview

- Introduction to FLUKA
- Nuclear reaction cross sections in FLUKA for helium ions
- **Radiobiological studies in FLUKA for hadron therapy**

Definition of RBE



Relative biological effectiveness:

$$RBE = \frac{D_\gamma}{D_{ion}}\bigg|_{isoeffect}$$

RBE depends on:
- LET
- Dose
- Particle type
- Radiosensitivity

Radiobiological models

Protons: RBE = 1.1

Carbon and Helium ions: radiobiological models

- Local Effect Model (LEM) used in clinics in Europe (developed at GSI)
- Microdosimetric Kinetic Model (MKM) used in clinics in Japan
- BIophysical ANalysis of Cell death and chromosome Aberrations (BIANCA) developed at the University and INFN of Pavia

Radiobiological models

- Local Effect Model I (LEM I) :

  the damage in a cellular sub-volume is related to the expected energy deposition in that sub-volume,

  tested against survival curves of CHO and V79 cells in vitro, and against in vivo data of rat spinal cord.

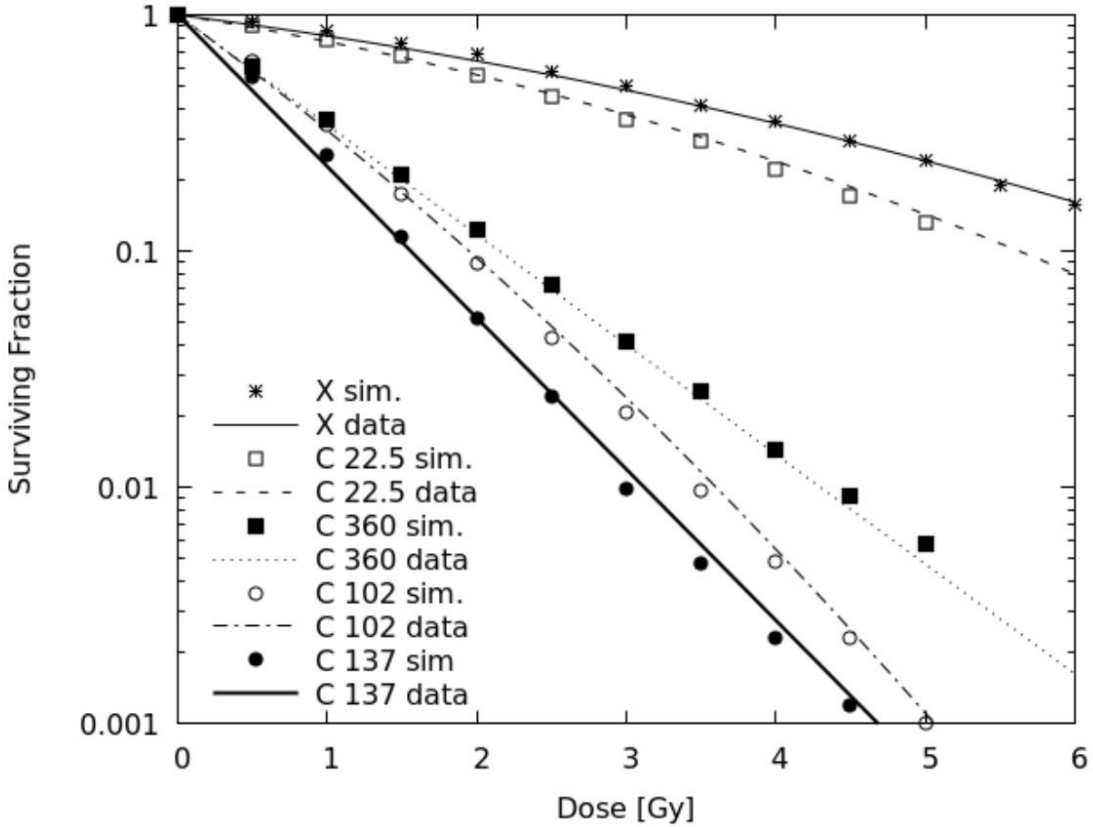
- BIophysical ANalysis of Cell death and chromosome Aberrations (BIANCA) :

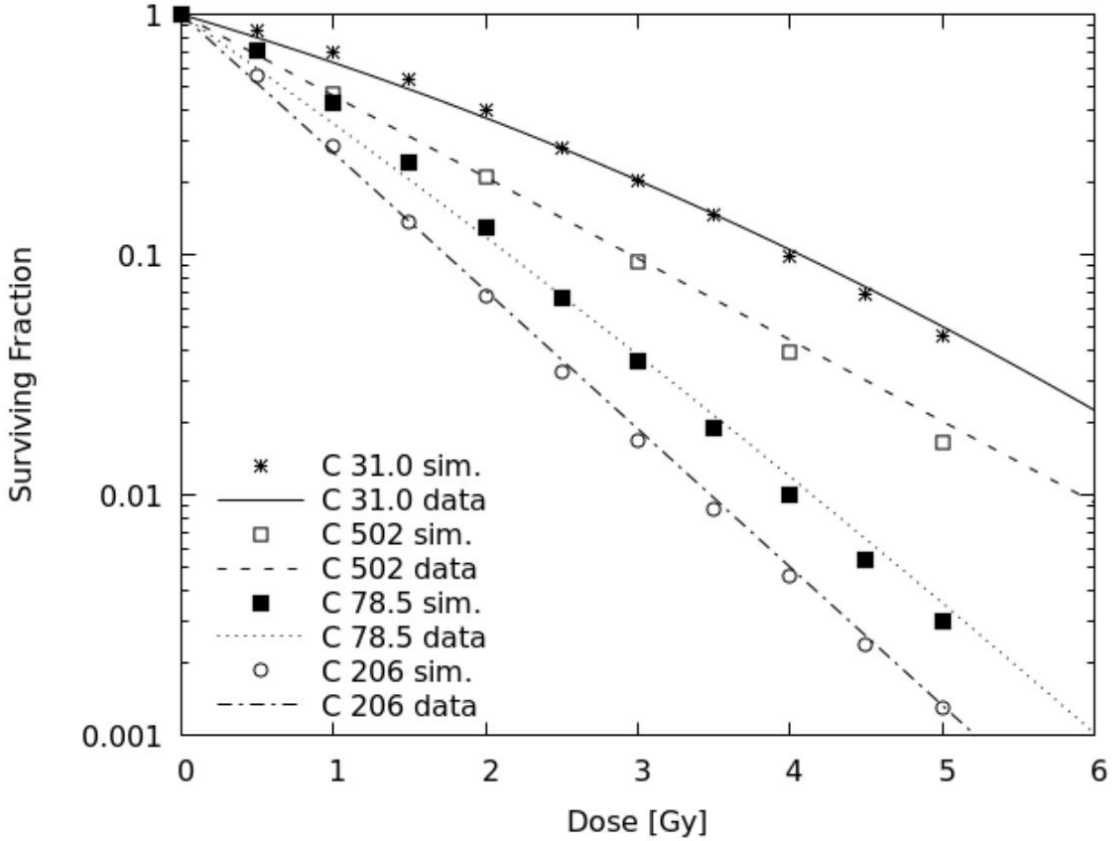
  the cell death is directly correlated to the chromosome aberration,

  tested against survival curves of V79, AG01522, U87 and CHO cells in vitro.

Benchmarking of BIANCA

Survival of V79 cells irradiated by **carbon ion** beams of different (dose-averaged) LET [keV µm^{-1}]



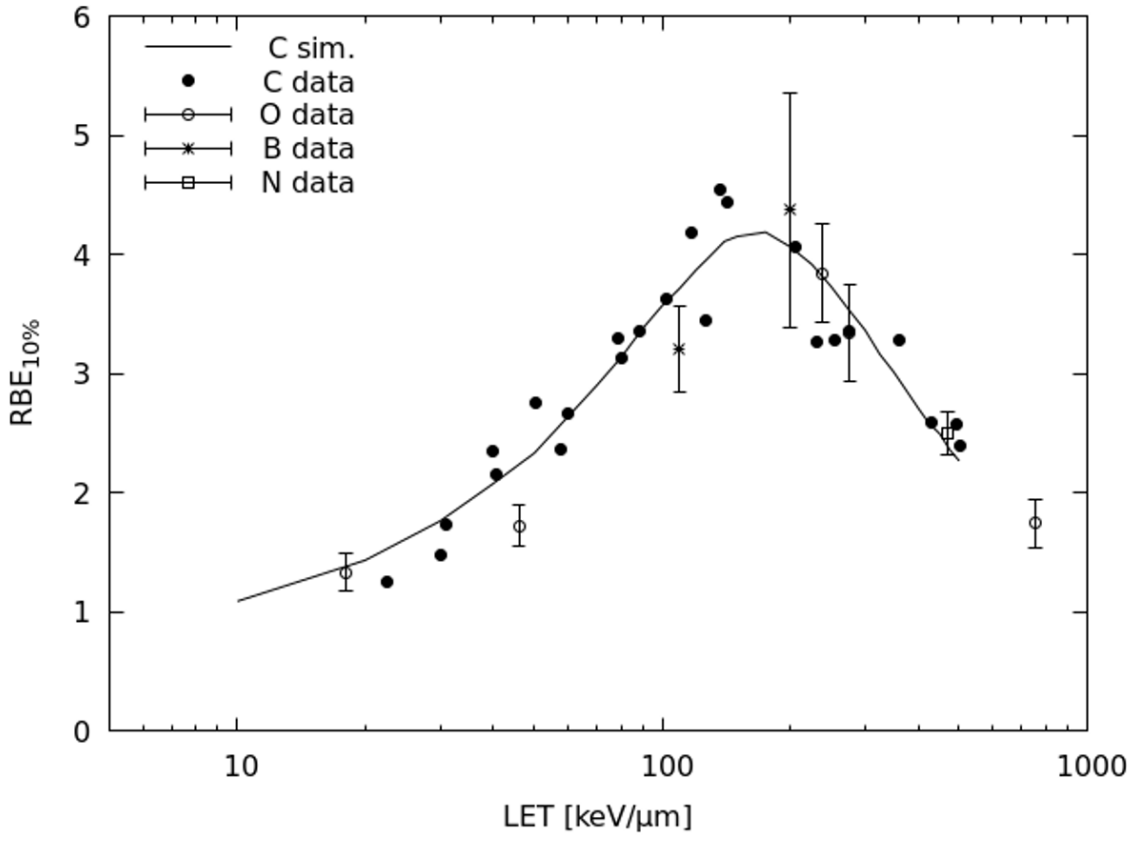


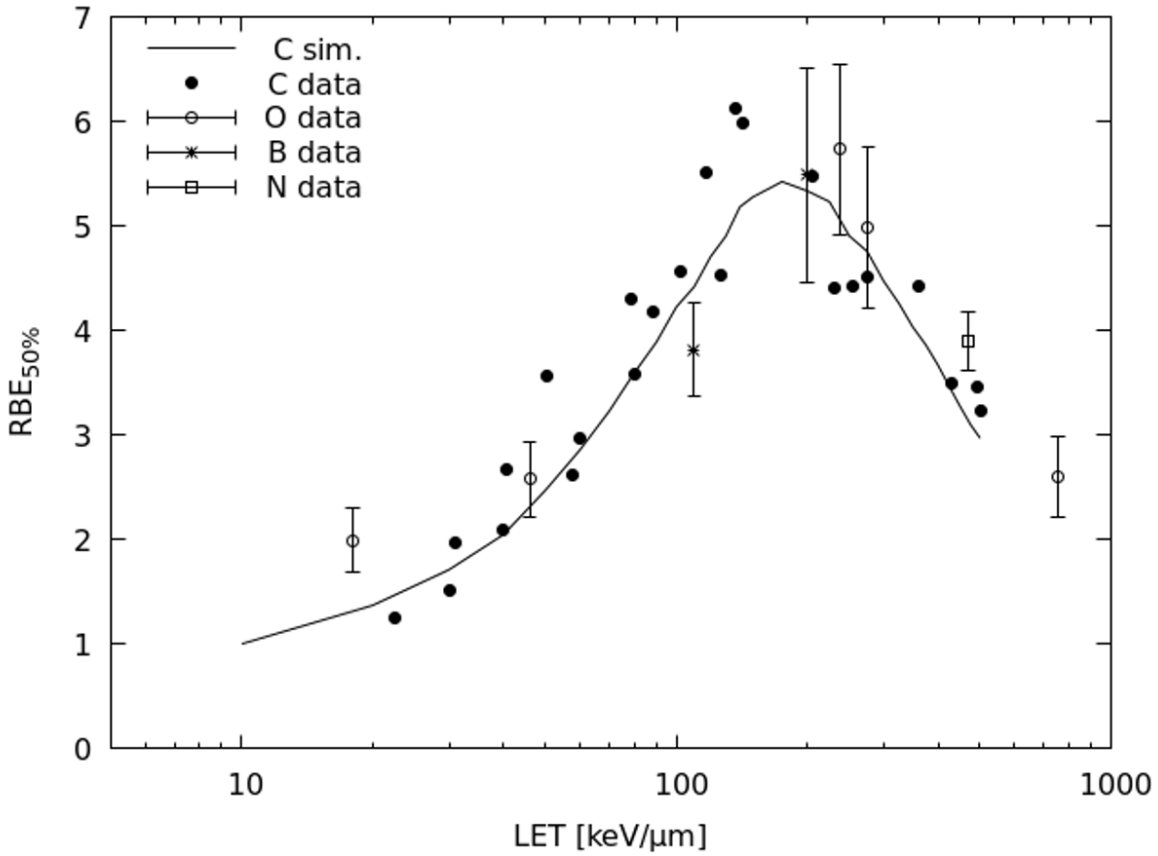
Carante MP *et al.* 2018 Phys. Med. Biol. 63 075007

Exp data from Furusawa Y *et al.* 2000 Radiat. Res. 154 485–96

Benchmarking of BIANCA

RBE at 10% and 50% survival of V79 cells





Carante MP *et al.* submitted to Phys. Med. Biol.

Method

1) FLUKA simulations + radiobiological model (tabulation of α and β for mixed ion fields)

2) Scoring of α, β, and absolute dose in FLUKA, in each bin, in water or in a patient case

3) Computation of survival cells :

$$-\ln(S) = \begin{cases} \overline{\alpha} D + \overline{\beta} D^2 & D \leqslant D_t \\ \overline{\alpha} D_t + \overline{\beta} D_t^2 + (D - D_t) s_{\max} & D > D_t \end{cases}$$

D_{RBE} :

$$D_{\mathrm{RBE}} = \begin{cases} \sqrt{-\ln(S)/\beta_X + (\alpha_X/(2\beta_X))^2} - (\alpha_X/(2\beta_X)) & -\ln(S) \leqslant -\ln(S_t) \\ (-\ln(S) + \ln(S_t))/s_{\max} + D_t & -\ln(S) > -\ln(S_t) \end{cases}$$

and RBE :

$$\mathrm{RBE} = D_{\mathrm{RBE}}/D$$

Similar approach* for LEM and BIANCA, but :

different α, β, α_x and β_x values, and no D_t and S_t in BIANCA

*Mairani A *et al.* 2010 Phys. Med. Biol. **55** 4273–4289
Carante MP *et al.* submitted to Phys. Med. Biol.

Comparison with SOBP experimental data

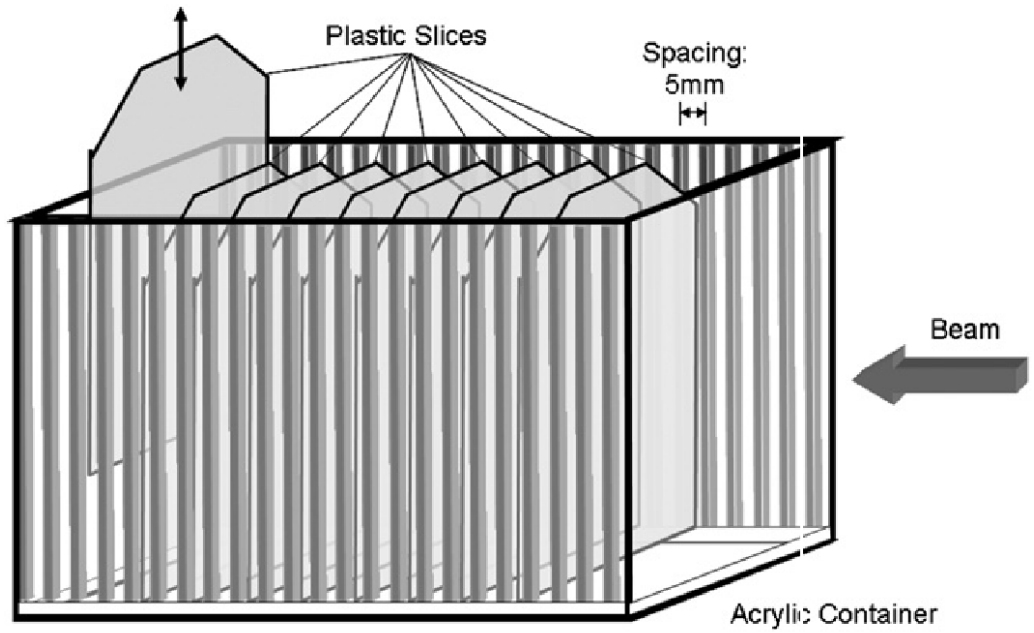


Fig. 1. Schematic view of the acrylic phantom used for the experiments.

Acrylic container 5 cm x 10 cm x 16 cm.
Cells grown as monolayers on 25 cm^2 polyethylene slices.
Chinese hamster ovary cells (CHO-K1) grown under standard conditions.

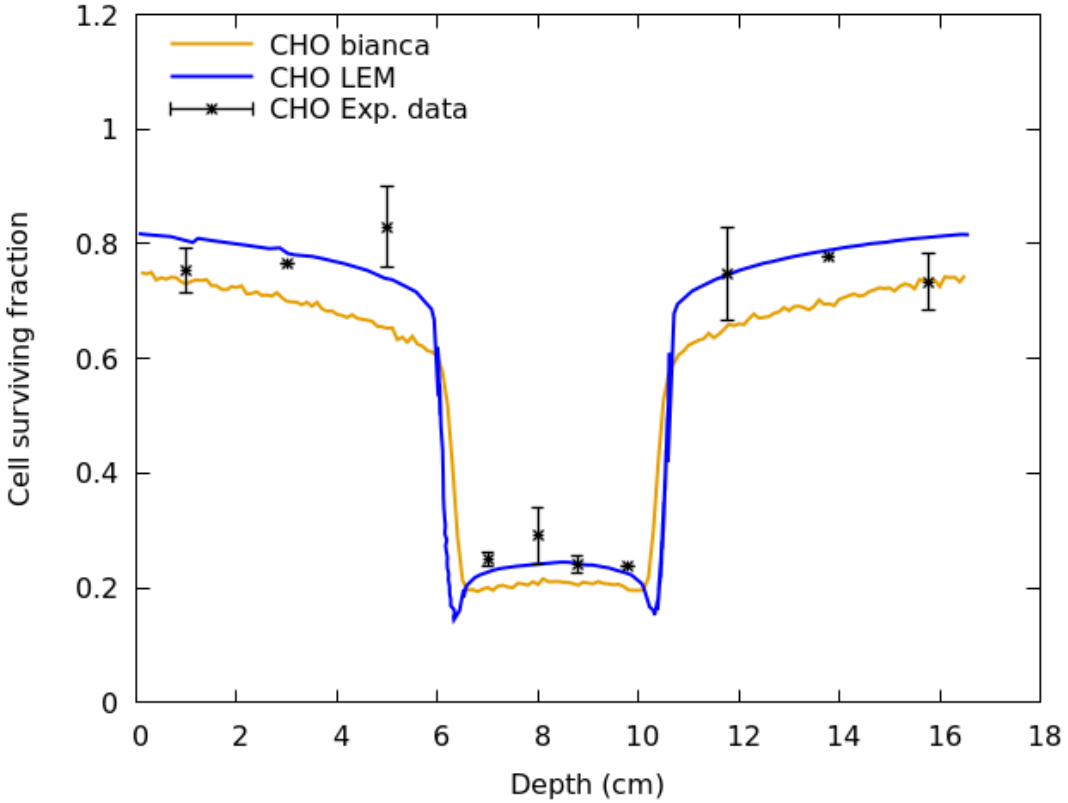
Measurements performed at HIT (proton and carbon ions) or at GSI (helium ions).

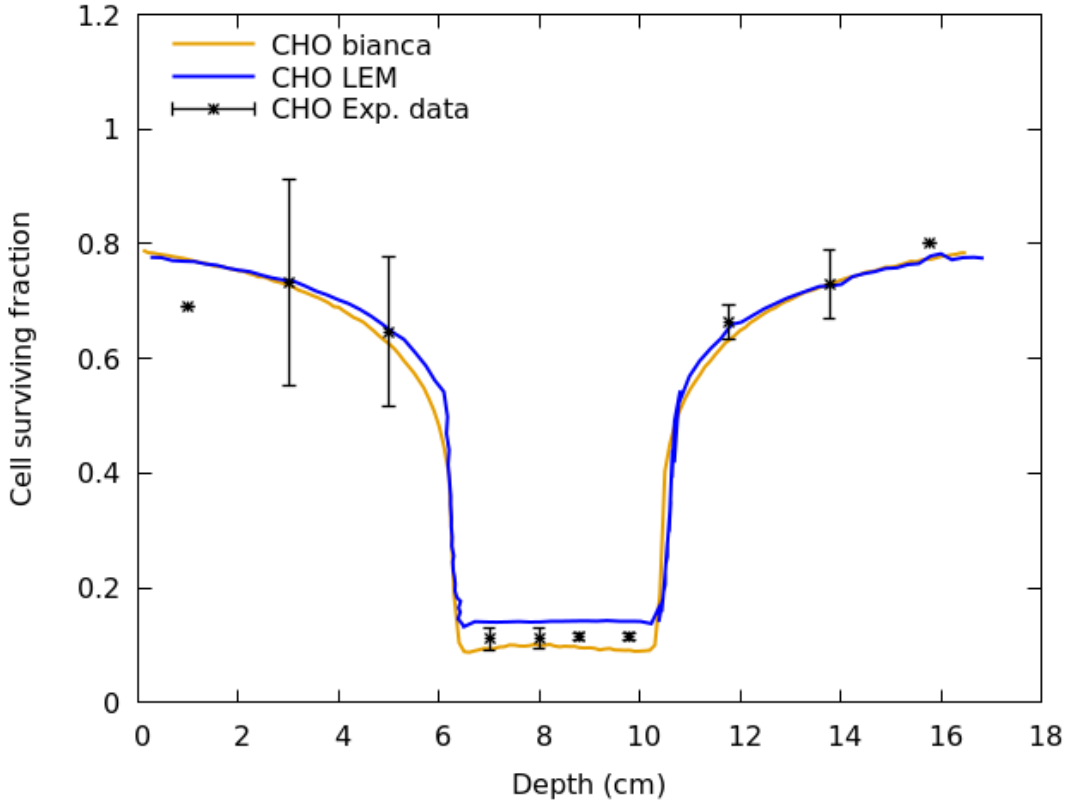
Experimental data were compared with TRIP+LEM predictions.

Experiment from Elsässer *et al* 2010, Int J Radiat Oncol Biol Phys 78(4) 1177-80

Results

Surviving fraction for CHO cells in a typical two-port irradiation with protons (left) and carbon ions (right)





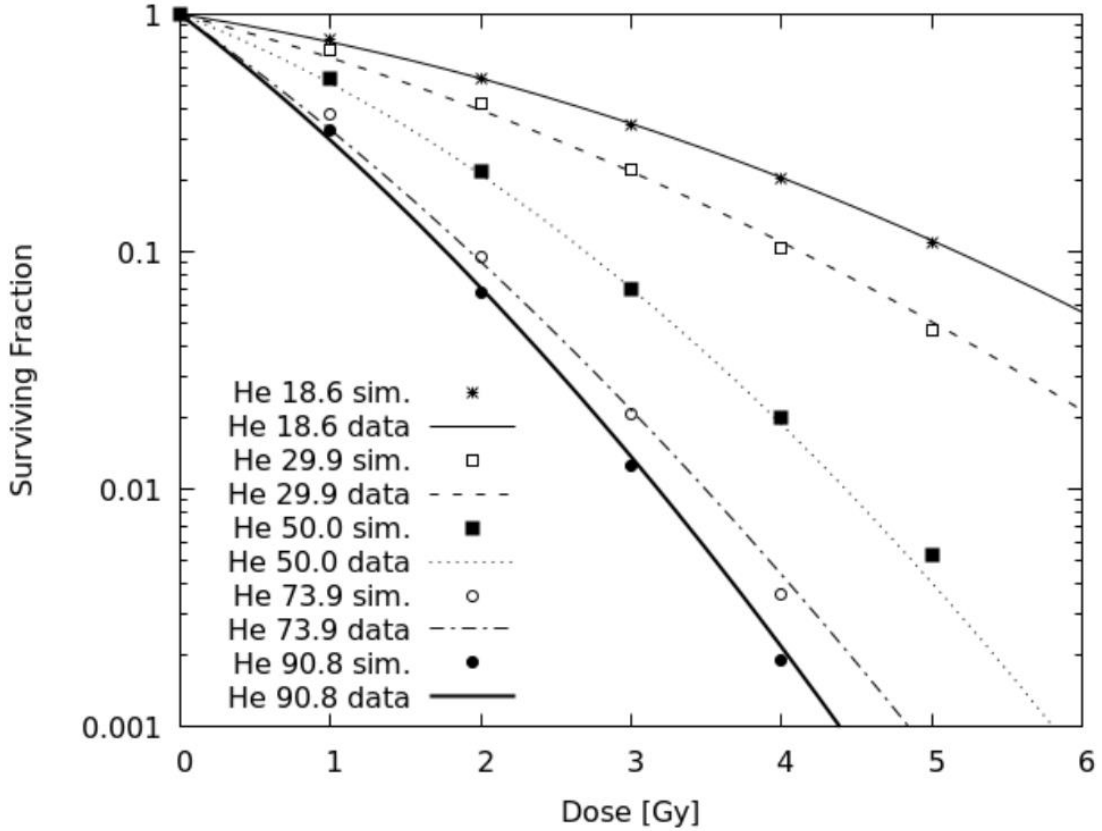
Please see **Wioletta Kozlowska**'s poster, **P57**, for examples in **patient** cases

Carante MP *et al.* submitted to Phys. Med. Biol.

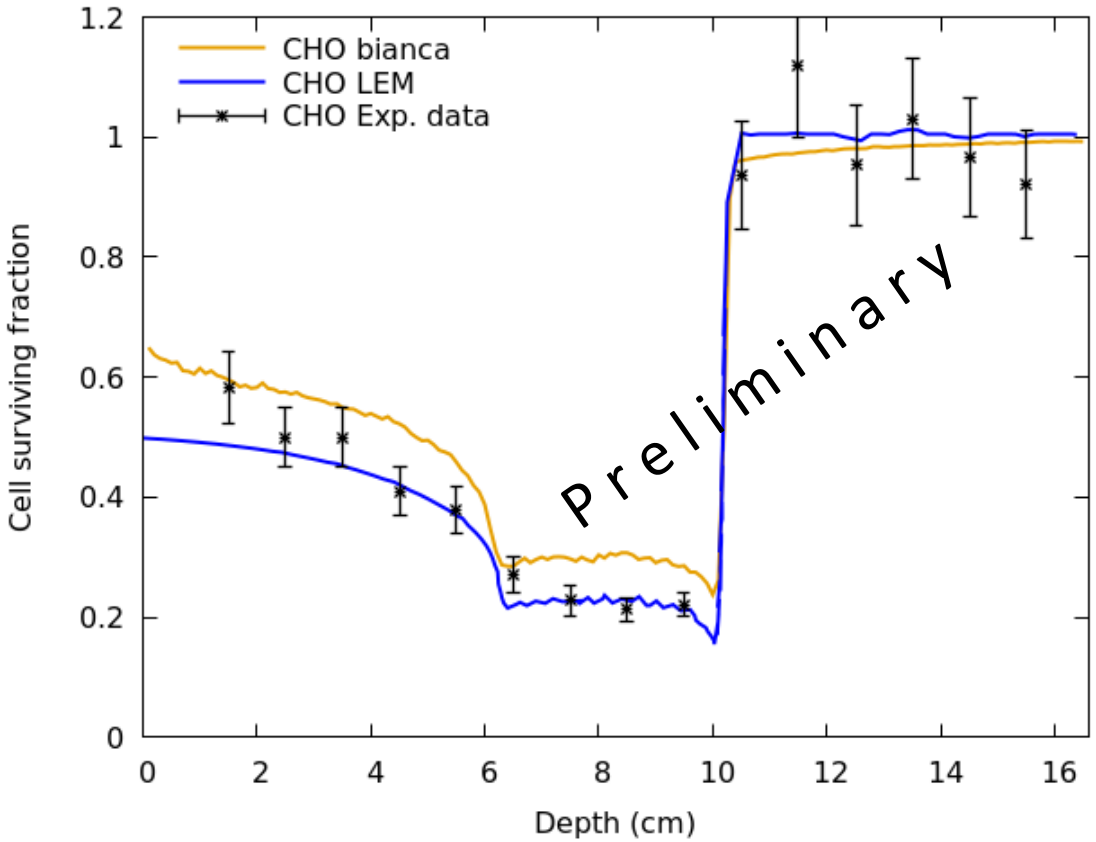
Helium?

Results

Survival of V79 cells irradiated by **helium ion** beams of different (dose-averaged) LET [keV μm^{-1}]



Surviving fraction for CHO cells in a one beam irradiation with **helium ions**



Carante MP *et al.* 2018 Phys. Med. Biol. 63 075007

Summary and Conclusions

BIANCA is a biophysical model developed in Pavia that can predict chromosome aberrations and cell death.

- BIANCA can be used for cell survival and RBE predictions, in principle for any cell line.
- Following interface with FLUKA, BIANCA was used to predict cell survival in SOBP, with proton, carbon and helium ions.

- We plan to complete this work for helium ion beams,
- and to benchmark BIANCA against *in vivo* chordoma data.

Thanks for your attention

Acknowledgments:

CERN: Alfredo Ferrari, Wioletta Kozlowska
University and INFN of Pavia: Francesca Ballarini, Mario Carante
GSI: Felix Horst, Christoph Schuy, Uli Weber
HIT: Andrea Mairani, Stuart Mein, Judith Besuglow
CNAO: Giuseppe Magro

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