Radiobiological needs for FOOT

E. Scifoni, F. Tommasino

- Target Fragments in proton beam irradiation (inverse kin)
- Projectile Fragments in Oxygen beam irradiation (direct kin)

Trento Institute for Fundamental Physics and Applications

MoVe IT

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

Sebastian Hild (TIFPA)

WP1 – RB modeling for TPS

- ***T1.1:*** *RBE modeling for protons*
- ***T1.2:*** *OER and ITH modeling*

MG Pugliese (NA)

WP2 – NTCP/TCP

- ***T2.1:*** *NTCP models on proton patient data including RBE*
- ***T2.2:*** *TCP/NTCP including hypoxia for different ions*

Giorgio Russo (LNS)

WP3 – Biological Dosimetry

- ***T3.1:*** *Devices for spatially resolved proton RBE measurement*
- ***T3.2:*** *Hypoxic, Coculture and Stem cells devices*
- ***T3.3:*** *In vivo and Molecular biomarkers*

Pablo Cirrone (LNS)

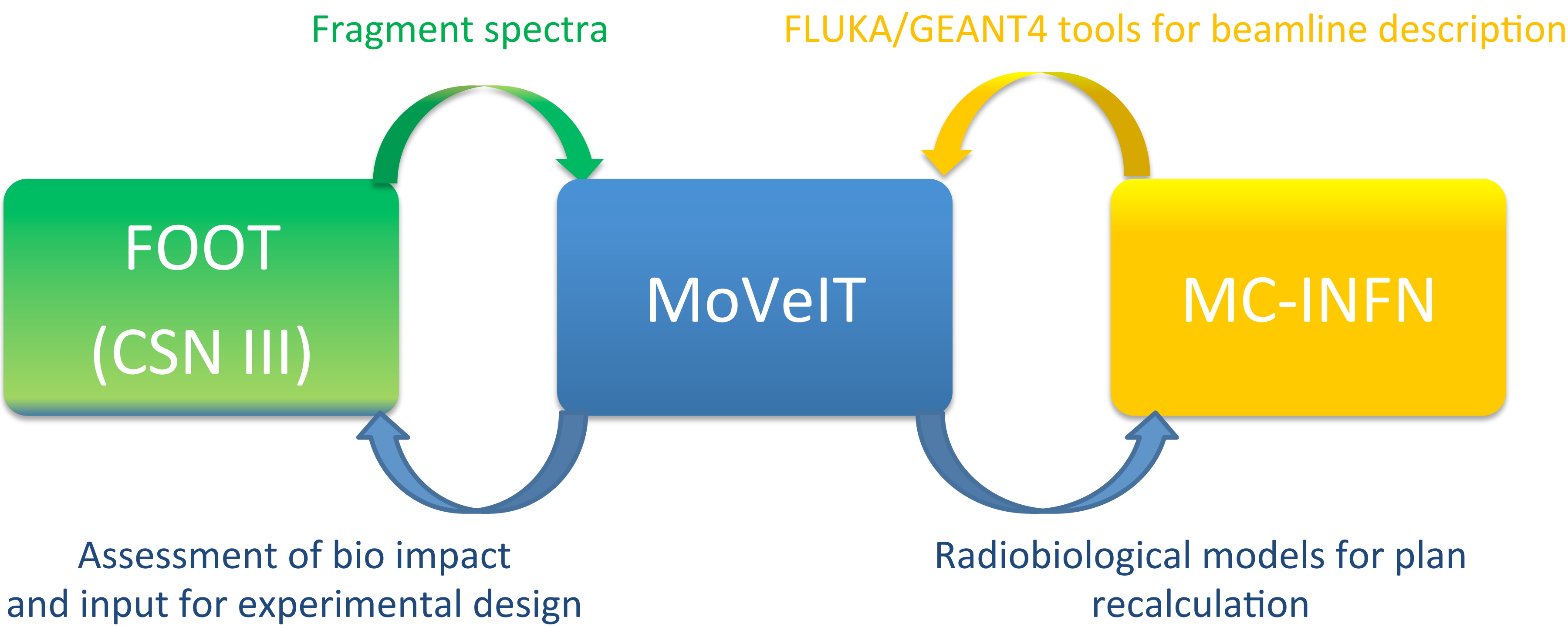
WP4 – Facilities

- ***T4.1:*** *CNAO/TIFPA/LNS lines development for beam delivering*
- ***T4.2:*** *MC Simulations for beamlines/target stations for in vitro/in vivo exp*
- ***T4.3:*** *Detectors for beam flux and beam energy measurement*

WP0
Coordination& Dissemination

Emanuele Scifoni (TIFPA)

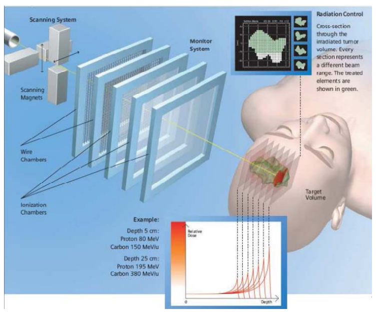
Interaction with INFN projects

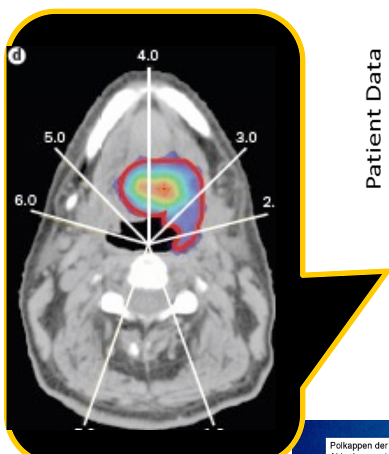


+ Feed from previous related projects: TPS, RDH, UFSD

TRiP98 – Biological Based Treatment planning for Particles

Clinical use in pilot project, Research use in GSI, HIT, Aarhus, Lyon etc.
Reference for: Siemens SynGo/PT, RaySearch





Planning task input

Beam Data

Irradiation specifics (beam angles, available energies etc..)

Patient Data

Morphological map (CT; Contours)

Functional map (pO_2 distribution e.g. from PET)

TRiP98

Physical beam calculation

- Field update
- Dose
- LET

Optimization

Biological effect calculation

- OER (x,y,z)
- RBE Calculation
- Beam mixing

Base Data input (tables)

Physics

- Depth dose profile $dE/dz\ (E, Z)$
- Fragment spectra $dN/dE(E_b,z,Z,E)$
- ...etc.

Radiobiology

- $RBE(E,Z)$ (e.g. from LEM)
- $OER\ (pO_2,LET)$ (from present or different model)

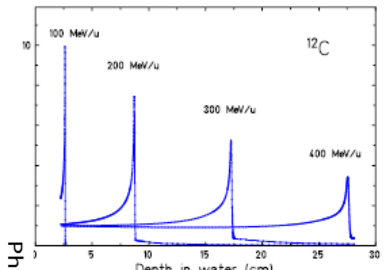
Output

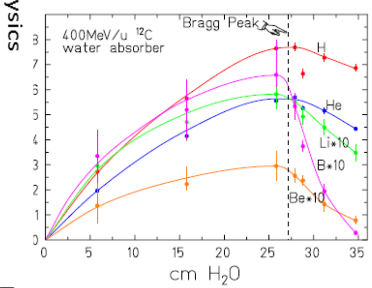
Optimized Scan Parameters

- Energies E_b
- Fluences $F(E_b,x,y)$

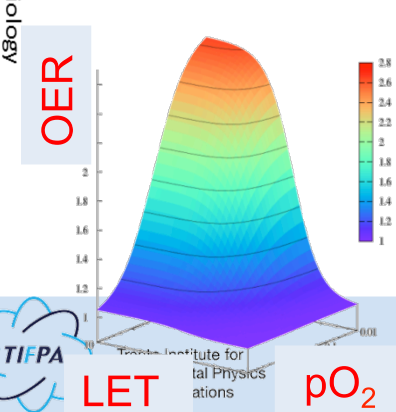
Outcome Plan

- Dose, LET distribution
- Full biological Effect S(x,y,z)

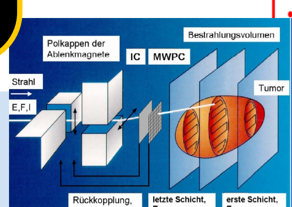


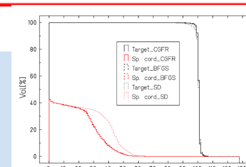


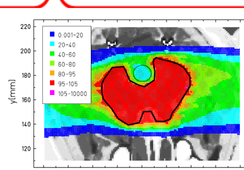
Schardt et al. Rev Mod Phys 2010



Tinganelli et al. Sci.Rep.2015







Kraemer et al. EPJD 2014

Biological-based treatment planning

- Bio-TPS for ion beams aims to include as much as possible biological effect information in the planning strategy.
- Relevant for plan recalculation but ideally needed for inverse planning.
- Substantial for assessing differential benefits of different irradiation modalities and selecting the most suitable choice for a given patient case.
- Additional physics data needed, since the different components (E,Z) of the mixed field in a beam should be properly accounted in order to get an overall biological effect.

IOP PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY
Phys. Med. Biol. 57 (2012) 5169–5185 doi:10.1088/0031-9155/57/16/5169

The impact of modeling nuclear fragmentation on delivered dose and radiobiology in ion therapy

Armin Lühr[1,2,3], David C Hansen[1,2], Ricky Teiwes[2],
Nikolai Sobolevsky[4], Oliver Jäkel[5,6] and Niels Bassler[1,2]

- SHIELD-HIT (MC) + TRiP98
- C beam
- 20% in xs => only 3% in RBE

Role of Target fragmentation in proton therapy

Differently from Projectile fragments, their Energy distribution being peaked at very low E
Combines with the peak of RBE at low E

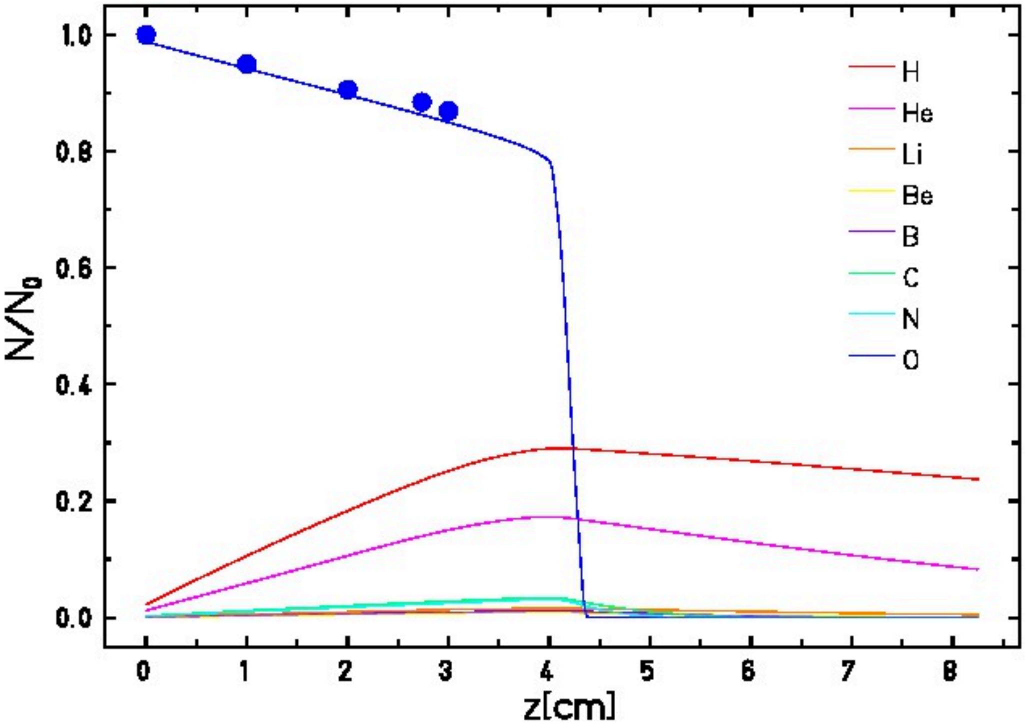
Fragment	E (MeV)	LET (keV/µm)	Range (µm)
^{15}O	1.0	983	2.3
^{15}N	1.0	925	2.5
^{14}N	2.0	1137	3.6
^{13}C	3.0	951	5.4
^{12}C	3.8	912	6.2
^{11}C	4.6	878	7.0
^{10}B	5.4	643	9.9
^{8}Be	6.4	400	15.7
^{6}Li	6.8	215	26.7
^{4}He	6.0	77	48.5
^{3}He	4.7	89	38.8
^{2}H	2.5	14	68.9

Heavy fragments have low residual energies and release low doses -> high RBE

Tommasino & Durante 2015 Cancers

^{16}O beam in TRiP

Yield of secondary particles with depth in water for ^{16}O at 160 MeV/u (TRiP98)



Exp attenuation data courtesy of C. La Tessa (BNL)

- Large number of fragments
- Few experimental data available
- New data for full spectral characterization are highly needed to assess impact of fragments

Exploiting O beams for hypoxia

www.nature.com/scientificreports

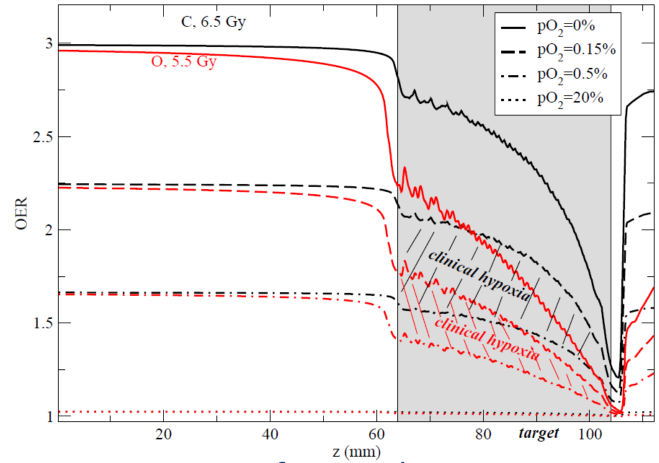
SCIENTIFIC REPORTS

OPEN

Kill-painting of hypoxic tumours in charged particle therapy

Walter Tinganelli[1,2], Marco Durante[1,3], Ryoichi Hirayama[2], Michael Krämer[1], Andreas Maier[1], Wilma Kraft-Weyrather[1], Yoshiya Furusawa[2], Thomas Friedrich[1] & Emanuele Scifoni[1]

Received: 03 July 2015
Accepted: 23 October 2015



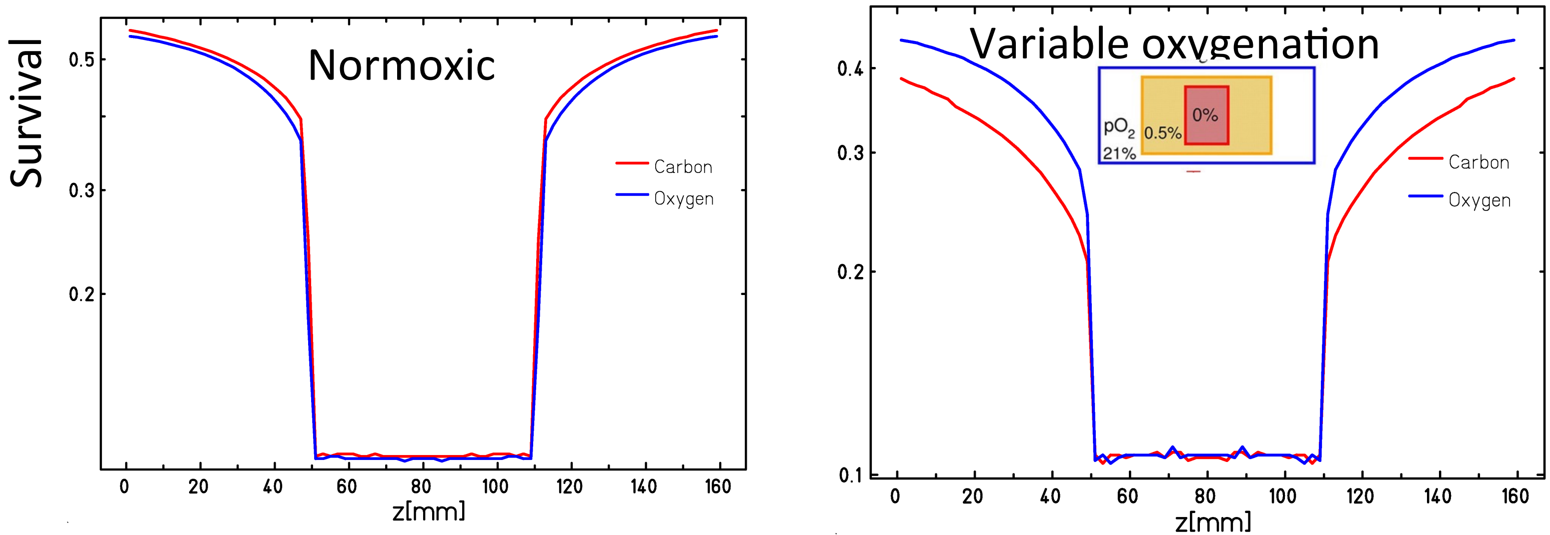
Scifoni et al PMB 2013

Oxygen beams for therapy: advanced biological treatment planning and experimental verification

O Sokol[1], E Scifoni[1,2], W Tinganelli[1,2], W Kraft-Weyrather[1], J Wiedemann[1], A Maier[1], D Boscolo[1], T Friedrich[1], S Brons[3], M Durante[1,2] and M Krämer[1]

Submitted to PMB

OER optimized plans with O (kill painting)



Sokol et al. submitted to PMB

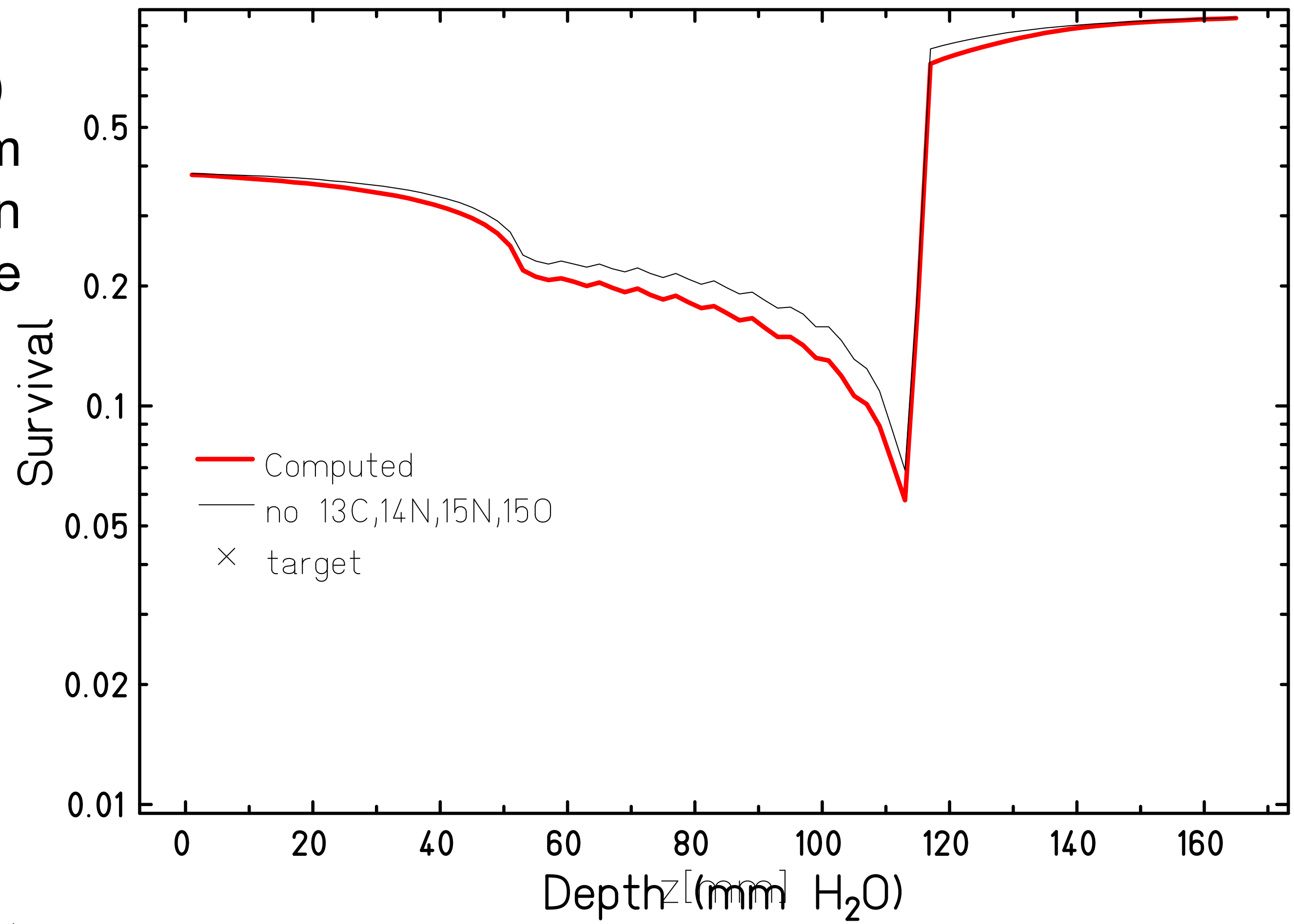
- In case of hypoxia, proper optimization accounting for OER may lead to **Inverted peak-to-entrance ratios** as compared to a normoxic case

- According to actual oxygenation, O beam may overcome the price of larger entrance channel with the LET advantages

- Trade-off between better **LET distribution** and worse **Fragmentation** in entrance and tail

Impact of "high" fragments

Survival profile (CHO) along an O beam SOBP, optimized on physical flat dose (4Gy)



Desiderata for Protons

Target fragment producton, at 100-200 MeV:

- Heavy fragment ($Z>2$) production cross section with uncertainty < 5%
- Fragment energy spectrum (i.e. $d\sigma/dE$) with energy resolution of ≈1 MeV/u
- Charge ID at the level of 2-3%
- Isotopic ID at the level of 5%
- Not needed accurate angular measurement
- Study light ions production at large angle

Desiderata for Oxygen

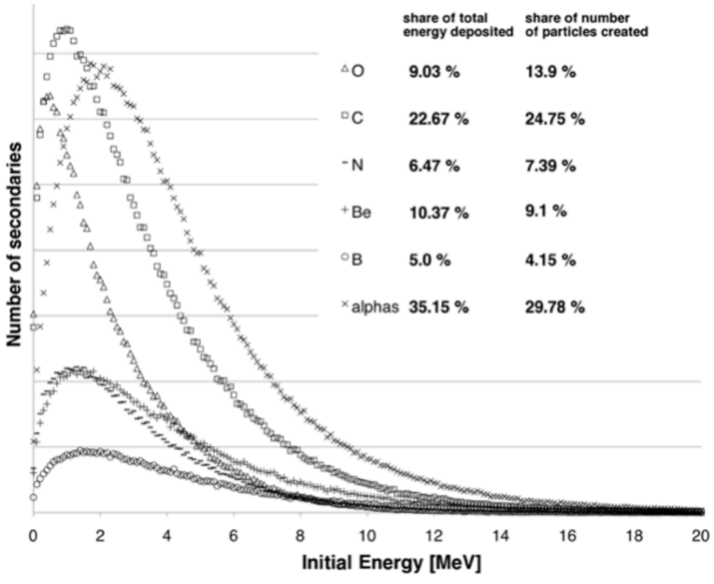
Projectile Fragment producton, at 150-400 MeV/u:

- Cross section of projectile fragments with maximum uncertainty of 5-10%
- Fragment energy spectrum (i.e. $d\sigma/dE$) with an energy resolution of ≈10 MeV/u
- Charge ID at the level of 2-3%
- Isotopic ID at the level of 5%
- Angular distribution needed for out-of-field biological dose

Our strategy for better figures design

MC Spectra from WP4 (LNS-GEANT4, MILANO-FLUKA)
2 options:

- Voxelized (layered) Spectra dN/dE(Z,**z**,E,E_0) including eventual buidup
- Pure Fragment Spectra dN/dE(Z,E,E_0) -> YIELD-> TRiP98



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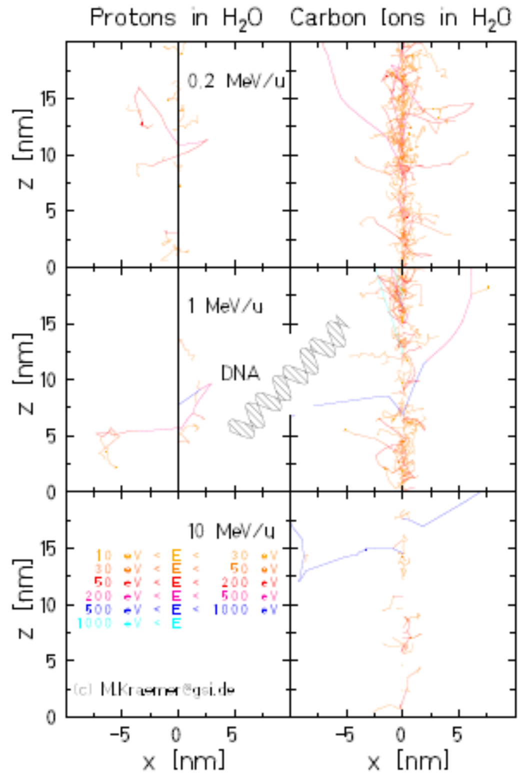
Parallel approaches for T_frag impact assessment

Track structure simulations of low energy ions
-with no Energy/space cutoff in secondary electrons-

- TRAX
- GEANT4DNA



Milestones related to FOOT

Milestone	Description	Date
M1.1.1	Initial RBE description with tentative cross sections	November 2017
M1.1.2	Final RBE description with FOOT cross sections	July 2019
M2.1.2	Comparison between proton NTCP estimations	November 2019
M2.2.1	NTCP/TCP estimations with different ions, on imported plans	April 2019

Thank you