



# 4th European Advanced Accelerator Concepts Workshop

15-21 September 2019

Hotel Hermitage, La Biodola Bay, Isola d'Elba, Italy

Europe/Rome timezone

## Dosimetry of laser-accelerated carbon ions for cell irradiation at ultra-high dose rate

Giuliana Milluzzo

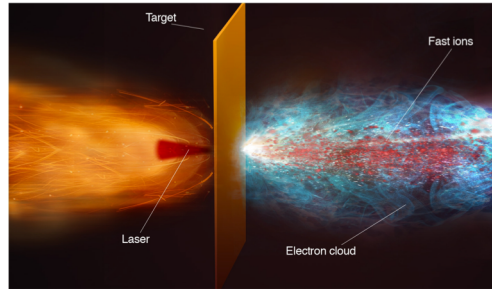
Queen's University Belfast



**QUEEN'S  
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# Laser-acceleration of ions for biomedical applications



## A-SAIL's vision

*All-optical delivery of dense, high-repetition ion beams at energies above the threshold for deep-seated tumour treatment and diagnosis*

### Activities:

**WP1:** Exploration of different acceleration regimes

**WP2:** Investigation of the extreme interaction physics underlying the acceleration processes

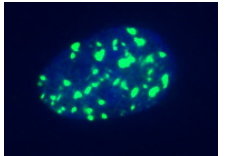
**WP3:** Development of enabling technology (targetry, advanced optics, diagnostics)

**WP4:** Investigation of highly pulsed ion radiobiology

## Novel regime of radiobiology

### Short pulse irradiation

High dose rates  $> 10^9$  Gy/s (cfr 10 Gy/min with conventional beams)

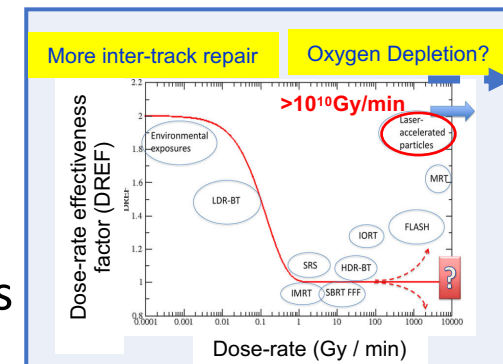


### Possible effects

- Spatio-temporal overlap of independent tracks
- Local depletion of oxygen
- Lack of interaction between prompt DNA lesions and indirect lesions

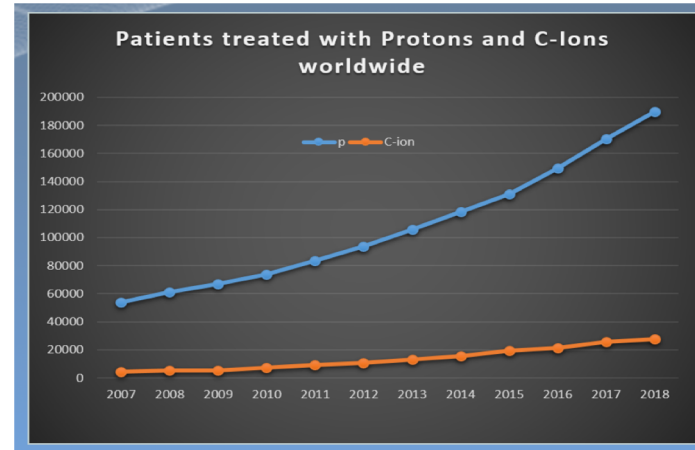
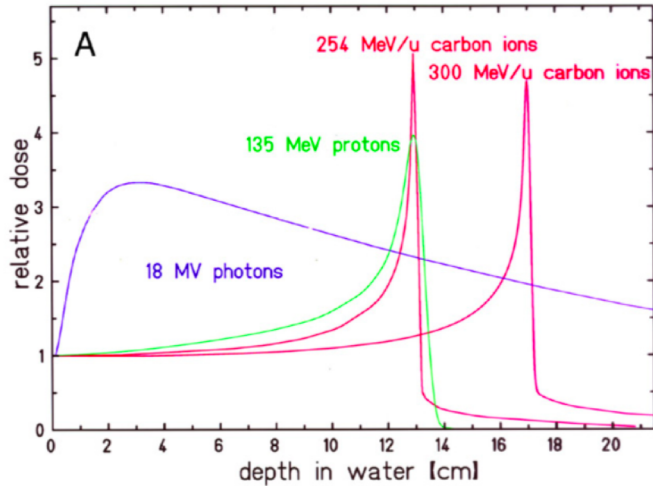
### Studies

- Investigations of DNA damage and repair dynamics
- Survival studies
- Sub-lethal damage investigations



# Hadrontherapy VS Protontherapy

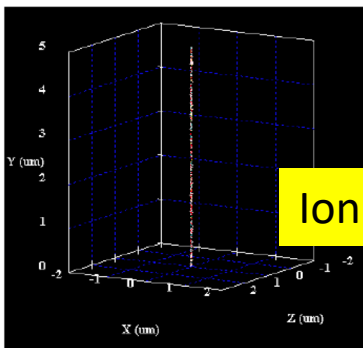
Proton and Carbons from RF accelerators such as cyclotrons are currently used for treating a number of tumours



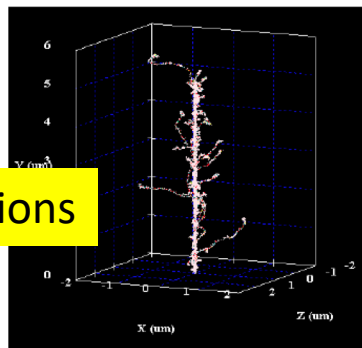
**Radiation quality index for cell response**

Linear Energy transfer (LET)  
Relative Biological Effectiveness (RBE)  
Medium ionization

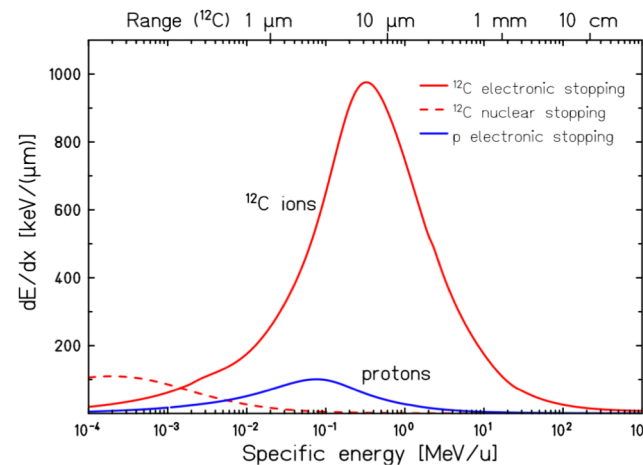
10 MeV Protons



5 MeV/nucleon  
Carbon Ions



Ionizations



**Advantages of carbon ions**

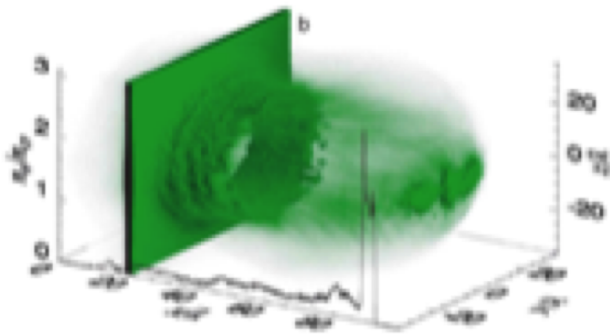
- ✓ More complex damages to the cell DNA
- ✓ Higher LET > 100 KeV/ $\mu\text{m}$
- ✓ Higher biological efficiency
- ✓ Higher efficiency for the treatment of radioresistant tumours

# Recent results for carbon ion acceleration @ ASTRA GEMINI (RAL)

## Laser characteristics

- Pulse duration  $\sim 40$  fs
- Energy on target up to 15 J
- $I \sim 0.5 - 1.0 \cdot 10^{21}$  W/cm<sup>2</sup> (f/2 focusing)

**Energy dependence from target thickness and laser polarization for carbon ions and protons**



Efficient **Radiation Pressure Acceleration** of Carbon ions (up to 400 MeV) achieved by polarization control  
C. Scullion et al, PRL, **119**, 054801 (2017)

See talk Aodhan McIlvenny  
WG2 Thursday h 17:00

17:00

**Bulk ion acceleration from ultrathin foils in PW-class interactions on the ASTRA GEMINI laser**

20m

During the interaction of ultra-intense laser pulses with ultrathin foils, advanced mechanisms of ion acceleration take place which can be controlled and optimized in view of further progress towards high energy ranges of medical relevance on upcoming multi-PW facilities. In the framework of the activities of the UK-wide A-SAIL project, recent campaigns at the ASTRA GEMINI laser facility (Rutherford Appleton Laboratory) have investigated and characterised ion acceleration from 2-100 nm thick Carbon foils irradiated by 40 fs laser pulses at intensities of  $10^{20}$ - $10^{21}$  W/cm<sup>2</sup>. The experiments have highlighted a strong dependence of the ion energy from the target thickness and the laser polarisation, and suggested the onset of Light Sail Radiation Pressure acceleration from the bulk of the target when using circularly polarized pulses. Following initial results (published in PRL, 119, 054801, 2017), following campaigns have led to an enhancement of the ion energies (up to  $\sim 35$  MeV/n for Carbon 6+) and to observations of an intensity-dependent optimal thickness, consistently with analytical predictions. Comparison with extensive Particle-in-Cell simulations clarifies the complex interplay of multispecies dynamics during the acceleration, as well as the role of relativistically-induced transparency, and allows predictions of future performance at increased laser power and intensity.

Speaker: Mr McIlvenny Aodhan (Queen's University Belfast)



# Experimental setup @ ASTRA GEMINI (RAL)

## PURPOSE

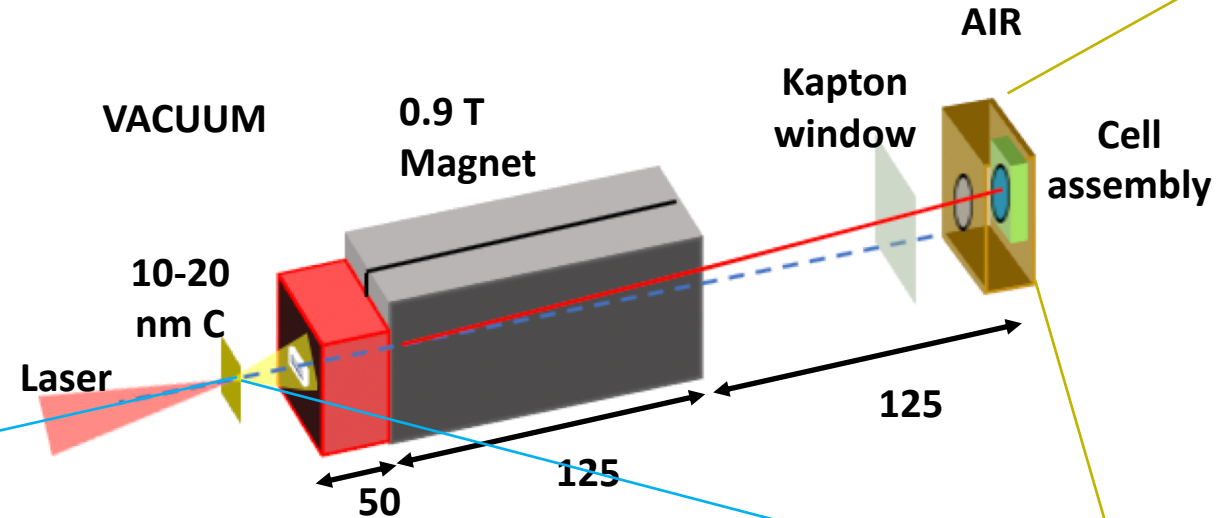
GBM stem cells irradiation with 10 MeV/u carbon ions

## REQUIREMENTS

Separation of carbon from proton contribution for a pure carbon irradiation

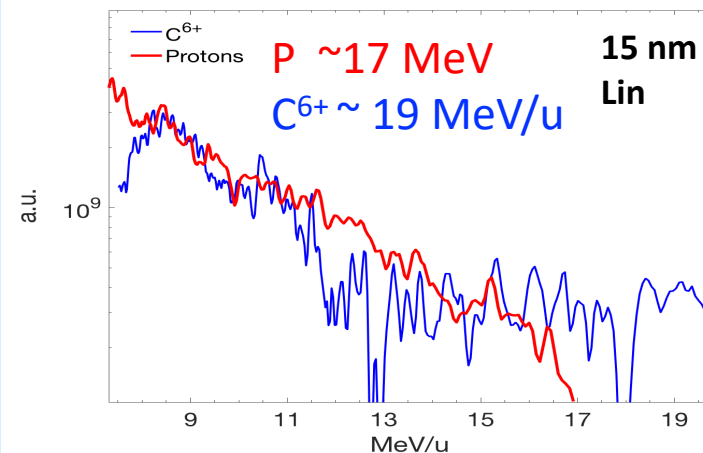
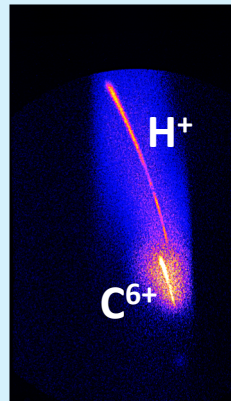
## CHALLENGES

Dosimetry at low-energy high LET carbon ions

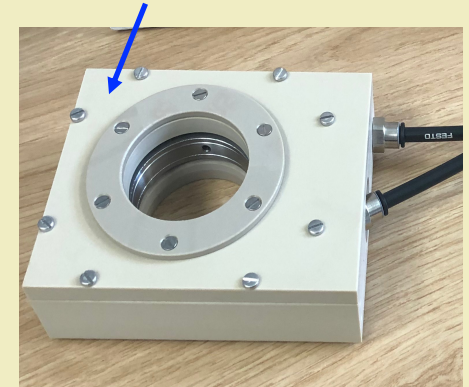


## Input ion beam characteristics

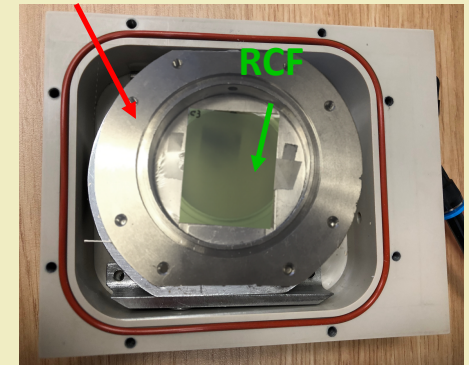
- Thomson Parabola Spectrometer
- RadioChromic film stacks



## HOLDER CHAMBER

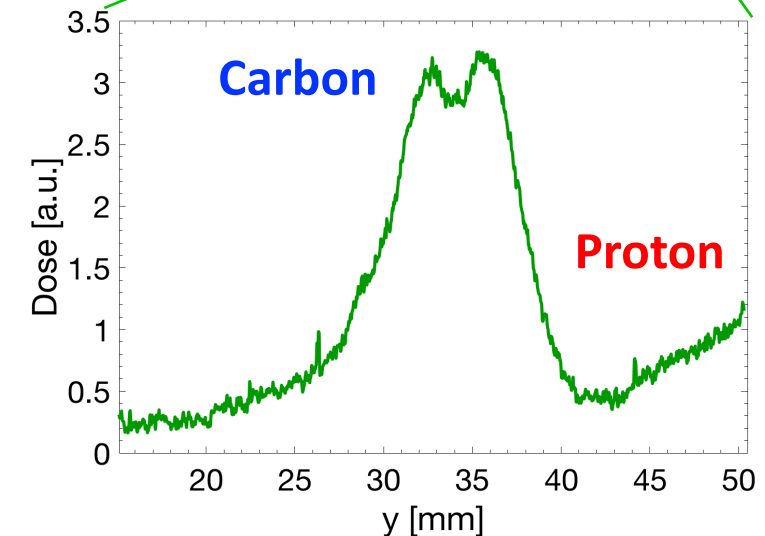
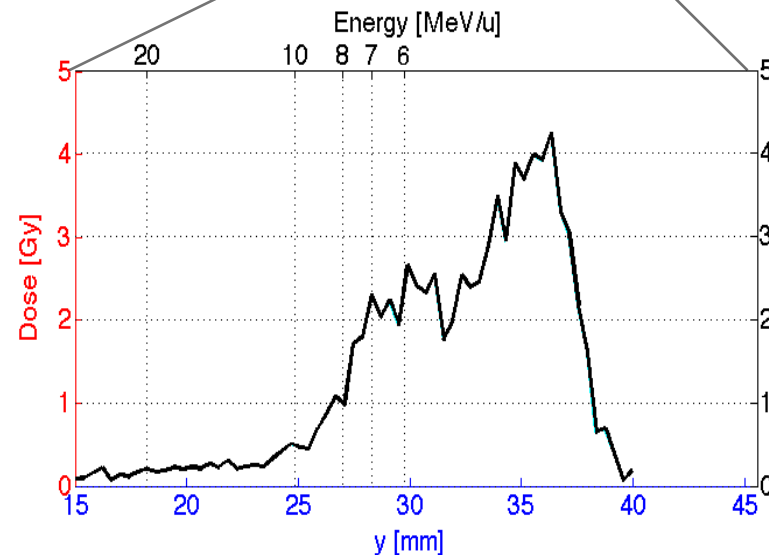
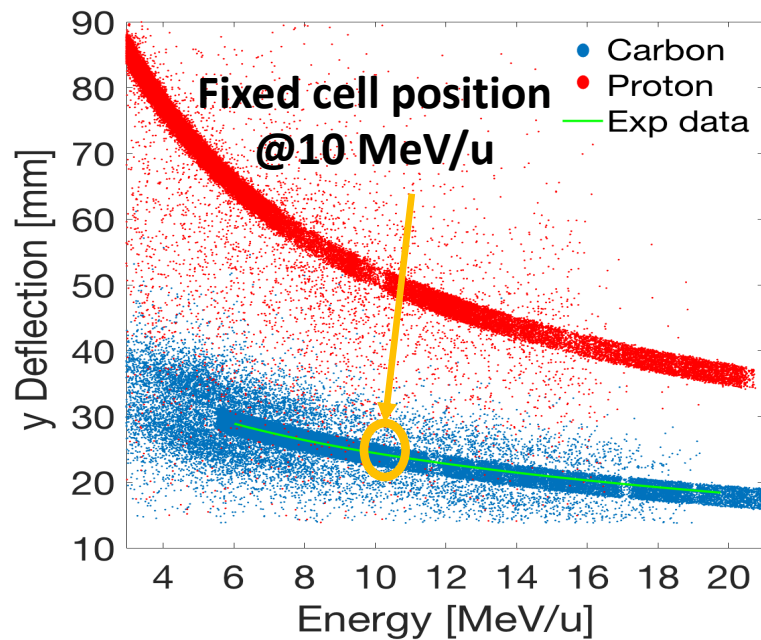
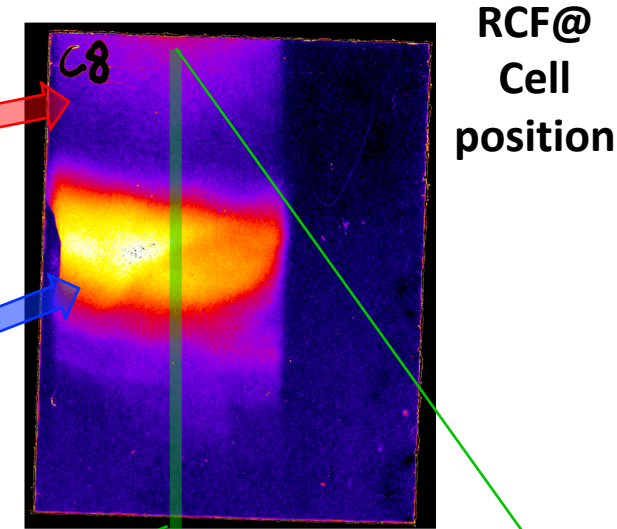
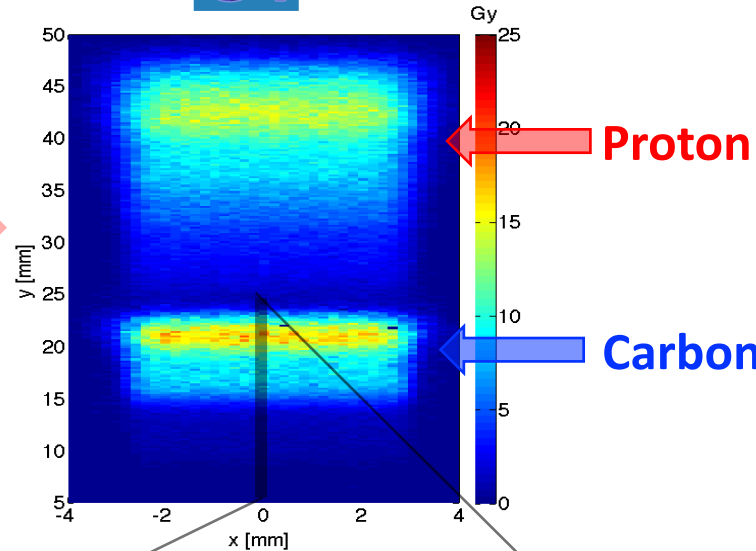
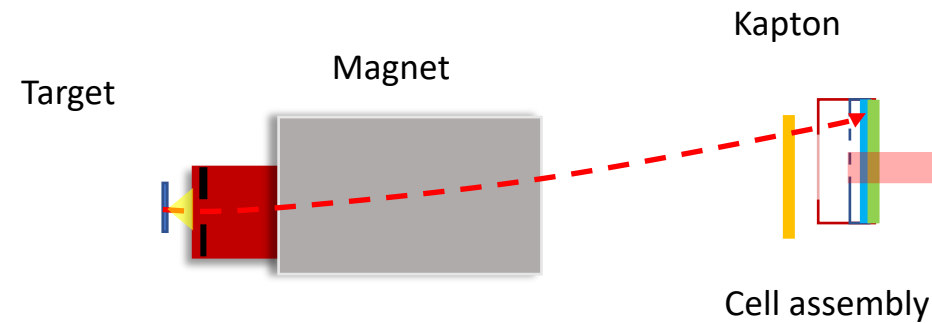


## CELL DISH



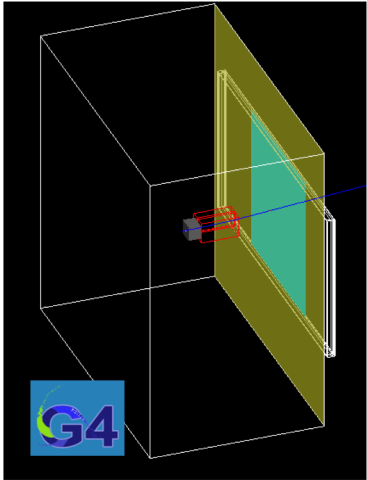
Monolayer 2D cells :  
Glioblastoma (GBM)  
stem cells

# Proton & Carbon dose and energy transversal distribution at the cell plane

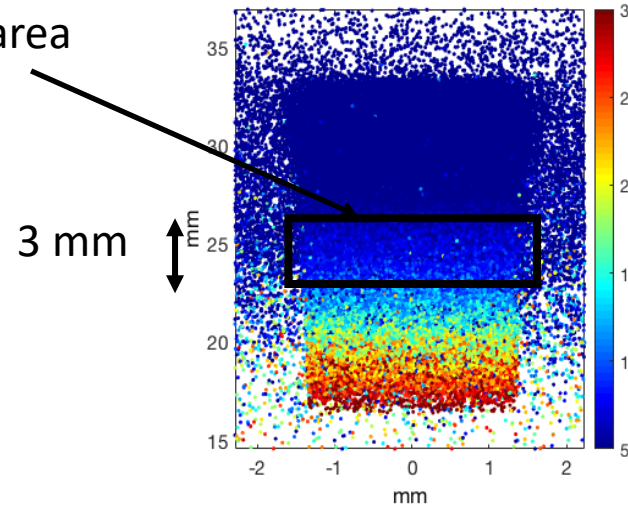


# Carbon energy and LET distribution at the cell plane-MC simulation

MC simulations to estimate the energy and the LET distribution on the cell plane



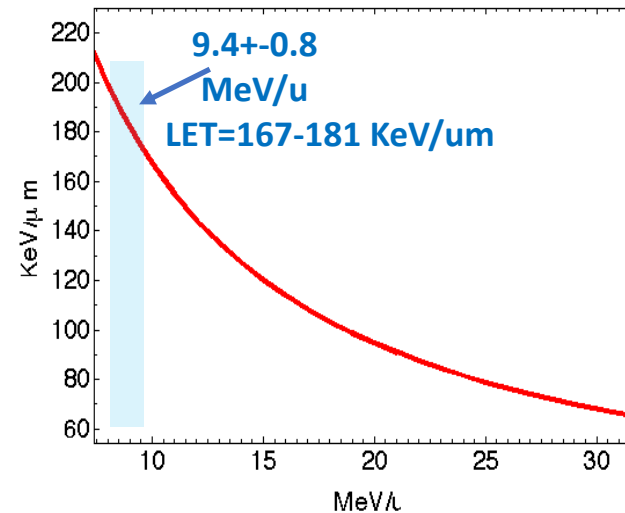
Irradiation area



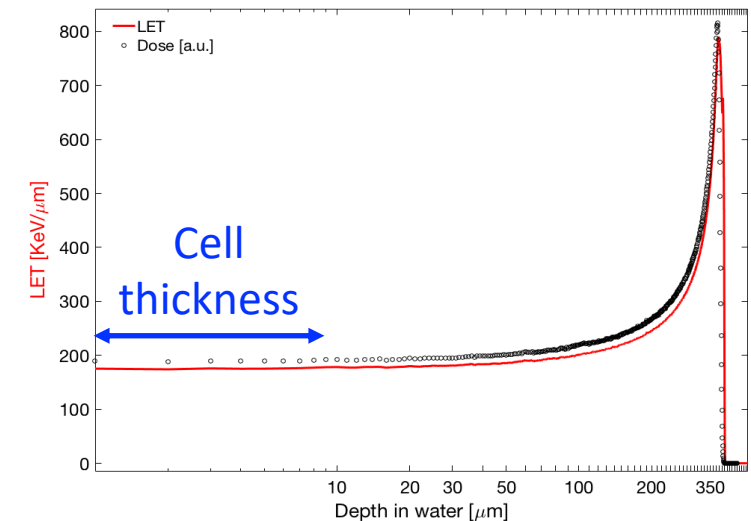
## REQUIREMENT FOR CELL IRRADIATION

- Reduced energy spread at the cell plane
- Reduced Dose and LET variation in the transverse and longitudinal plane

## LET VS Energy

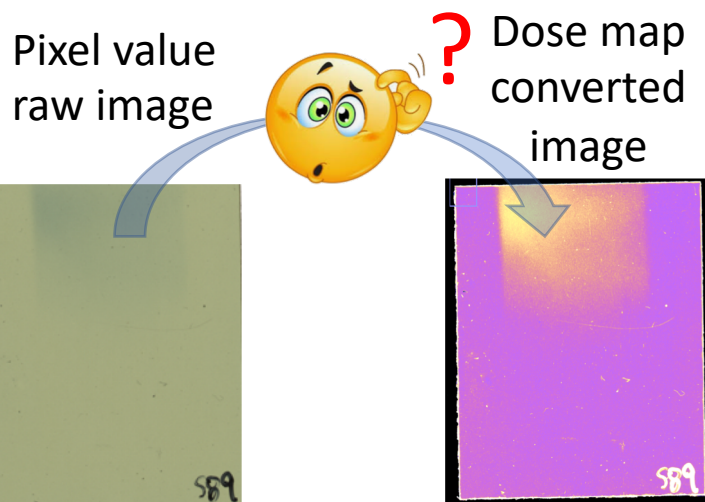


## Depth LET & Dose profile in water



8% energy and LET variation

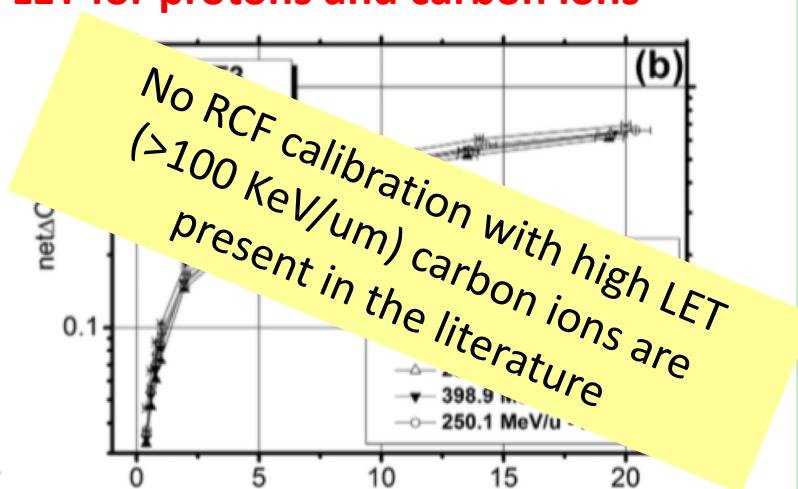
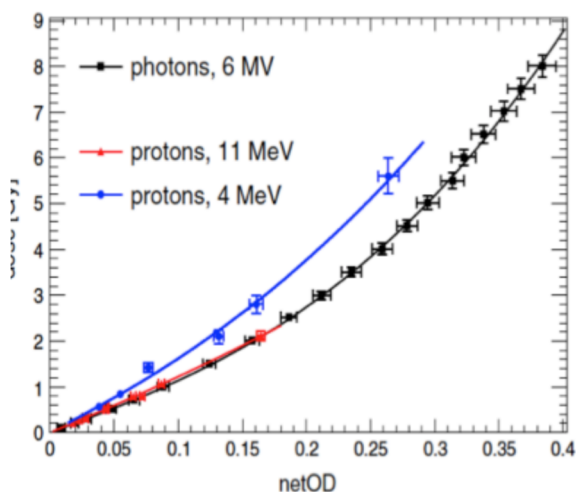
# Dosimetry with EBT3 RadioChromic films: low energy carbon ions



## Issues

- Low energy carbon ions (10 MeV/u) do not traverse the polyester layer
- High LET value 200 KeV/um
- OD dependence from LET

## OD dependence from LET for protons and carbon ions



No RCF calibration with high LET (>100 KeV/um) carbon ions are present in the literature

## Solution

Unlaminated EBT3: active layer+1 polyester dead layer

Active Layer - 12 um  
Polyester- 97 um

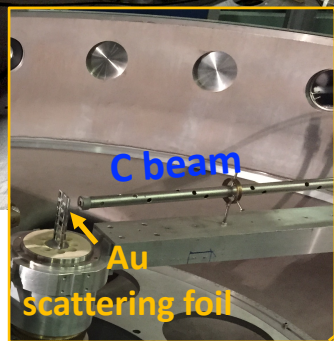
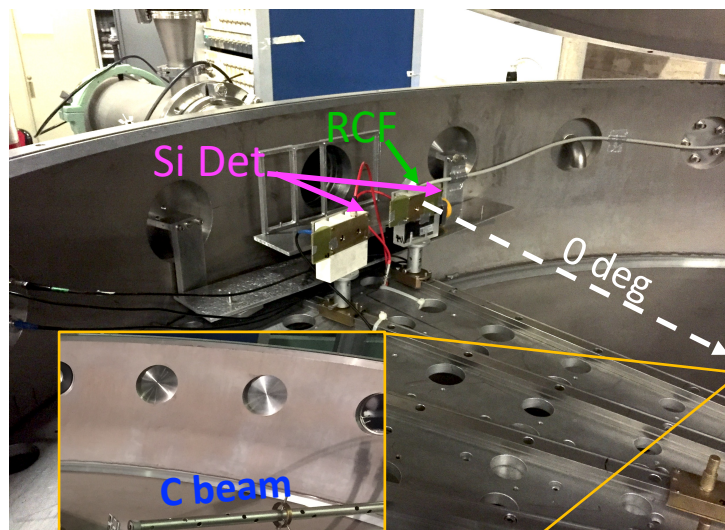
New procedure for EBT3 unlaminated calibration at low energy



# EBT3 customized calibration with 6 MeV/u C @ LNS-INFN

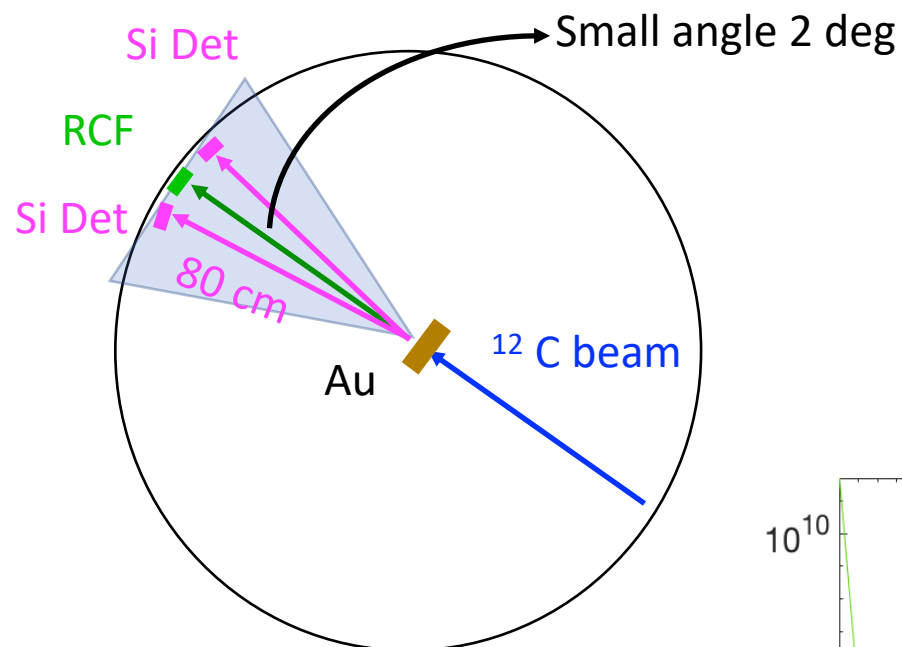


## EXPERIMENTAL SETUP



### Devices

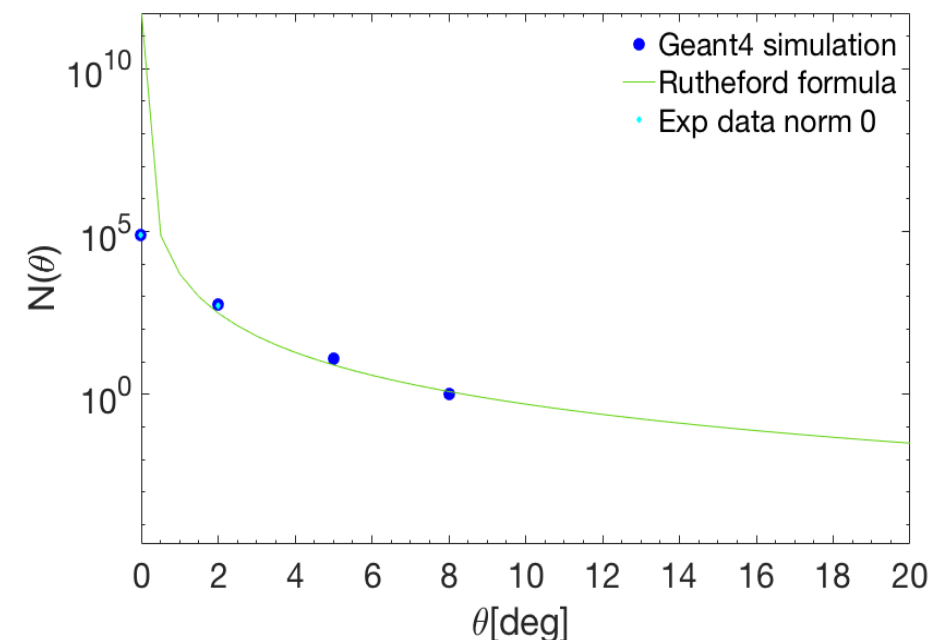
- EBT3 customized
- CR39
- 100/500 um thick Si detector acting as monitor for the beam current at small angles



### Beam characteristics

- 6 MeV/u C beam from Tandem accelerator (1% E spread)
- Tunable incident current

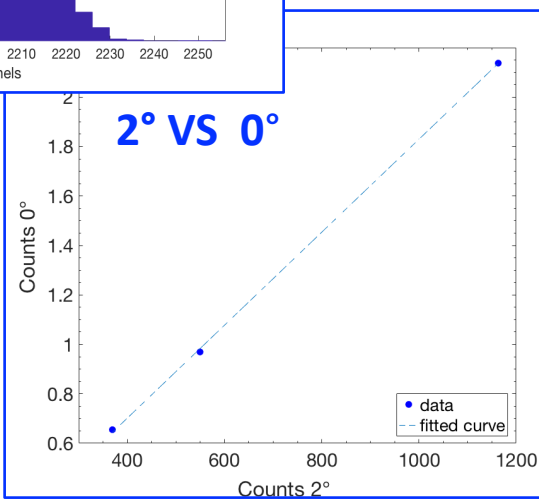
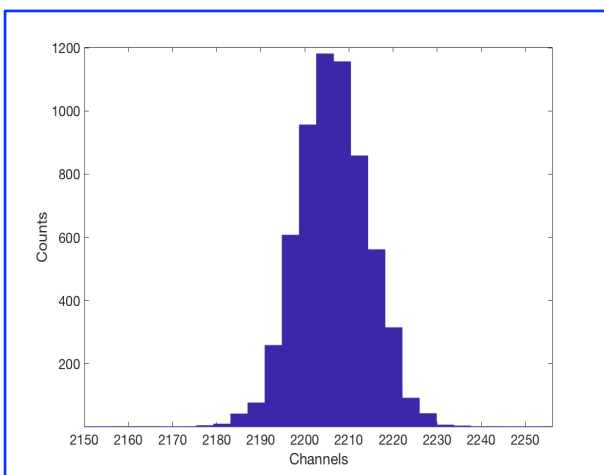
### Rutherford scattering



# EBT3 customized calibration with 6 MeV/u C @ LNS-INFN



Si counts @ 2°

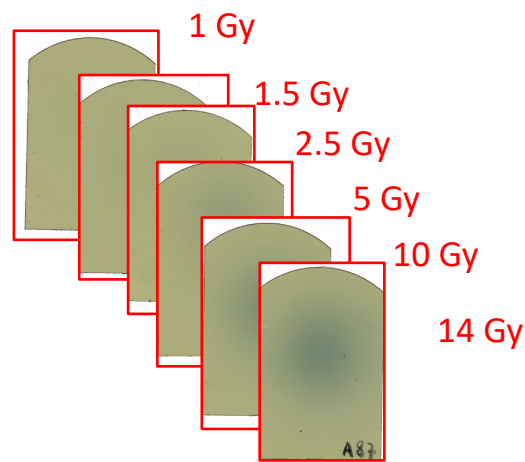


netOD VS Dose calibration curve



Lower RCF response to dose for carbon ions than protons

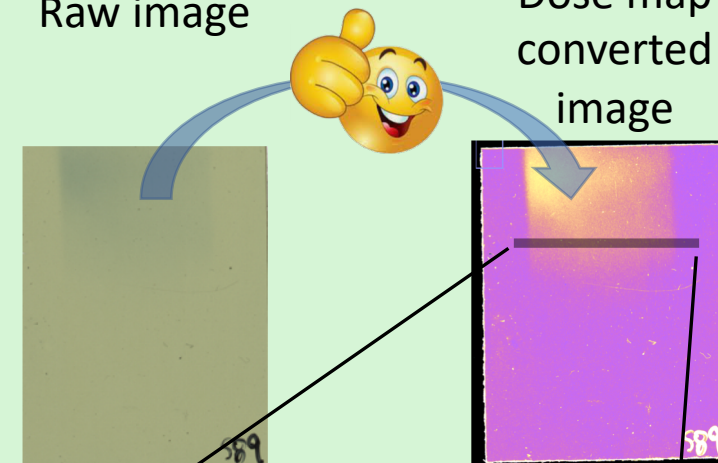
OD conversion



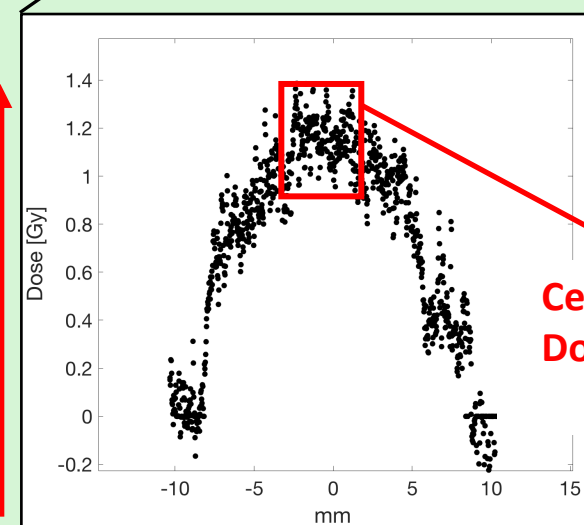
Dose profile at cell plane

Raw image

Dose map converted image



FOCI



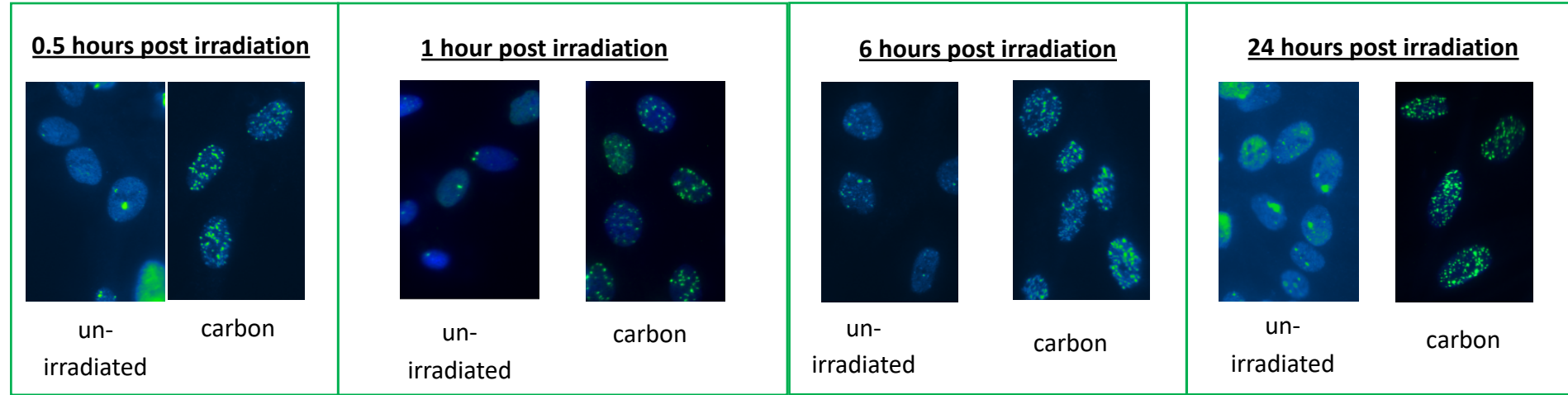
Cell position  
Dose=1 Gy ± 15%



# More complex, unreparable damage is inflicted by the Carbon ions

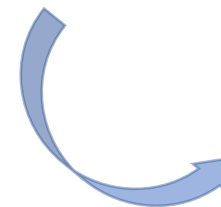
## DNA damage and repair (53BP1 immunofluorescence):

Foci (regions of accumulation of the agent) are highlighted, e.g. by fluorescence



GBM stem cells

Conventional comparator data needs to be generated



See talk Dr. Pankaj Chaudhary  
Plenary session Tuesday h 12:10

# Contributors

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# Summary

- **Dosimetry of laser-driven carbon beams @ 10 MeV/u**
  - New approaches for dose measurement with high LET and low energy carbon ions
  - New procedure for RCF-EBT3 calibration
- **Radiobiology investigations using laser-driven carbon beams @ 10 MeV/u with GEMINI laser**
  - Test unexplored regimes of ultrahigh dose rates
  - Cell irradiation with high-LET carbon ions
  - may provide a flexible, unique source for novel biological studies

## **Future perspectives**

- Careful comparison with dedicated “conventional “ data ongoing to assess any variation in biological effectiveness associated to the peculiar nature of the source

**Thanks for the attention**