Istituto Nazionale di Fisica Nucleare

Activities at INFN-LNS in Catania, Italy

GAP Cirrone, F Farrokhi, S Fattori, L Pandola, G Petringa, A Sciuto

Group presentation

INFN-LNS group is active **since 2002**

G.A.Pablo Cirrone: responsible for "hadrontherapy" and "radiobiology" examples
pablo.cirrone@lns.infn.it

Serena Fattori: contact person for UHDR simulations in Geant4-DNA; Geant4-DNA tutorials (chem6)
serena.fattori@lns.infn.it

Alberto Sciuto: machine learning development in Geant4 / Geant4-DNA
alberto.sciuto@lns.infn.it

100 % for Geant4 work

Giada Petringa: LET/RBE simulations vs. microdosimetric data
giada.petringa@lns.infn.it

Luciano Pandola: Coordination of the EM Working Group; Maintenance and bug fix of Penelope; STT shifts; Evolution Task Force
luciano.pandola@lns.infn.it

A **new post-doc** will join the group on November 2023

100 % for Geant4 work

Geant4 activities

Geant4 activities

`Hadrontherapy` progress, maintenance and G4Med connections

LET/RBE simulations vs **microdosimetry data**

Contribution into the **EM Working group**

Developing and maintenance of the `Hadrontherapy` example

`Hadrontherapy` was published in 2002 and it has been evolved during the years;

Details in the dedicated talk on the "Examples" Session;

Part of the example output inserted in the **G4-MED** framework.

Coordination / service tasks within LNS

Deputy coordination of the EM Working Group (Low Energy)

Maintenance and bug fix of the Penelope (and other EMLowEnergy) models

- Bug #2465 on fluorescence after Livermore photoelectric still open
- Could not reproduce with TestEm5 (a lot of support by Zhuxin!)

Contribution to the **STT shifts** (3 weeks/year)

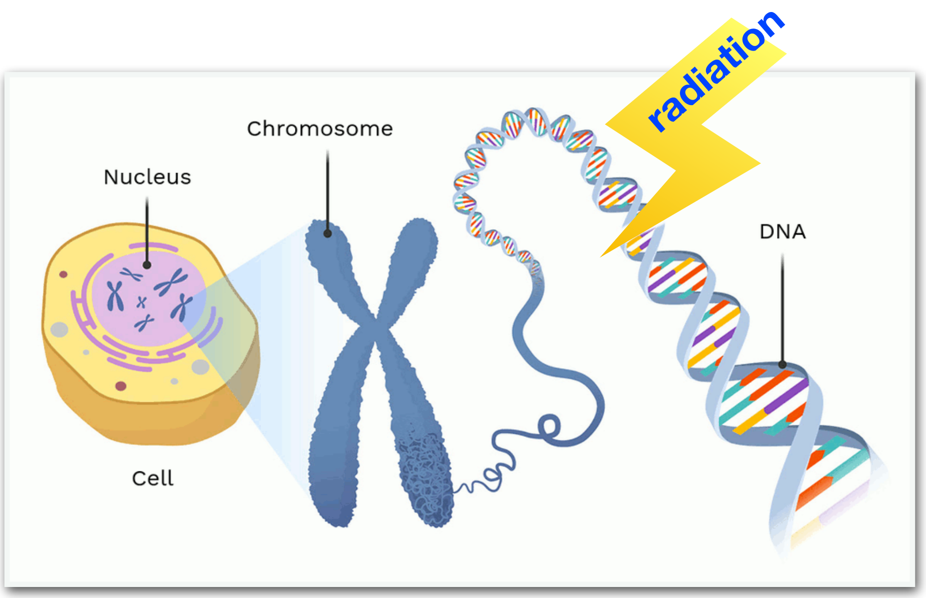
Contribution to the **Collaboration Evolution Task Force**

Technical support to the **Ferrara group** for the implementation of the Baier-Katkov model --> See talk by A. Sytov

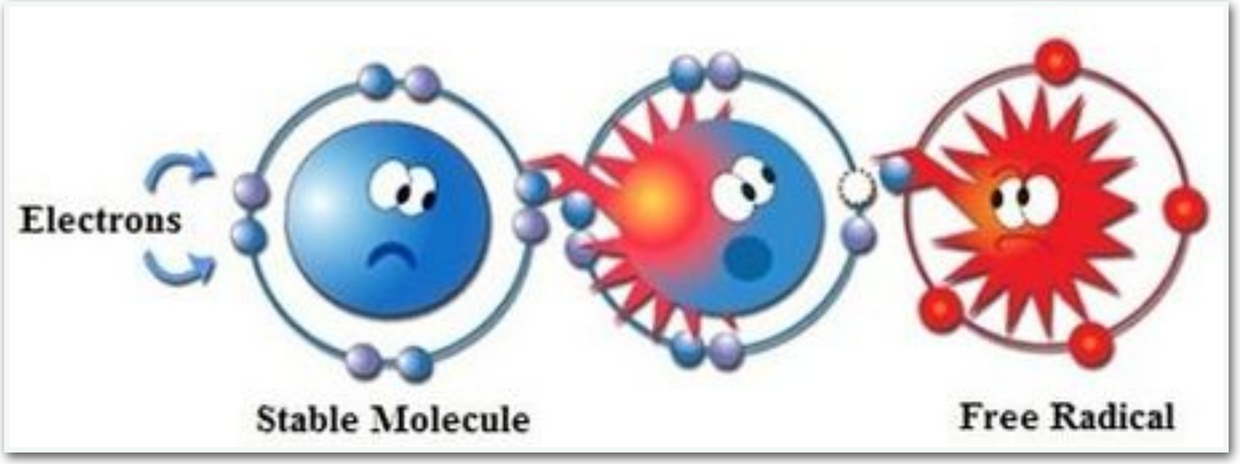
G4DNA activities
(from macro to micro and nano)

G4DNA activities

Biological side

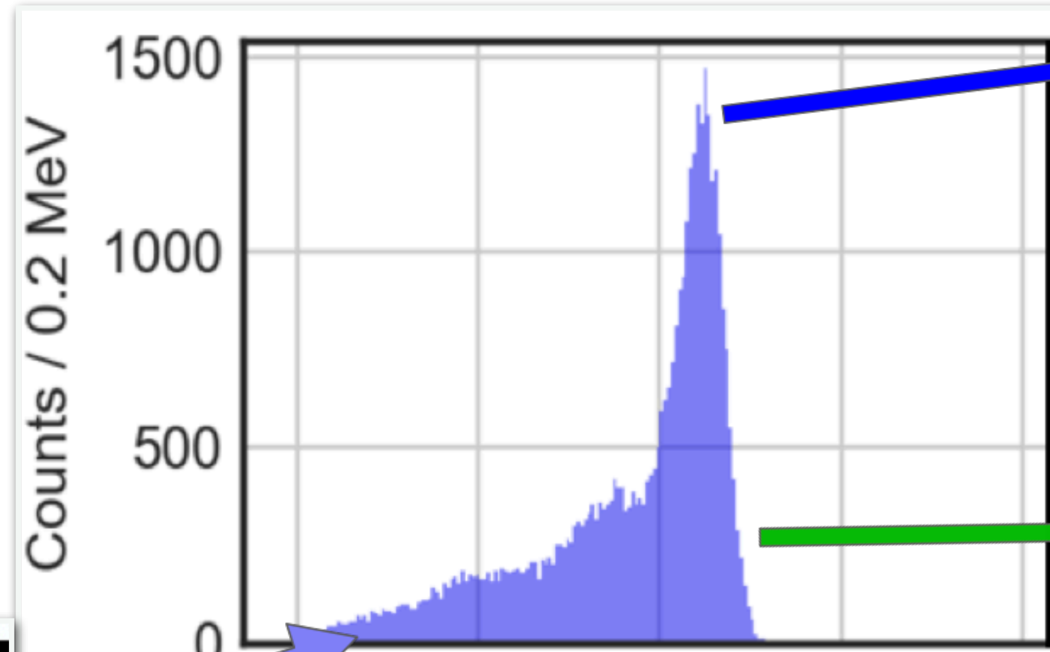


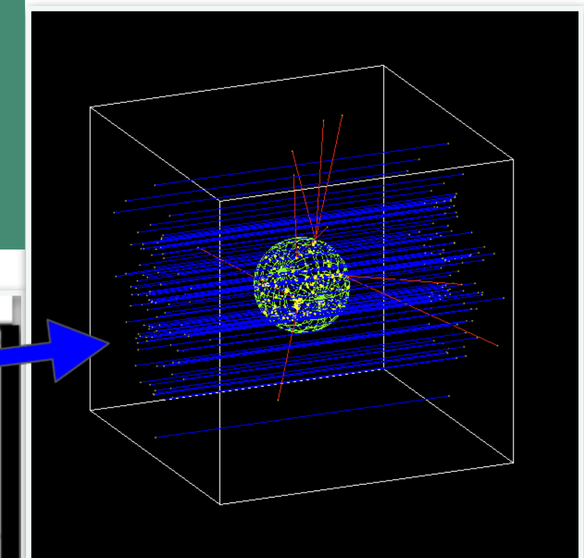
Chemical side

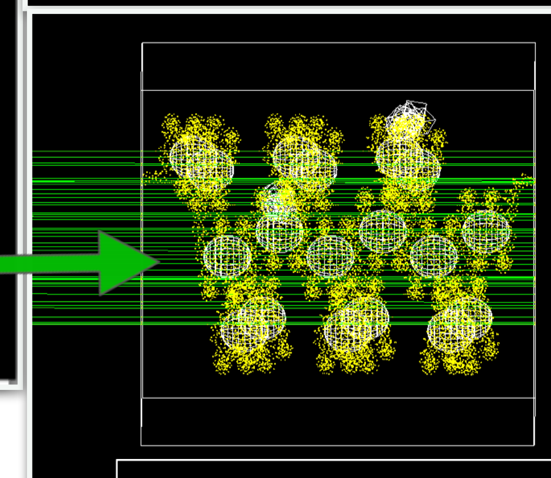


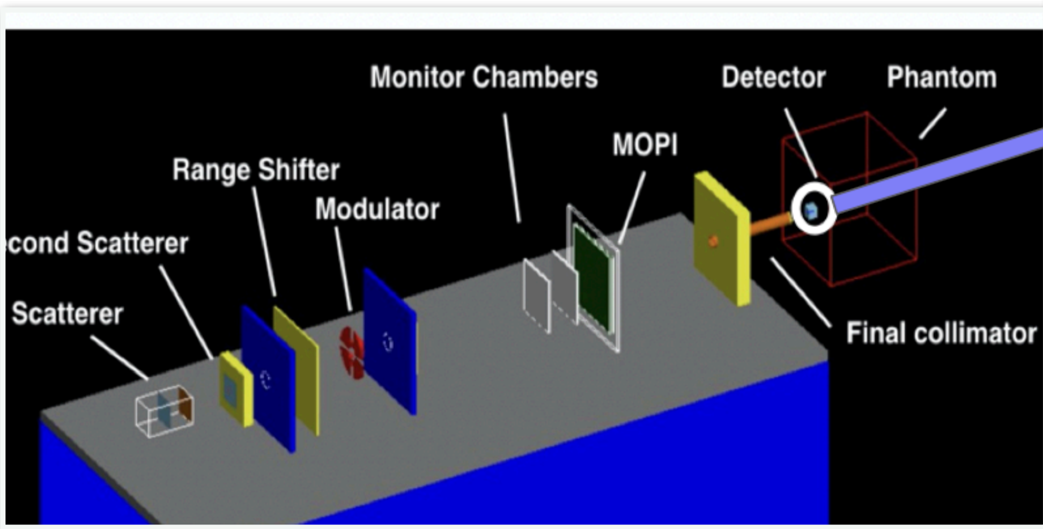
G4DNA activities: biological side

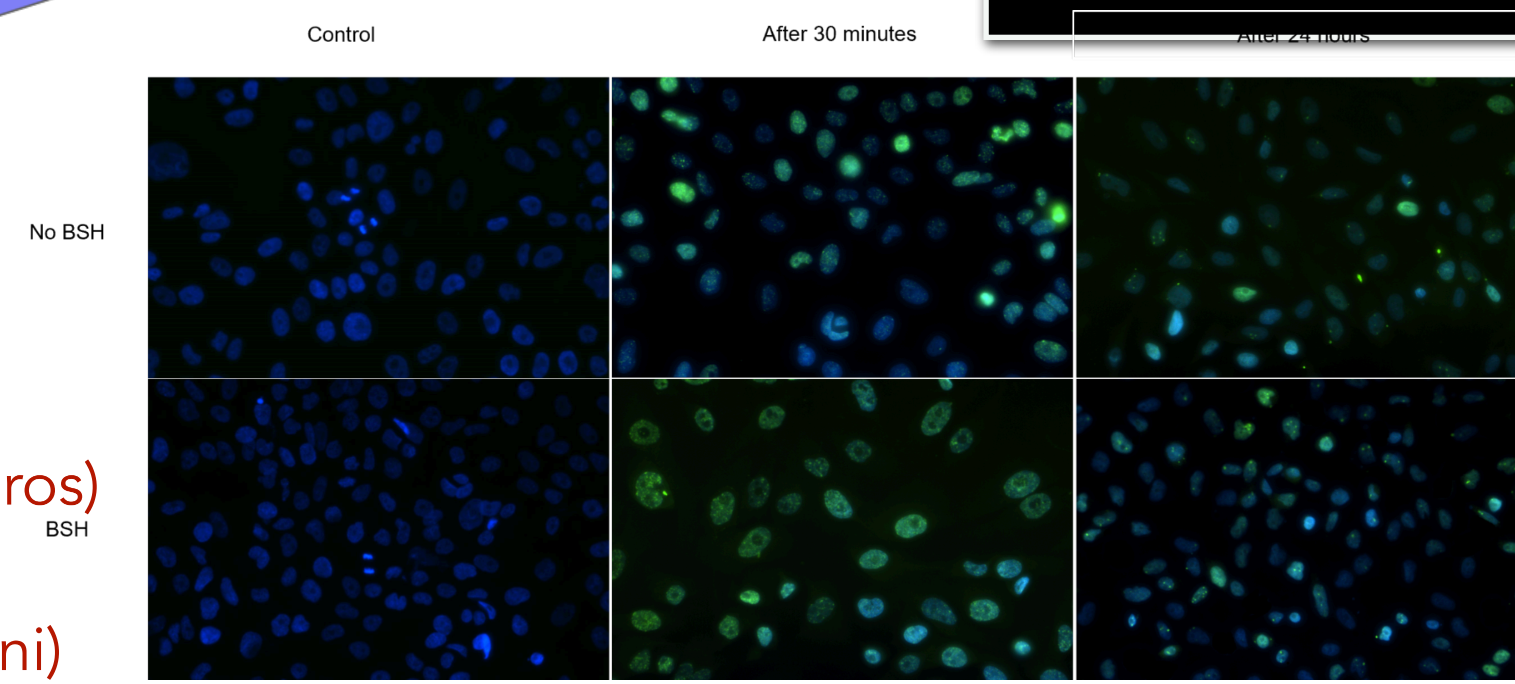
"Clustering" and "dnadamage1" examples against exp. data











--> Erasmus Master Thesis (Dr A. Matamoros)

--> Paper submitted with NTU (Dr K Ruhani)

G4DNA activities: chemical side

Oxygen depletion studies with Geant4-DNA: Geant4-DNA (scavenger) compared to TRAX-CHEM

Radiation Physics and Chemistry 212 (2023) 111184
Contents lists available at ScienceDirect
Radiation Physics and Chemistry
journal homepage: www.elsevier.com/locate/radphyschem

Effects of the Oxygen depletion in FLASH irradiation investigated through Geant4-DNA toolkit

Fateme Farokhi [a,b], Babak Shirani [a,*], Serena Fattori [b,**], Mohammad Ali Asgarian [a], Giacomo Cuttone [b], Sayyed Bijan Jia [c], Giada Petringa [b], Alberto Sciuto [b], G.A. Pablo Cirrone [b,d,e]
[a] Faculty of Physics, University of Isfahan, Isfahan, Iran
[b] Istituto Nazionale di Fisica Nucleare (INFN), Laboratori Nazionali del Sud, Catania, Italy
[c] Department of Physics, University of Bojnord, Bojnord, Iran
[d] Centro Siciliano di Fisica Nucleare e Struttura della Materia, Catania, Italy
[e] Dipartimento di FISICA ED ASTRONOMIA "Ettore Majorana" - Università degli Studi di Catania, Catania, Italy

(2023) doi.org/10.1016/j.radphyschem.2023.111184

Radiotherapy and Oncology 162 (2021) 68–75
Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

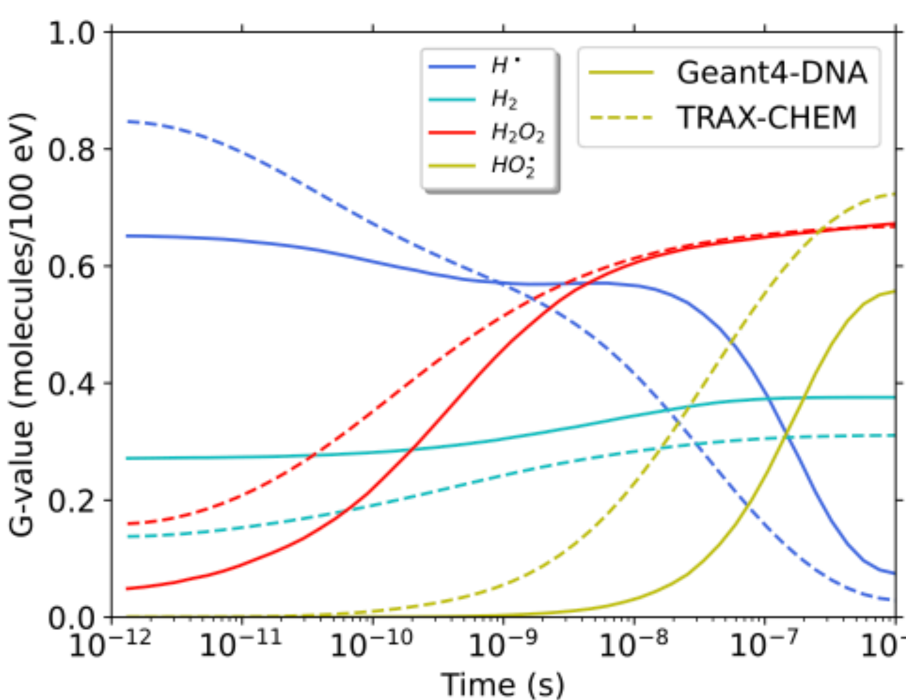
Original Article

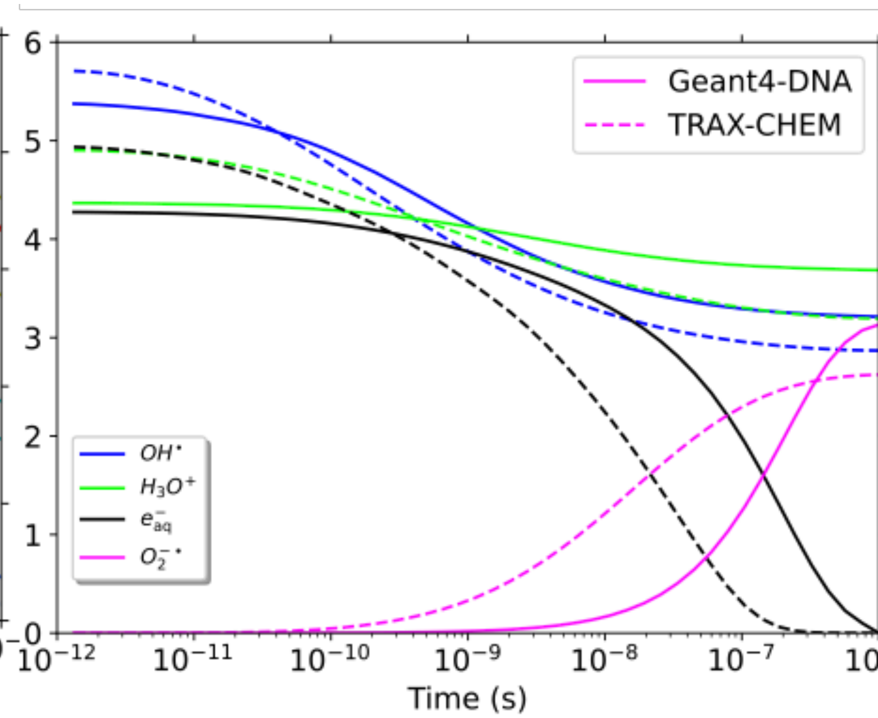
May oxygen depletion explain the FLASH effect? A chemical track structure analysis

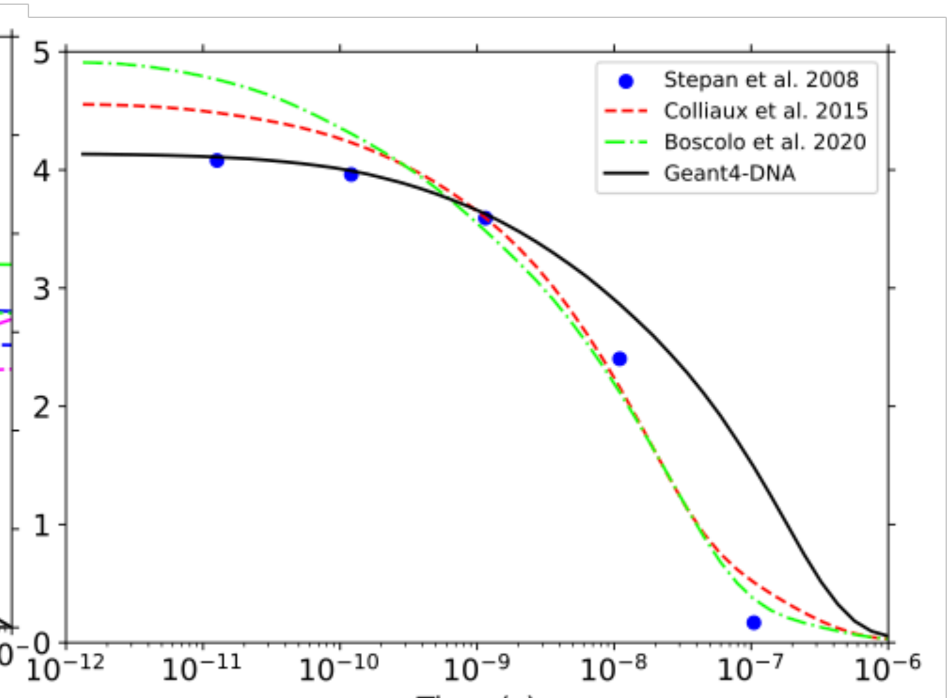
Daria Boscolo [a], Emanuele Scifoni [b], Marco Durante [a,c,*], Michael Krämer [a], Martina C. Fuss [a,*]
[a] GSI Helmholtzzentrum für Schwerionenforschung GmbH, Darmstadt, Germany; [b] Trento Institute for Fundamental Physics and Applications (TIFPA), National Institute for Nuclear Physics (INFN), Trento, Italy; [c] Institut für Physik Kondensierter Materie, Technische Universität Darmstadt, Germany

G-values of different radiolitic species after **proton and electron irradiation**.

--> Study of the **oxygen depletion** hypothesis in comparison with TRAX-CHEM







Side activities:

the BIORAD III project

The BIORAD-ESA activity

Experimental biological damage quantification and simulation

Institutes

INFN (Italy), IBFM (Italy), IRSN (France), CENBG (France), VINCA (Serbia), Univ. Sevilla (Spain)

Experimental radiobiological data database for comparison against Monte Carlo simulation (i.e. the output from the "Hadrontherapy" example (RBE module from Survival Fraction)

Christelle ADAM-GUILLERMIN, Pierre BEAUDIER, Marco CALVARUSO, Giovanni CANTONE, Konstantinos CHATZIPAPAS, Davide CHIAPPARA, Giuseppe Antonio Pablo CIRRONE, Miguel CORTES-GIRALDO, Milos DORDEVIC, Serena FATTORI, Orsola GIAMPICCOLO, Franck GOBET, Sébastien INCERTI, Giada PETRINGA, Ivan PETROVIC, Aleksandra RISTIC-FIRA, Alberto SCIUTO, Hervé SEZNEC, Ngoc Hoang TRAN*

The BIORAD-ESA activity

Istituto Nazionale di Fisica Nucleare

Two kinds of biological endpoints:

FOCI via the H2AX protein Phosphorylation and

Survival Fraction (or Clonogenic)

ClonogenicSurvival_Data_example 〉 No Selection

```
U-87; 5., 55., 25., 15.; Proton; SOBP; vertical; 24.2; 60.3; 1.0; 1.0;
    50.0; -1; -1; -1; -1; 0.292; 0.036; 0.010; 0.003; 28.6; -1;
    10.3390/jpm11040308

DOSE, SF, SEM_SF
0, 1.000, 0.185
1, 0.756, 0.126
2, 0.516, 0.066
3, 0.409, 0.069
4, 0.257, 0.050
10, 0.109, 0.022
21, 0.056, 0.015
```

Example of **Clonogenic** data file

FOCI_Data_example_normal

FOCI_Data_example_normal 〉 No Selection

```
92-1; 5., 55., 25., 15.; 60Co-gamma; SOBP; vertical; 24.0; 1.0; 1.0; immuno-γH2AX; 10.3109/09553002.2010.481322

TIME, FOCI, SEM_F, DSB, SEM_D, LET, ENERGY, DURATION
-0, 5.82, 0.87, 0.97, 0.14, 36.0 20. 5.
0.5, 22.13, 0.62, 3.69, 0.10, 36.0 20. 5.
24.2, 11.63, 1.07, 1.94, 0.18, 36.0 20. 5.
```

Example of **FOCI-H2AX** data file

The BIORAD-ESA activity

Readme for the different part

Structure of the Clonogenic information

Structure of the FOCI information

Structure of the Cell-lines information

Format of the data file and data list

```
CellName; CellCycle; BeamParticle; BeamType; BeamOrientation; Depth; Dose;
DoseRate; Assay; DOI

TIME, FOCI, SEM_F, DSB, SEM_D,     LET, ENERGY, DURATION
Time_1, Foci_1, Err_F_1, DSB_1, Err_D_1, Let1, Energy1, Duration1
Time_2, Foci_2, Err_F_2, DSB_2, Err_D_2, Let2, Energy2, Duration2
```

```
============
CellName: String of one word containing the "code-name" of the irradiated cell
line, according to the cell line file;
CellCycle: Group of 4 float values, comma separated with each other, indicating
the percentage of cells in each cycle phase during the irradiation, listed in
the following order: sub-G1, G1, S, G2/M;
BeamParticle: String of one word containing the type of beam (use: Proton, 4He,
12C, 16O, 60Co-gamma, etc.);
BeamType: String indicating the beam type with the acronym:
        "FE":     for Full Energy peak beam
        "SOBP": for Spread Out Bragg Peak
        "uBF": for micro Beam Focused (using particle by particle in a specific
subcellular compartment)
        "uBD": for micro Beam Defocused (using several particles as a defocused
beam irradiating a large cell surface)
BeamOrientation: String indicating the beam orientation with the words
"horizontal" or "vertical";
Depth: Float value indicating the depth in water in mm;
Energy: Float value indicating the kinetic energy at the cell-layer point, in
AMeV;
Dose: Float value indicating the dose in Gy;
DoseRate: Float value indicating dose-rate in Gy/min;
Assay: String of one word indicating the method used to quantify foci;
DOI: doi of publication related to the data contained in the file.
```

```
Database/
├── IBFM/
│   ├── FOCI_92-1_Proton_CNR-IBFM
│   ├── FOCI_ARPE19_Proton_CNR-IBFM
│   ├── FOCI_MCF10A_Proton_CNR-IBFM
│   └── ClonogenicSurvival_U87_Proton_CNR-IBFM
├── IRSN/
│   ├── FOCI_Data_Layout_example92.1_NEW-updated_MICRO_GononG1_Proton_gH2AX
│   ├── FOCI_Data_Layout_example92.1_NEW-updated_MICRO_GononG2_Proton_53BP1
│   ├── FOCI_Data_Layout_example92.1_NEW-updated_MICRO_GononG3_Alpha_gH2AX
│   └── FOCI_Data_Layout_example92.1_NEW-updated_MICRO_GononG4_Alpha_53BP1
├── US/
│   └── USE_U2OS_2019
└── VINCA/
    ├── 92.1 cell line gamma irradiation
    ├── 92.1 cell line proton irradiation
    ├── ARPE19 cell line gamma irradiation
    ├── ARPE19 cell line proton irradiation
    ├── HTB177 cell line gamma irradiation
    └── HTB177 cell line proton irradiation
```

Machine learning approaches

Machine Learning and Geant4

Istituto Nazionale di Fisica Nucleare

Current activities

We are currently developing a **post-processing tool** to bridge results across Geant4 and Geant4DNA in medical physics applications;

Tree based **regression models** are used to learn damage behaviours at the DNA scale in the form of **SSBs and DSBs**

Trained models are used at the end of macroscopic simulations to give **an estimate of DNA damage**

Machine Learning

Future activities

Improve computational efficiency in Geant4 based simulations for medical physics trough the **integration of a ML super-resolution models** in voxelized detectors

Post-processing tool based on a CNN (Convolutional Neural network) model trained with high density voxelized detector data.

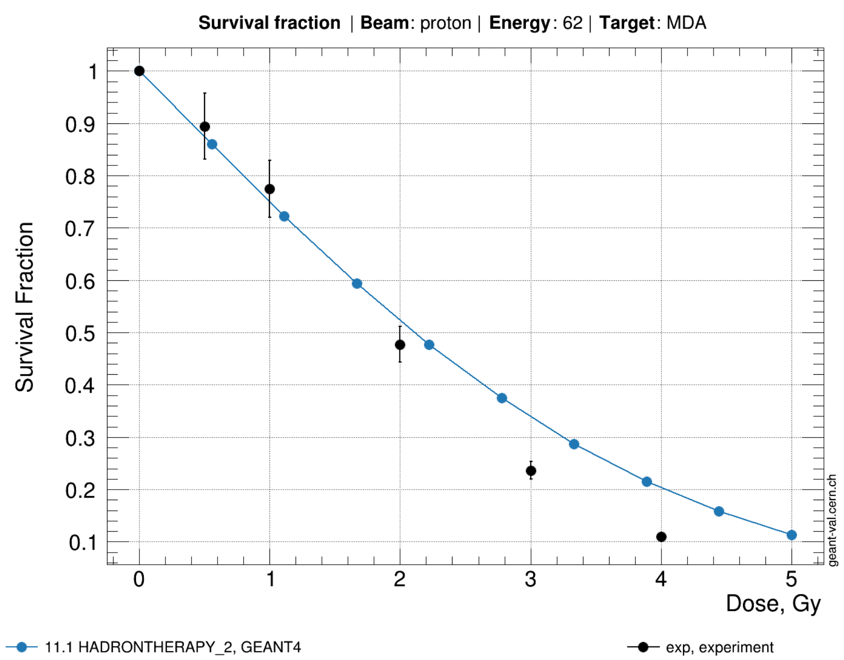
Application of the model to **retrieve spatial distribution of secondary particles** on low resolution voxelized detectors.

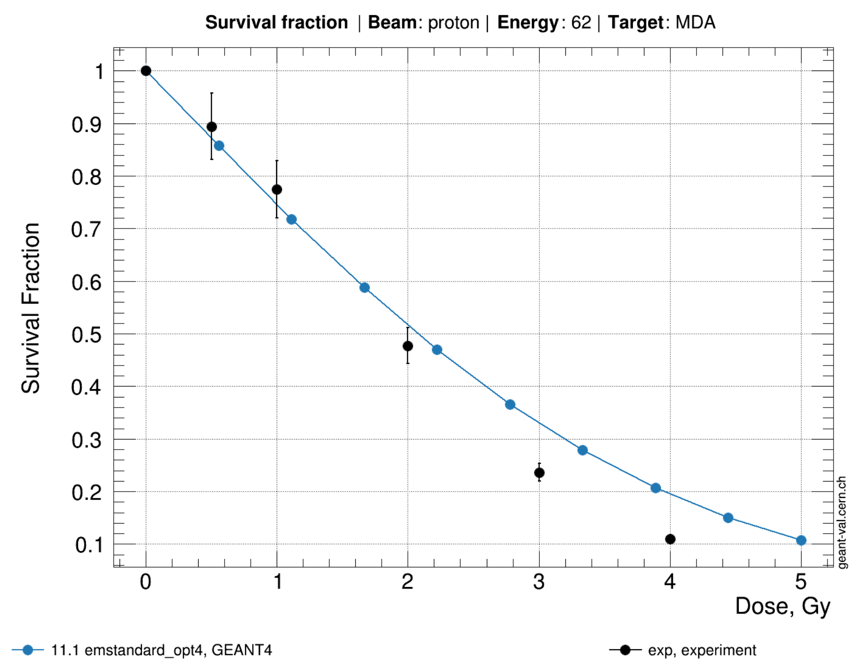
Thanks for listening

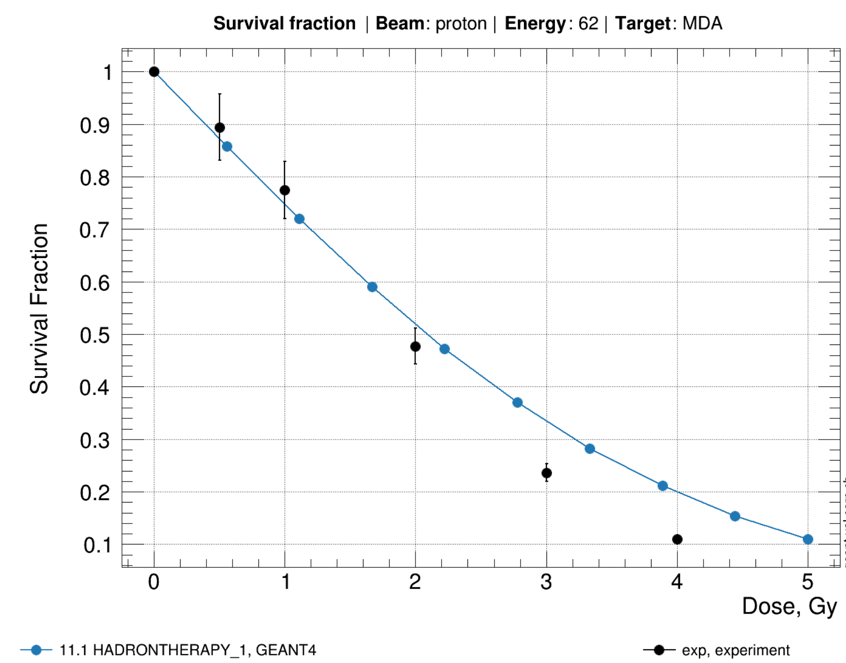
Left to right:
Roberto Catalano, Davide Passarello, Pablo Cirrone, Emilio Zappalà, Nino Amato, Luciano Pandola, Giuliana Milluzzo, Michele Costa, Mariacristina Guarrera, Serena Fattori, Antonio Russo, Beatrice Cagni, Alma Kurmanova, Carmen Altana,Andrea Matamoros, Giuliana Navarra, Salvo Tudisco, Giacomo Cuttone, Giada Petringa, Gustavo Messina
INFN-LNS Medical Physics Group - Catania, April 30, 2021

Hadrontherapy testing in G4-MED

Hadrontherapy is one of the examples present in the **Geant-Val platform**







Current version monitories the cell **Survival Fraction and RBE calculation** for a 62 MeV Proton Beam with the three em options of the example: emstandard_opt4, HADRONTHERAPY_1 and HADRONTHERAPY_2;

LET calculation and comparison with data for proton, Carbon, Helium and Oxygen beams of clinical interest, are being inserted

LET simulations vs microdosimetry data: protons

Physics in Medicine & Biology
IPEM Institute of Physics and Engineering in Medicine

PAPER

Monte Carlo implementation of new algorithms for the evaluation of averaged-dose and -track linear energy transfers in 62 MeV clinical proton beams

G Petringa[1], L Pandola[1], S Agosteo[2,3], R Catalano[1], P Colautti[4], V Conte[4], G Cuttone[1], K Fan[5], Z Mei[5], A Rosenfeld[6], A Selva[4] and GAP Cirrone[1,*]

(2020) doi.org/10.1088/1361-6560/abaeb9

$$\bar{L}_d = \frac{\sum_{i=1}^{N} L_i \varepsilon_i}{\sum_{i=1}^{N} \varepsilon_i}$$

$$\bar{L}_d^{Total} = \frac{\sum_{j=1}^{n} [\sum_{i=1}^{N} L_i \varepsilon_i]_j}{\sum_{j=1}^{n} [\sum_{i=1}^{N} \varepsilon_i]_j}$$

$$\bar{L}_T = \frac{\sum_{i=1}^{N} L_i l_i}{\sum_{i=1}^{N} l_i}$$

$$\bar{L}_T^{Total} = \frac{\sum_{j=1}^{n} [\sum_{i=1}^{N} L_i l_i]_j}{\sum_{j=1}^{n} [\sum_{i=1}^{N} l_i]_j}.$$

L: total electronic stopping power

ε: energy loss

t: track length

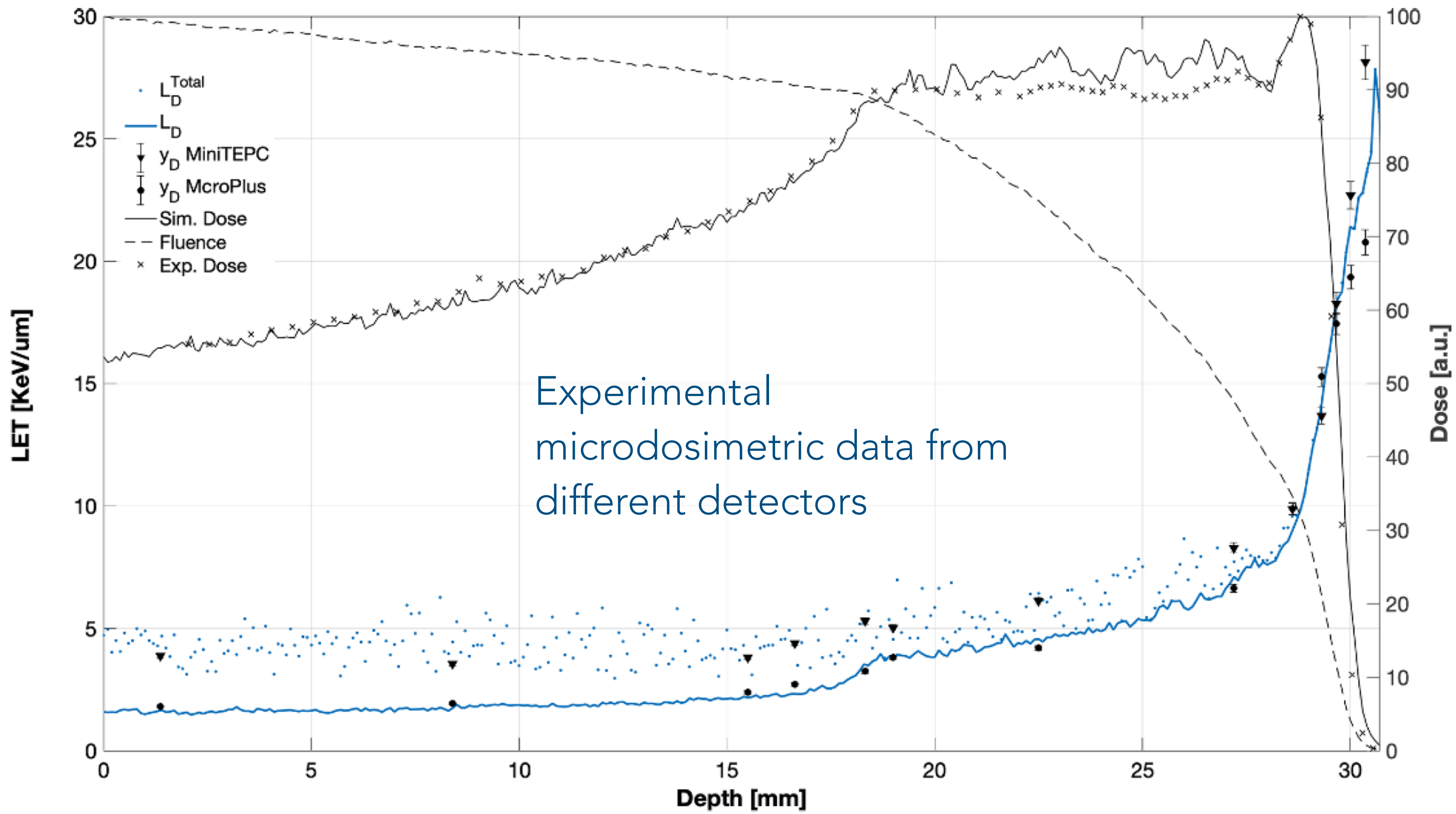
New formulation for LET-dose and LET-track

Independence from the **production cut**

Extensible to **higer-Z ions**

Taking into account the **primary** beam and the **secondaries produced** in hadronic interactions

LET simulations vs microdosimetry data: protons



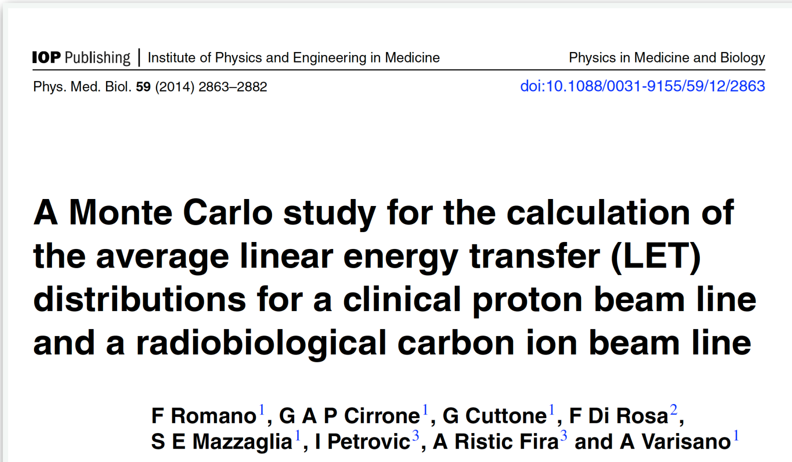
Experimental microdosimetric data from different detectors

Contribution of **secondaries**;

Agreement with detectors able to also evaluate the **fragments**;

Projectile fragmentation already predicted in 2014 by our group

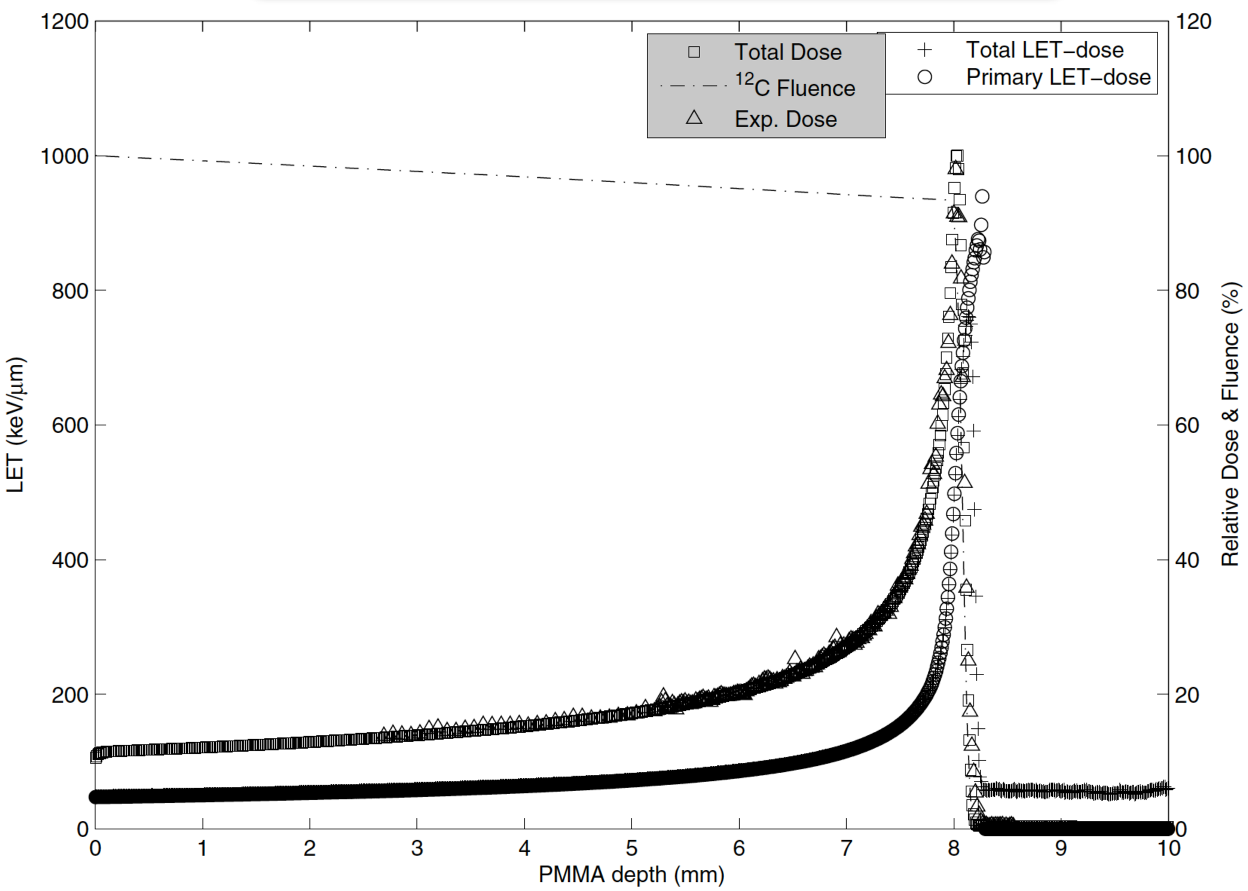
LET simulations vs microdosimetry data: Carbon

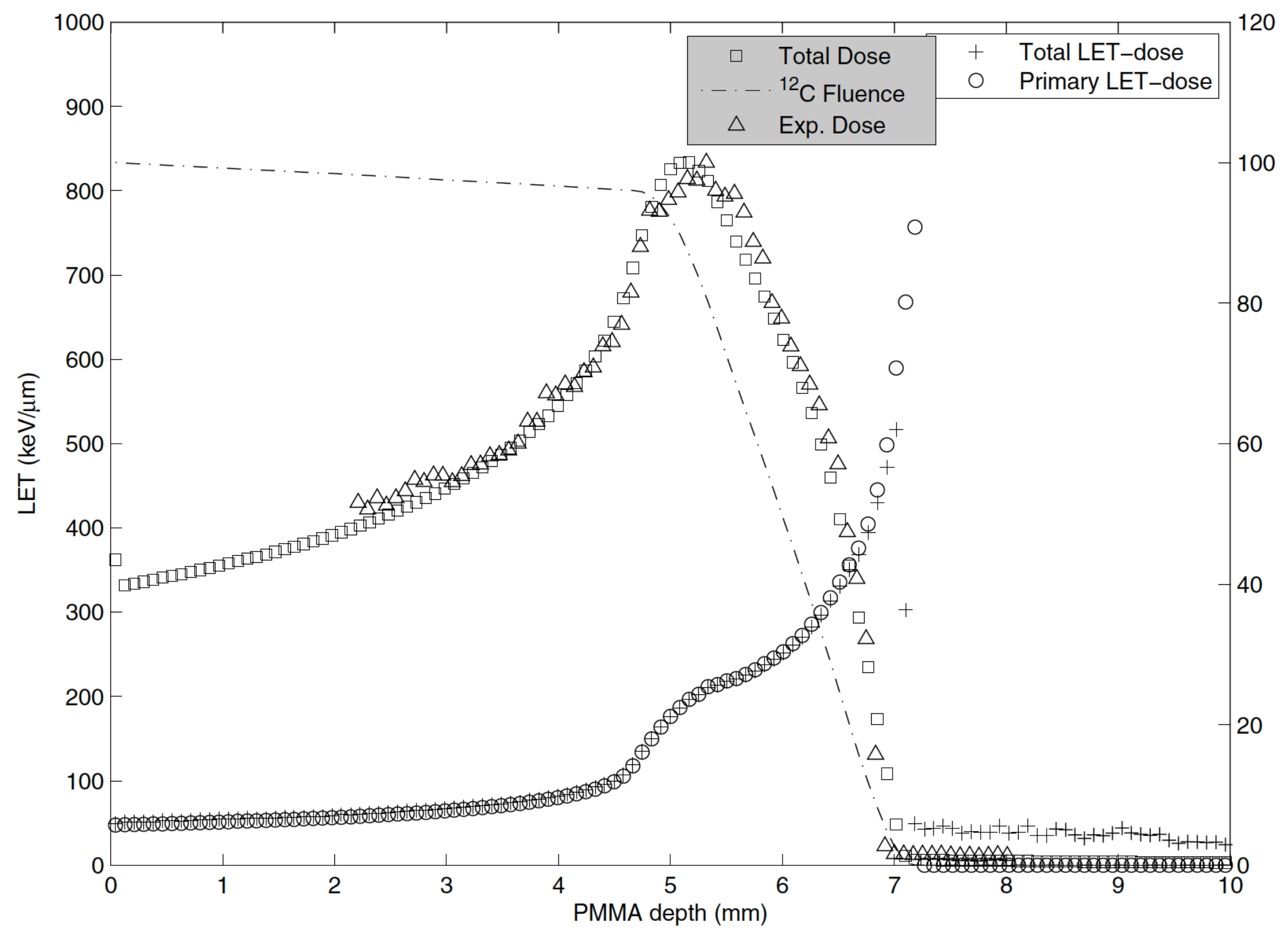

IOP Publishing | Institute of Physics and Engineering in Medicine — Physics in Medicine and Biology
Phys. Med. Biol. 59 (2014) 2863–2882 — doi:10.1088/0031-9155/59/12/2863

A Monte Carlo study for the calculation of the average linear energy transfer (LET) distributions for a clinical proton beam line and a radiobiological carbon ion beam line

F Romano[1], G A P Cirrone[1], G Cuttone[1], F Di Rosa[2], S E Mazzaglia[1], I Petrovic[3], A Ristic Fira[3] and A Varisano[1]

(2014) doi.org/10.1088/0031-9155/59/12/2863



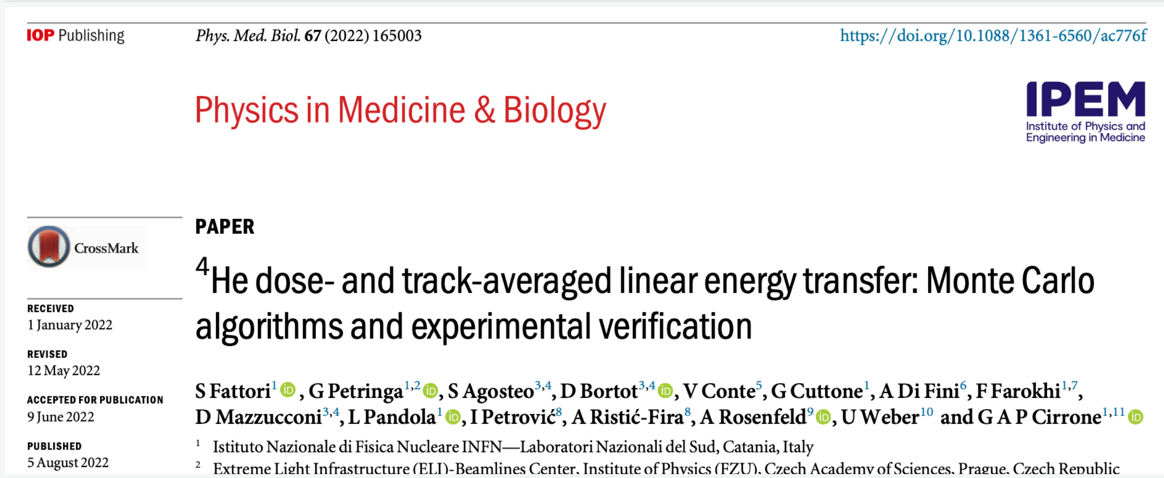


Mono- and poly-chromatic 62 AMeV Carbon beam

Also validated against microdosimetric data

GAP Cirrone, PhD - pablo.cirrone@lns.infn.it

LET simulations vs microdosimetry data: Helium, 62 AMeV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IPEM Institute of Physics and Engineering in Medicine
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12 May 2022
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9 June 2022
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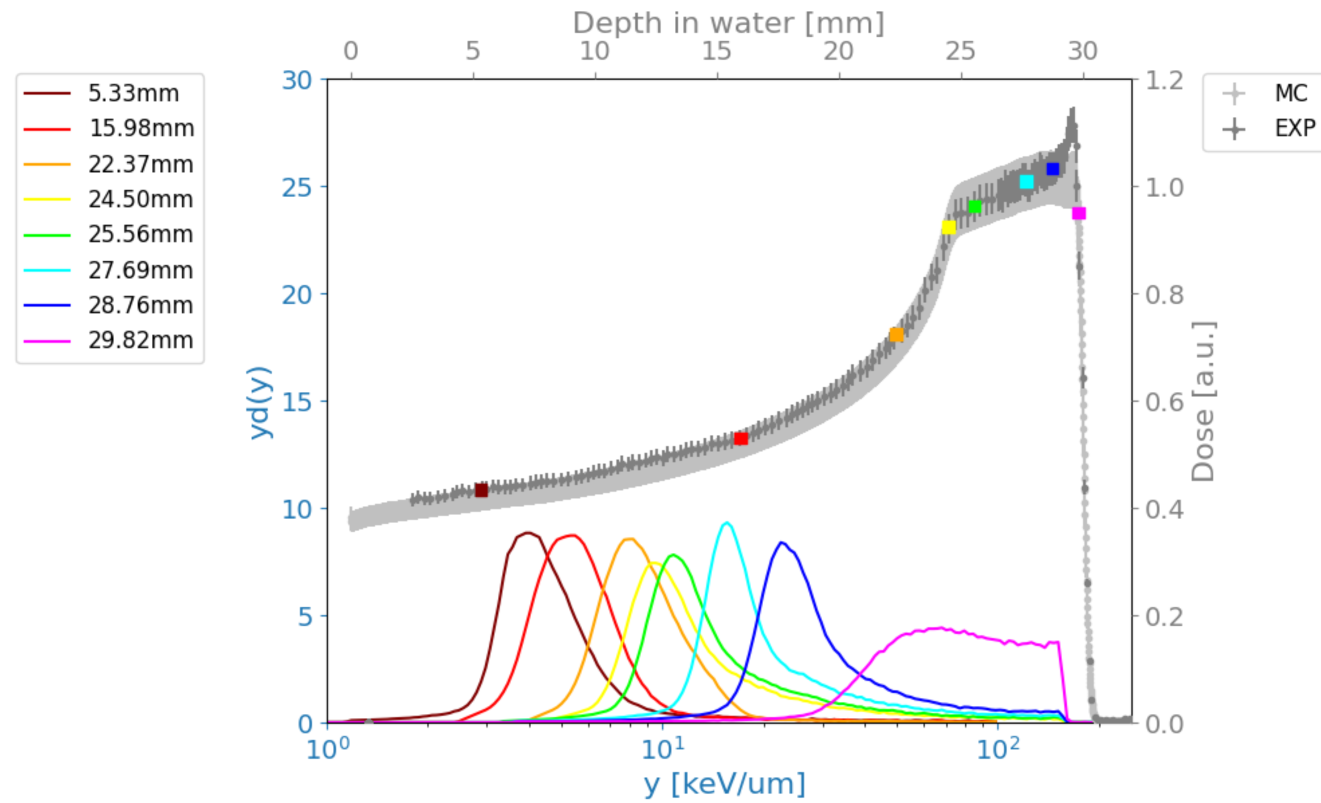
5 August 2022

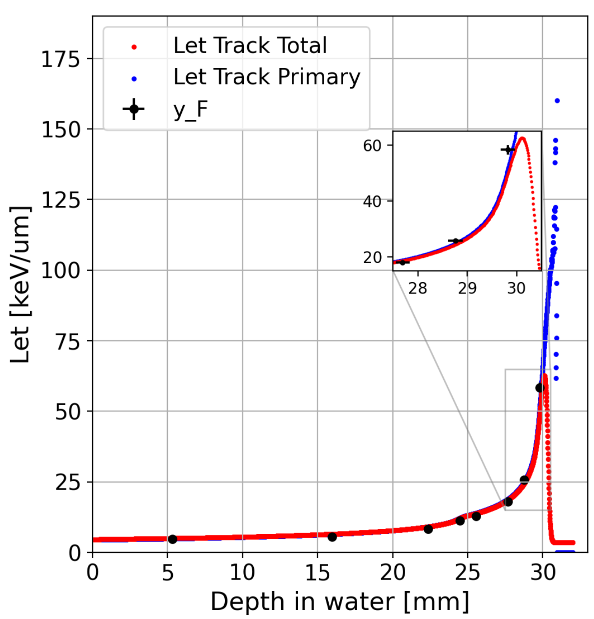
PAPER

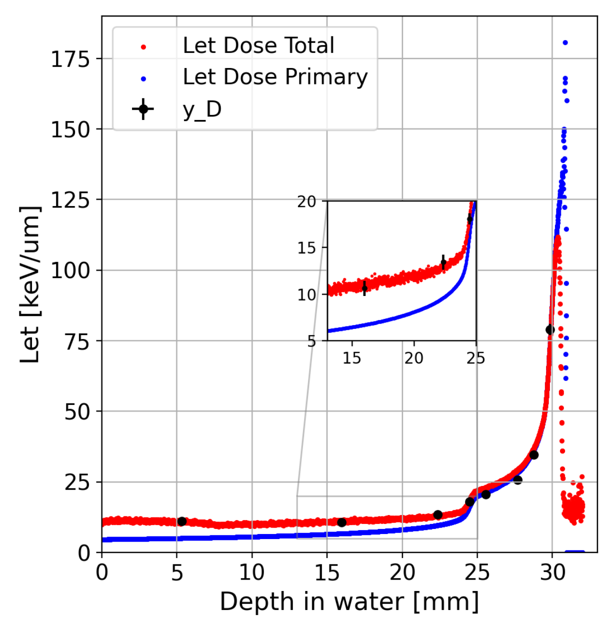
^{4}He dose- and track-averaged linear energy transfer: Monte Carlo algorithms and experimental verification

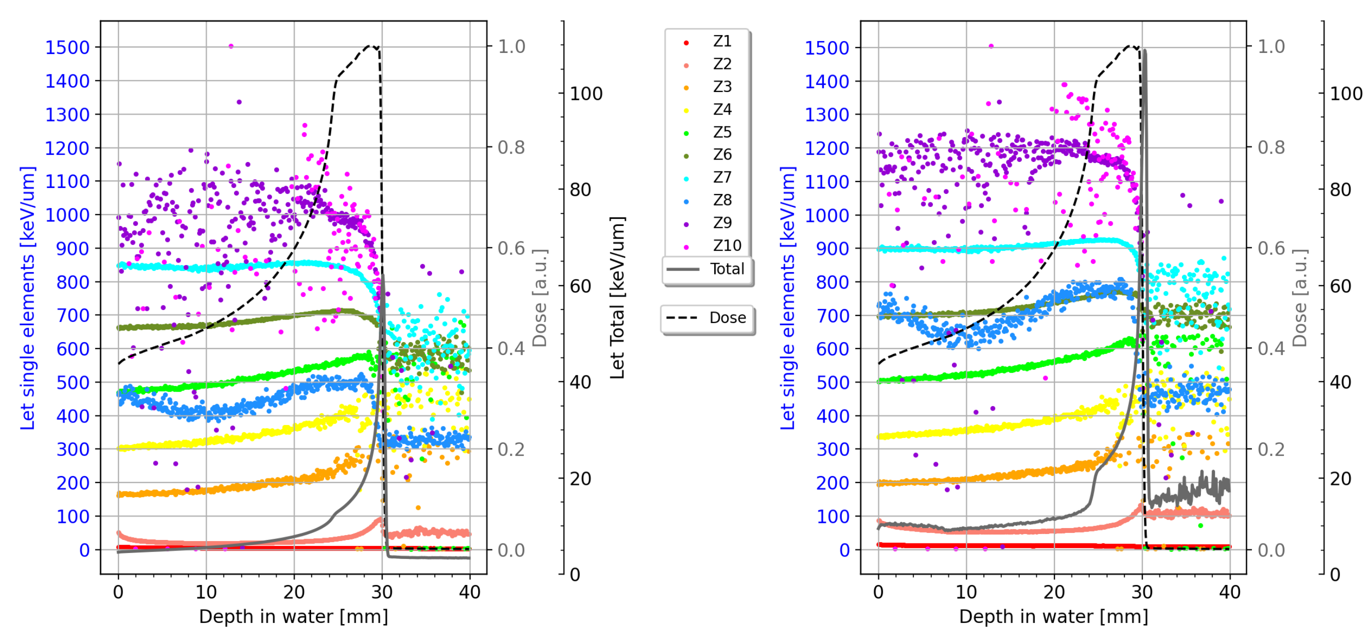
S Fattori[1], G Petringa[1,2], S Agosteo[3,4], D Bortot[3,4], V Conte[5], G Cuttone[1], A Di Fini[6], F Farokhi[1,7], D Mazzucconi[3,4], L Pandola[1], I Petrović[8], A Ristić-Fira[8], A Rosenfeld[9], U Weber[10] and G A P Cirrone[1,11]
[1] Istituto Nazionale di Fisica Nucleare INFN—Laboratori Nazionali del Sud, Catania, Italy
[2] Extreme Light Infrastructure (ELI)-Beamlines Center, Institute of Physics (FZU), Czech Academy of Sciences, Prague, Czech Republic

(2022) doi.org/10.1088/1361-6560/ac776f









Oxygen study is ongoing