An Open Access Facility for Heavy Ion Radiobiology

Why do we need it?

What do we need it for?

What do we need?

Who can provide it?

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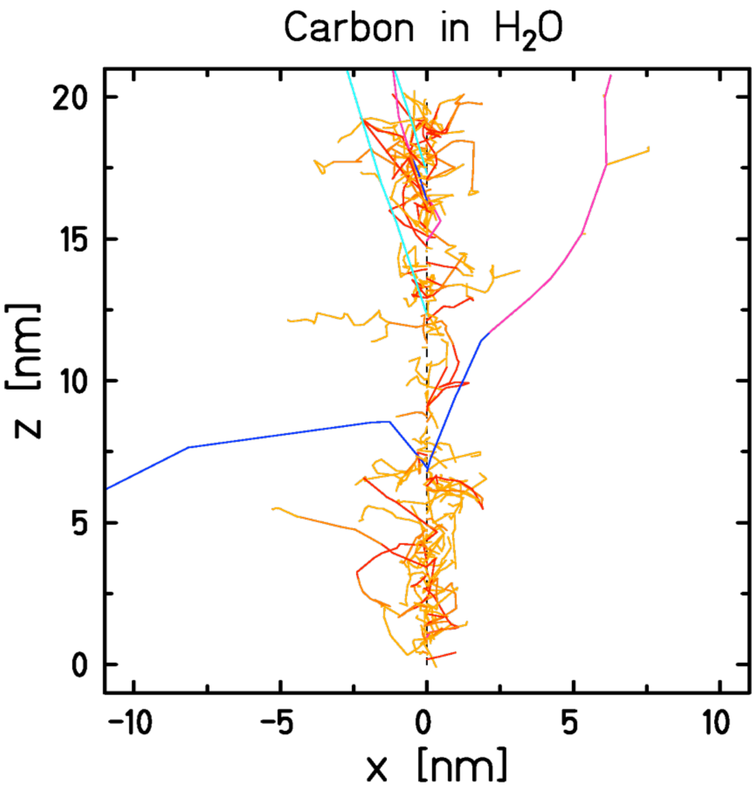
What makes the difference between ions?

Biological effectiveness is directly linked to the distribution of ionization events along the particle tracks (track structure)

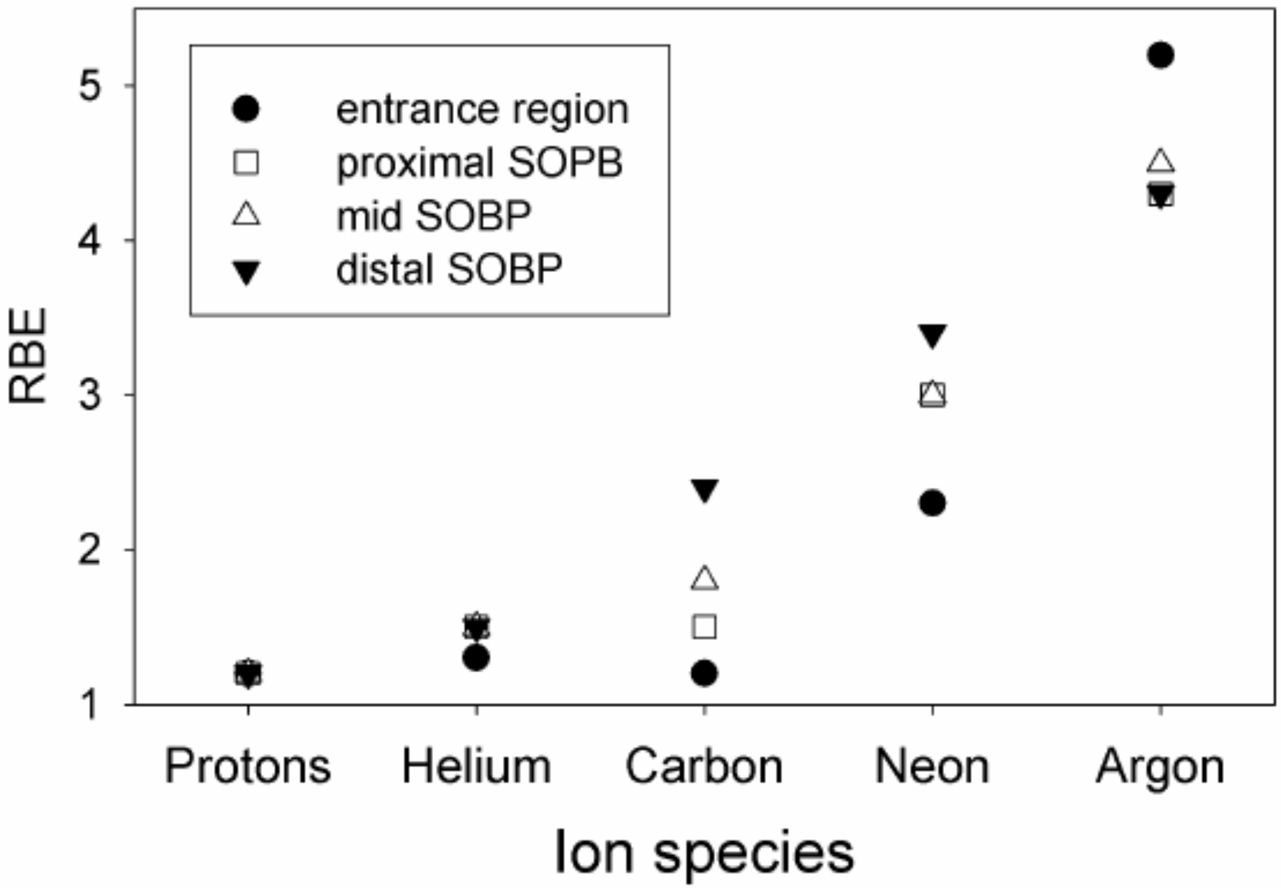
Ionization density depends on stopping power and is best represented by LET

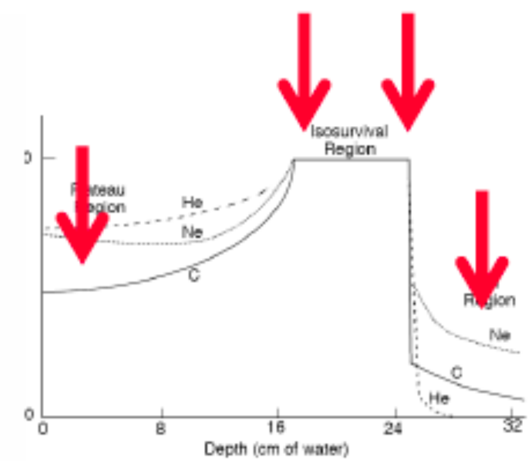


Higher LET particles have higher biological effect

Which is the best ion for RT ?

RBE for a fractionated irradiation of jejunal crypt cells of mice (SOBP of 8 cm)





Courtesy Oliver Jäkel, HIT

Proton data: Tepper et al 1977,
Ion data: Goldstein et al. 1981.

The differential RBE peak/plateau is optimal for Li…O

Tumor Hypoxia

Treatment failures

Tumors with compartments containing hypoxic cells are well known to have reduced radio-sensitivity compared to normoxic cells resulting in lower control rates in radiotherapy

Nordsmark et al. R&O 57 (2000) 57 and R&O 77 (2005)

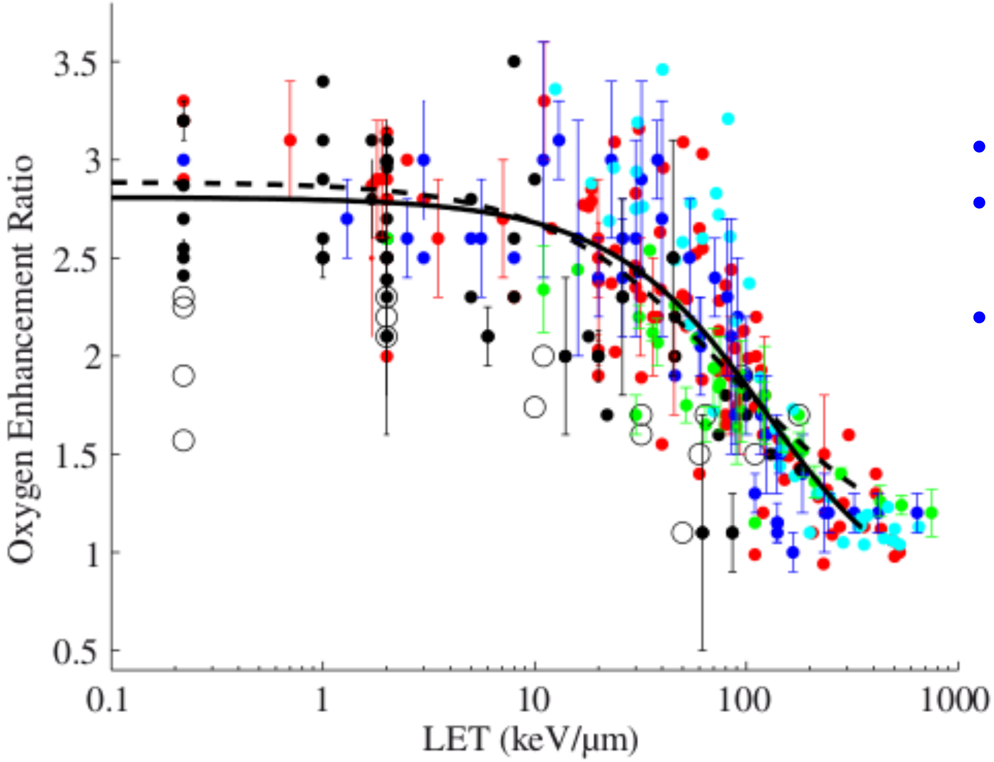
Possible Treatment Strategy

Functional imaging (hypoxic markers + PET) and application of heterogeneous dose and/or LET distributions

Dose painting; LET painting

Bassler N, Jäkel O, Søndergaard CS, Petersen JB; Acta Oncol. 49 (2010)

Radio Resistant Tumors and OER



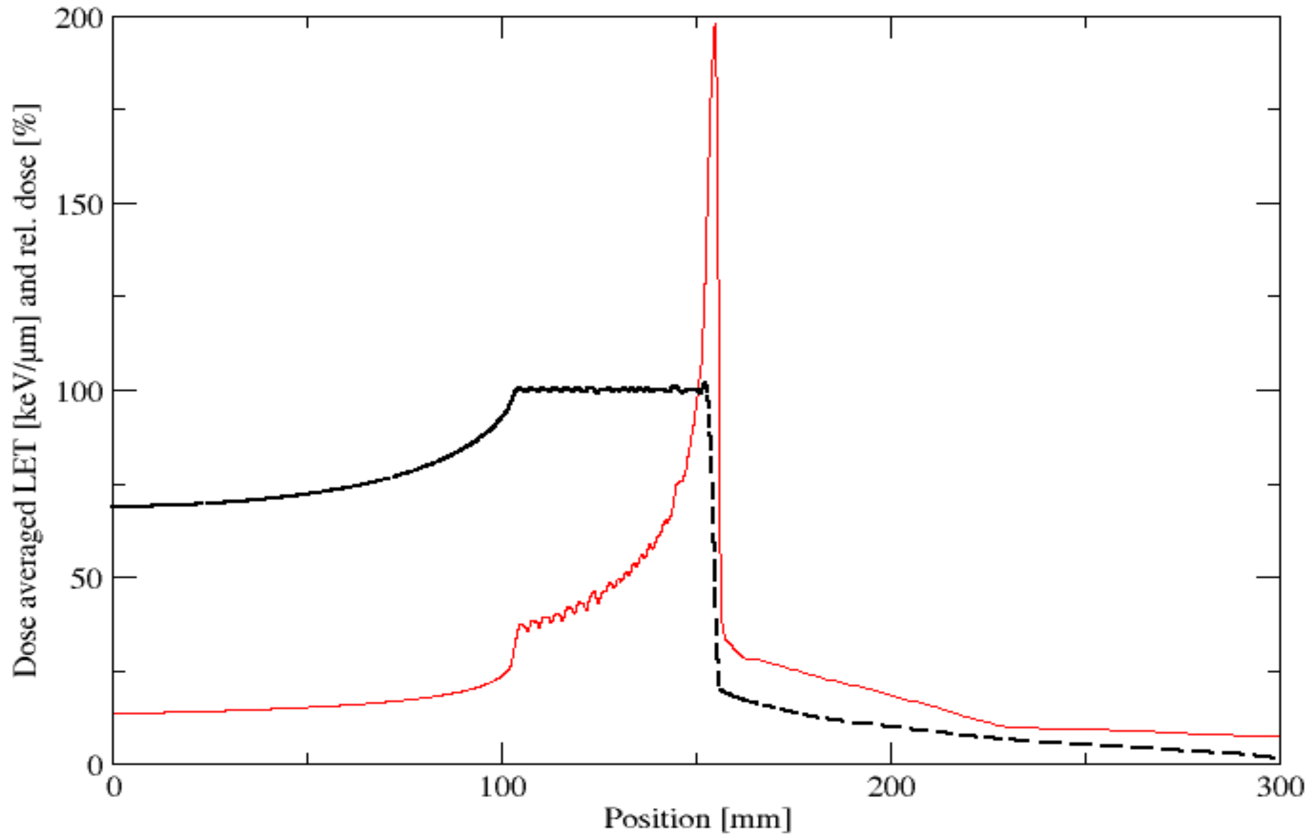
- OER strongly depends on LET
- Significant in vitro enhancement at LET > 100 keV/μm
- Notice: Results in vivo differ

Figure 1. Experimental data from the literature (see tables 1 and 2) for the OER dependence on LET *in vitro* (filled circles) and *in vivo* (open circles) at 10% cell survival. The error bars are shown according to the original publications (if provided). Different colours (online only) correspond to different cell lines: red: V79; blue: T1; green: R1; cyan: HSG; black: other. The solid line represents the OER calculated *in vitro* for 10% cell survival at $p_a = 160$ mmHg and $p_h = 0.01$ mmHg according to equation (12). The dashed line shows results for the same survival level and pO_2 values but now with an LET dependent β parameter according to equation (13).

Wenzl and Wilkens, PMB 2011

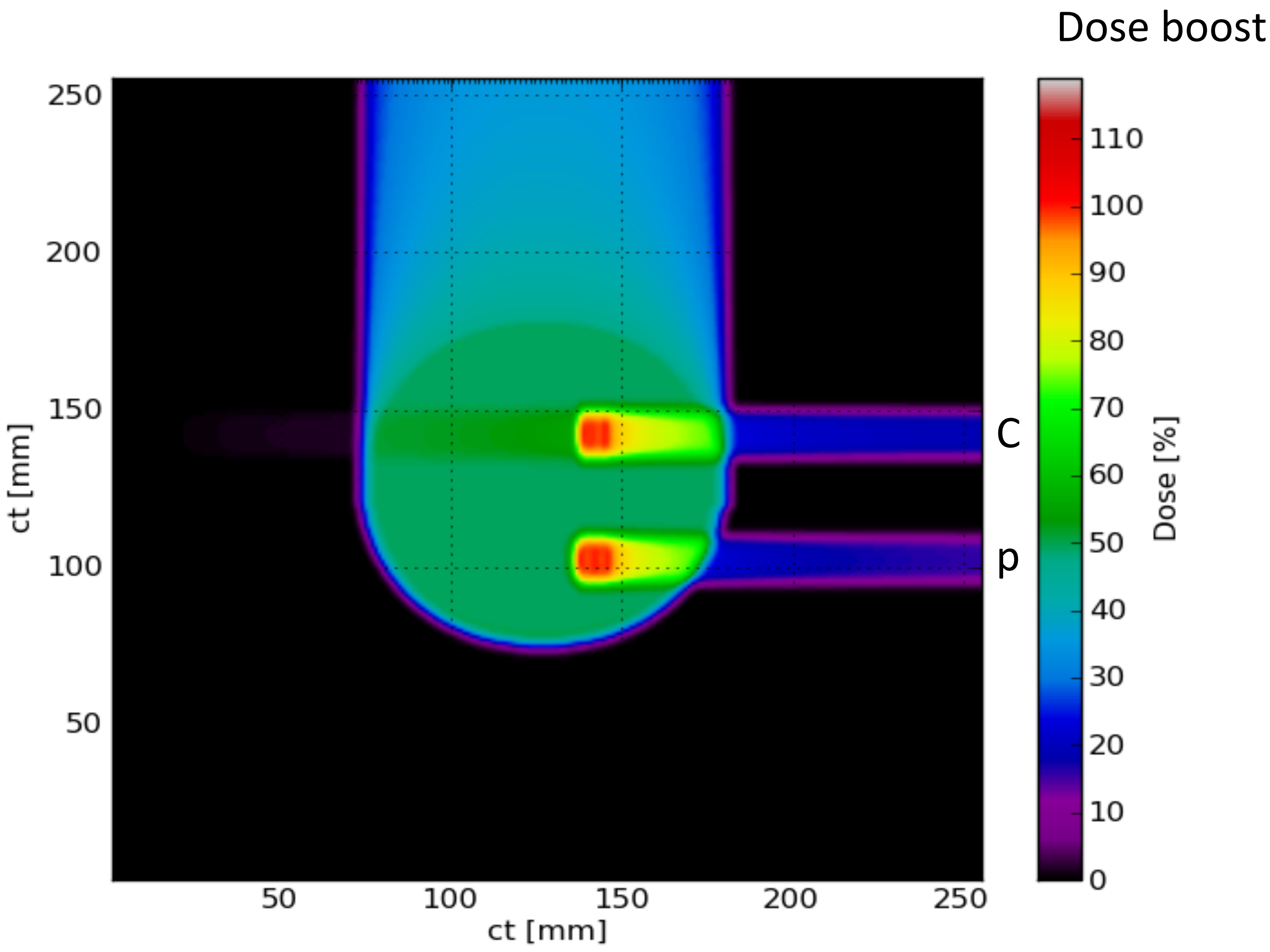
What do we need for Painting ?

Dose averaged LET for 12C beam with 5 cm SOBP; Niels Bassler, Aarhus

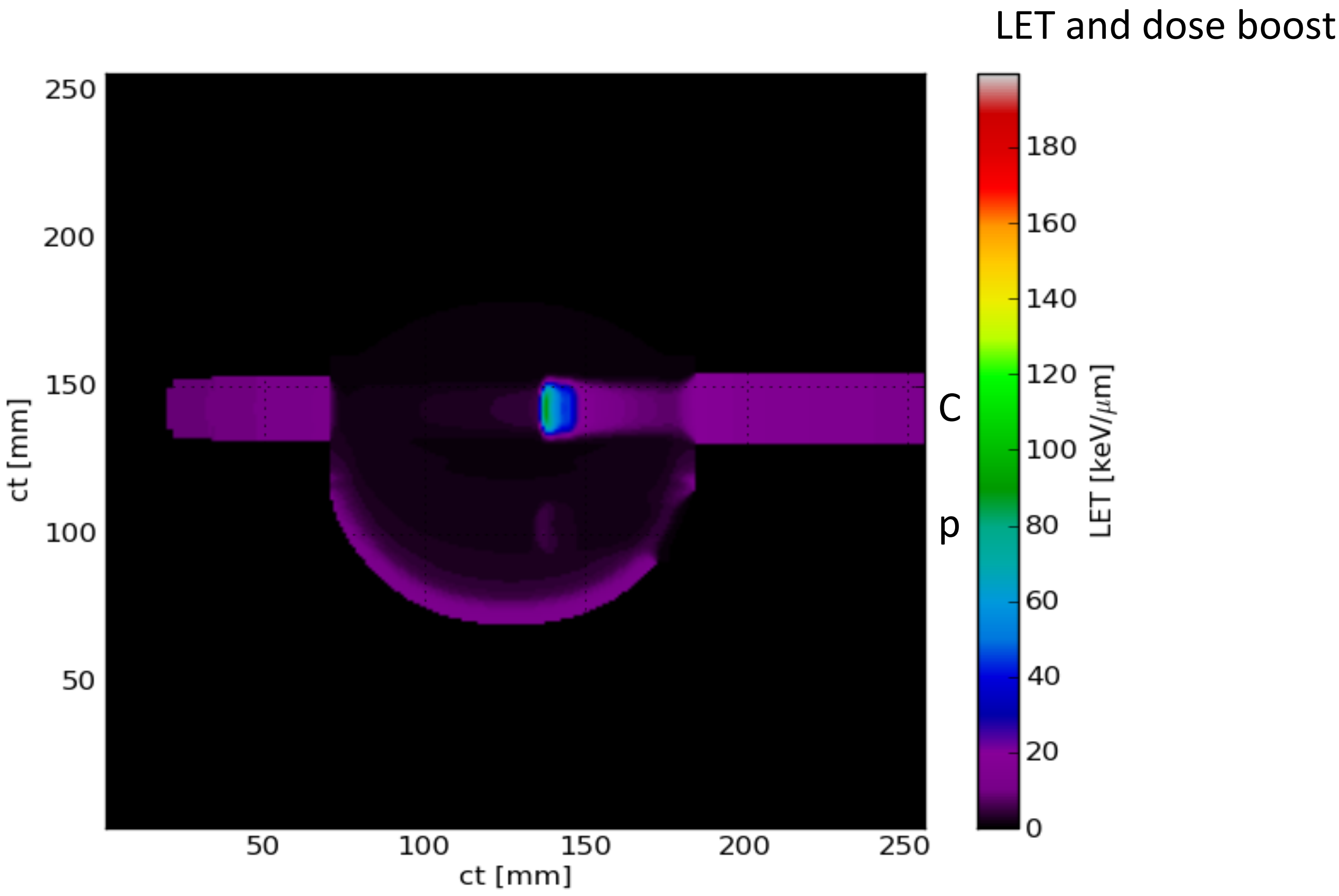


➔Need heavier ions to achieve higher LET (O, N, ….??)

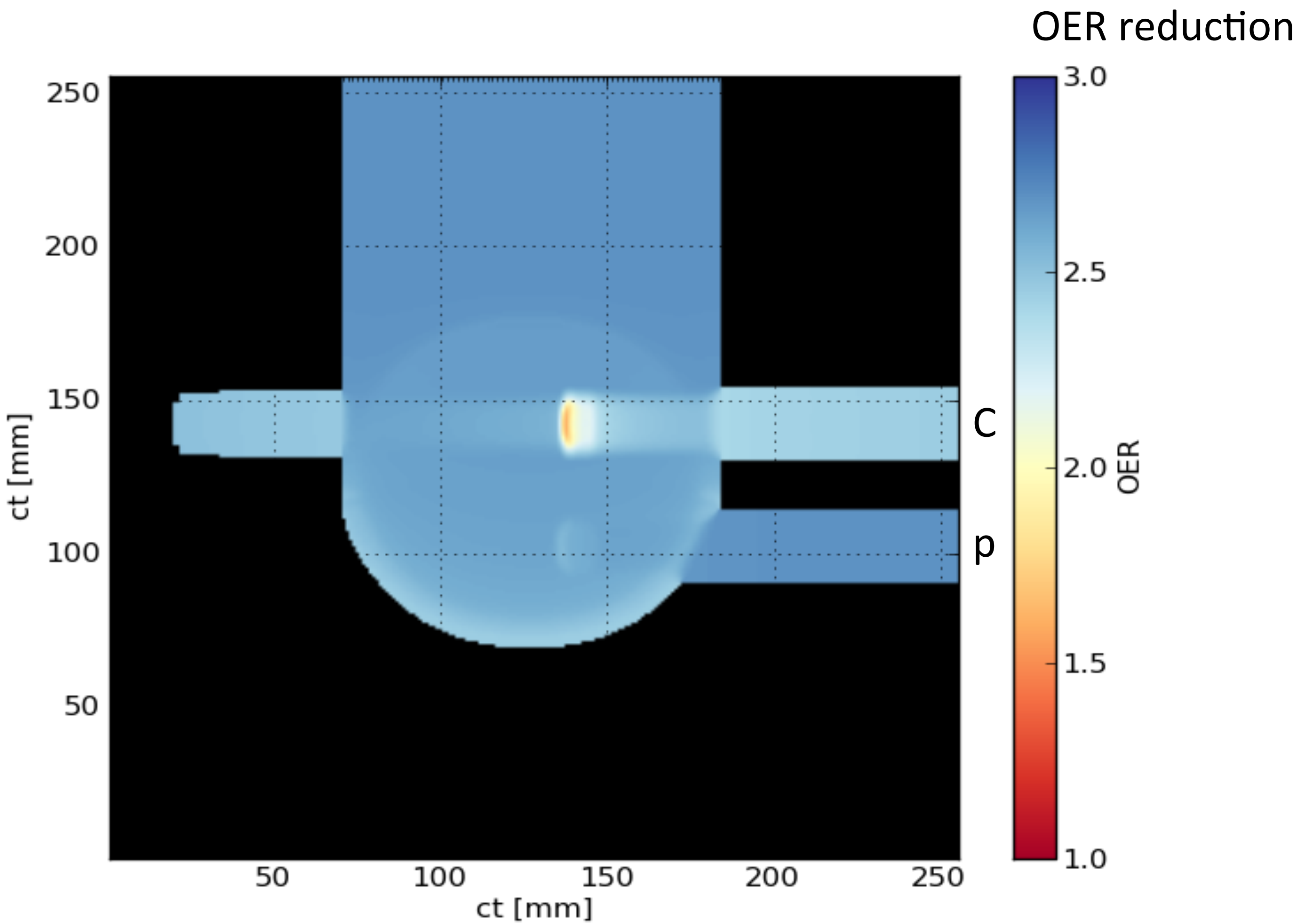
Proton + proton and carbon ion boost



Proton + proton and carbon ion boost



Proton + proton and carbon ion boost



Accelerator requirements

Different ions

Up to Fe but does not need to be complete range of Z

Laser Ion Source (Brookhaven) or multiple ion sources.

Energy range and control

Low energy (< 70 MeV/u) desirable

in-vitro tests

detector characterization with “clean” beams

up to 400 MeV/amu for ^{12}C

to study samples in a clinically relevant beam (fragmentation)

Fast uncomplicated energy switching

(spill by spill)

directly in synchrotron (much preferred over a range shifter)

Beam delivery

Two beamlines for optimal use of accelerator

vertical for low energies (up to 50 or 70 MeV/u)
horizontal for all energies
target stations sufficiently shielded from each other (access for set up)
shared experimental stations (no permanent installations)

Slow extraction

need for clinical dose rates

Irradiation field

at least 5x5 cm^2 at isocenter, 1-2 % homogeneity over entire field,
pencil beams, with good knowledge of FWHM, divergence, and focal point
could be achieved by passive scattering or scanning (preferred)

Dosimetry and fluence monitoring

Good knowledge of fluence at isocenter (2% or better)
basic dosimetry support, equipment (ionization chambers, dose meters)

Experimental infrastructure

At the isocenter

XYZ translator, with sub mm precision
water phantom (PTW MP3 or similar)
laser guides (complete)
Video surveillance

Access to machine shop facilities

building custom sample holders
custom phantoms

Reference units

Co-60 reference unit (2 Gy/min)
X-ray reference unit (e.g. 220 kV, variable dose rate, 0.5 Gy/min - app. 5 Gy/min)

Tissue culture lab

a dedicated room which is clean for biology setups which contains

4 or more incubators (bottle neck)
3 flow benches for handling of sterile samples
1 fume hood
refrigerators for growth media
freezer -20^{0}C and -80^{0}C for cell cultures
Centrifuges, cell counter, autoclave, special glassware dish washer
2x standard microscopes, 1x UV microscope (nice to have)
Biohazard disposal?
Gas supply (CO2 for incubators), Water-sterilizer
~10 meters of bench space
.............and much more

All this shall be shared amongst many groups

(both usage and purchase cost)

General support infrastructure

Dedicated office space for visiting groups

Counting huts

with ample cabling possibilities to exp. stations (BNC, RS232, Ethernet...)

Resident Personnel

primary responsible for Bio-Lab
physicist/technician responsible for beam line

Any facility built will immediately turn out too small

Conclusions

- Radiobiological research is still needed to develop the full potential of particle therapy
- Clinical installations can neither offer the necessary beam time nor is this research in their core mission
- CERN can provide a crucial contribution to global health providing access to an accelerator facility standing idle for large parts of the year
- A collaboration has to be set up amongst interested groups to facilitate and promote the synergy between CERN and the medical and radio-biological communities
- Let me know at michael.holzscheiter@gmail.com