Comparison of treatment plans with different light ions

Emanuele Scifoni, Olga Sokol, Sebastian Hild, Andrea Attili, Summit Jalota, Marco Durante and Michael Kraemer

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TIFPA Trento Institute for Fundamental Physics and Applications

GSI

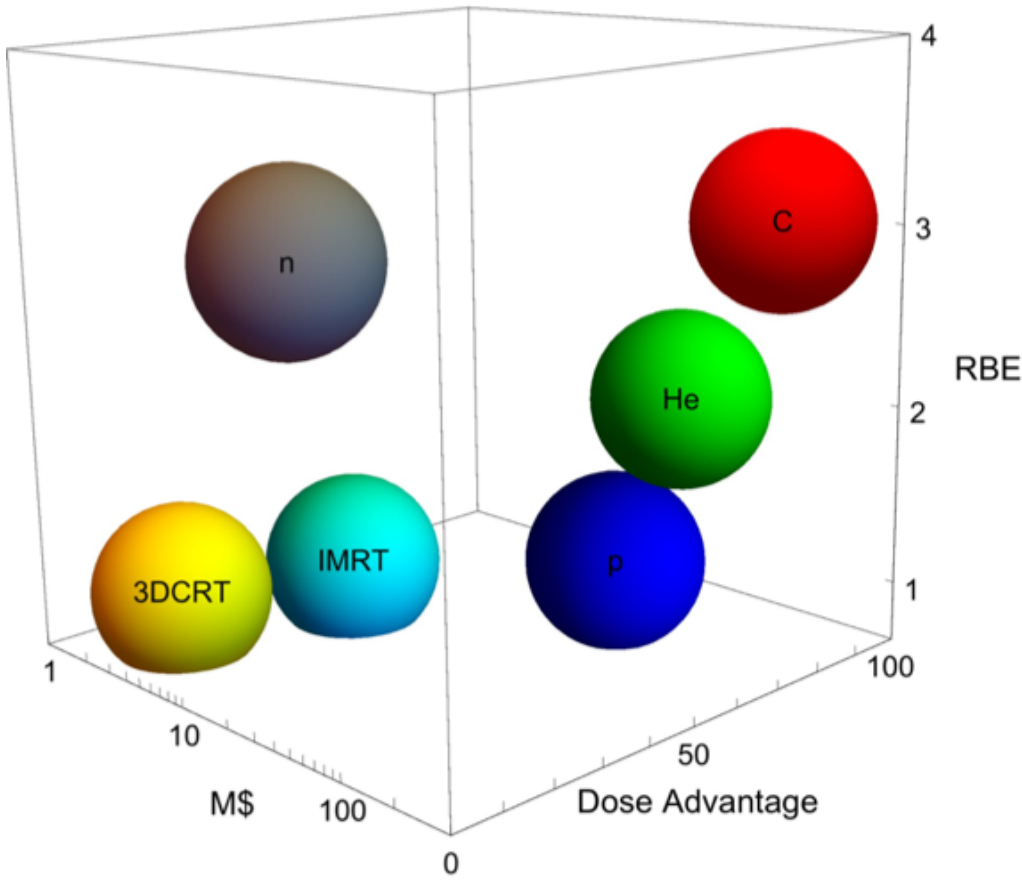
Outline

- **Biological Treatment planning (Bio-TPS) for ion beams:**
  - **RBE-weighted dose optimization and beyond**
  - **Adaptive Bio-TPS including hypoxia**

- **Bio-TPS with different ions**
- **Nuclear physics data need and their impact**
- **Impact of biophysical models**
- **Bio-TPS with Multiple Ions**

What's the best ion?

- What means the best?
- Most probably no unique choice
- The choice depend on morphological and biological features
- We need specific (Bio)-TPS studies



Biological-based treatment planning

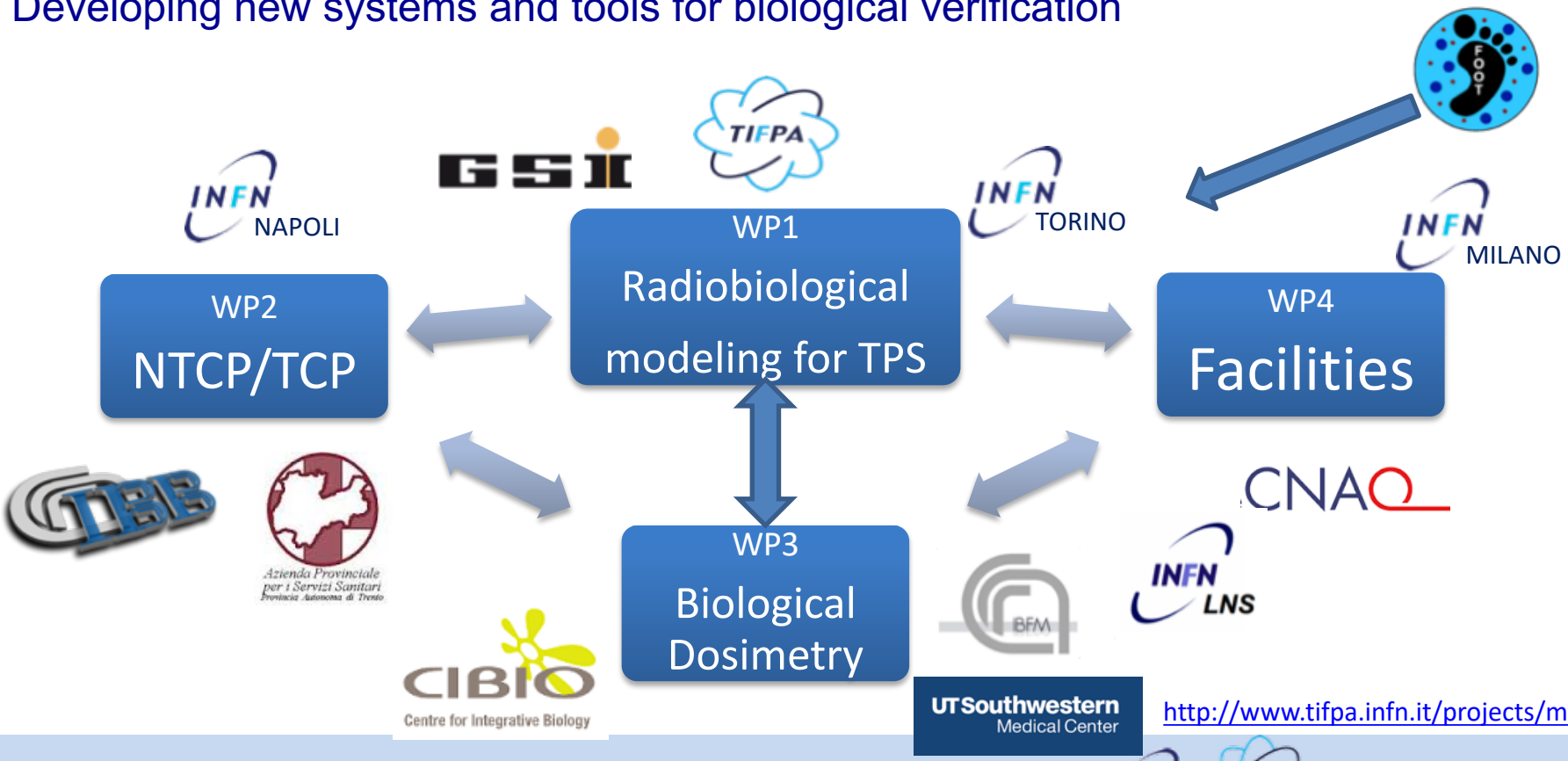
- Bio-TPS for ion beams aims to include as much as possible biological effect information in the planning strategy.
- Relevant for plan recalculation but ideally needed for **inverse** planning.
- Substantial e.g., for assessing differential benefits of different irradiation modalities and selecting 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 a proper overall biological effect.

MoVe IT

Modeling and Verification for Ion beam Treatment planning

INFN Network - Call group V - funded 2017-2019- Coordinator: E. Scifoni

- Advancing biolological treatment planning (e.g. impact of full nuclear spectra (including target fragments from FOOT) on RBE, hypoxia, intra-tumour heterogeneities)
- Developing new systems and tools for biological verification



http://www.tifpa.infn.it/projects/moveit

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Advancing biological treatment planning: a graphical summary

Physics

- Depth dose distributions
- Nuclear fragment spectra (including target)
- Stopping power data

Radiobiology

(= Biological effects + micro/nanoscale physics)

- RBE (eg. LEMx, MKM)
- OER
- DEF

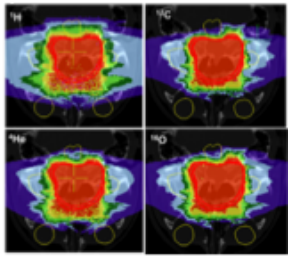
TPS

Beamline specifics

Patient Imaging data

Including intratumor heterogeneity

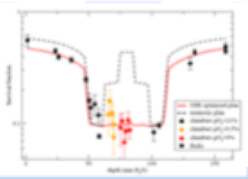
Effective Dose profile



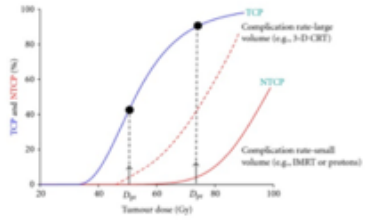
Verification

advanced beam monitoring

"Bio"-dosimetry



Clinical Impact



TCP/NTCP

Advancing clinical prescription for Particle therapy

optimized quantity:

- Absorbed Dose

- Biologically effective Dose (RBE weighted)

Optimization of the RBE-Weighted Dose

$$\chi^2_{\mathrm{Bio}}(\vec{N}) = \sum_{i\in \mathrm{target}} \frac{[D^i_{\mathrm{pre}} - D^i_{\mathrm{Bio}}(\vec{N})]^2}{\Delta D^2_{\mathrm{pre}}} + \sum_{i\in \mathrm{OAR}} \frac{[D^i_{\mathrm{max}} - D^i_{\mathrm{Bio}}(\vec{N})]^2}{\Delta D^2_{\mathrm{max}}} \Theta(D^i_{\mathrm{Bio}}(\vec{N}) - D^i_{\mathrm{max}})$$

RBE-weighted dose:

Biophysical model

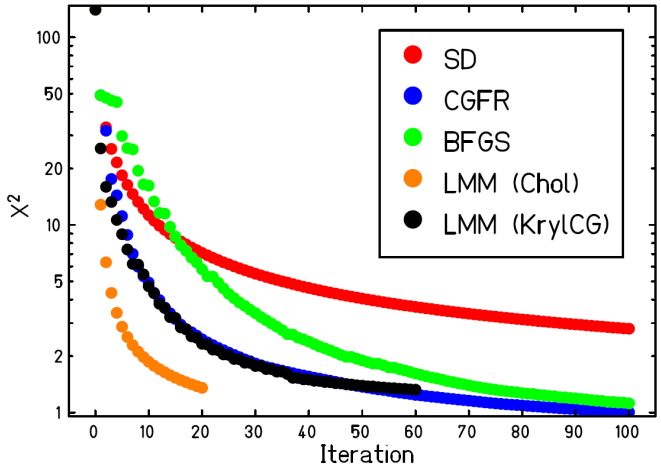
$$D^i_{\mathrm{act}}(\vec{N}) = D^i_{\mathrm{bio}}(\vec{N}) = D^i_{\mathrm{abs}}(\vec{N}) \cdot \mathrm{RBE}^i(\vec{N})$$

Optimization Task

$$\chi^2_{\mathrm{Bio}}(\vec{N}) \rightarrow \min$$

nonlinear RBE-weighted dose

-> solution only with numerical methods



Algorithms for the optimization of RBE-weighted dose in particle therapy

Horcicka et al. PMB 2013

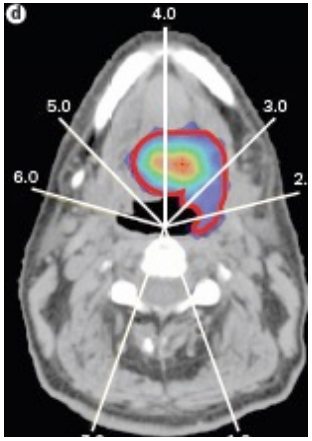
The kill painting basic idea

optimized quantity:

- Absorbed Dose

- Biologically effective Dose (RBE weighted)

- Biologically isoeffective Dose in the local microenvironment

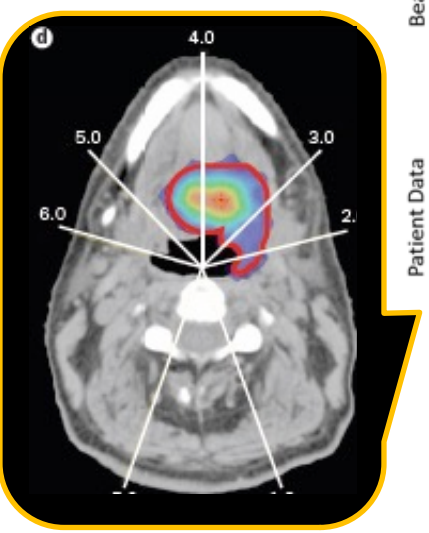


Intra-tumour
Heterogeneity
revealed by functional imaging
e.g. CT/PET(FMISO)
Horsman NRCO 211

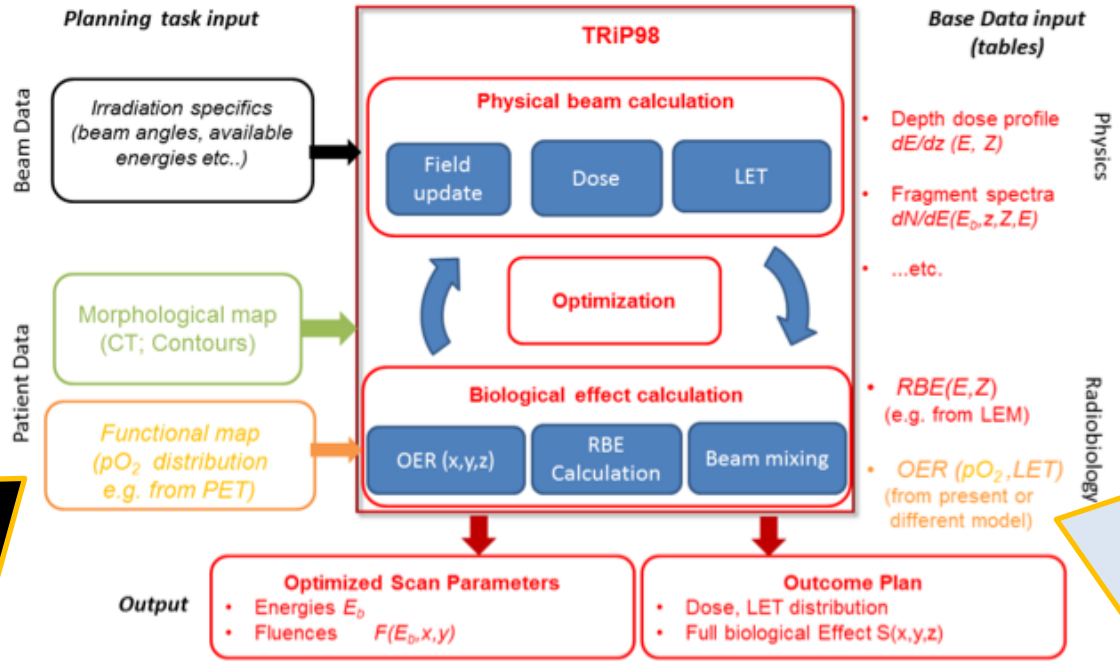
What is needed:

- ✓ Physical beam modeling
- ✓ RadioBiological modeling
- ✓ Implementation in TPS
- ✓ Experimental Verification

Kill painting implementation in TPS

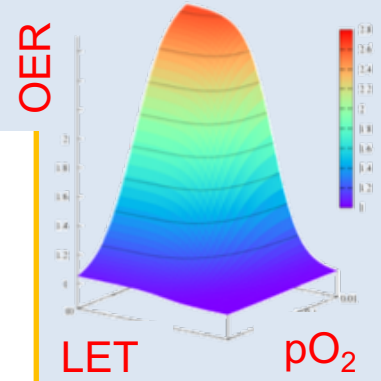


Horsman et al
Nat. Rev. Clin. Oncol. (2012)

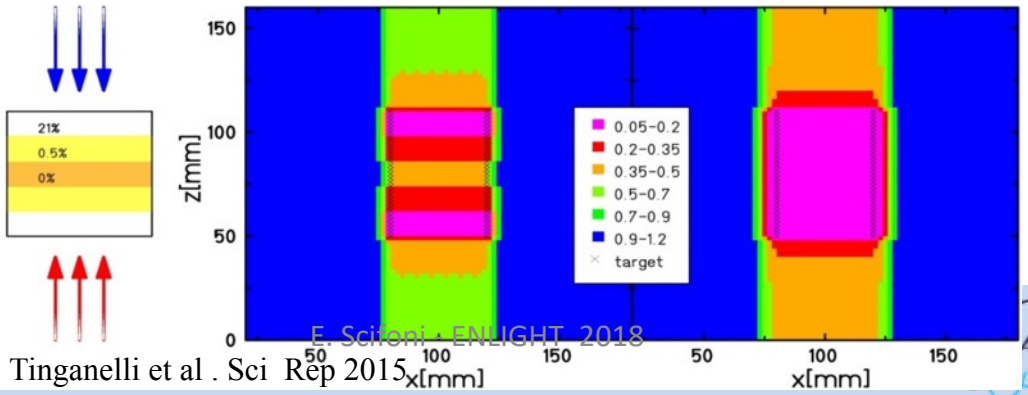


Semi-empirical model for OER (pO_2,LET)

Scifoni et al .
Phys Med Biol 2013



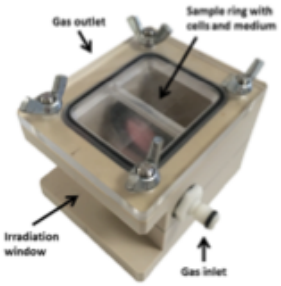
LET and dose distribution of the particle fields automatically adjusted from the optimization to the oxygen distribution

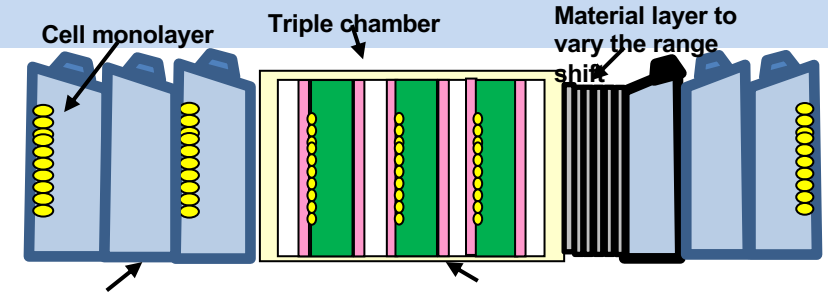


Tinganelli et al . Sci Rep 2015

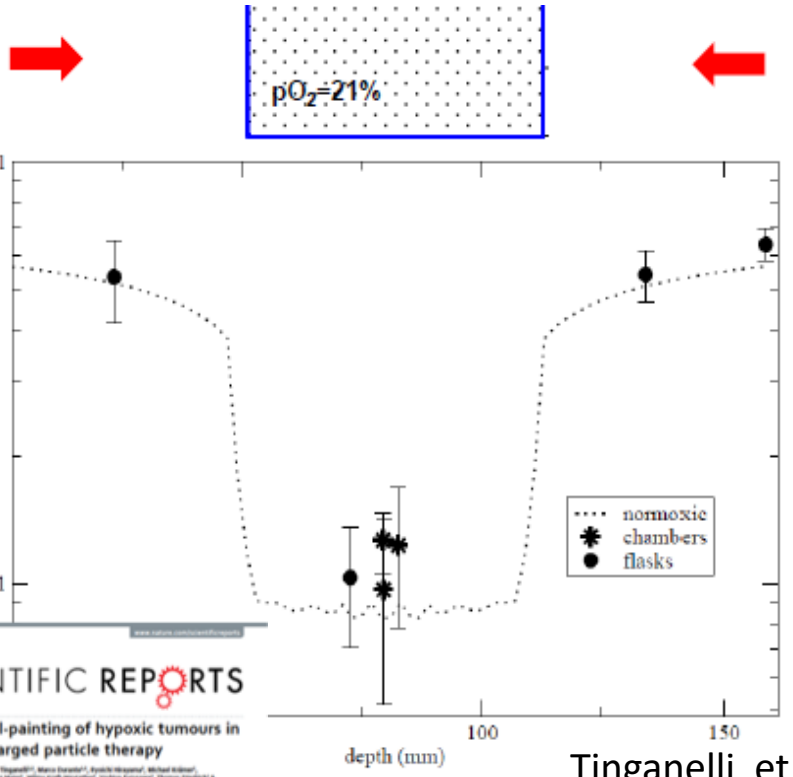
Experimental verification: Hypoxic cell chambers

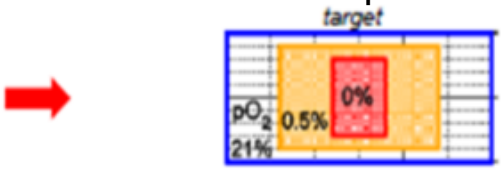
2 Fields C ions@GSI

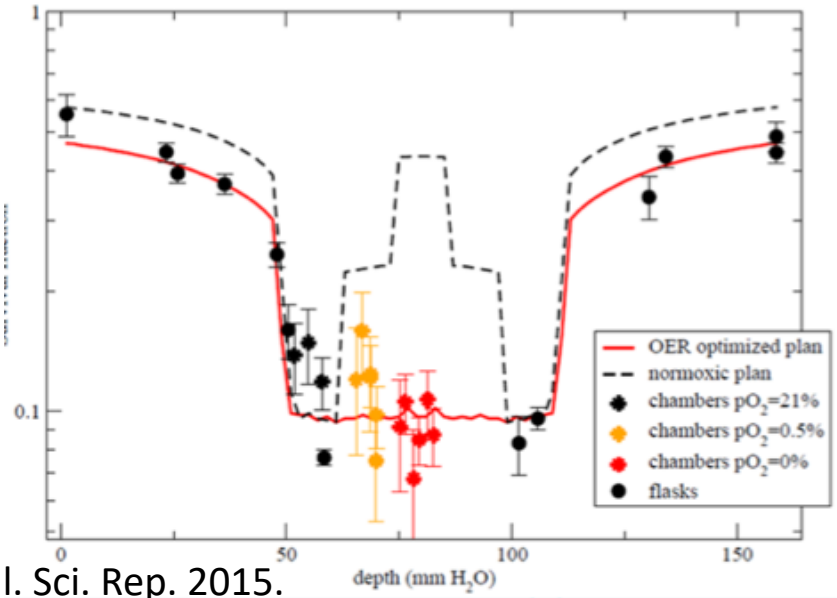




Example of the 'anoxic' phantom







Tinganelli et al. Sci. Rep. 2015.

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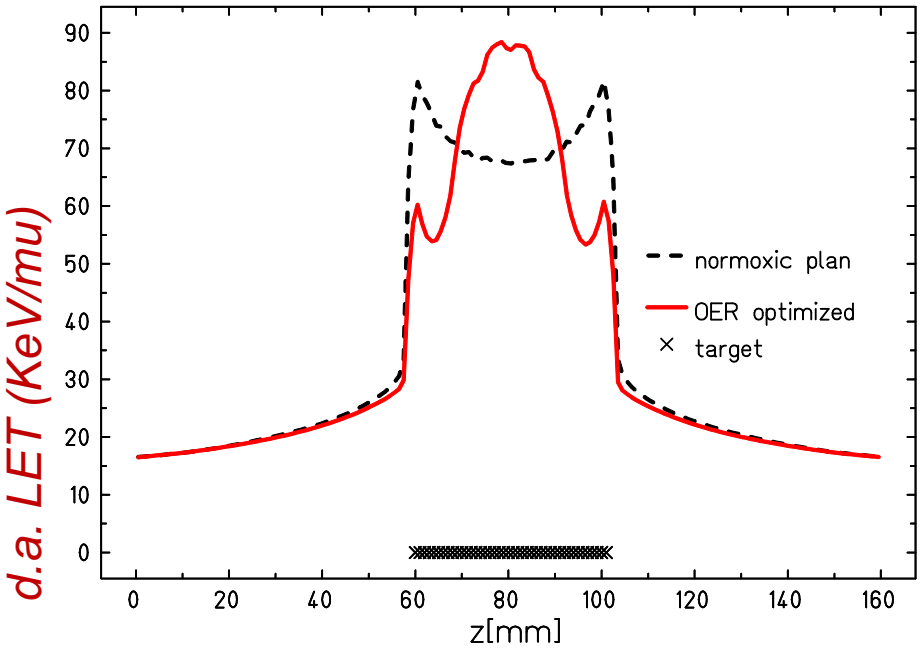
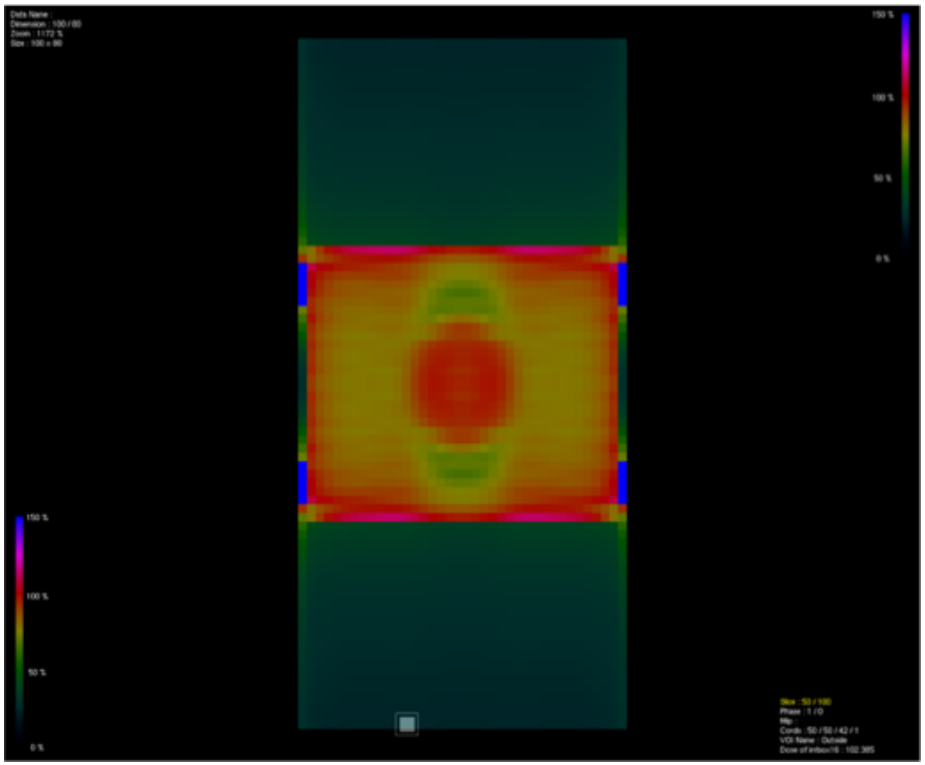
Proof of principle of 3D kill painting

Automatic optimal LET distribution



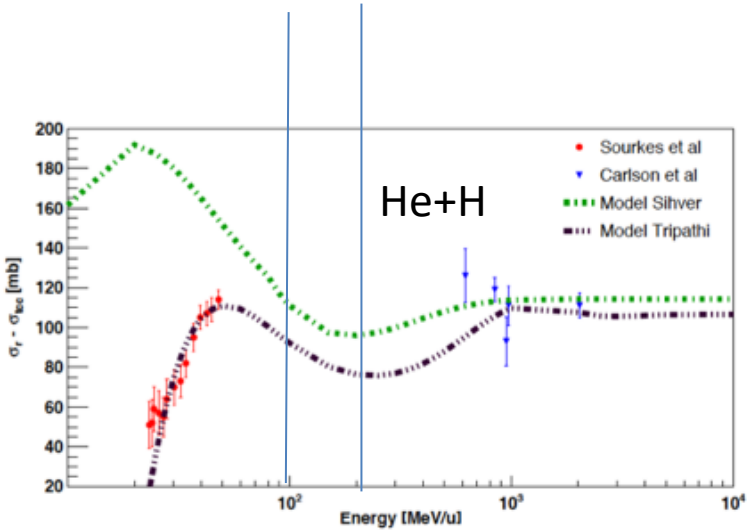
1D Kraemer et al. EPJD 2014

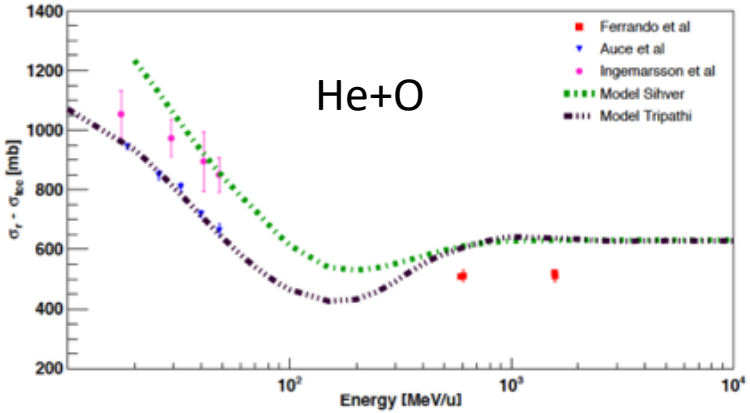


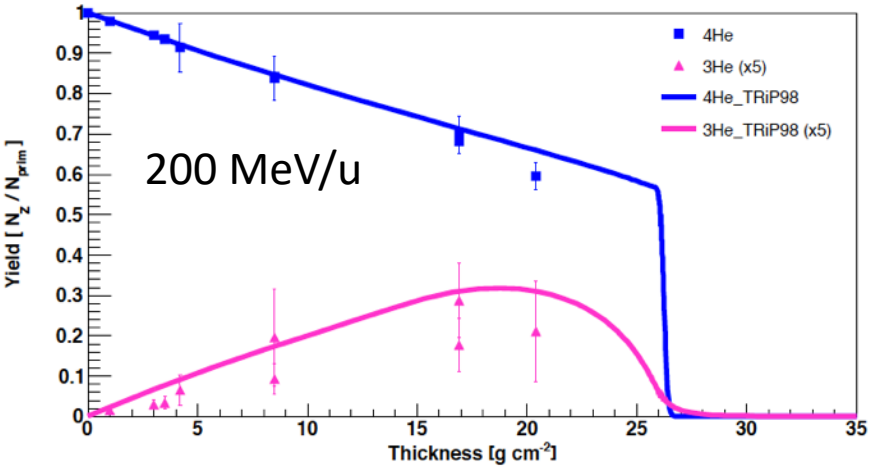
3D Sokol et al. in prep. for PMB

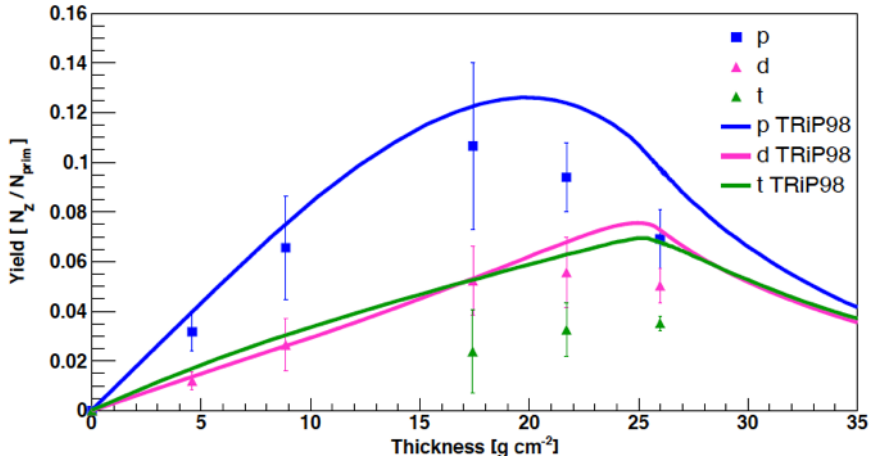
Similar to LET painting (*Bassler et al. 2014)* BUT no ramp applied, simple result of the optimization

^{4}He beam model





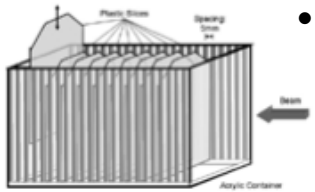


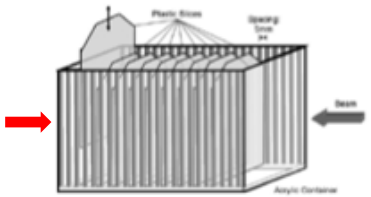


Kraemer et al. Med Phys 2016
Rovituso et al. PMB 2017

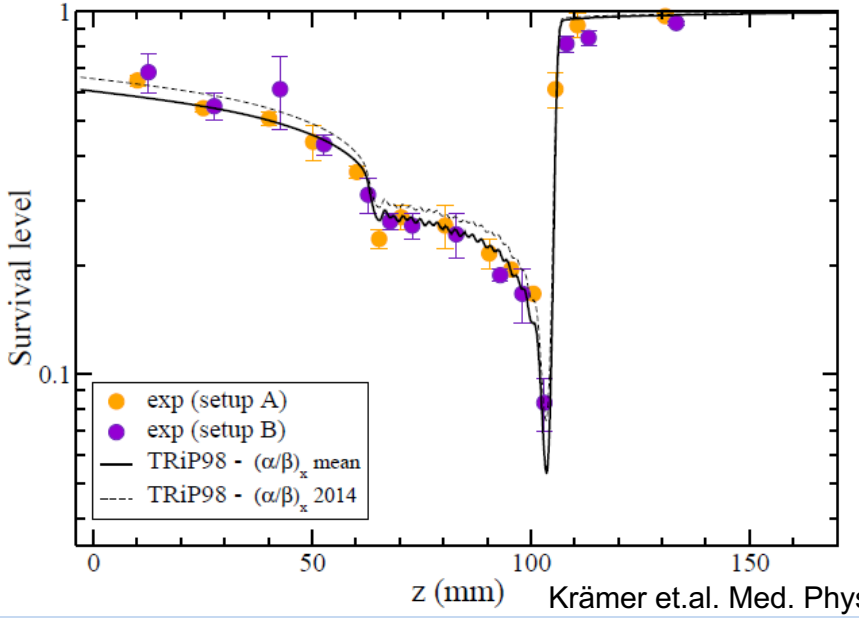
^{4}He biological verification

- New Beam model + LEMIV
  - CHO cells Survival on a He planned extended volume
  - spatial resolution : 2.5 mm



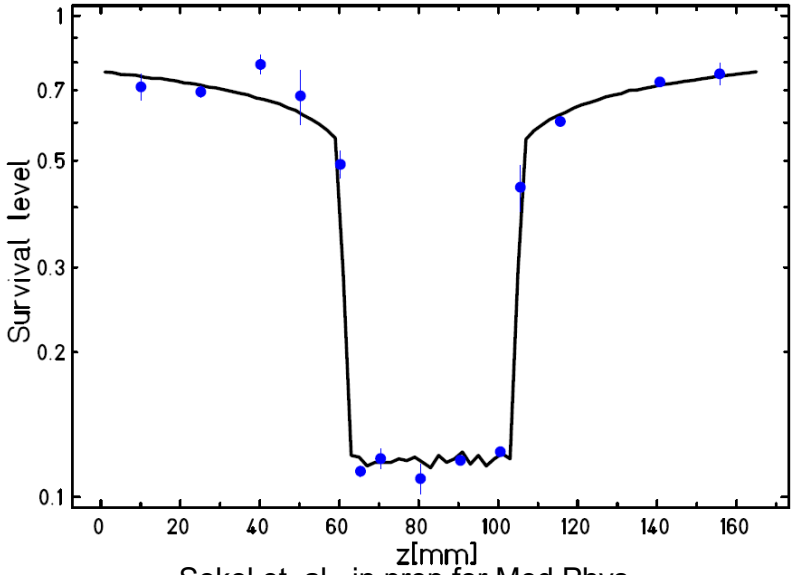


- Single field, optimized on flat physical dose =4Gy



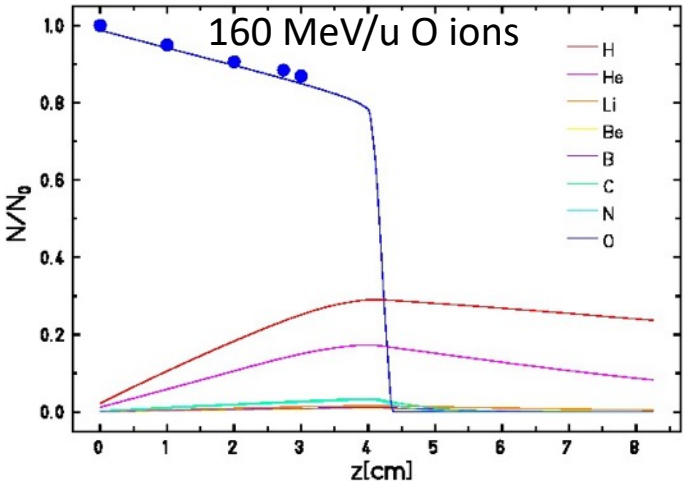
Krämer et.al. Med. Phys. 43, 2016

- 2 Fields bio-optimized (MFO) on uniform survival



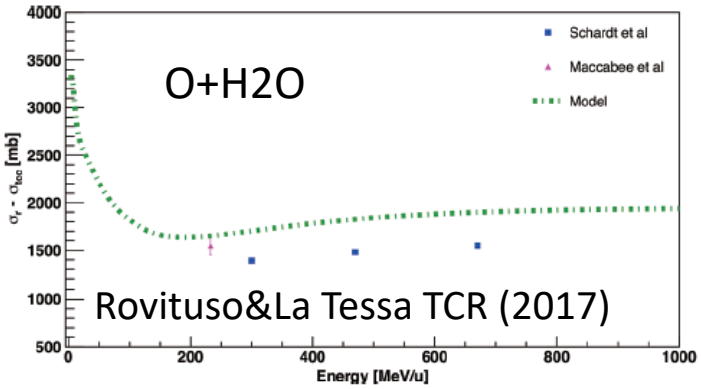
Sokol et. al. in prep for Med Phys.

^{16}O beam fragmentation

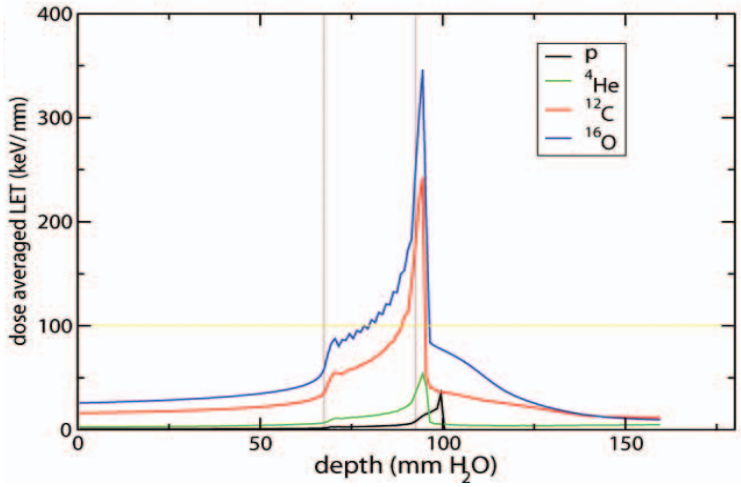


(TRiP98) Yield of secondary particles in water

Exp attenuation C. La Tessa (@BNL)

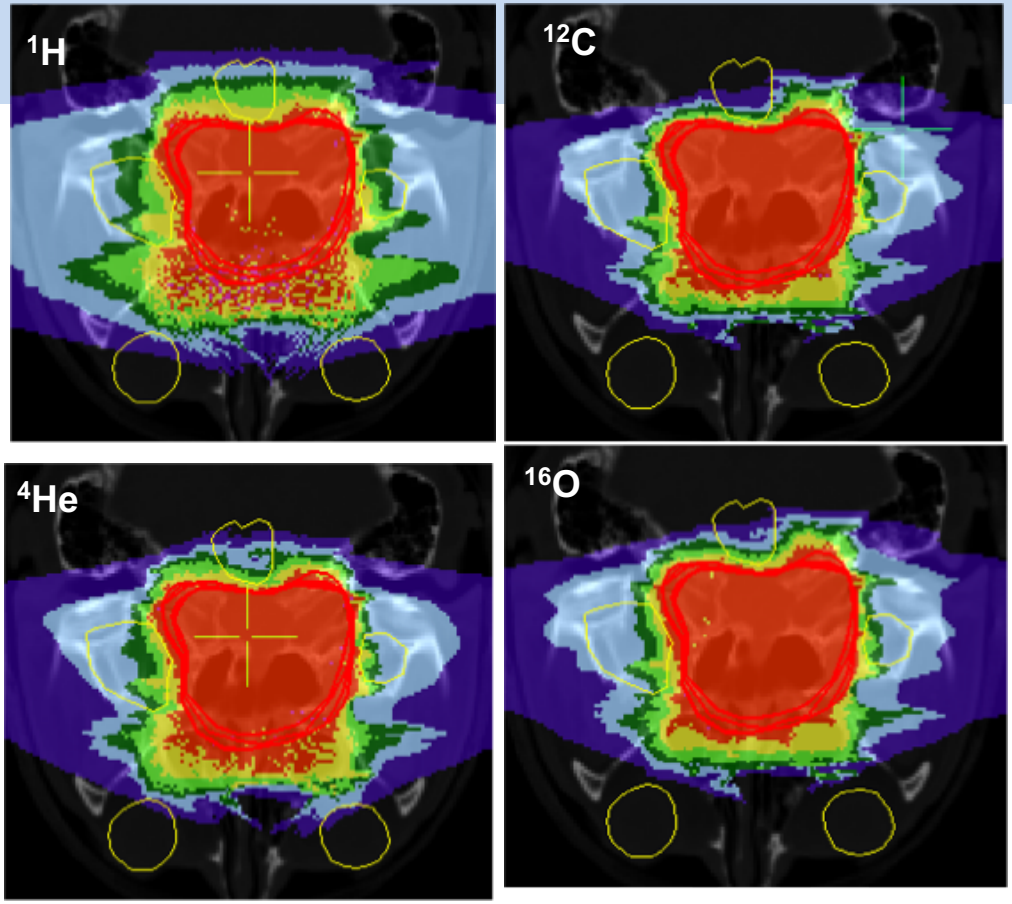


- Large number of fragments
- Few solid data available
- High need of additional data especially for light fragments (will be provided by FOOT exp)
- Relevant for hypoxic targets for broad high LET distribution



Tommasino Scifoni Durante Int J Part Ther 2015

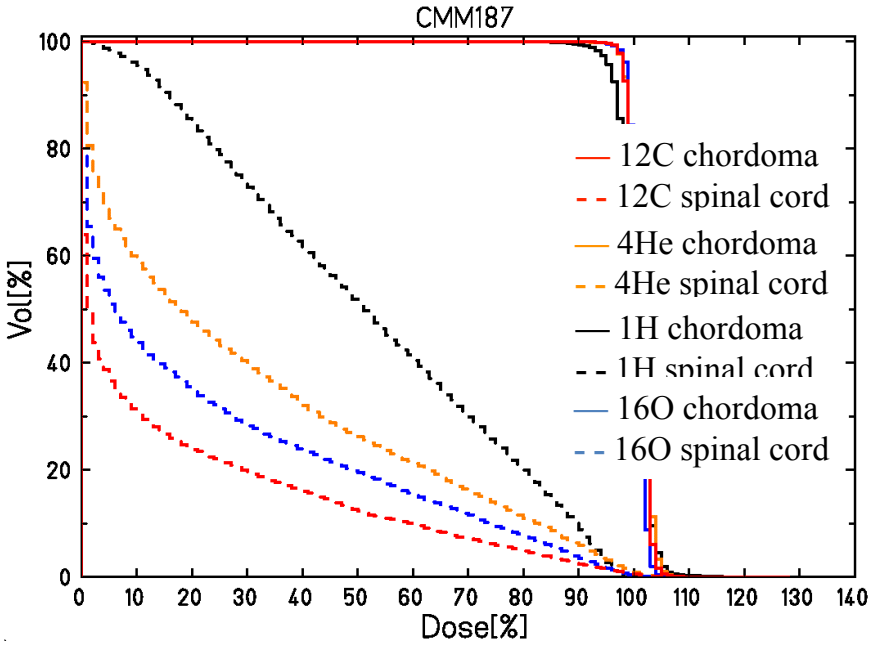
Treatment plans comparison - a patient example



Two-dimensional dose distributions for GSI pilot project patient CT slice
Plans for double-field irradiation of chordoma with ^{1}H, ^{4}He, ^{12}C

R. Grün et al, Med.Phys. 42, 1037 (2015)

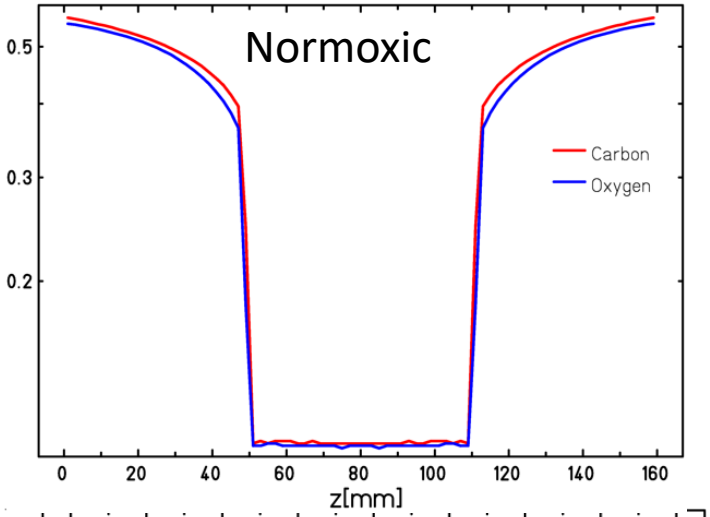
Extended + **^{16}O** (Sokol et al. PTCOG 2017)

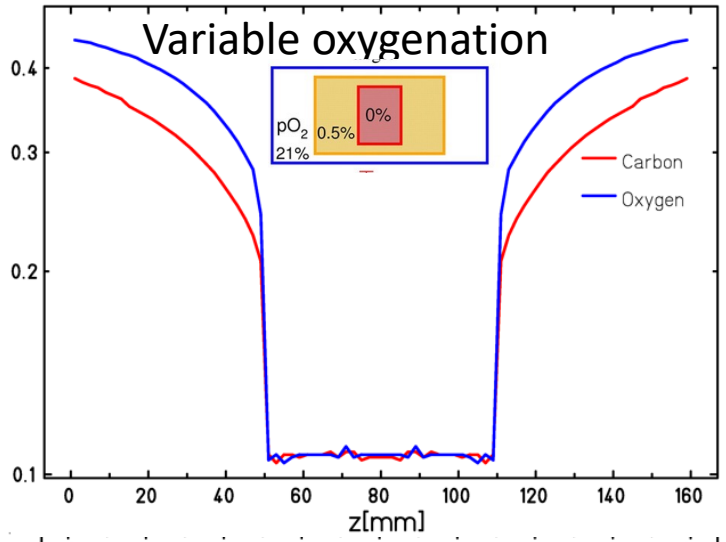


- RBE –weighted dose (LEMIV)
Helium: a promising alternative for carbon and protons

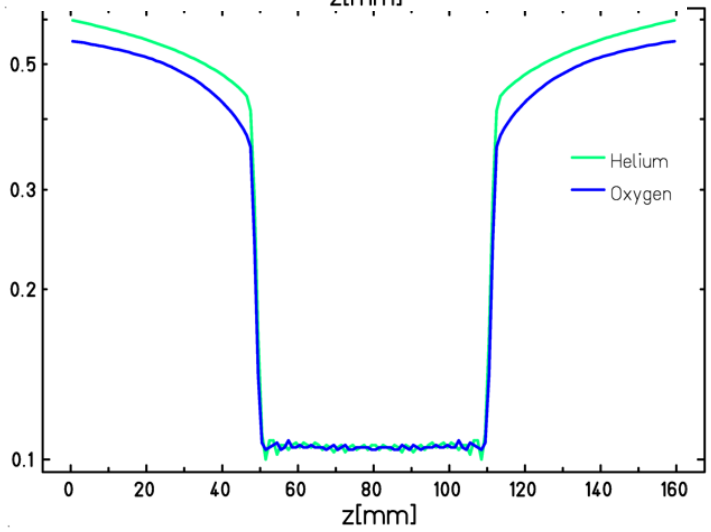
Kill painting with O: Inverted peak-to-base ratios

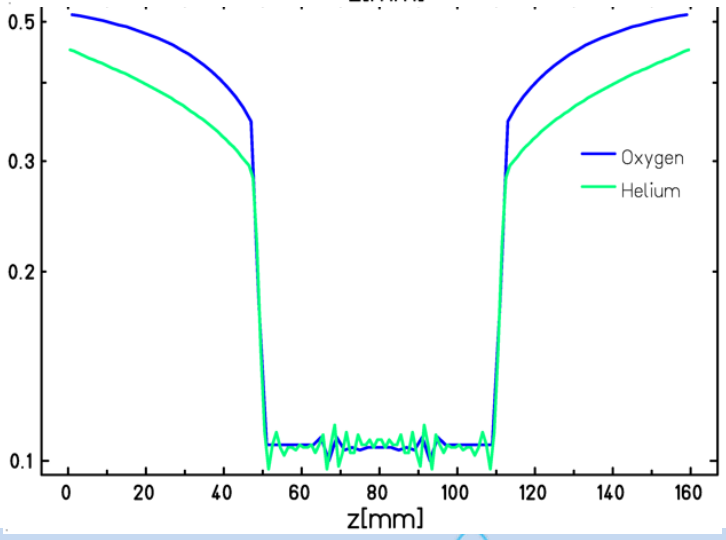
O vs C





O vs He



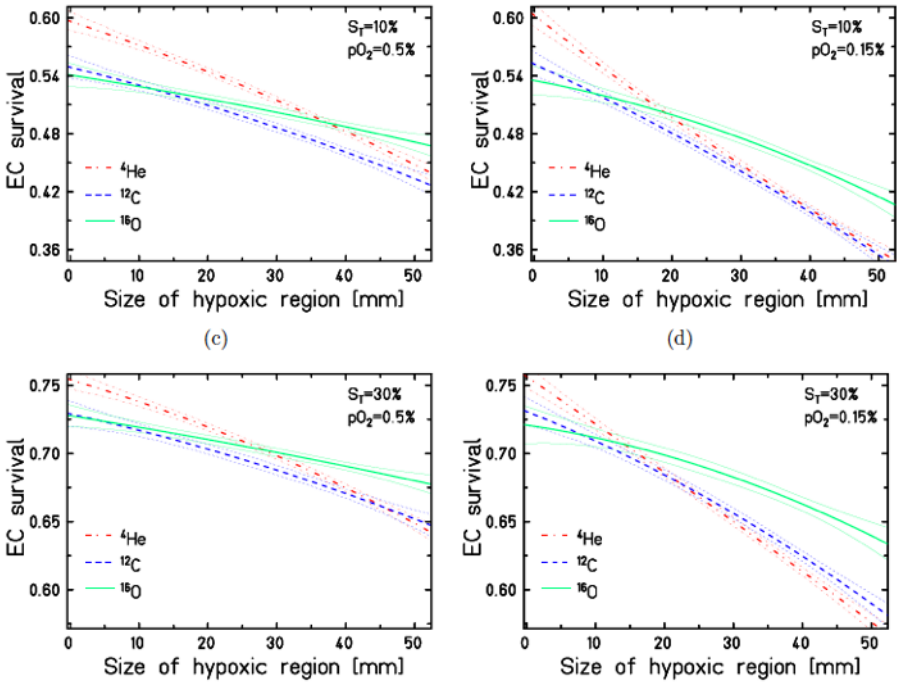


^{16}O beam bio-TPS in hypoxia

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]

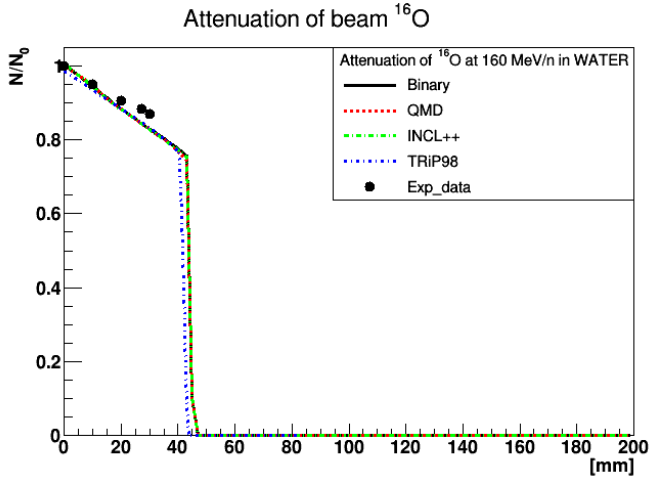
Phys Med Biol 2017

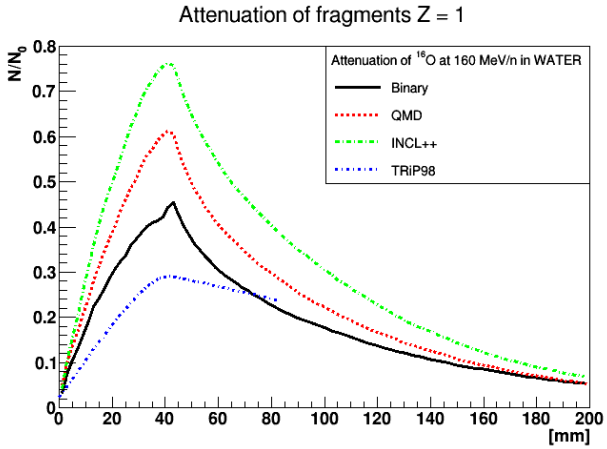


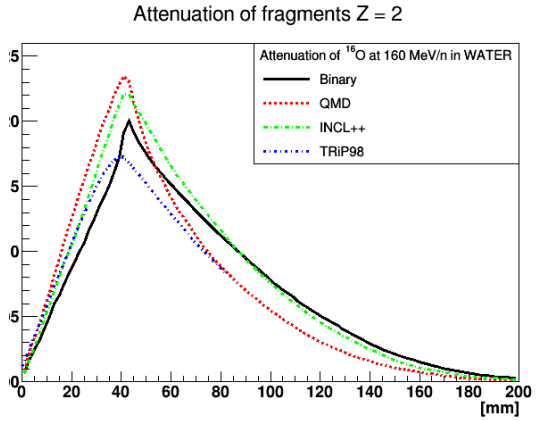
- Differential advantage of Oxygen beams with respect to other ions is a
- Trade-off between better **LET distribution** and worse **Fragmentation** in entrance and tail. Thus fragmentation description is crucial

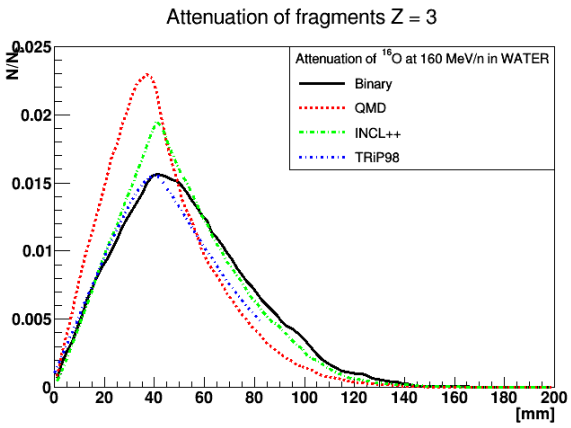
^{16}O beam fragmentation sensitivity

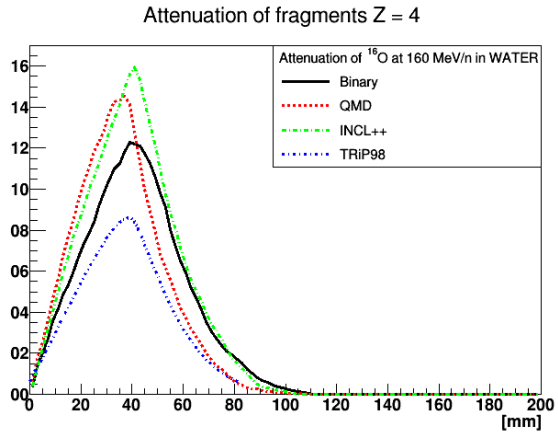
1st step: Physics test GEANT4 + 3 Nucl Models (Summit Jalota)

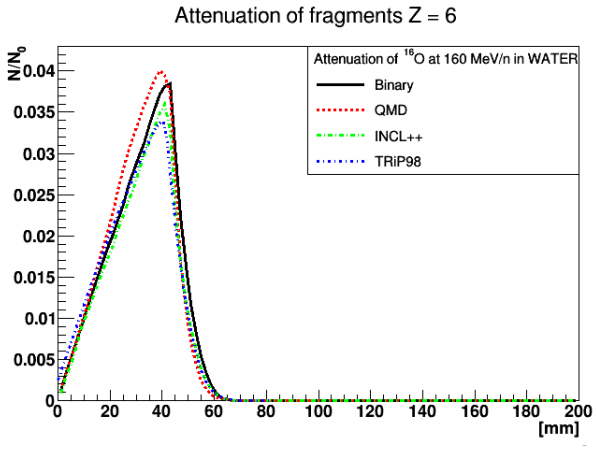






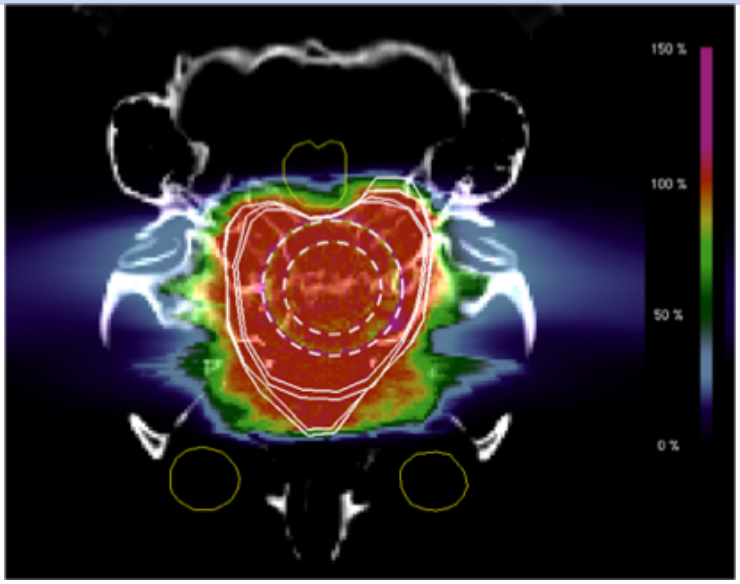




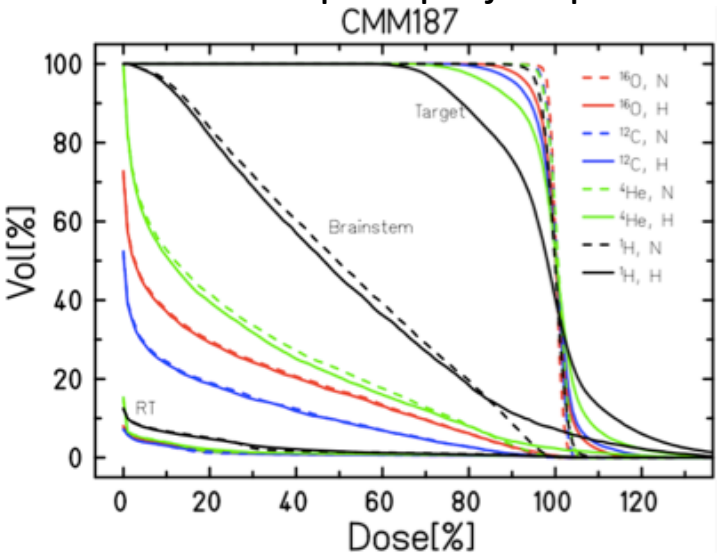


Most spread as expectable in protons production (small effect in LETd and then in OER)

Patient case

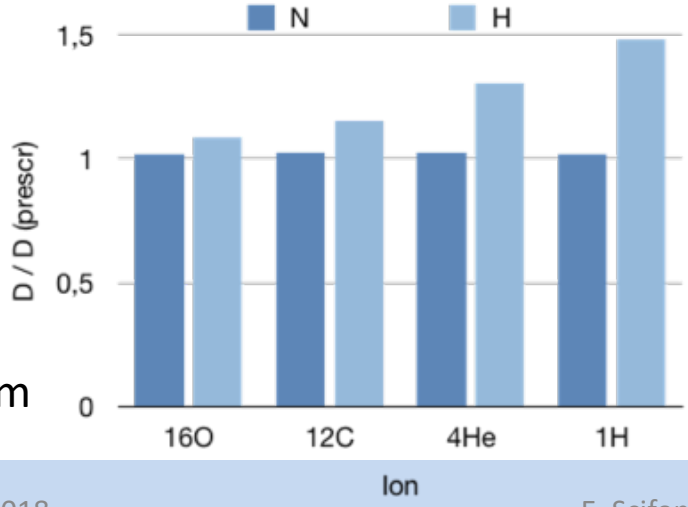


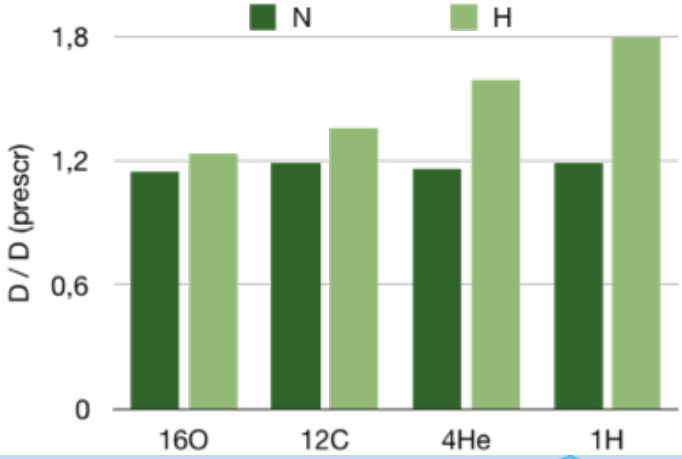
Chordoma from GSI pilot project patient pool



O. Sokol PhD Thesis TUD Darmstadt 2018

Max brainstem

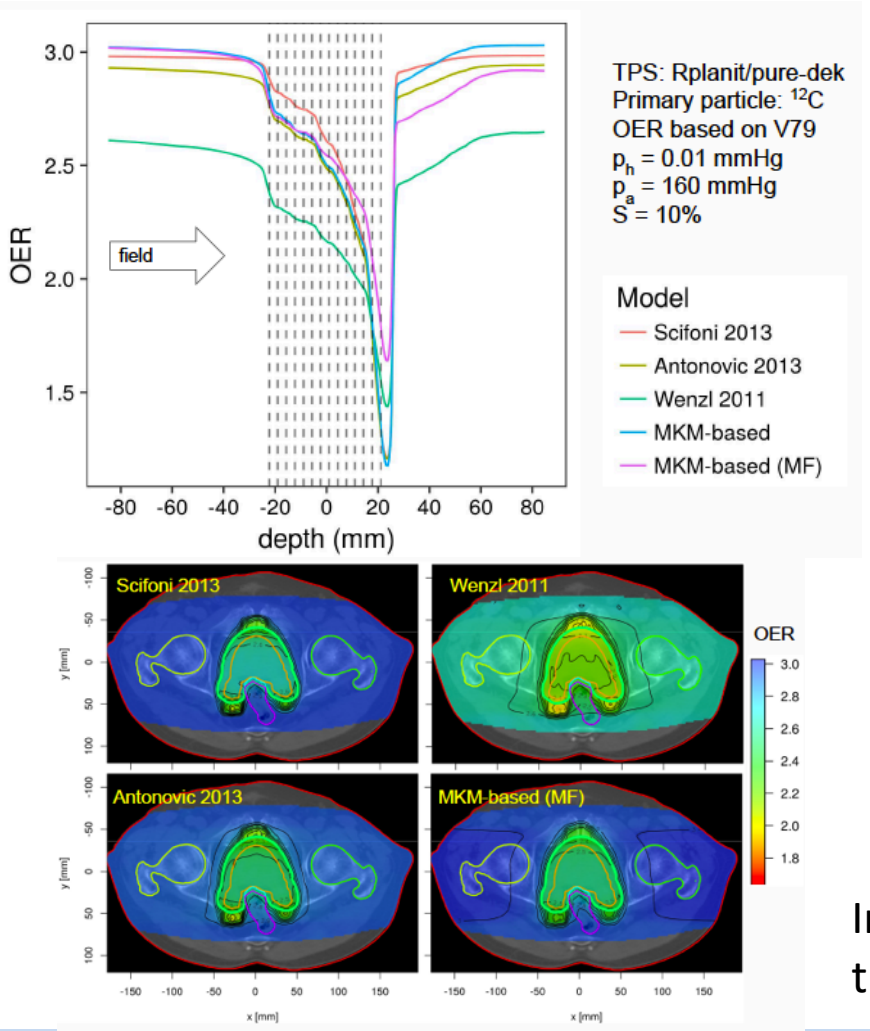




residual

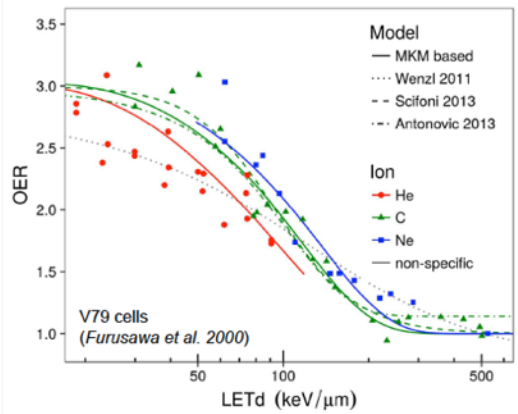
Ion INFN TIFPA Trento Institute for Fundamental Physics and Applications

OER Modeling with modified MKM



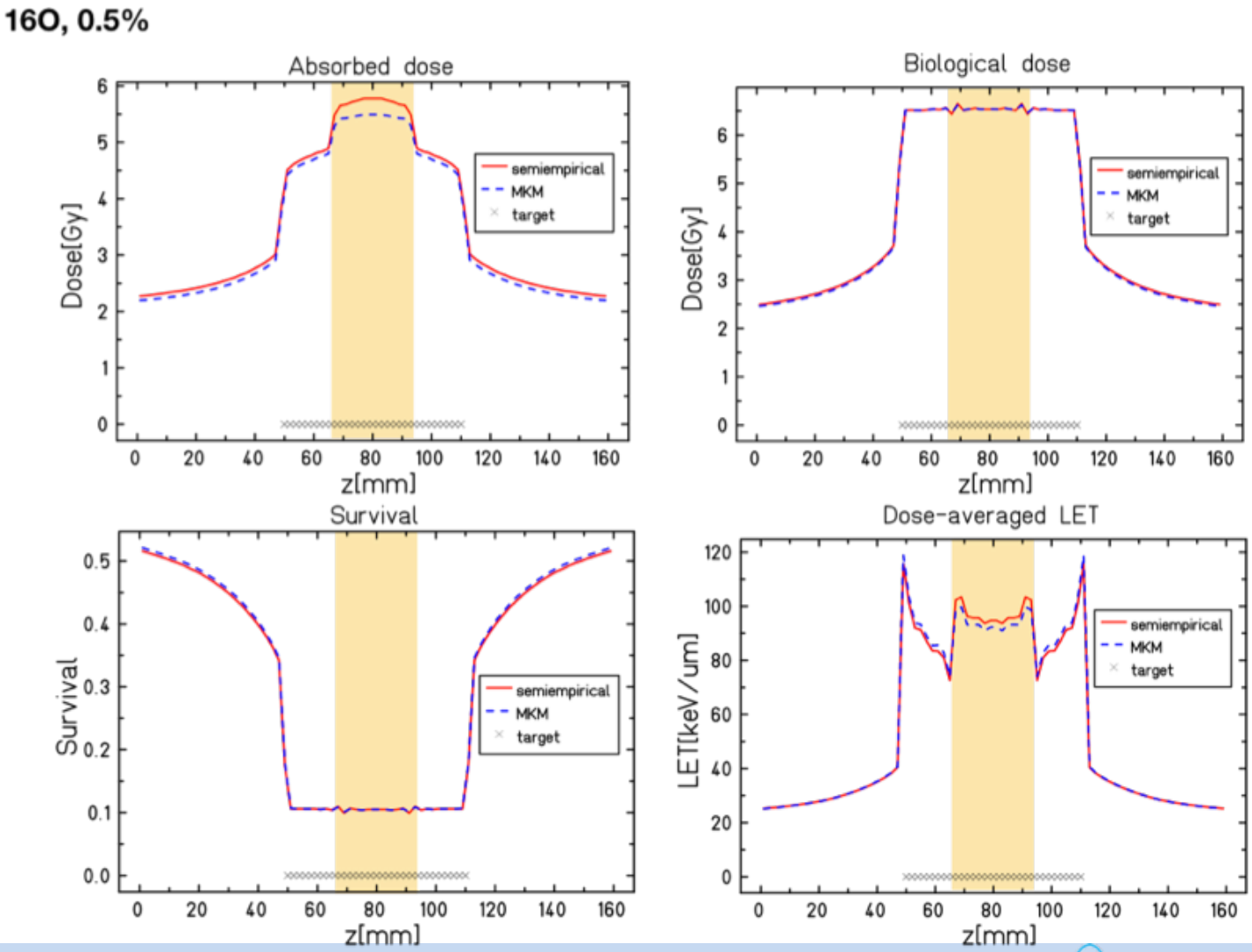
- New mechanistic model based on MKM, explicitly accounting for particle dependence and dose fraction

Strigari,Attili et al.PMB 2017
See also Bopp,Inaniwa et al. PMB 2016

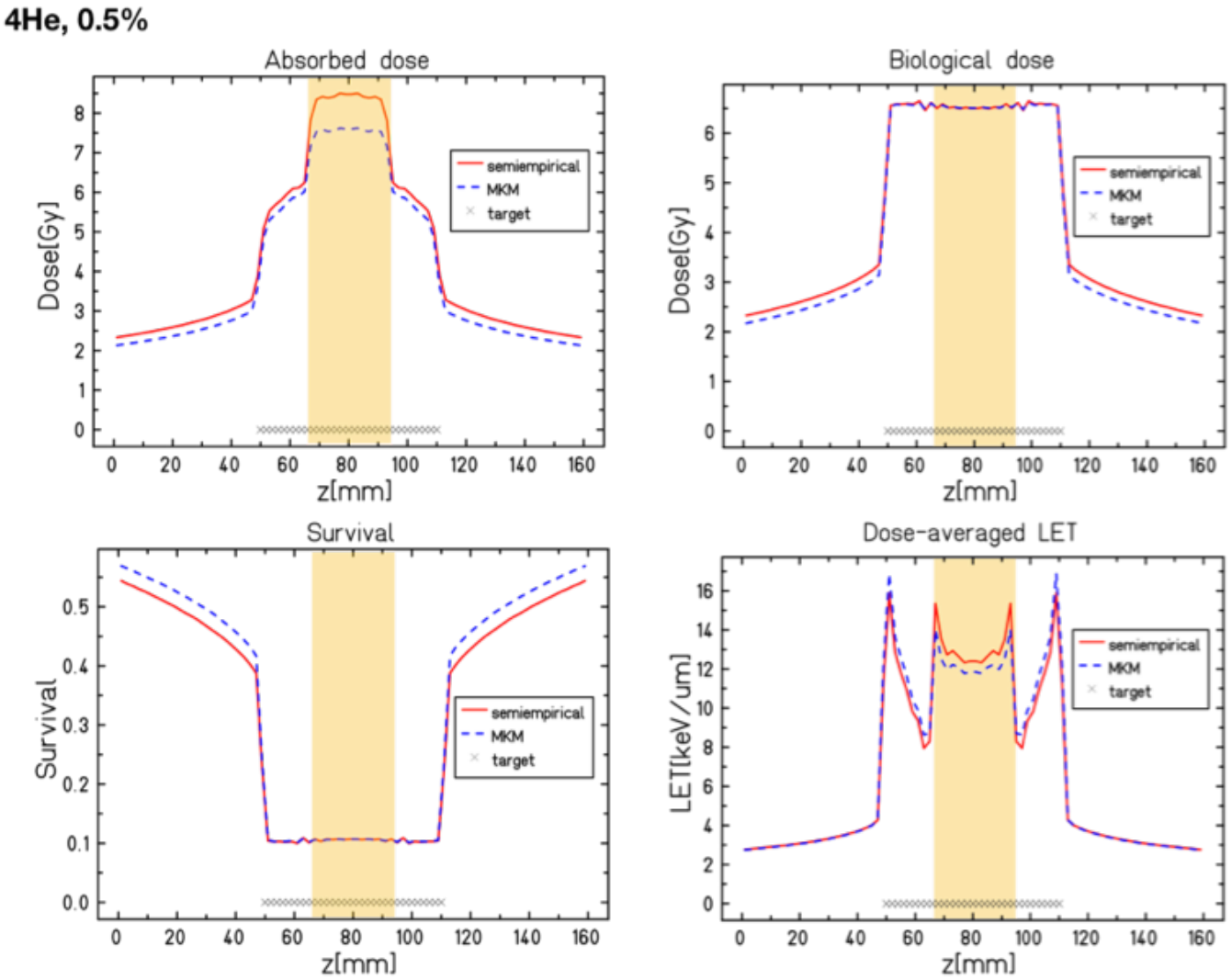


Impact of different OER models on a prostate tumor

Impact of biophysical models (Z dependence)



Impact of biophysical models (Z dependence)



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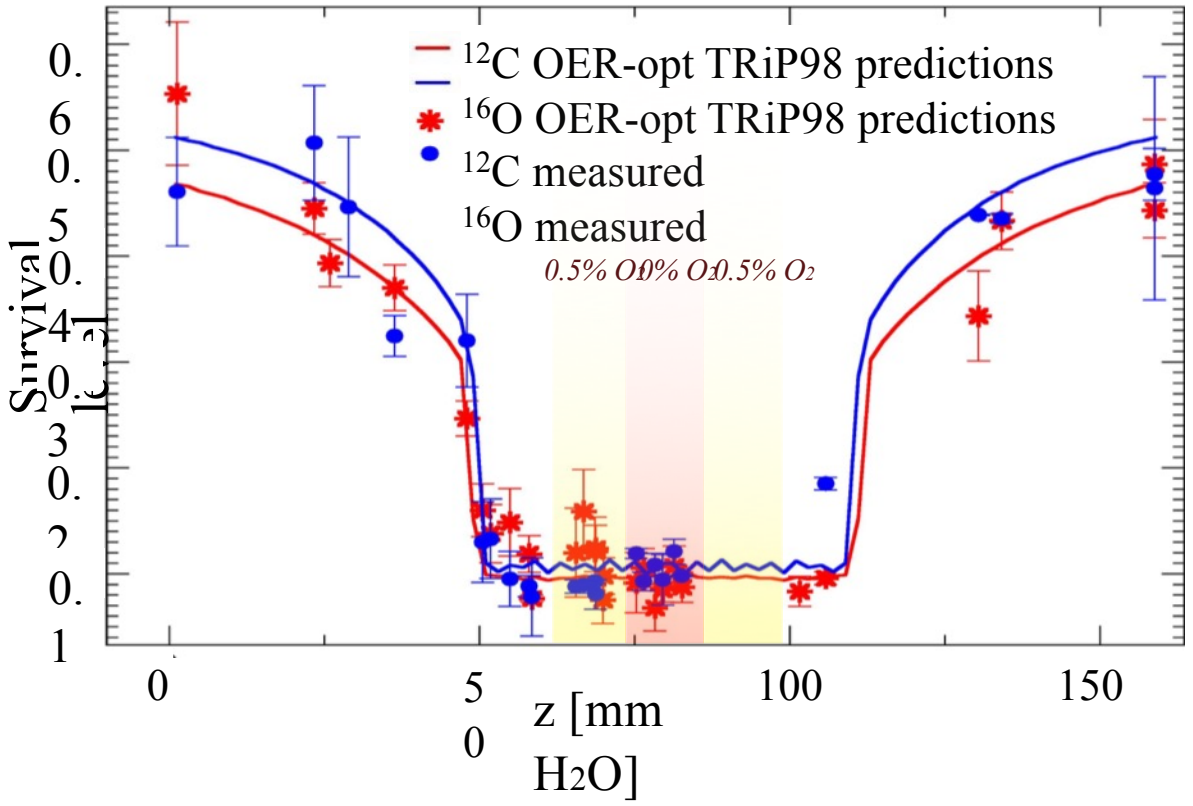
O vs C experimental verification

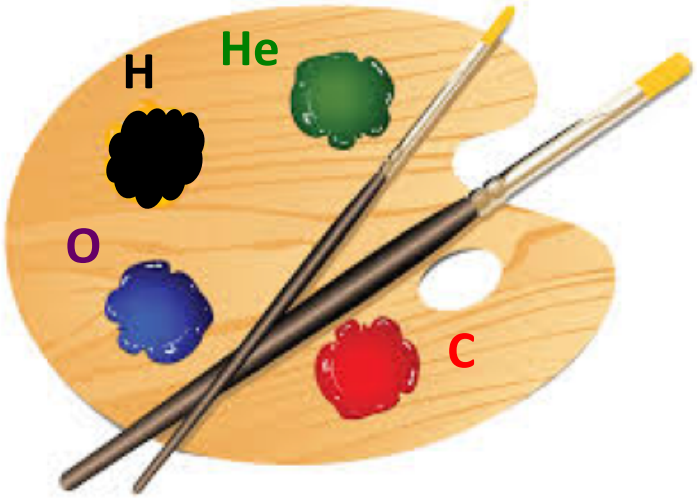
Carbon data: Tinganelli et al, Sci Rep 5, 17016 (2015)

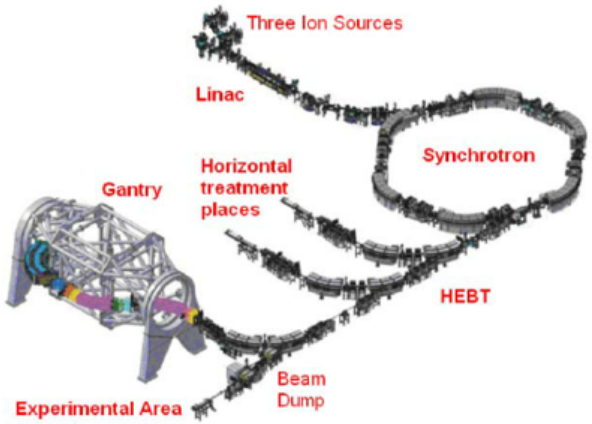
Sokol et al. PMB 2017



Oxygen in same cases can be really better than carbon, what's next?

Can we do better?





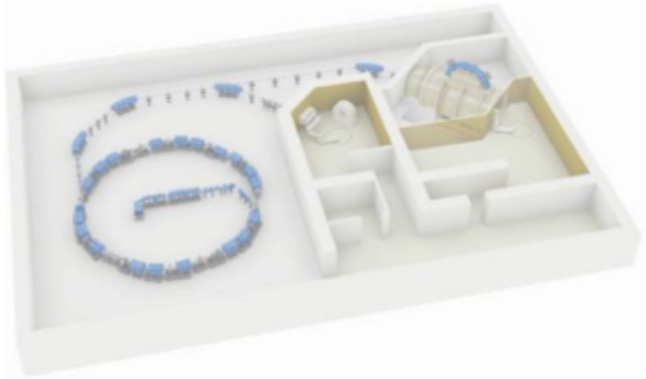
V. Van Gogh – *National Gallery*

Multiple ion therapy

T. Furukawa (ISIT 2017, Dallas):

- Multi-ion capability is a must for new Toshiba systems in Japan
- Fast switching (less than 1 min)
- Development of pulse-by-pulse (~ 5 s) is planned

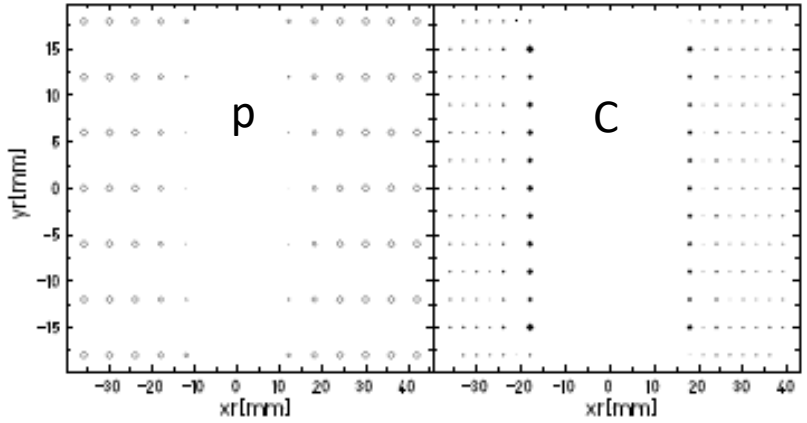
- Similar possibility available at HIT

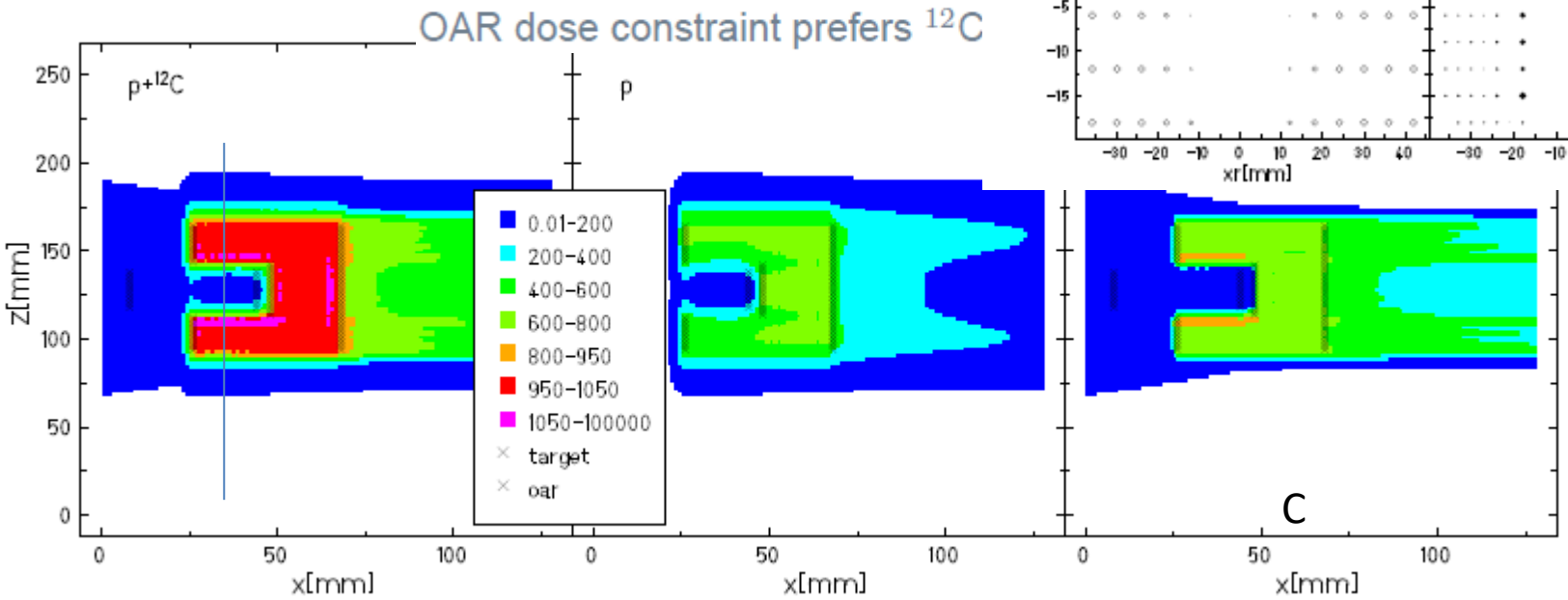


Multi-ion treatment planning

- TRiP version for a biologically optimised multi-ion treatment plan
- TPS enhanced to handle more than one ion beam modalities at once (including full spectra etc.)

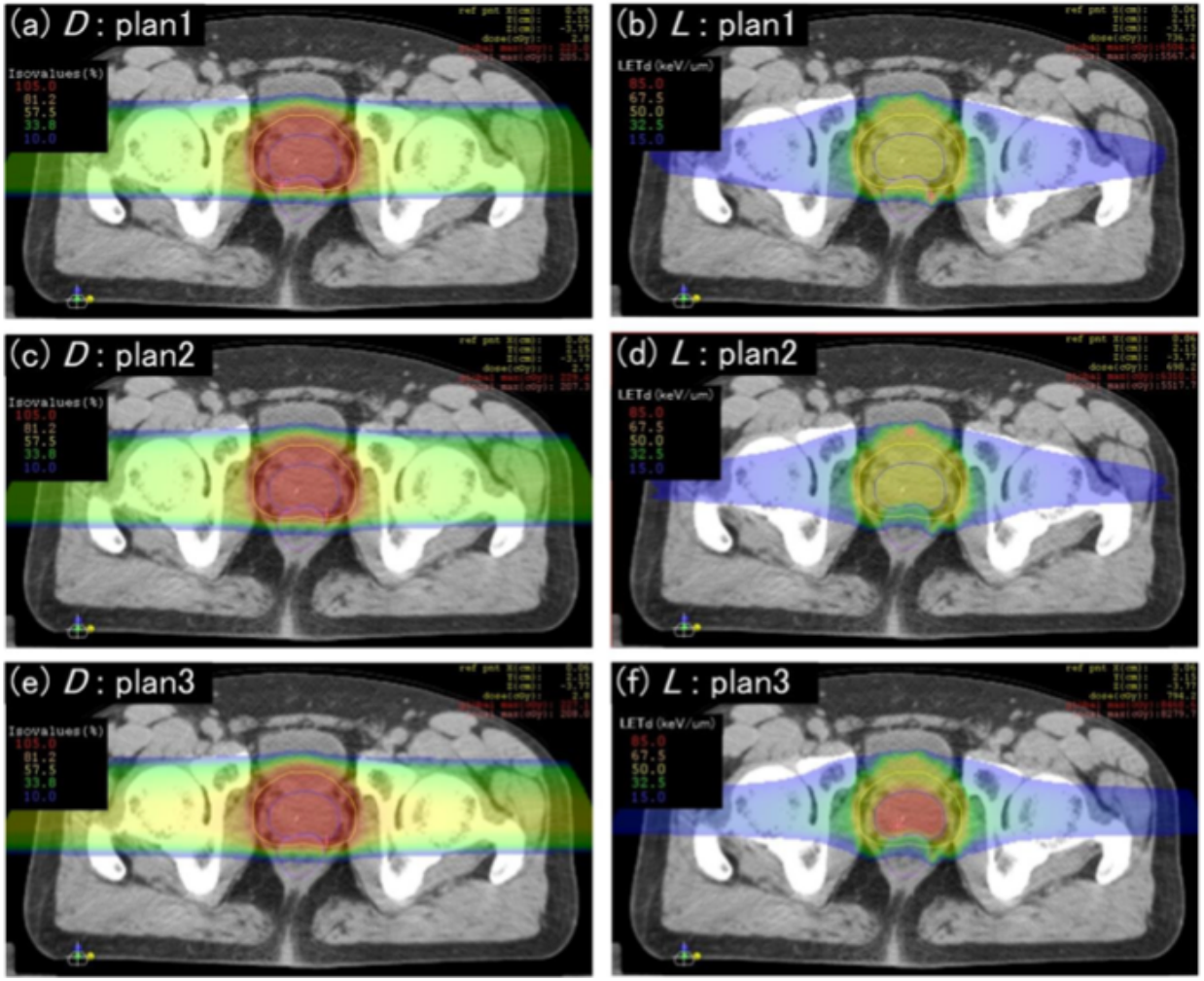
e.g. p+12C





Krämer, Scifoni, ,Schmitz, Sokol, Durante, *EPJD 68 (2014)*

Multi-ion treatment planning



The Japanese version

IMPACT: Intensity Modulated Composite Particle therapy

Inaniwa et al. PMB 2017

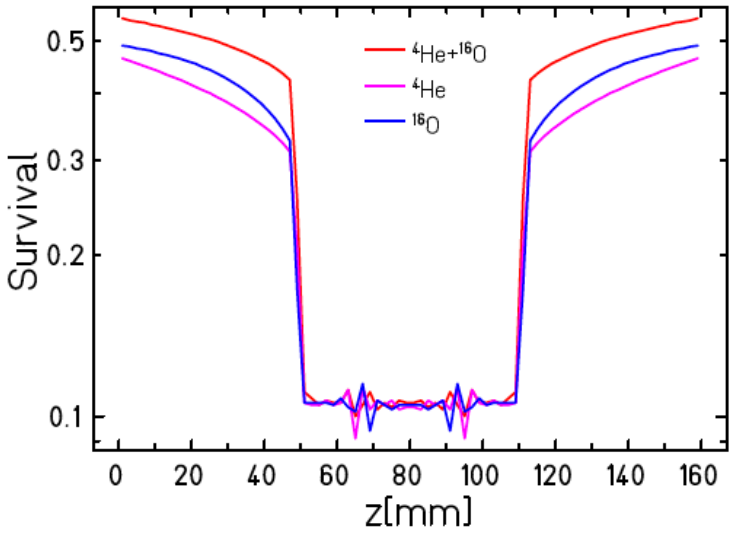
Multi-ion + kill painting

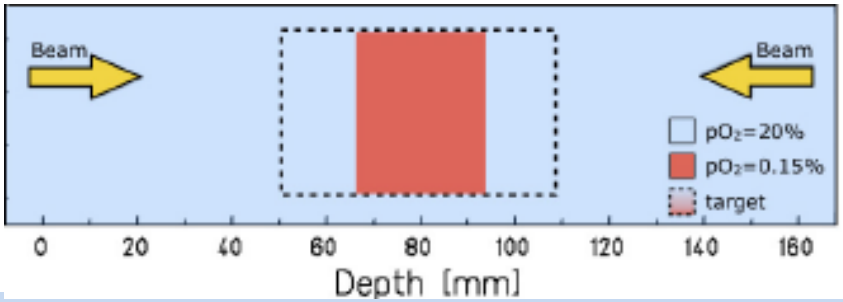
=**TRiP98-MIBO**: **M**ulti **I**on full **B**iological **O**ptimization

See Poster: **Kill-painting of hypoxic tumors with multiple ion beams**

O. Sokol[1], E.Scifoni[2], S. Hild[2,3], M. Durante[2] and M. Krämer[1]

GSI TIFPA

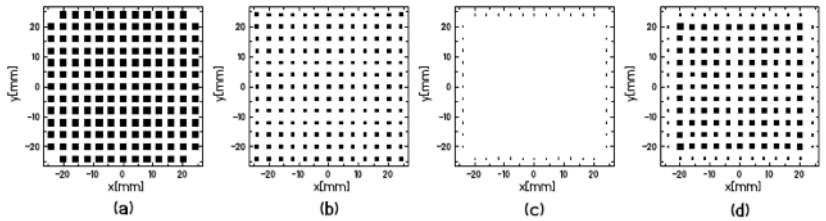




Survival distributions for single-ion double-field optimizations (^{4}He + ^{4}He and ^{16}O + ^{16}O), and multiion quadruple-field optimization (^{16}O + ^{16}O + ^{4}He + ^{4}He).

pO_2 =20%: z < 6.6 & z > 9.4
pO_2 = 0.5%: 6.6 < z < 9.4

Depth (mm)	EC survival, %		
	O	He	O+He
5	48.4	45.4	54.3
45	34.3	32.3	43.5



He normoxic hypoxic O Normoxic Hypoxic

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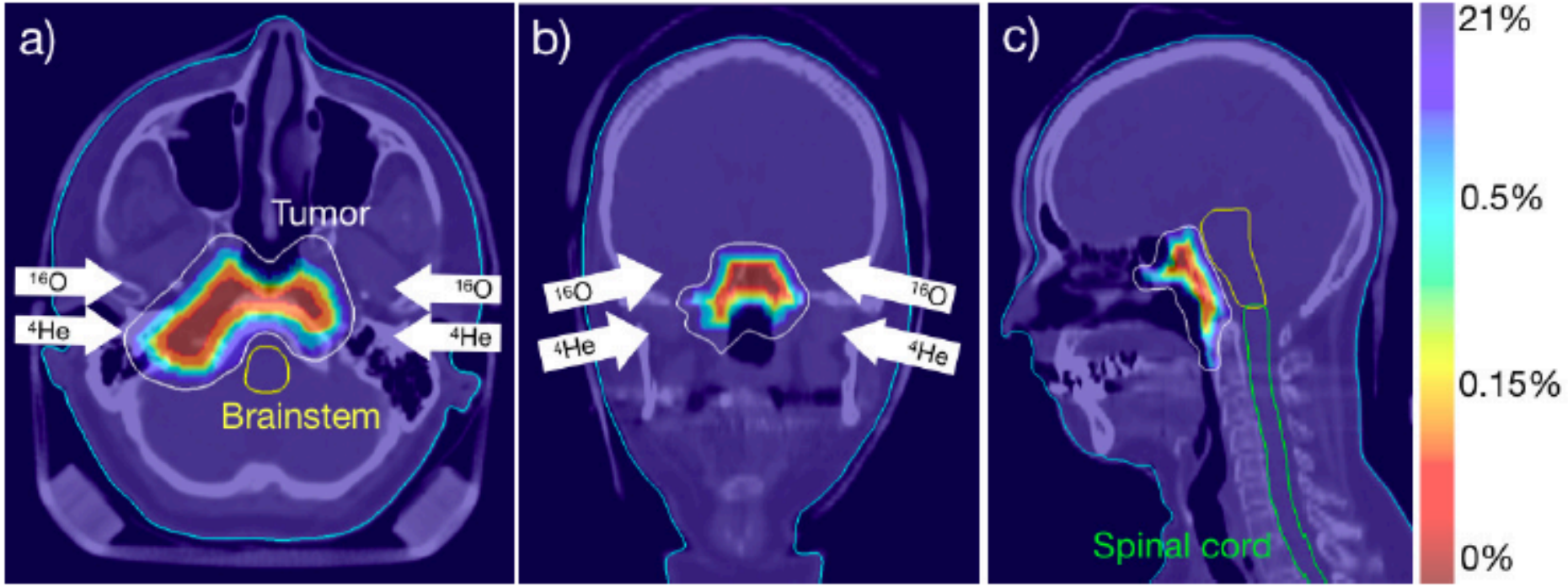
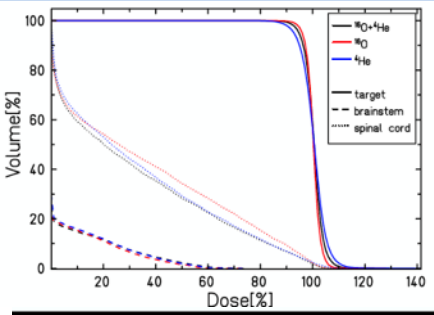
Kill Painting with Multi-ions

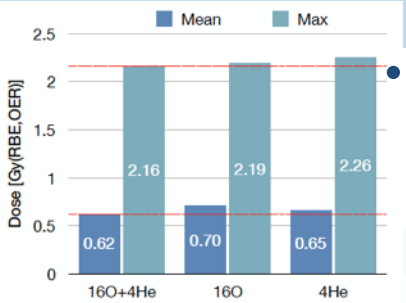
Generated pO2 smooth distribution



Sokol et al. in prep. for PMB

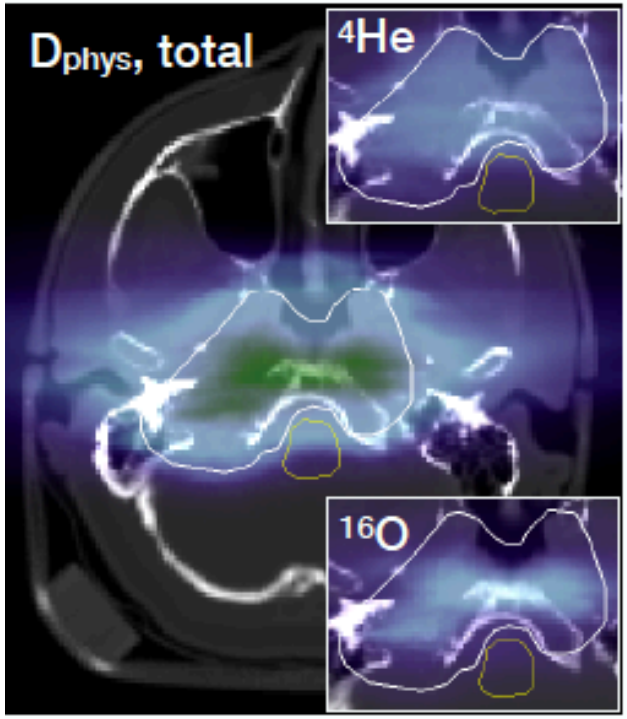
Kill Painting with Multi-ions

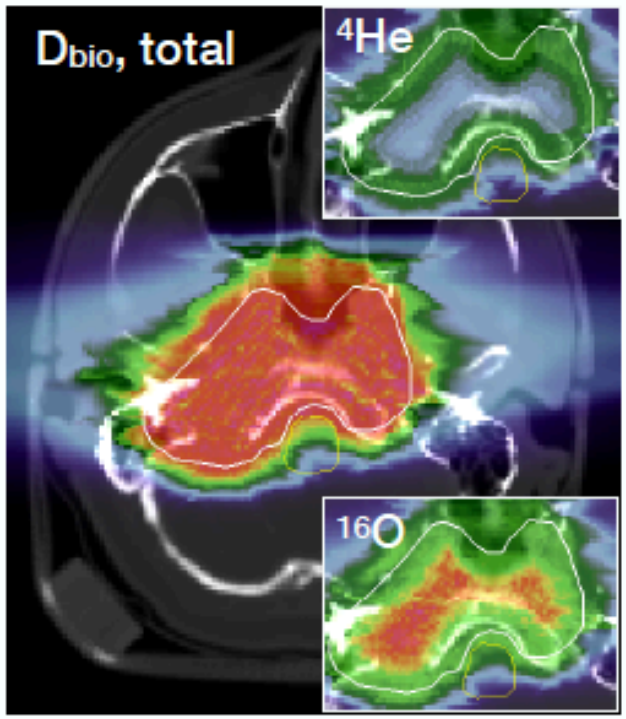


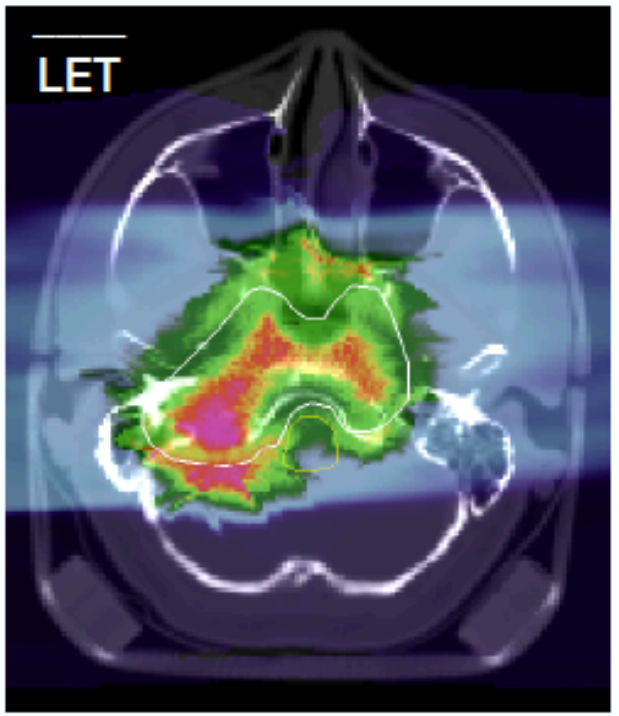


- The beamspots are currectly selected by the optimization in order to concentrate high LET particles in the hypoxic regions

*100% dose = 2 Gy 100% LET = 65 keV/um







0% 50% 100% 150%

Sokol et al. in prep. for PMB

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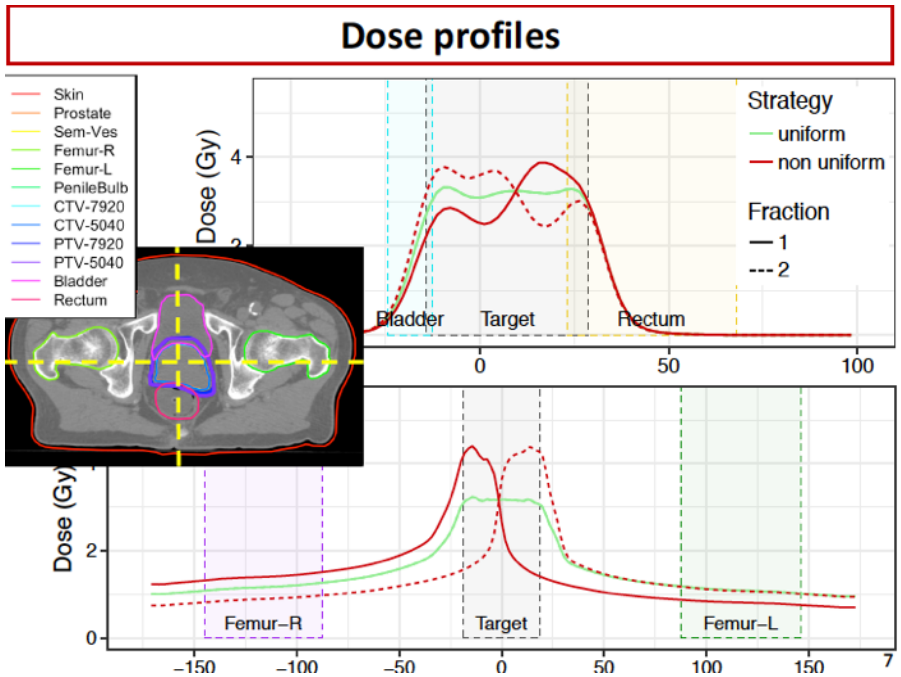
Summary

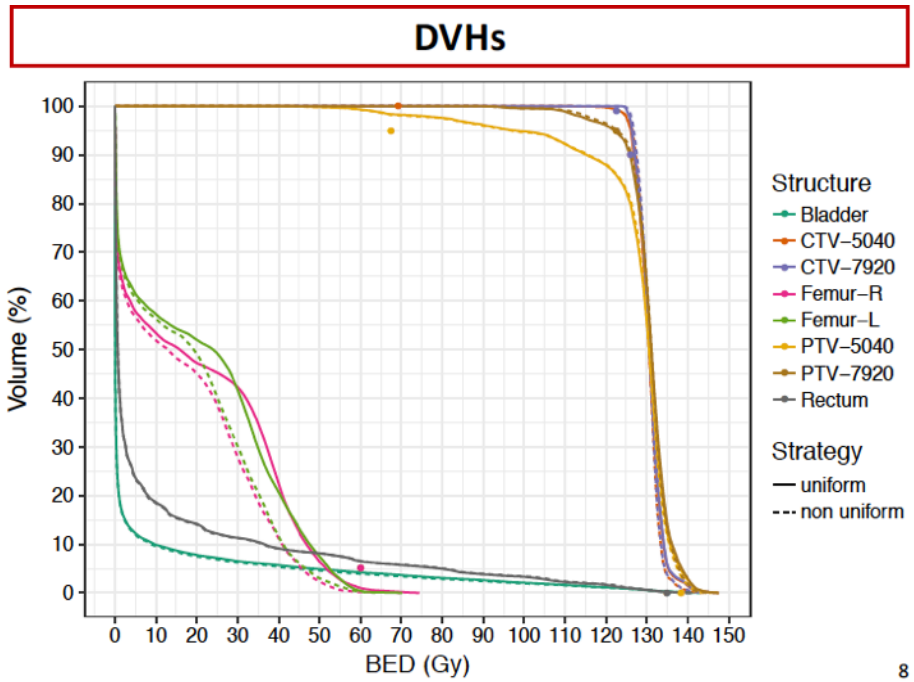
- Active scanned Particle therapy offer a maximum flexibility for adaptive, bio-optimization of a target
- Biologically optimized TPS needs accurate physics description e.g. for exploiting the different ion beams merits.
- New Ions may present specific biological advantages for selected cases or fractions
- Use of larger LET ions (^{16}**O**) quantitatively assessed and suggested for specific hypoxic cases
- **TRiP98-MIBO** offers the first TPS able to inverse plan with multiple ions fully accounting for RBE and OER weighted dose
- Multi-ion optimization may exploit combination of different ions peculiarities for specific biological scenarios
- Beam-time granted in Marburg for experimental (in vitro bio-phantom) verification

Outlook

Non uniform fractionation (L. Manganaro et al. Poster@PTCOG2108)

see also Unkelbach et al. (Radiother Onc 2017)





Yet, other degrees of freedom to explore: multi-ion+multi-fraction.
Strong robustness assessment needed

Thank you for your attention!

O. Sokol
M. Kraemer
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J. Wiedemann
D. Boscolo
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and to