LUDWIG-
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MÜNCHEN

Heavy Ion Therapy Research Integration

DEUTSCHES
KREBSFORSCHUNGSZENTRUM
IN DER HELMHOLTZ-GEMEINSCHAFT

Biological Dose Optimization

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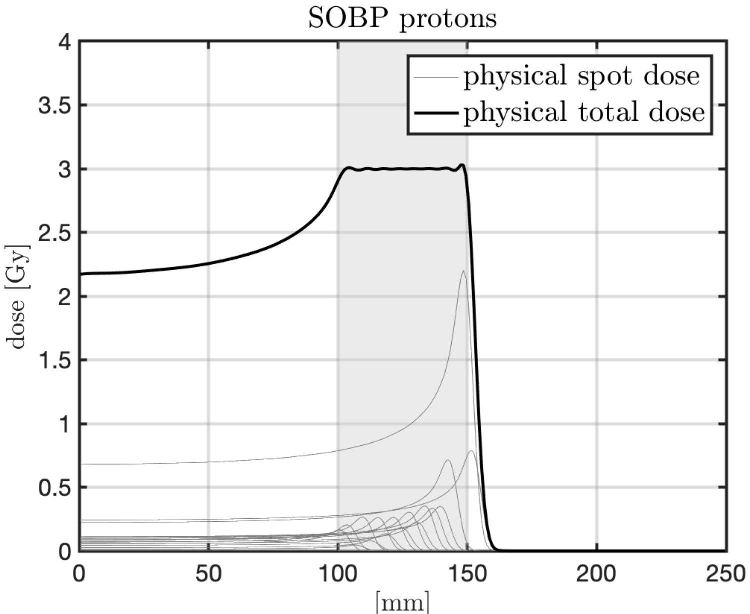
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

What we will learn today

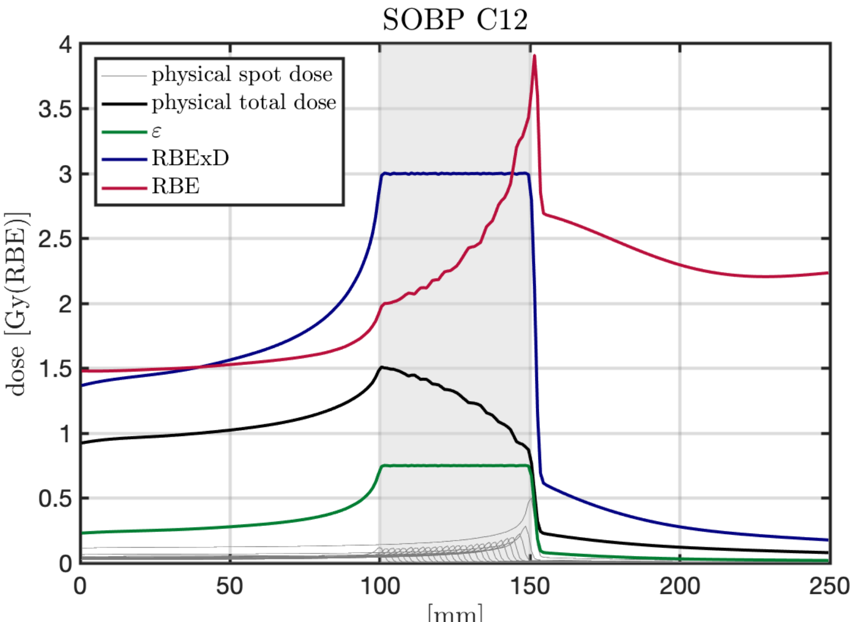
Linear dose mapping

$$d_i = \sum_{j=1}^{J} D_{ij} w_j \quad \text{or} \quad \mathbf{d} = D\,\mathbf{w}$$



Linear Quadratic dose mapping

$$\varepsilon_i = \sum_{j=1}^{J} w_j D_{ij} \alpha_{ij} + \left(\sum_{j=1}^{J} w_j D_{ij} \sqrt{\beta_{ij}} \right)^2$$

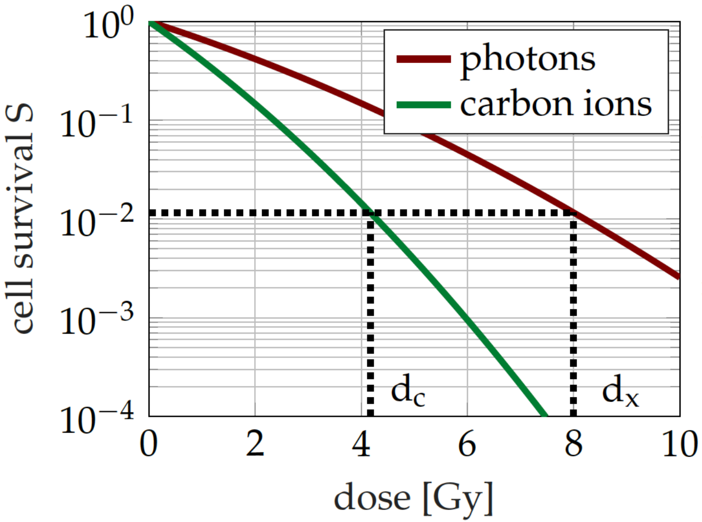


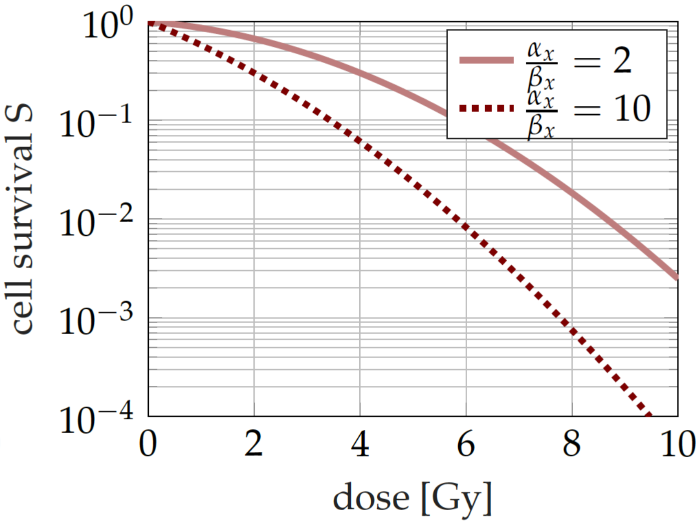
Recap: Radiobiology

$$RBE = \frac{d_x}{d_I}\Big|_{iso-effective}$$

Cell survival: linear quadratic model

$$S = e^{-\varepsilon} = e^{-(\alpha d + \beta d^2)} \quad \text{with:} \quad \varepsilon = \alpha d + \beta d^2$$

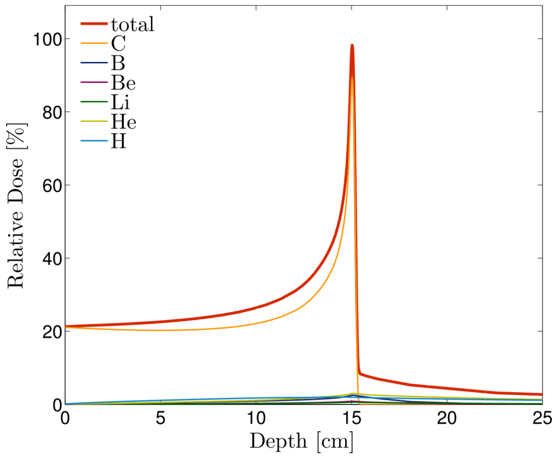




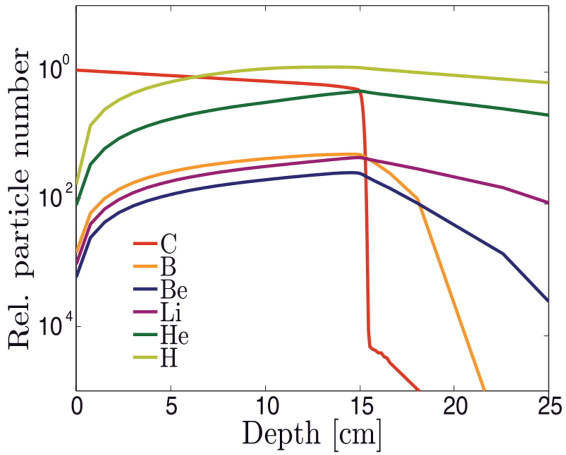
How to obtain the radio-sensitivity parameters for carbon ions α_c β_c?

Fragmentation – Mixed Radiation Field

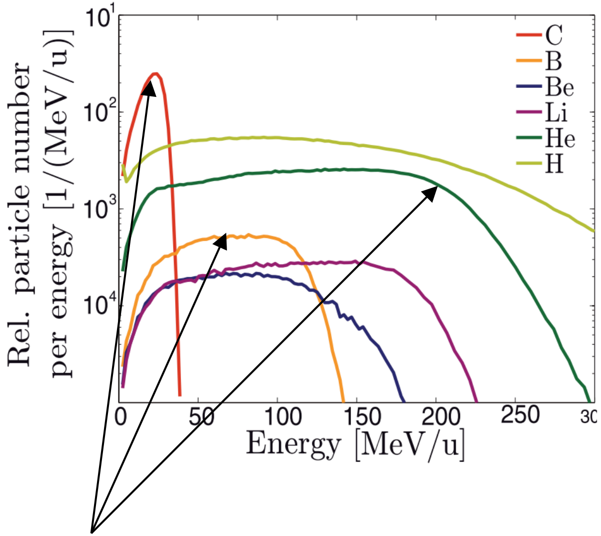
Depth dose profile



Fluence ϕ



Spectrum at 15 cm



- primary carbon ions fragment into lighter ions
- continuous fragmentation spectrum

What is the cell survival ?

$$\alpha_c = f(280MeV, 15cm, \alpha_H(E), \alpha_{He}(E), ..)$$

Figure courtesy Sarah C. Brünigk

Biophysical Models

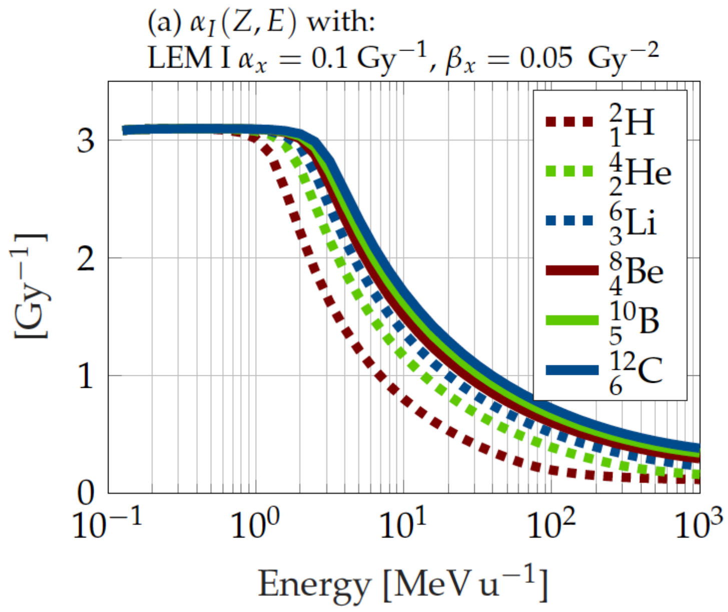
We need these radio-sensitivity parameters for treatment planning to account for these pronounced non-linear biological effects.

Radio-sensitivity parameters $\boldsymbol{\alpha_c}$ $\boldsymbol{\beta_c}$ posses various dependencies:

- initial beam energy
- depth
- particle type
- stopping power
- cell type
- …

cell line experiments → large effort

→ biophysical models have been developed to predict the radio-sensitivity



LEM,RMF,MKM

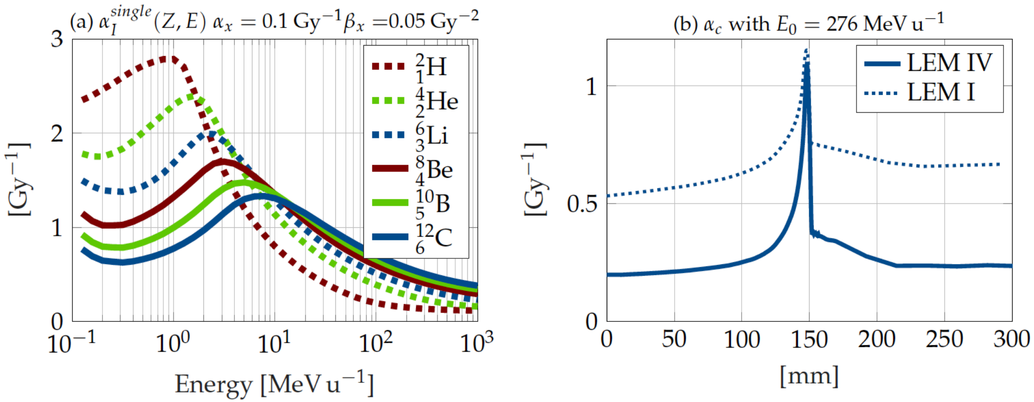
Putting things together in a TPS

Full simulation :

1. sample the number of cell hits (account for particle fluence)
2. get biological effect using biophys. model for each particle type from local spectrum
3. derive total biological effect
4. repeat this procedure N-times to account for different particle combinations

Needs to be redone if pencil beam intensities change !

Analytical Approximation & beam mixing model



- account for all fragments Z
- only valid for <10Gy (RBE)
- can be integrated in analytical dose calculation and optimization
- only needs to be done once

$$\alpha_c(x, E_0) = \frac{\sum_Z \int_0^\infty \alpha_I^{single}(Z,E)\phi(x,Z,E,E_0)\, S_{el}(Z,E)\, \mathrm{d}E}{\sum_Z \int_0^\infty \phi(x,Z,E,E_0)\, S_{el}(Z,E)\, \mathrm{d}E}$$

Biological Treatment planning

For **each** tabulated carbon ion energy E_0 and for **each** cell type:→ triplet of curves

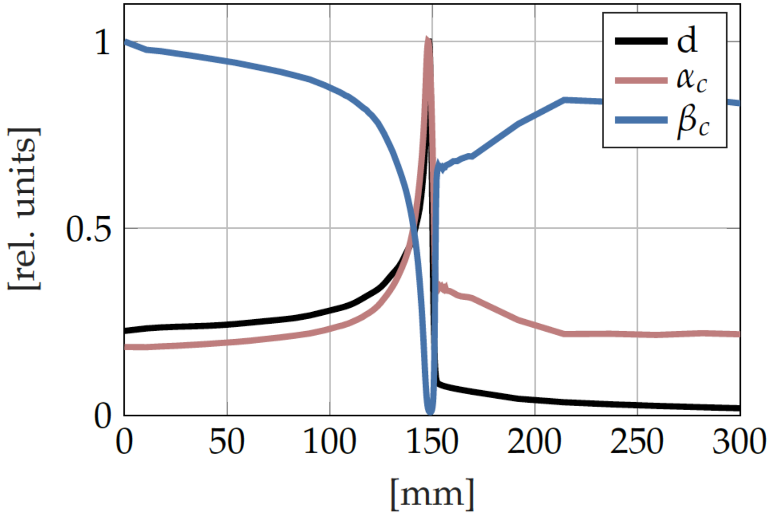
d(E0,z), $\boldsymbol{\alpha_c(E0,z,T)}$, $\boldsymbol{\beta_c(E0,z,T)}$

$$RBE = \frac{d_x}{d_I}\bigg|_{iso-effective}$$

biological effect

$$RBE \times d = \sqrt{\frac{\varepsilon}{\beta_x} + \gamma^2} - \gamma = \sqrt{\frac{\alpha_c d + \beta_c d^2}{\beta_x} + \left(\frac{\alpha_x}{2\beta_x}\right)^2} - \frac{\alpha_x}{2\beta_x}$$

277 MeV carbon ions



adapt dose influence concept to radio-sensitivity parameters for fast evaluation of ε_i for different intensities w during optimization.

$$\varepsilon_i = \sum_{j=1}^{J} w_j D_{ij}\alpha_{ij} + \left(\sum_{j=1}^{J} w_j D_{ij}\sqrt{\beta_{ij}}\right)^2 = \sum_{j=1}^{J} w_j A_{ij} + \left(\sum_{j=1}^{J} w_j B_{ij}\right)^2 \rightarrow \quad RBE \times d$$

Combing back …

Linear dose mapping

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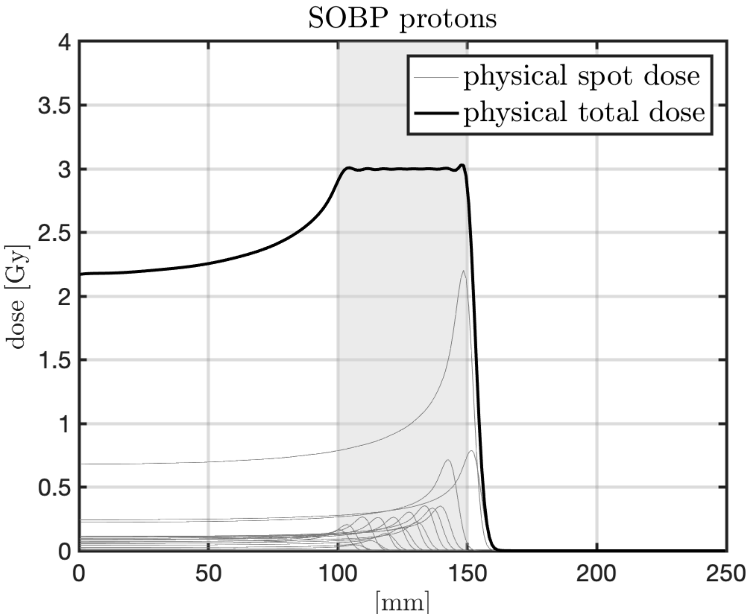

Linear Quadratic dose mapping

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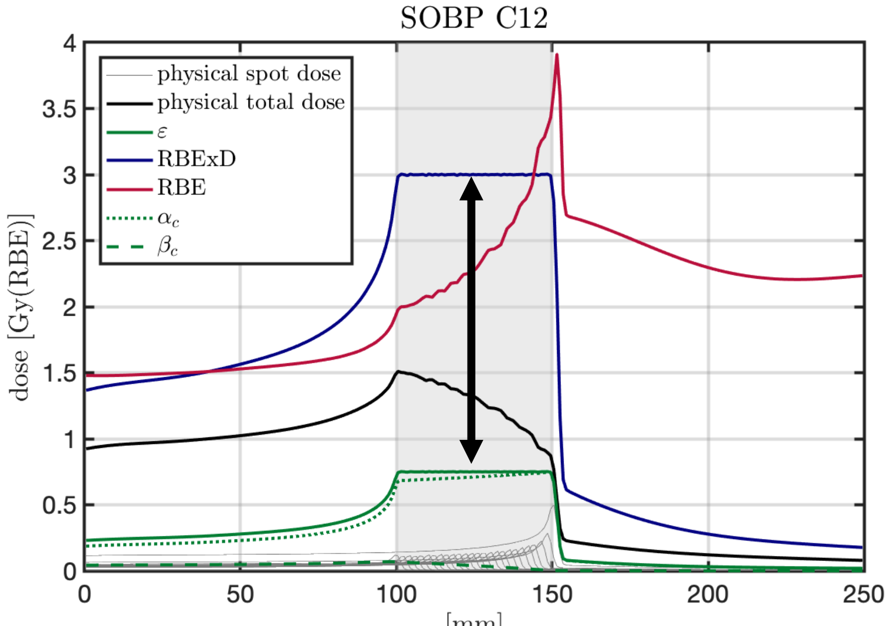


Outlook: Other Ion species

Protons **Helium** **Carbon**

const RBE of 1.1

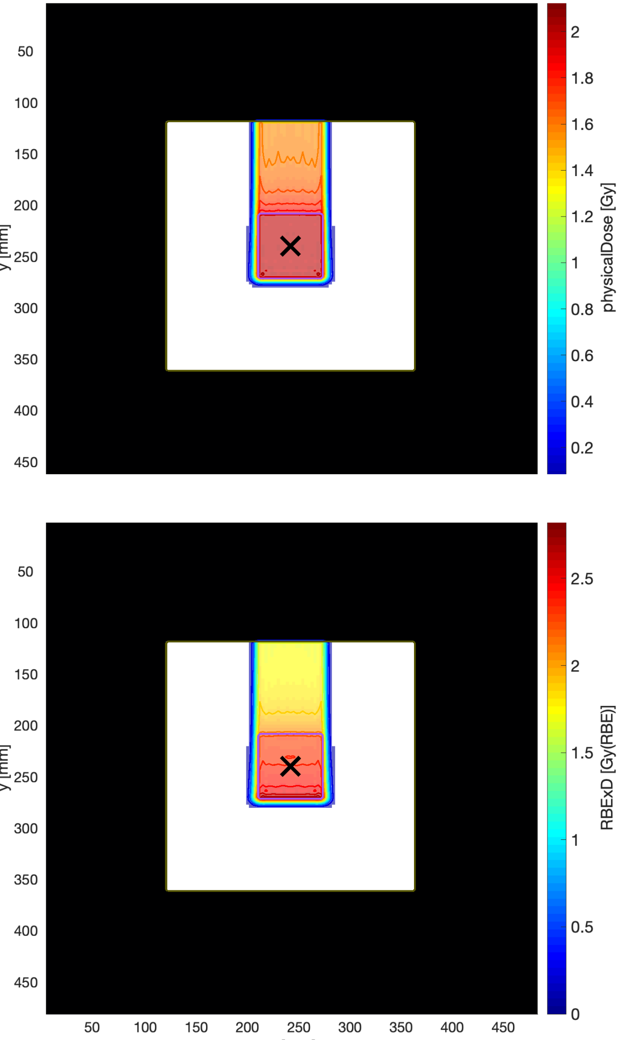
Analytical fits to in-vitro(vivo data):

$$\alpha_{P/H} = f(LET[E_0, z], \alpha_x, \beta_x)$$

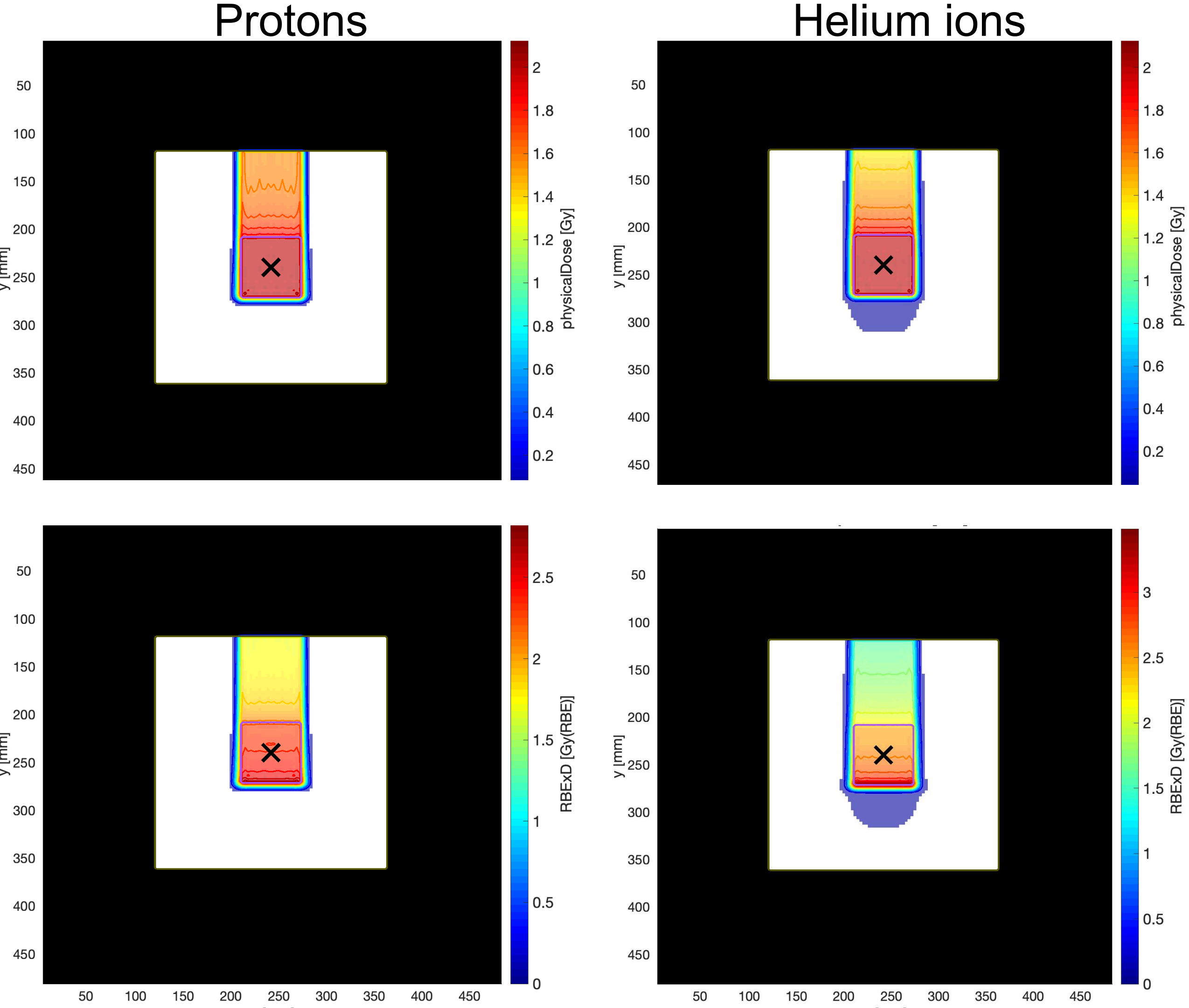
$$\beta_{P/H} = f LET[E_0, z], \alpha_x, \beta_x)$$

biophysical models

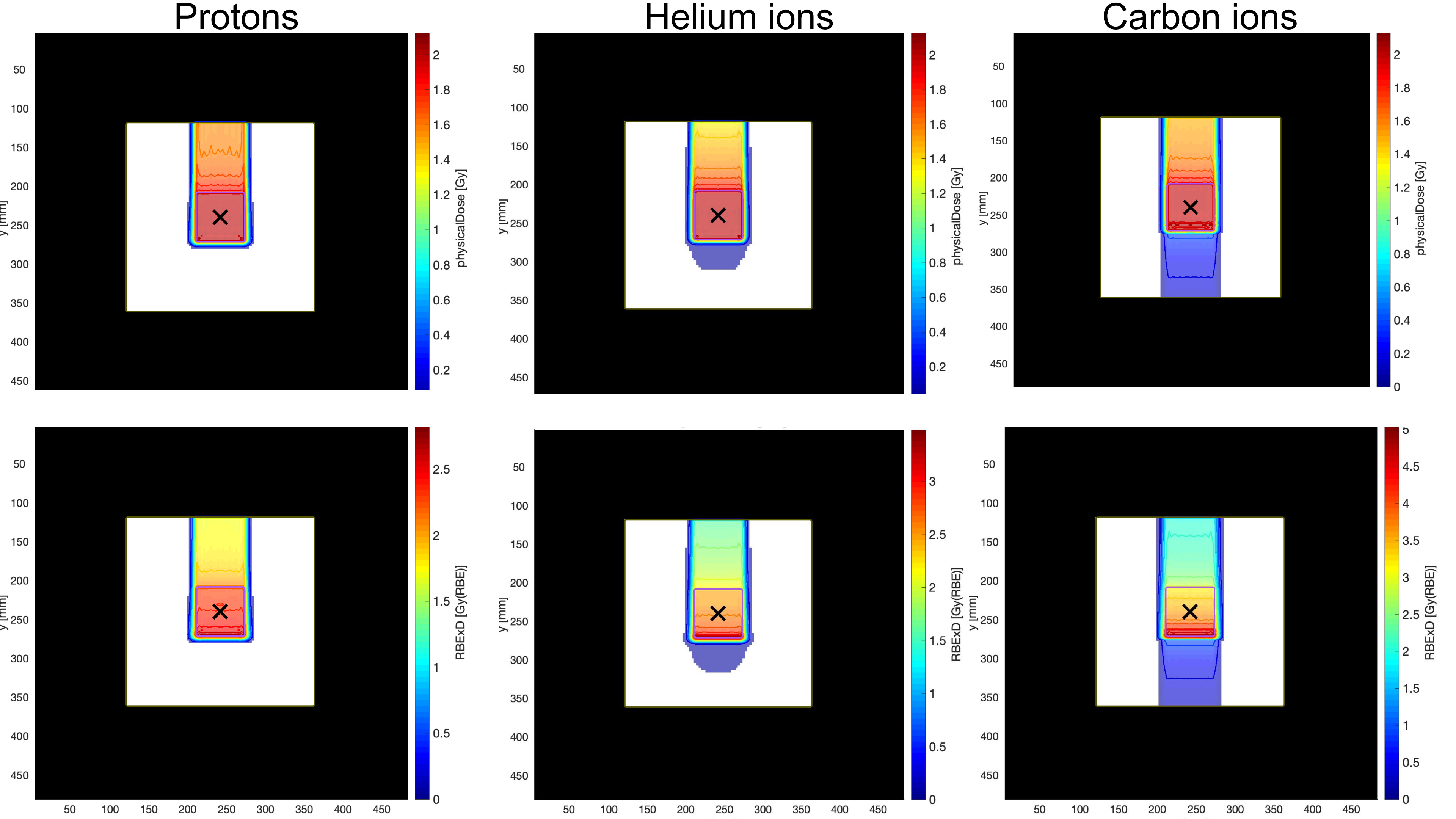
Protons



y [mm]
50
100
150
200
250
300
350
400
450
physicalDose [Gy]
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
RBExD [Gy(RBE)]
2.5
2
1.5
1
0.5
0



Protons
Helium ions
physicalDose [Gy]
RBExD [Gy(RBE)]
y [mm]



Protons
Helium ions
Carbon ions
physicalDose [Gy]
RBExD [Gy(RBE)]
y [mm]

Thank you !

This material was prepared and presented within the HITRIplus Heavy Ion Therapy MasterClass school, and it is intended for educational purposes to facilitate students; people interested to use any of the material for any other purposes (such as other lectures, courses etc.) are requested to please contact the authors

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