Calculations of the cell survival rate after irradiating with minibeams of protons and ^{12}C

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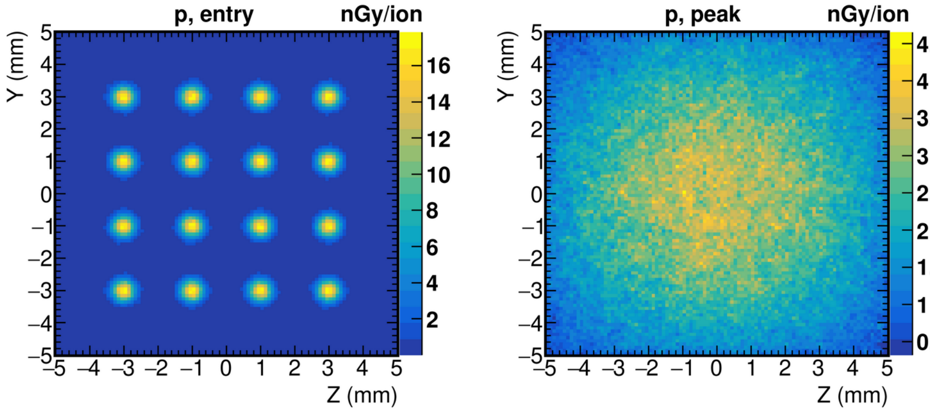
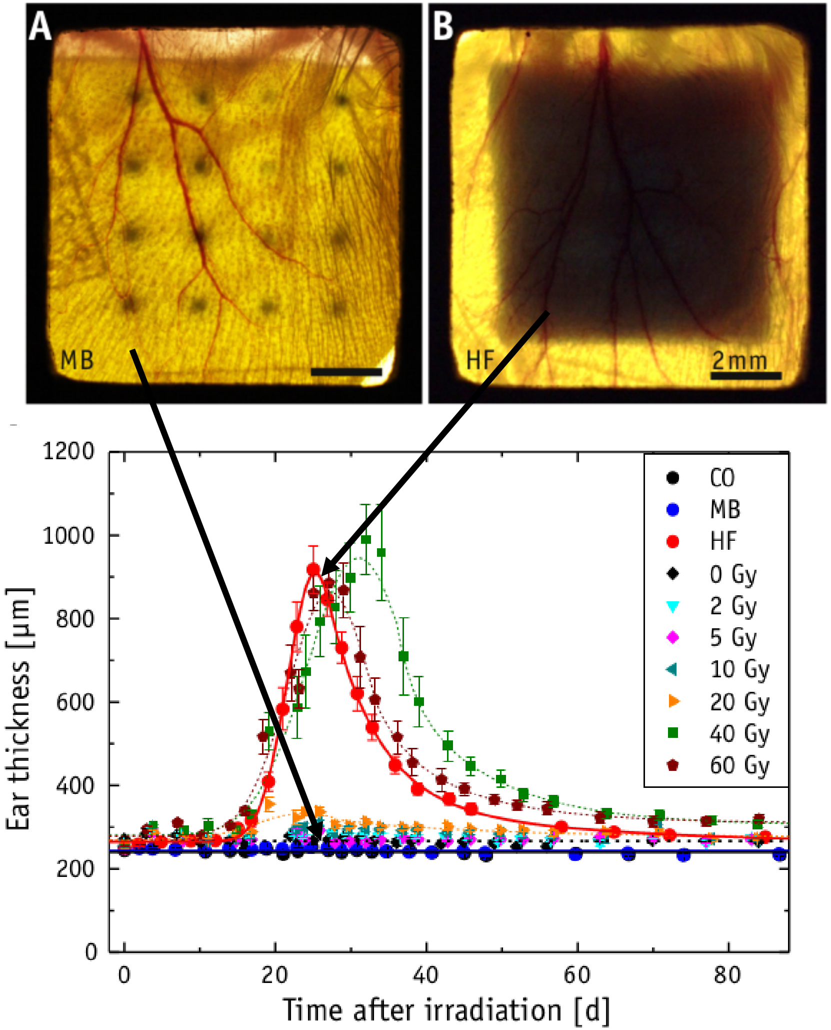


Motivation

- In conventional proton or ion therapy, the damage to healthy tissues from projectiles on their way to the target tumour volume is inevitable
- As reported[1,2,3], this damage can be reduced by using spacially fractionated dose field delivered by proton minibeams of ~0.5 mm FWHM with centre-to-centre distance of ~2 mm.
- Detailed modelling is necessary to obtain the dose distribution, relative biological efficiency and, finally, the cell survival rate in homogenous and spatially fractionated radiation fields[1]

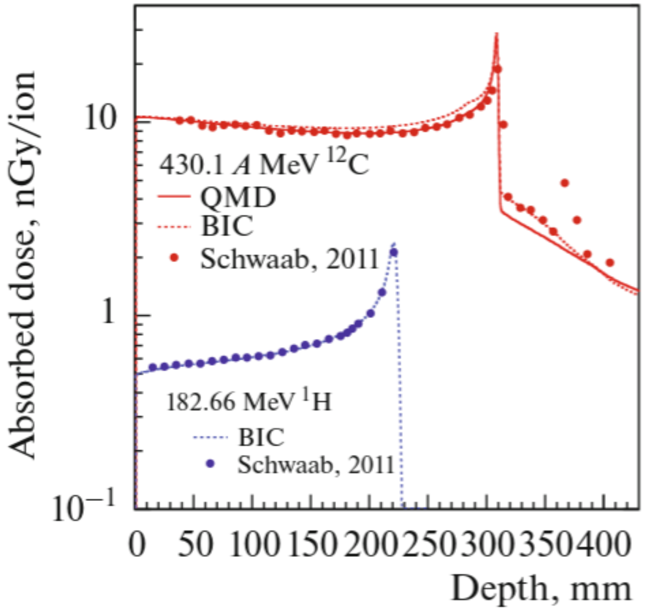


1) Prezado Y et al. Sci. Reports. (2017) 7 14403
2) Girst S et al. Int. J. Rad. Onc.* Biol.* Phys. (2016) 95 234.
3) Sammer M et al. PLoS ONE (2019) 14 e0224873.

Our calculations of dose

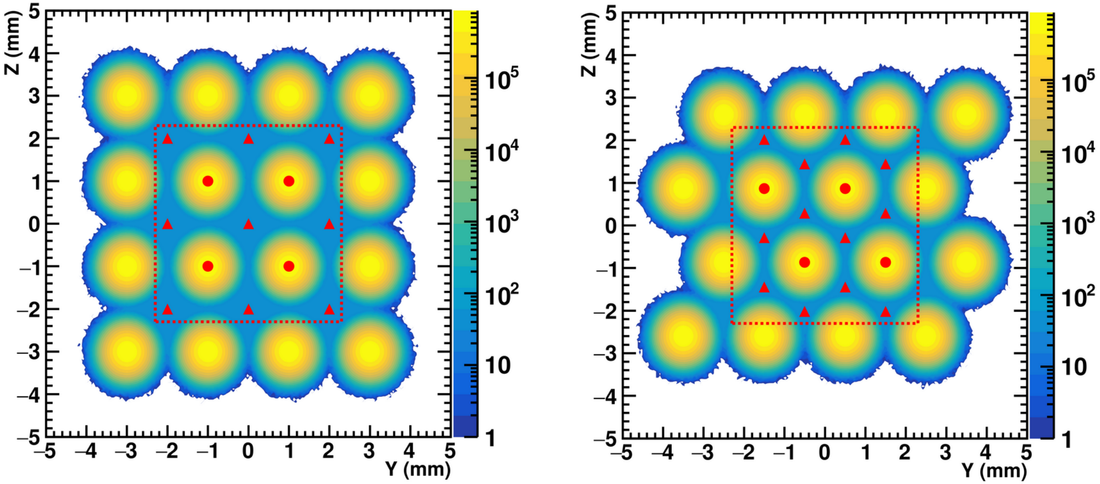
- Geant4 v10.3 Electromagnetic processes Standard_opt3
  - Binary cascade (BIC) model for proton-induced reactions
  - Quantum Molecular Dynamics (QMD) model for ion-induced reactions
- Arrays of 16 minibeams are propagating in water phantom

Depth-dose distributions are described well



Pshenichnov, I. et al. Phys. Part. Nuclei (2024) 55, 929

Distributions of beam intensity at the entrance, ctc = 2 mm, FWHM = 0.5 mm



The boundary of volumes to analyse are marked by dotted lines

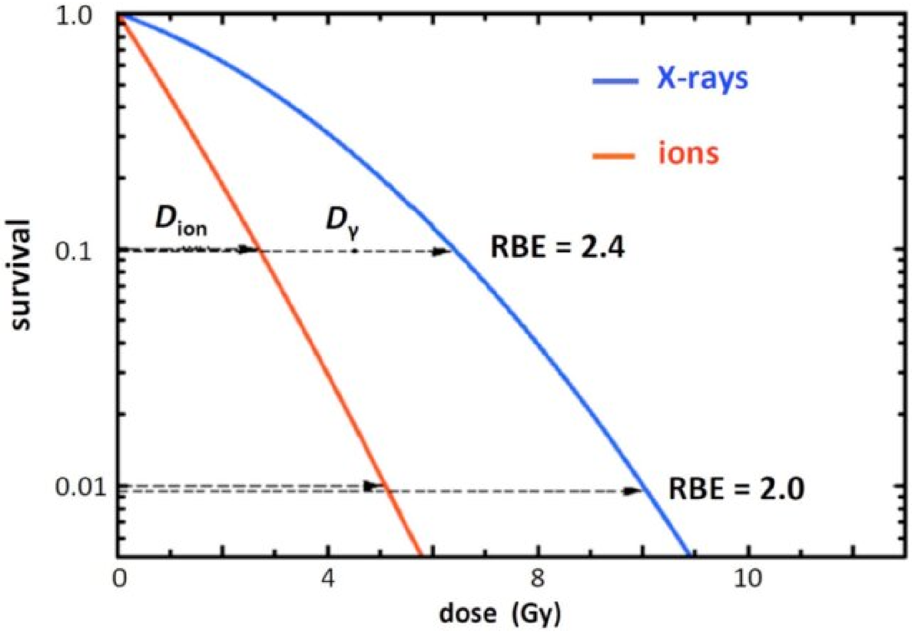
Three quantities to characterize biological effect

- Cell survival (CS) is the fraction of cells in tissue that survives the irradiation. It is described by the linear-quadratic model (LQM).

- Relative biological effectiveness (RBE) is a ratio between the dose from ions and the dose from reference x-ray radiation to provide the same cell survival rate

- Biological dose is the physical dose multiplied by RBE

$$S = \exp\left(-\alpha D - \beta D^2\right)$$



U. Amaldi, CERN Yellow Reports Vol. 2 (2019)

The modified microdosimetric kinetic model

- The cell survival Is related to the number of double strand breaks (DSB) of DNA molecule induced by protons and ions. This number is higher near the tracks of heavily ionizing particles and therefore it is related to linear energy transferred by the projectile.

- In the microdisometric kinetic model (MKM) the number of DSB is calculated from the linear energy y. The saturation correction is also considered, where f(y) is PDF for linear energy

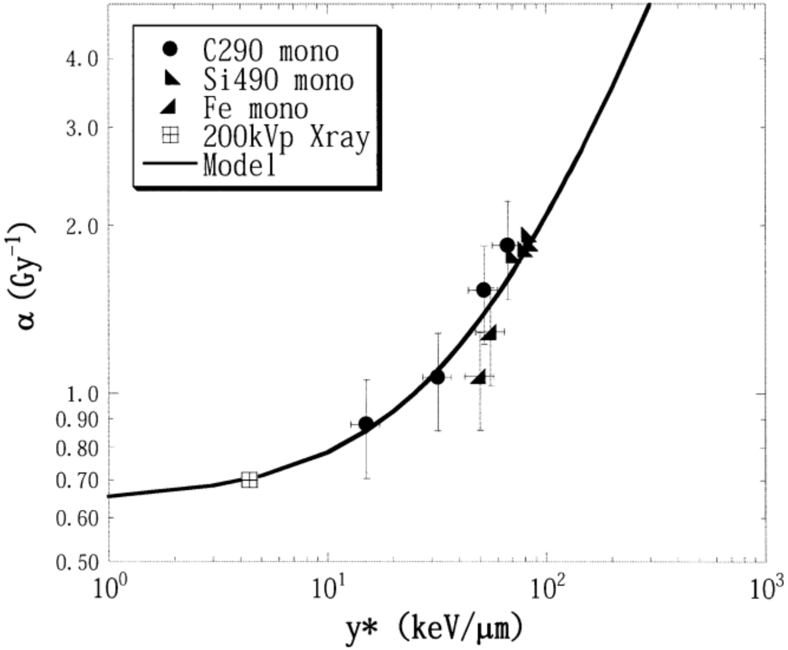
$$y^* = \frac{y_0^2 \int \left[1 - \exp\left(-y^2/y_0^2\right)\right] f(y) dy}{\int f(y) dy},\ y_0 = 150\ \mathrm{keV}/\mu\mathrm{m}$$

- α as a fuction of y* is calculated as follows

$$\alpha = \alpha_0 + \beta \frac{y^*}{\rho \pi R_d^2}$$

- R_d is domain radius, $\beta = 0.05\ \mathrm{Gy}^{-2}$ is taken for ions the same as for X-ray

- In this work the MKM is applied to human salivary gland (HSG) cells



Kase Y et al. Rad. Res. (2006) 166, 629

RBE is dose-dependent

- In LQM RBE is calculated via X-ray reference dose

$$\ln S = -\alpha D - \beta D^2 = \ln S_X = -\alpha_X D_X - \beta_X D_X^2$$

$$\Downarrow$$

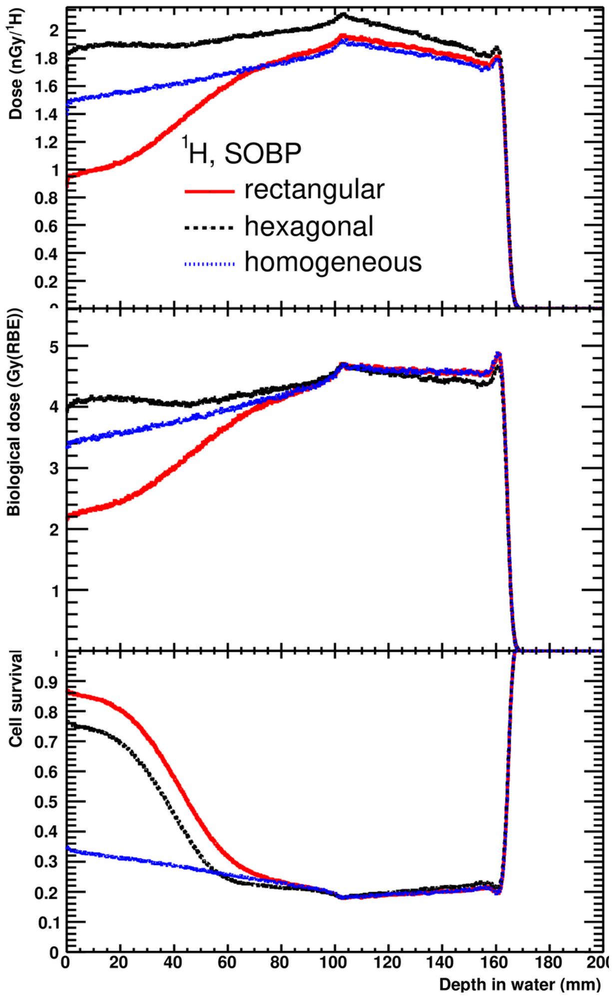
$$\mathrm{RBE} = \frac{\sqrt{(\beta/\beta_X)D^2 + (\alpha/\beta_X)D + 1/4(\alpha_X/\beta_X)^2} - 1/2(\alpha_X/\beta_X)}{D}$$

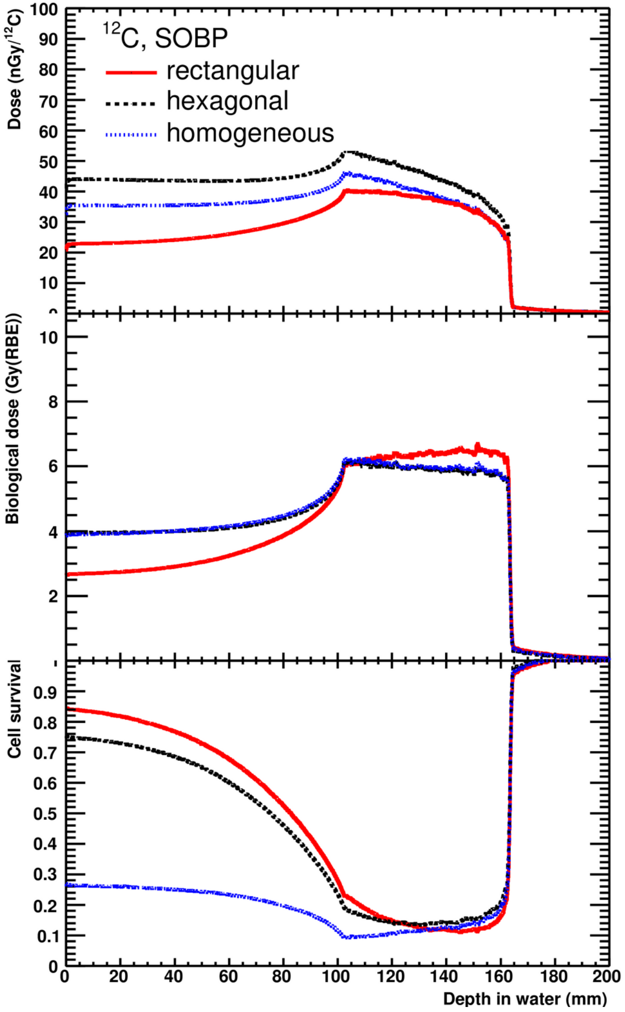
- Biological dose (RBE-weighted dose) is calculated as

$$D_{bio} = D \cdot RBE$$

- In further calculation the prescribed biological dose was taken as 5.1 Gy(RBE) in spread-out Bragg peak (SOBP) for the cell survival in the target volume at the level of 0.1 for HSG cells

The dependence on depth in phantom





The quantities were averaged in 2.6x2.6 mm square for a given depth.

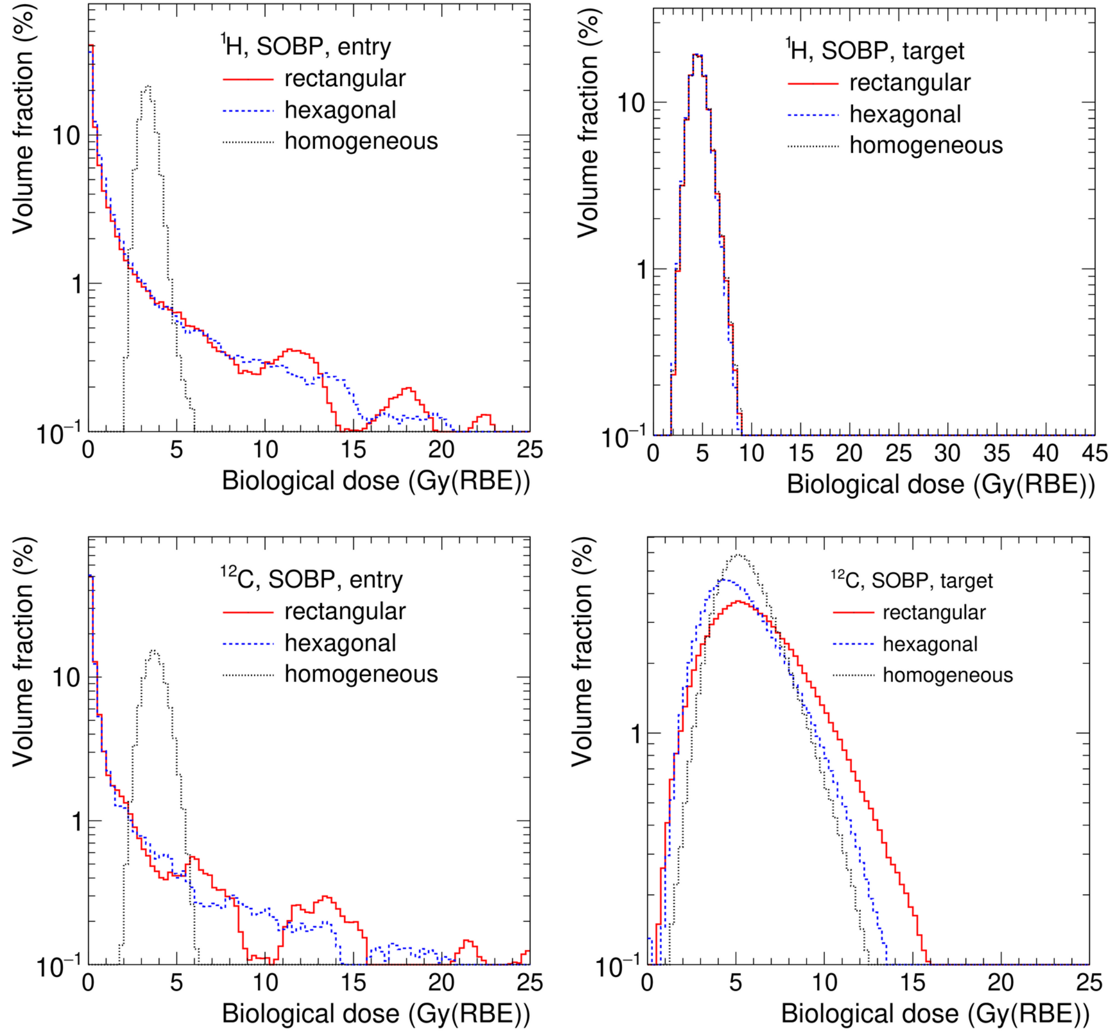
The physical and biological dose for the rectangular lattice is lower than for the homogenous field while for the hexagonal lattice it is higher for all depth

The CS at the entrance is ~0.7-0.9 for minibeams compared to homogenous field providing CS~0.3

For protons the CS is equal in all three cases

For ^{12}C the CS is slightly higher at 100 mm depth in comparison to homogenous field

Differential dose-volume histogram



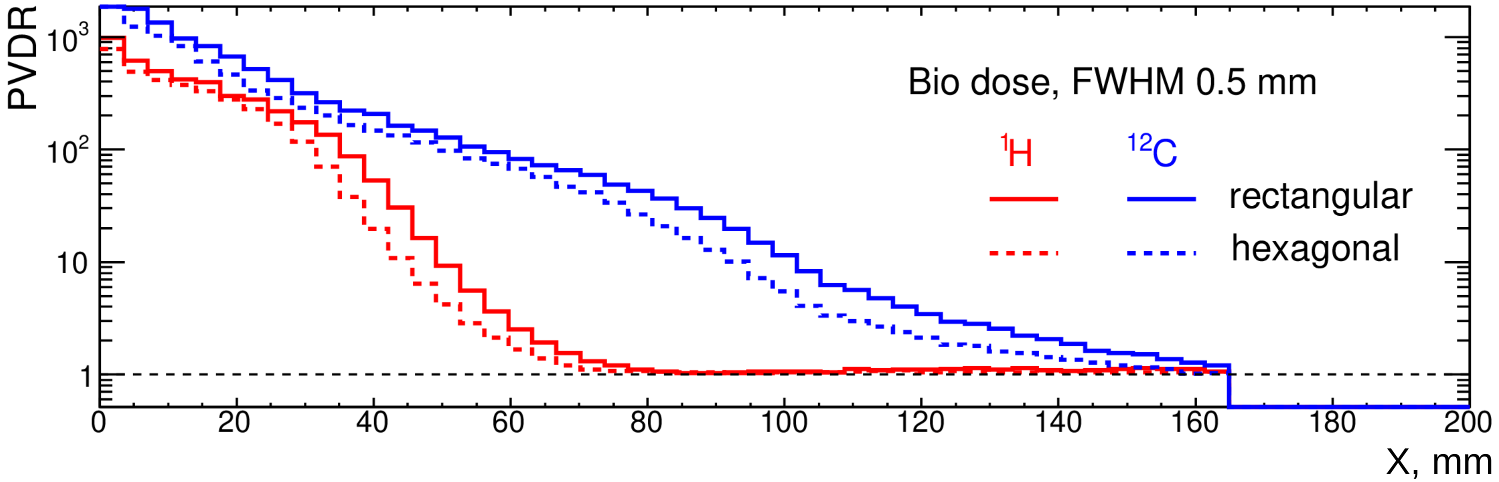
Differential dose-volume histogram (DVH) represents a fraction of volume that obtained a given biological dose

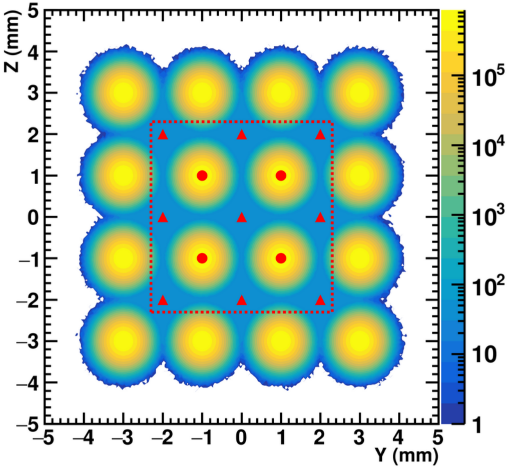
At the entrance, DVH are similar for all minibeam configurations. In the main part of the volume the biological dose is below 2 Gy(RBE) for minibeams.

In the target volume, DVHs are similar for minibeams and homogenous field for protons

For ^{12}C in target volume, hexagonal minibeam lattice provides DVH closer to that of homogenous dose field.

Peak-to-valey dose ratio

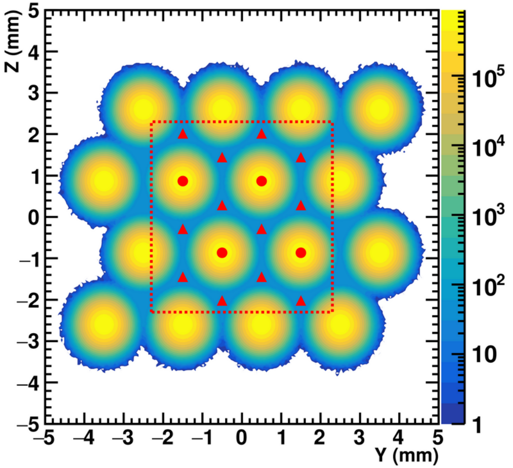




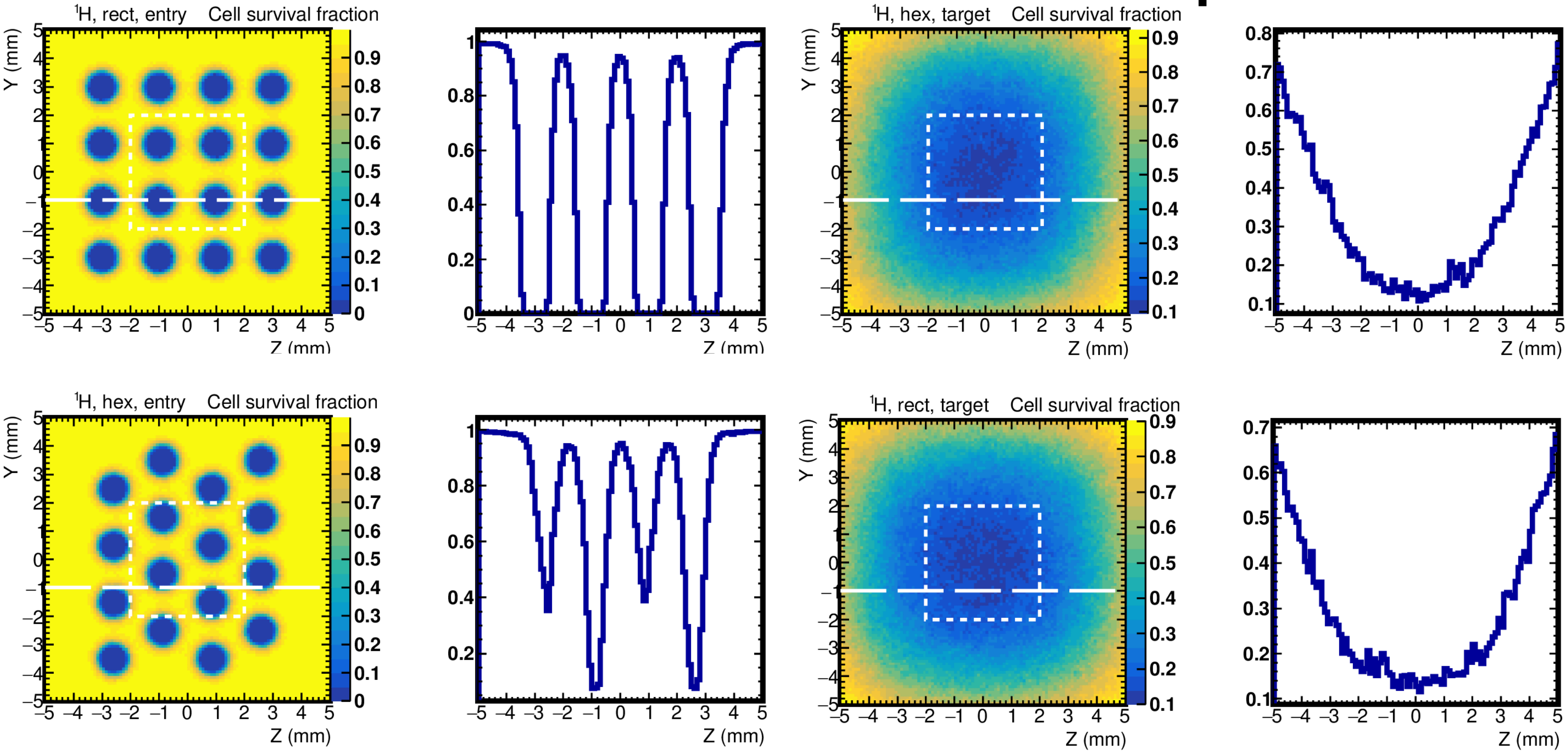
The sparing effect in tissue is typically associated with the ratio of doses in peaks (circles) and valleys (triangles) called PVDR

Proton minibeams fully overlap at the depth of ~80 mm while ^{12}C minibeams fully overlap at 160 mm at the distal edge of SOBP

Lower PVDR is calculated for hexagonal minibeam lattice



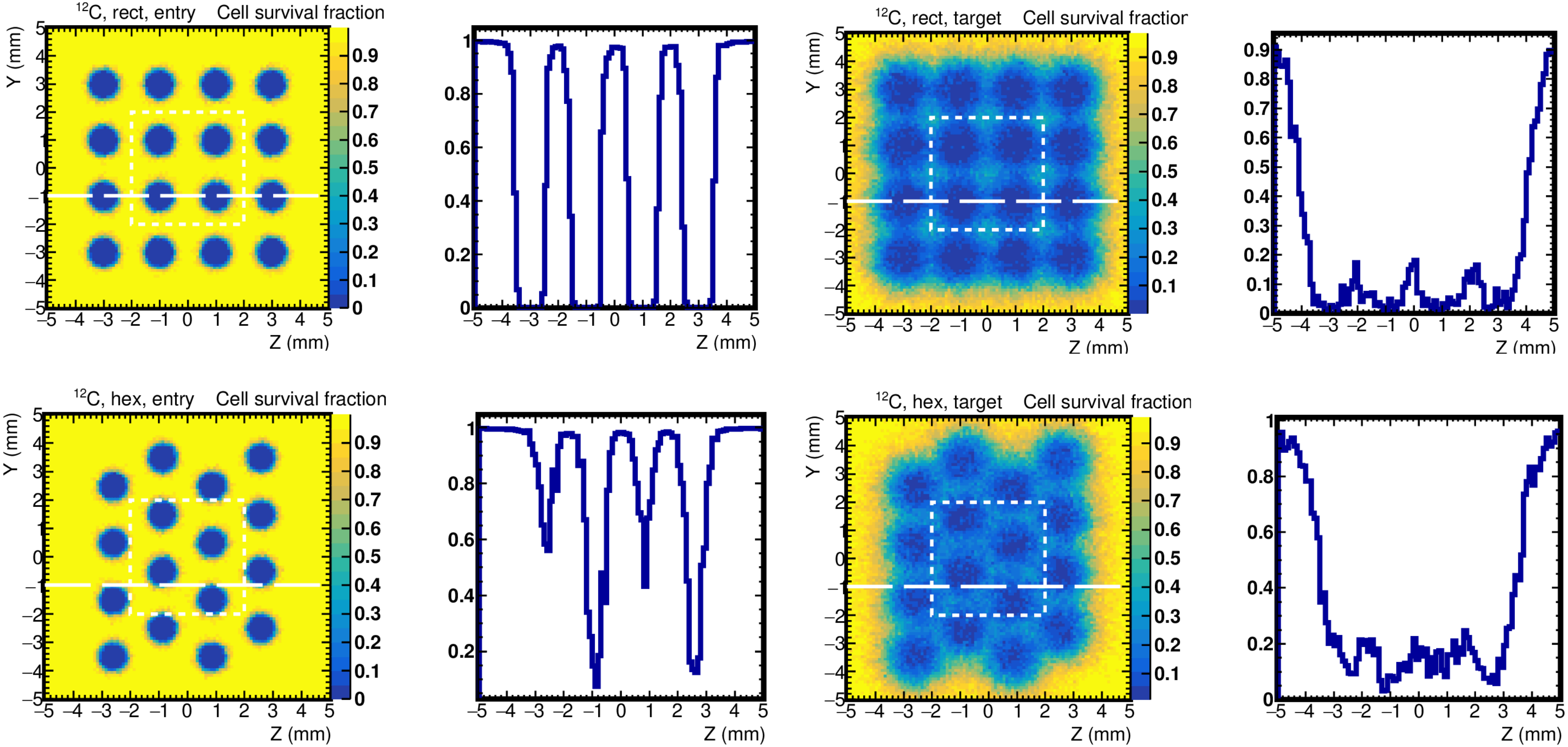
3D distributions of cell survival: protons



Cell survival distributions demonstrate submillimetre dead spots at the entrance.

In the target volume, the cell survival distribution become smooth like in the homogenous field.

3D distributions of cell survival: ^{12}C



The cell survival distributions demonstrate submillimetre dead spots at the entrance.
In the target volume, these distributions are less smooth than for protons.

Summary

- The average cell survival at the entrance is calculated to be higher for the rectangular minibeam lattice both for protons and ^{12}C

- At the entrance, DVH are similar for all minibeam configurations of the protons. For ^{12}C in target volume, hexagonal minibeam lattice provides DVH closer to that of homogenous dose field

- Proton minibeams overlap prior to proximal edge of the SOBP while ^{12}C minibeams overlap at the distal edge of the SOBP for the same width and centre-to-centre distance for the considered minibeam lattices

- The cell survival distributions at the entrance are represented by submillimetre spots of dead cells surrounded by large numbers of survived cells

- The obtained results can help in planning in vitro and in vivo measurements of biological effects in minibeam radiation

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Thank you for your attention!

Squares with Concentric Circles (1913) by Wassily Kandinsky