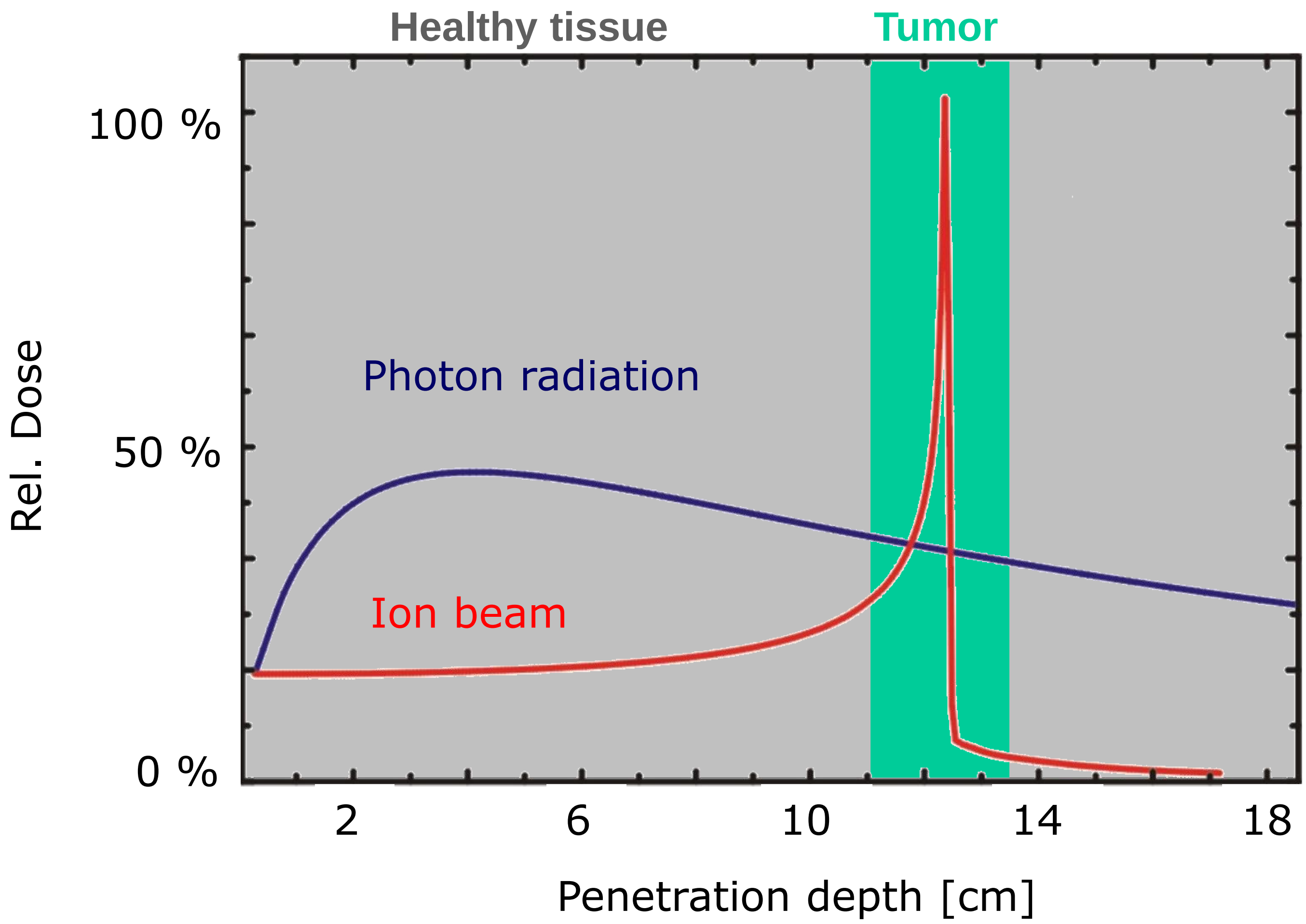
Radiation Quality in Ion Beam Therapy: How to take into account the RBE?

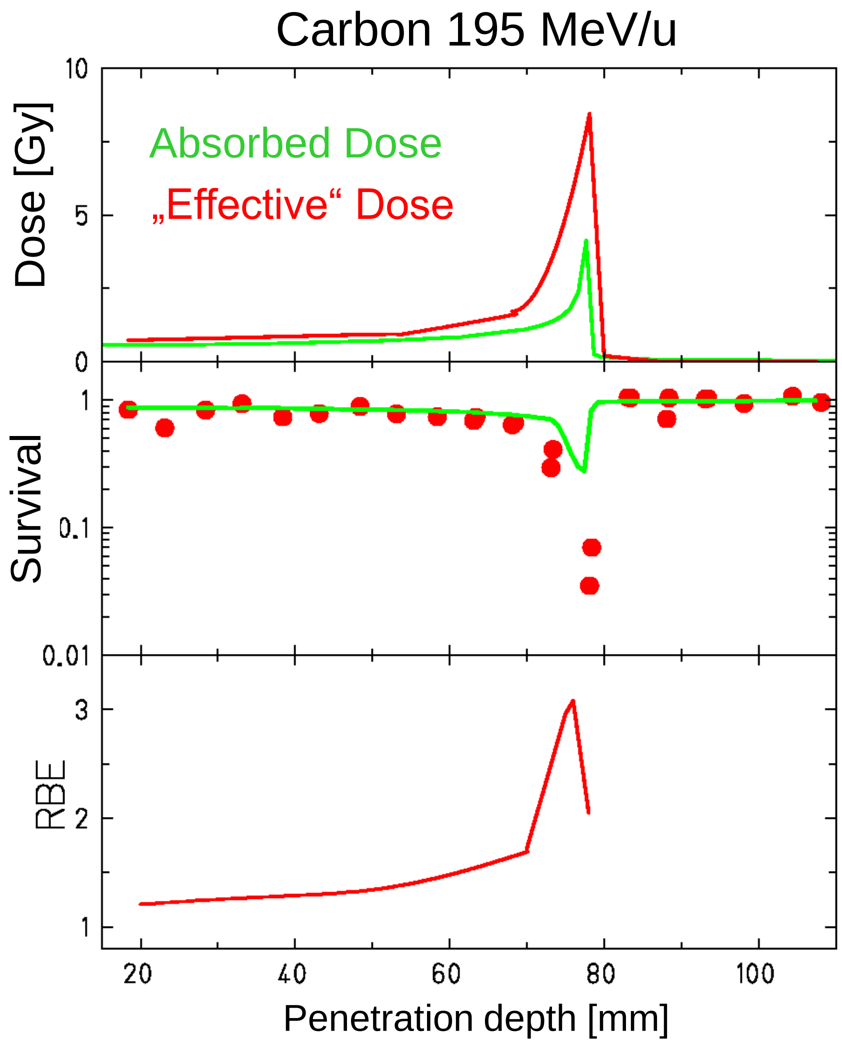
M. Scholz

GSI Darmstadt

Advantage of ion beams: physical



Increased Relative Biological Effectiveness: RBE



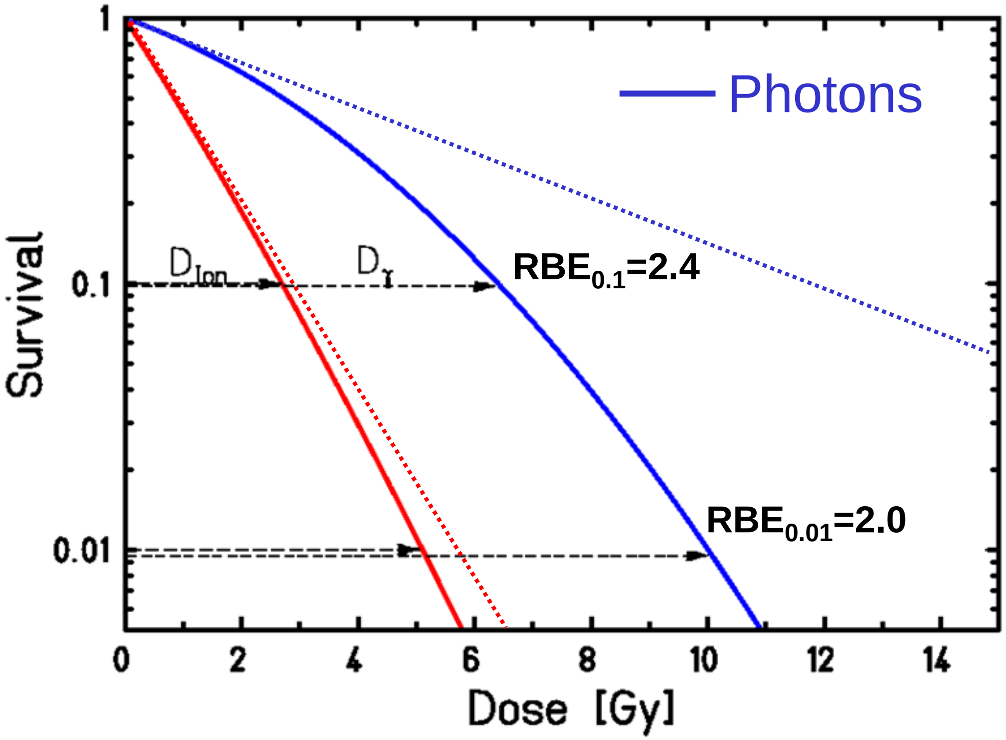
Weyrather et al.

Differential Effect:

Enhancement(Peak)
>>
Enhancement(Plateau)

(Neutrons:
Enhancement
everywhere!!!)

Definition: Relative Biological Effectiveness (RBE)



$$S = e^{-(\alpha D + \beta D^2)}$$

$$\alpha_{Ion} \geq \alpha_{Photon}$$

$$\beta_{Ion} \leq \beta_{Photon}$$

$$RBE = \left.\frac{D_{Photon}}{D_{Ion}}\right|_{Isoeffect}$$

$$RBE_{\alpha} = \frac{\alpha_{Ion}}{\alpha_{Photon}}$$

Requirements for Treatment Planning

Challenge:

Homogenous distribution of effective dose in treatment volume

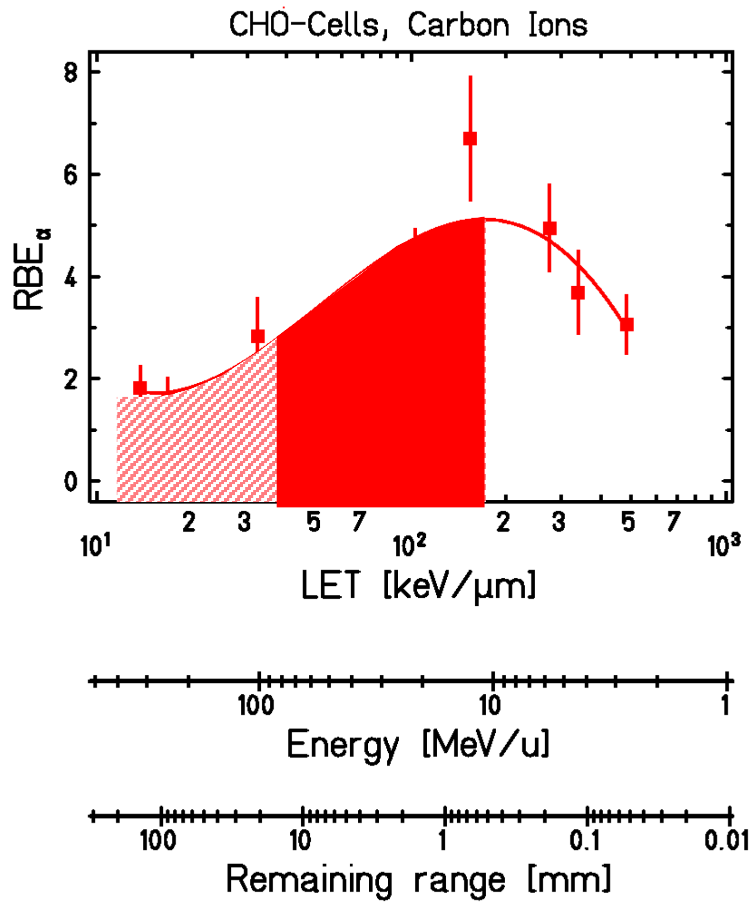
Effective dose distribution in normal tissues

$$D_{RBE} = D_{Phys} \cdot RBE(Z, E, D, \alpha, \beta, p_{O2}, \ldots)$$

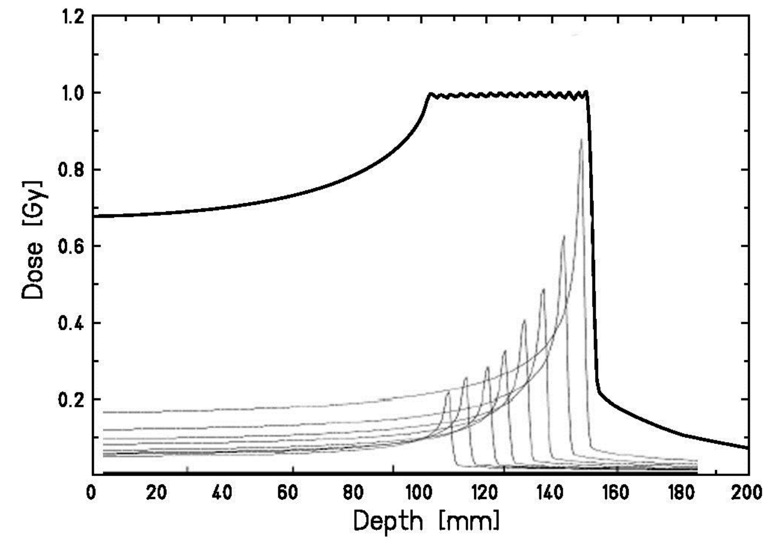
RBE depends on several factors:

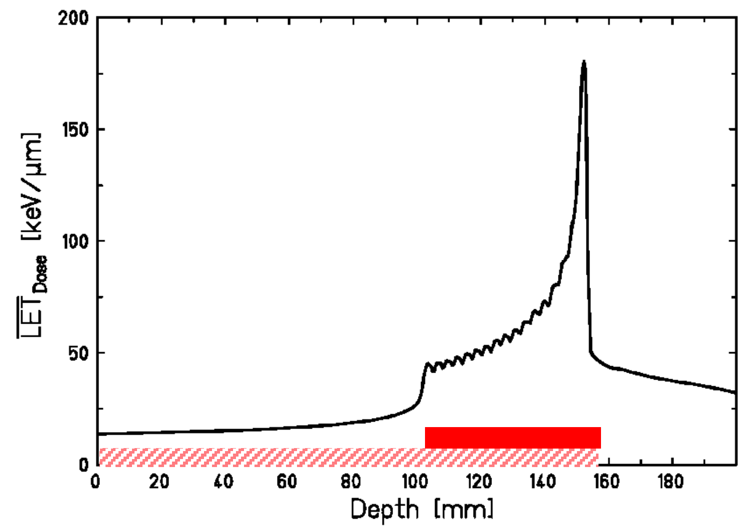
- Particle species / LET
- Dose
- Cell / Tissue type
- Oxygen status
- ...

LET ↔ Depth Dependence of RBE

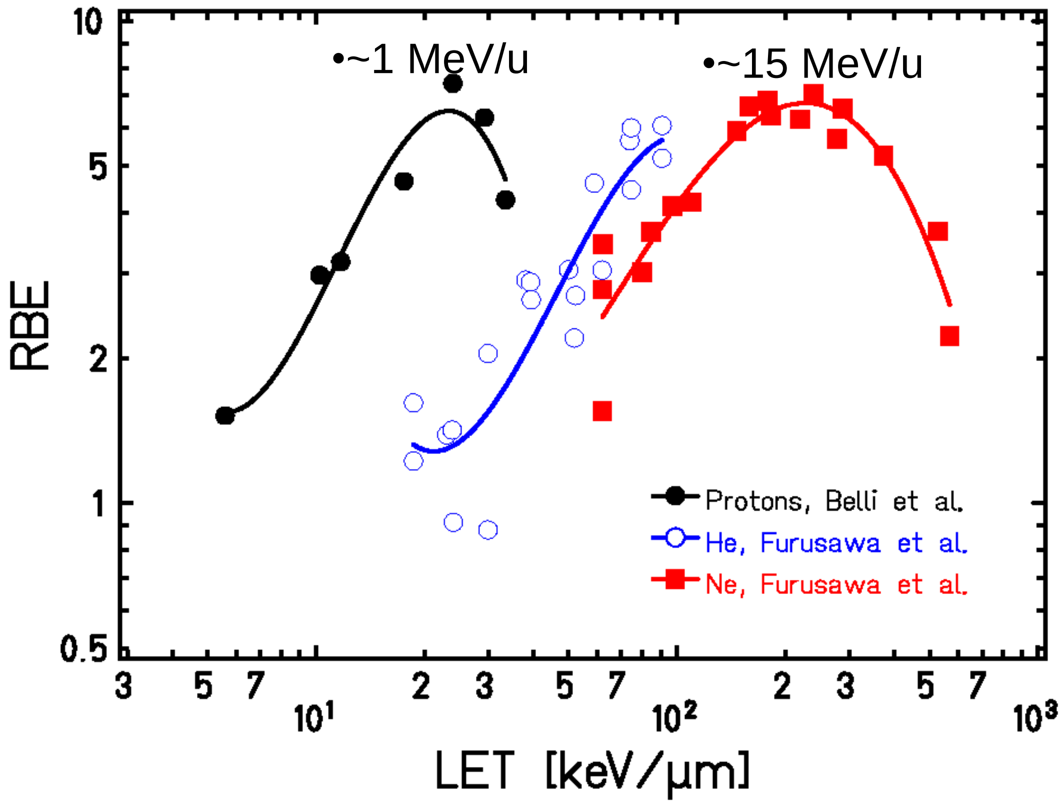


Weyrather et al. IJRB 1999



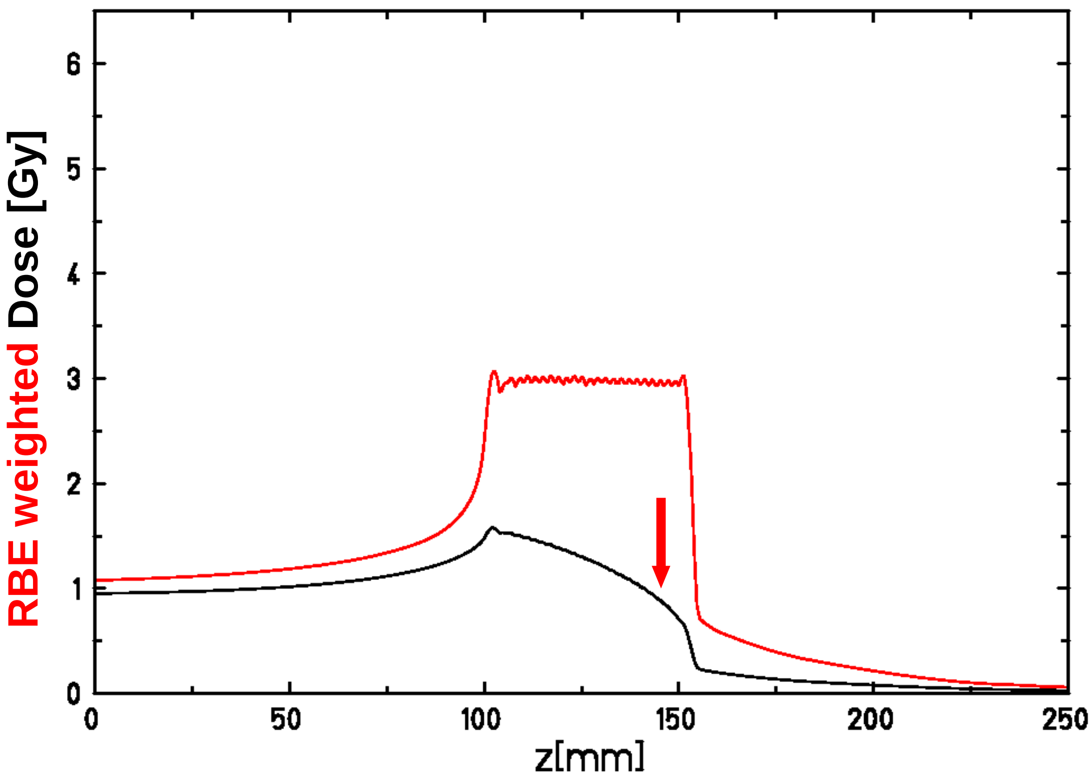


Dependence of RBE on ion species



RBE higher for light as compared to heavier ions at given LET

Depth Dependence of RBE



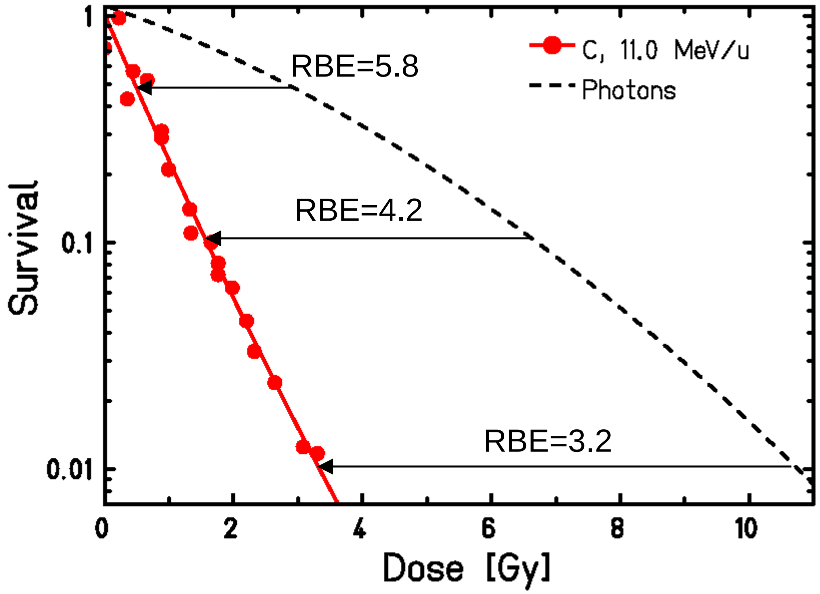
Reduction of dose towards distal peak

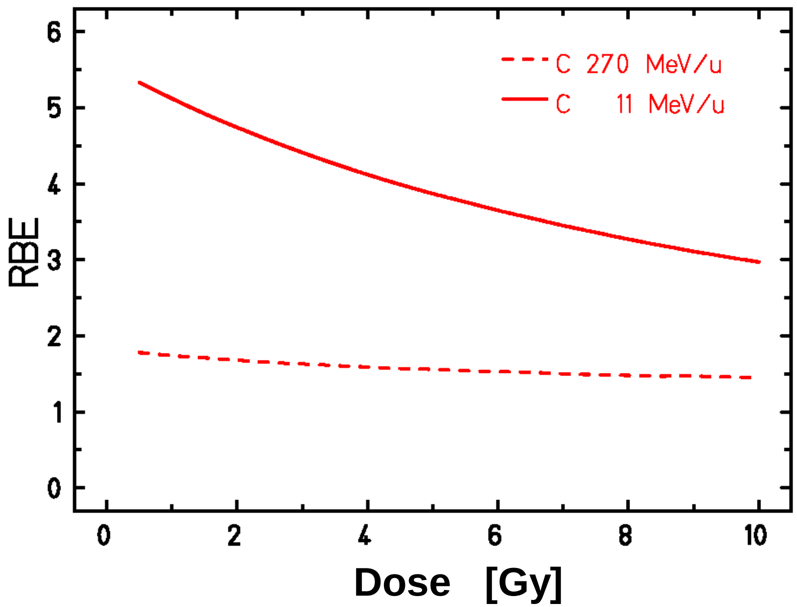
to account for increase of RBE

Dose Dependence of RBE

In-vitro:

Cell survival / CHO-cells

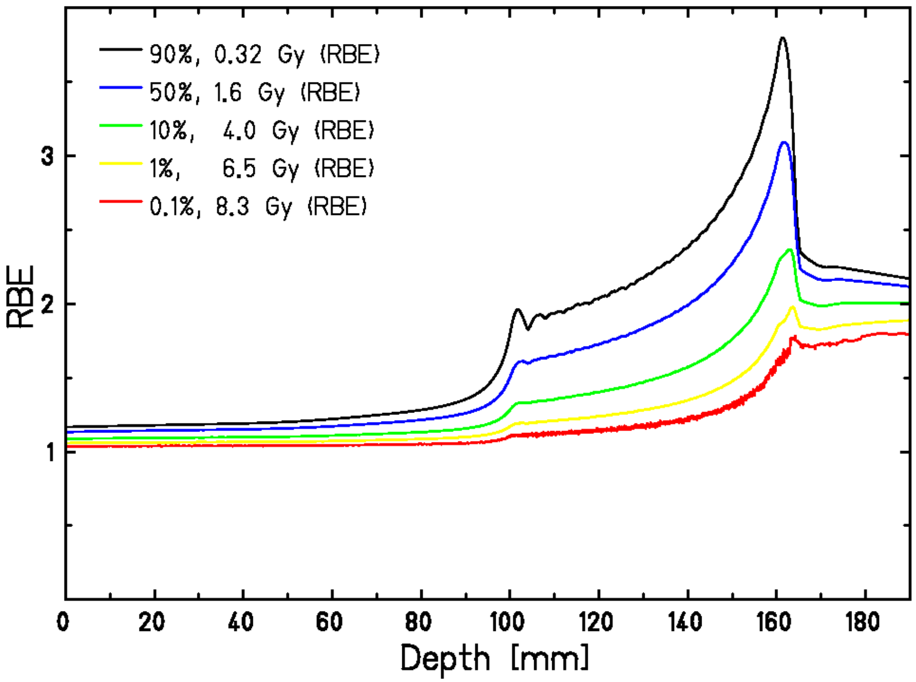


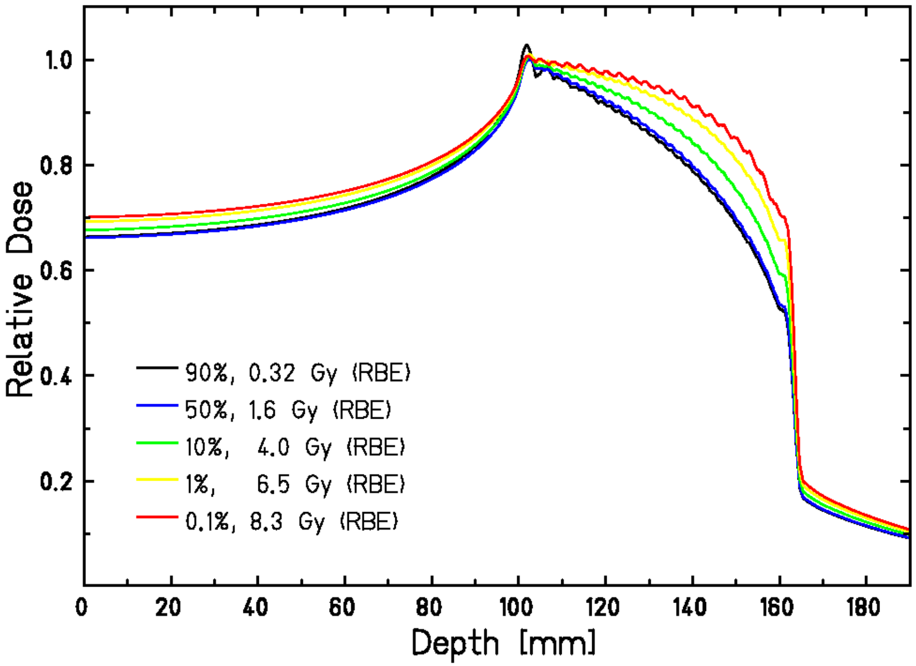


Weyrather et al., IJRB 1999

➡ RBE decreases with Dose

Dependence of RBE on Effect Level



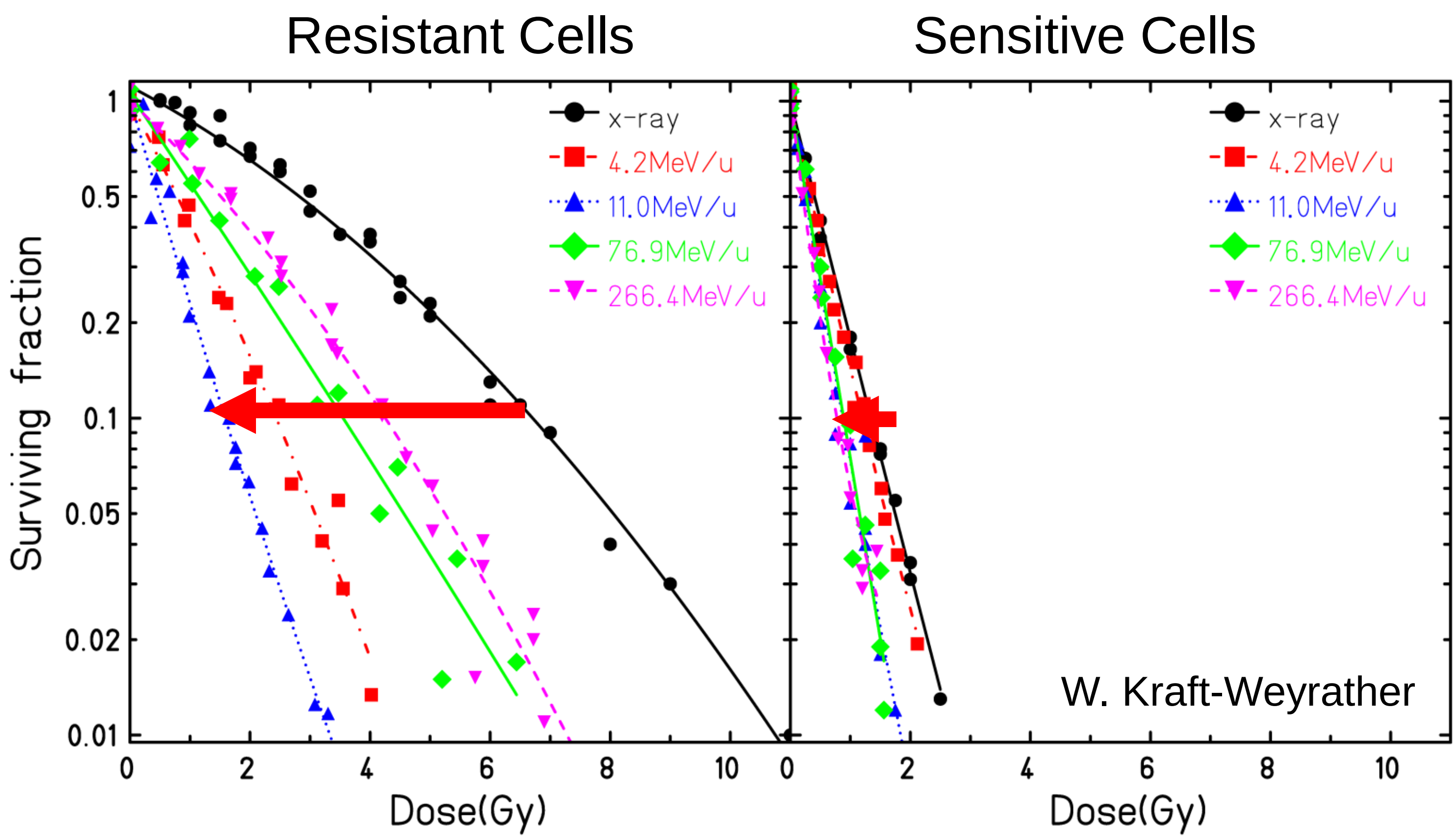


Endpoint: HSG cell survival in-vitro

➡ Shape depends on effect level

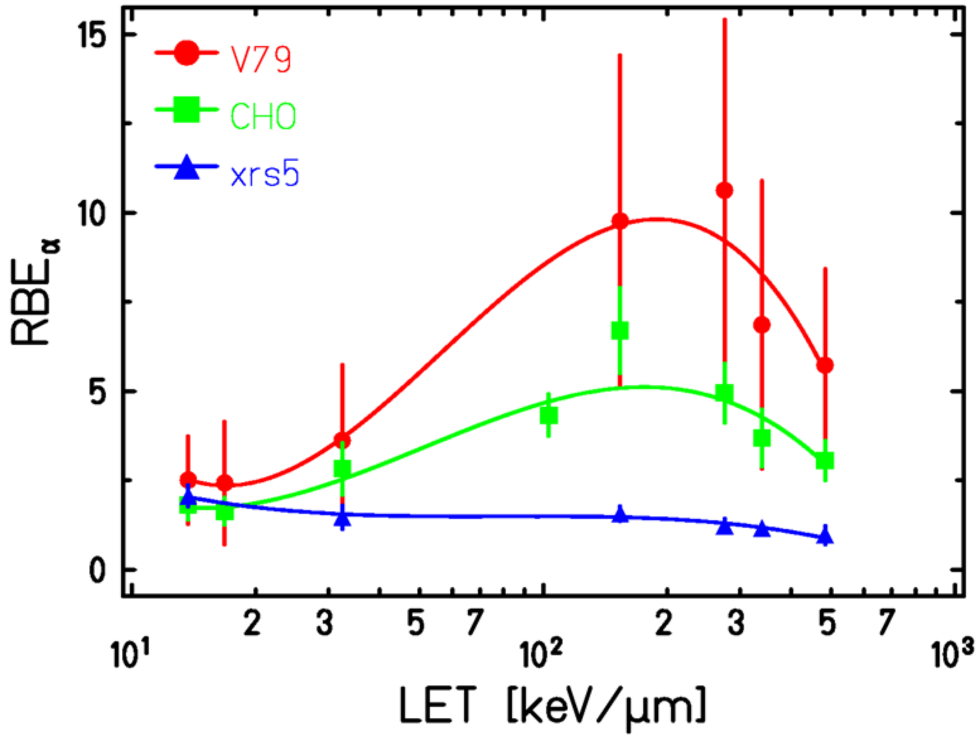
➡ Relevant for hypofractionation

Cell type dependence of RBE I



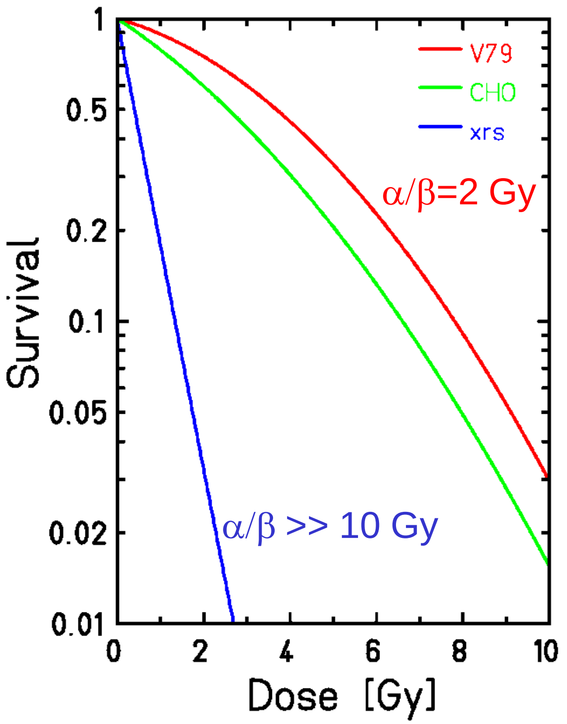
Increase of RBE more pronounced for resistant cells as compared to sensitive cells

Cell type dependence of RBE II



Weyrather et al. IJRB 1999

Photons



RBE is correlated with repair capacity

(In terms of LQ-model: with $(\alpha/\beta)_{\mathrm{Photon}}$-ratio)

Treatment planning for carbon ions

Complex RBE dependencies: E, LET, D, cell type,…

Interpolation/extrapolation required for treatment planning in HI therapy

HIMAC	GSI / HIT
Experimental Data + Clinical Neutron Experience (‚Fixed' RBE-scheme)	Biophysical Modelling (Local Effect Model LEM) (Variable RBE-scheme)

HIMAC - Approach

In-vitro Experiments
(Monoenergetic, high-LET)
$\alpha_{Carbon}(x), \beta_{Carbon}(x)$

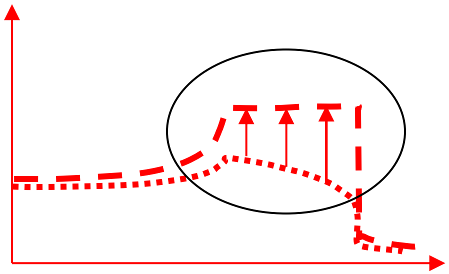
↓

Algorithm:
Dose Weighted Average
$\alpha_{Mix} = \sum f_i \alpha_i \qquad \sqrt{\beta_{Mix}} = \sum f_i \sqrt{\beta_i}$

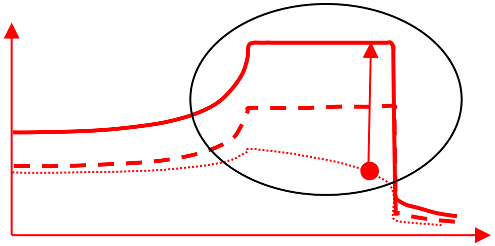
↓

Relative Shape of
Depth Dose Distribution

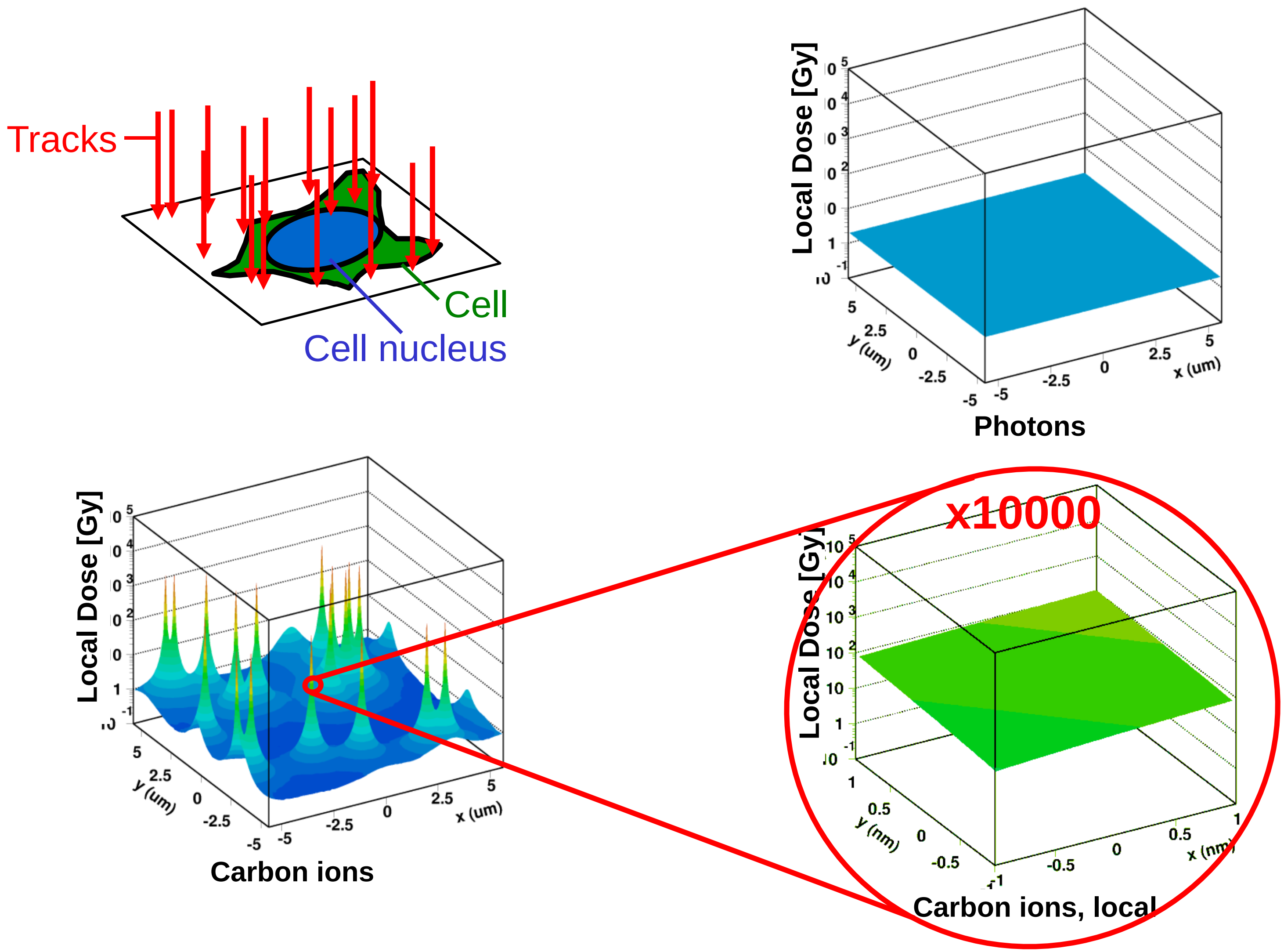
Absolute RBE:
Clinical Neutron Experience



Treatment Planning



GSI Approach: Basics of Modelling

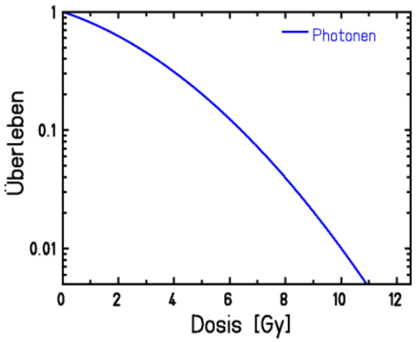


GSI Approach: Local Effect Model LEM

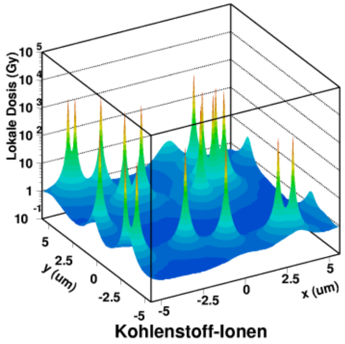
<u>Basic Assumption</u>:

Increased effectiveness of particle radiation can be described by a combination of the photon dose response and microscopic dose distribution

Local Effect (Photons) = Local Effect (Ions)



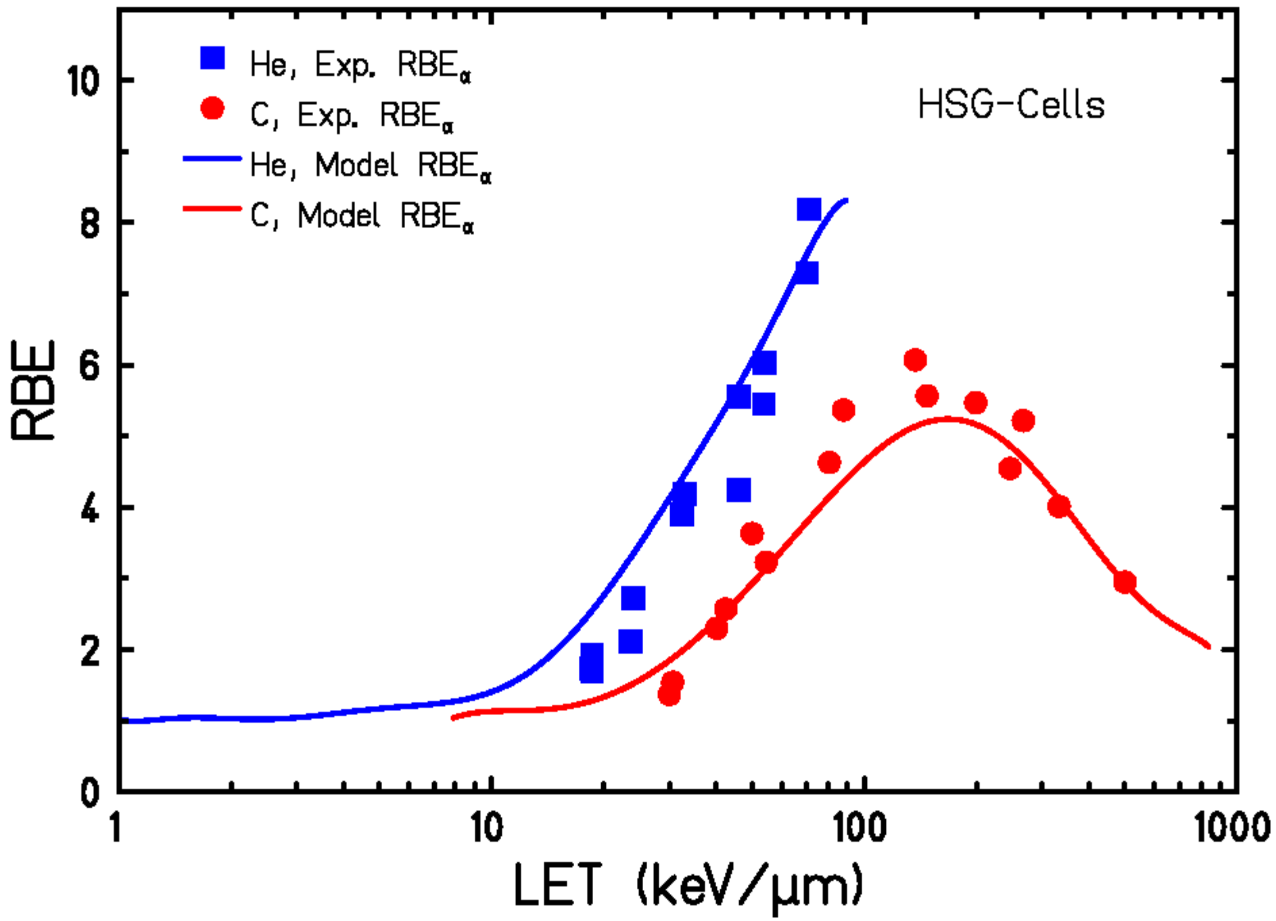
+



→ RBE !

LEM: Transfer of low-LET experience to high-LET

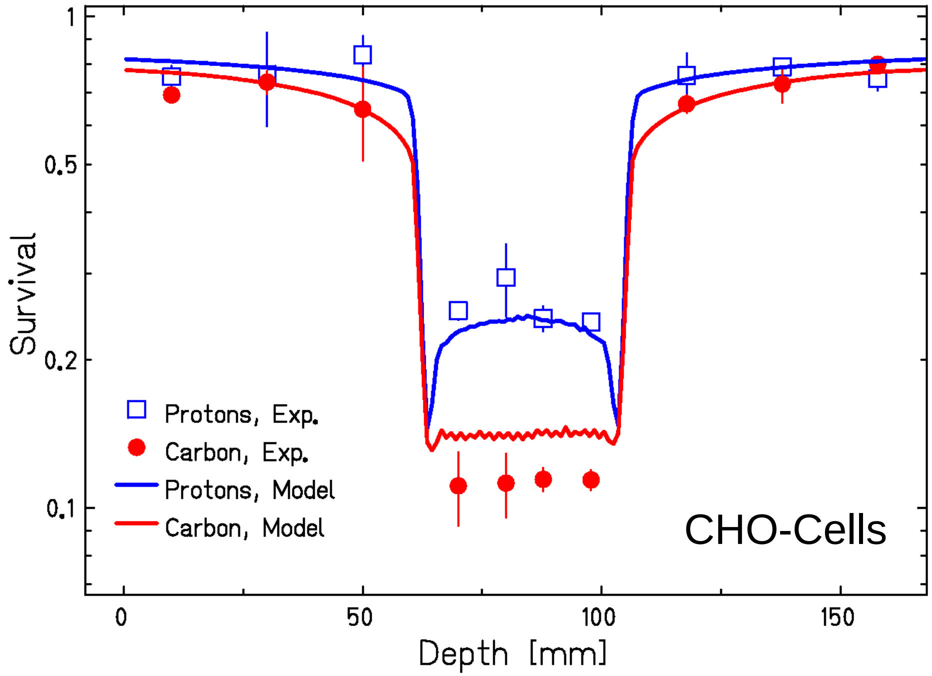
Comparison LEM IV – Experimental Data



Carbon ions vs. protons

First radiobiology experiments at HIT facility:

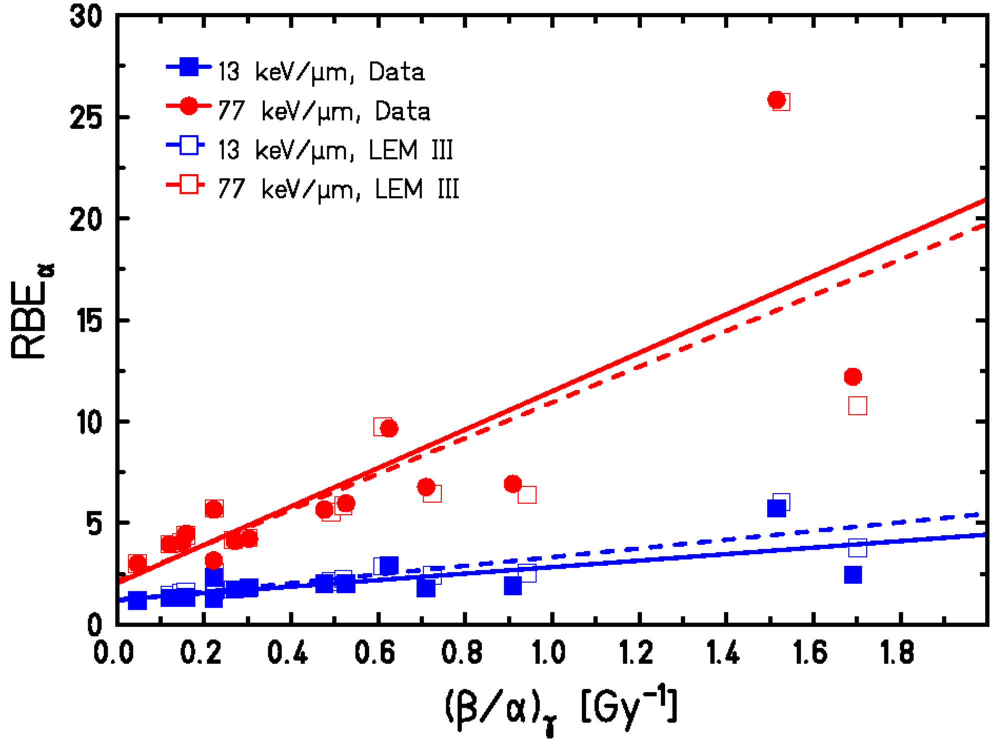
➡ Direct comparison of protons and carbon ions

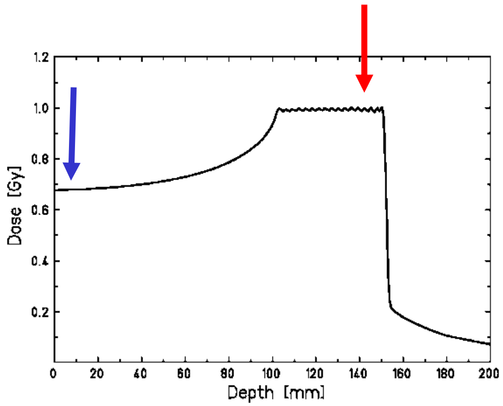


Experimental data: Weyrather et al.

Model: LEM IV (Elsässer et al, IJROBP 2010)

Cell type dependence: transfer to *in-vivo*





Experimental Data: Suzuki et al., *IJROBP* 2000
LEM III: Elsässer et al., IJROBP 2008

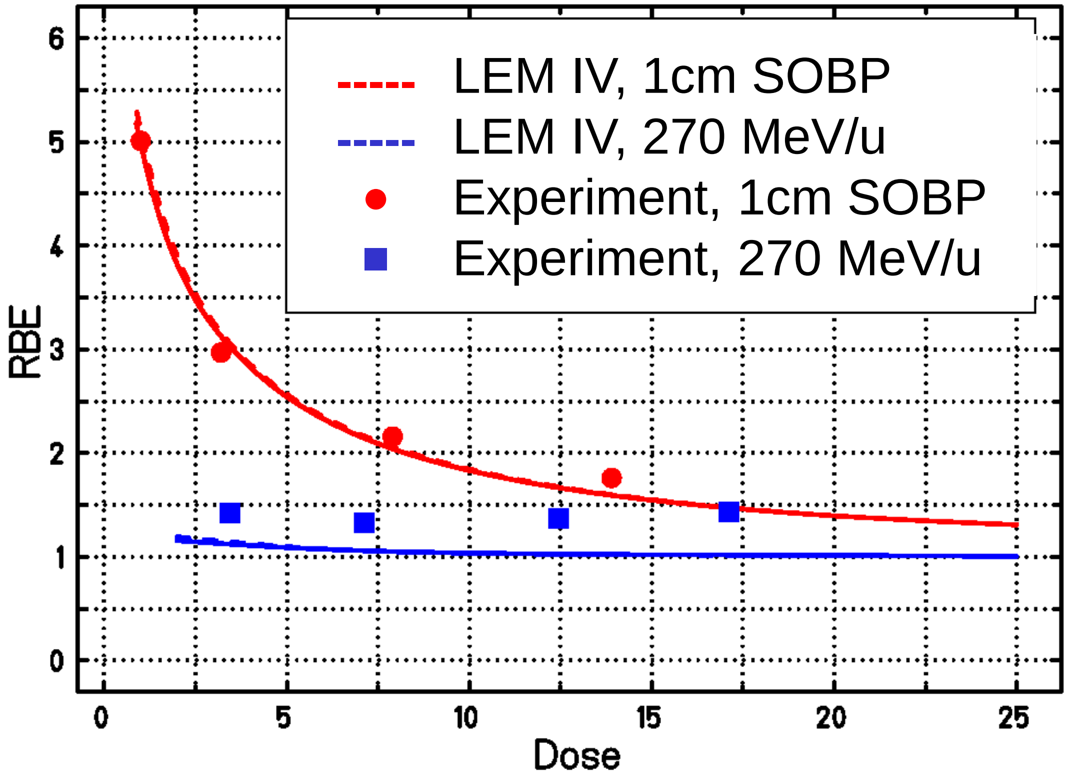
RBE increases with increasing $(\beta/\alpha)_\gamma$-ratio

Assumption for application in-vivo:

$$\mathrm{RBE}(\beta/\alpha)_{\textit{in-vitro}} = \mathrm{RBE}(\beta/\alpha)_{\textit{in-vivo}}$$

Comparison LEM – Experimental Data

In-vivo: Tolerance of Rat Spinal Cord



Exp. Data: Karger et al. IJROBP 2006

LEM IV: Elsässer et al., *IJROBP* 2010

Influence of Tissue Composition

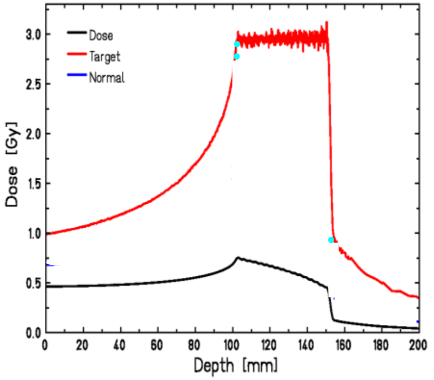
Tumor

Normal 1

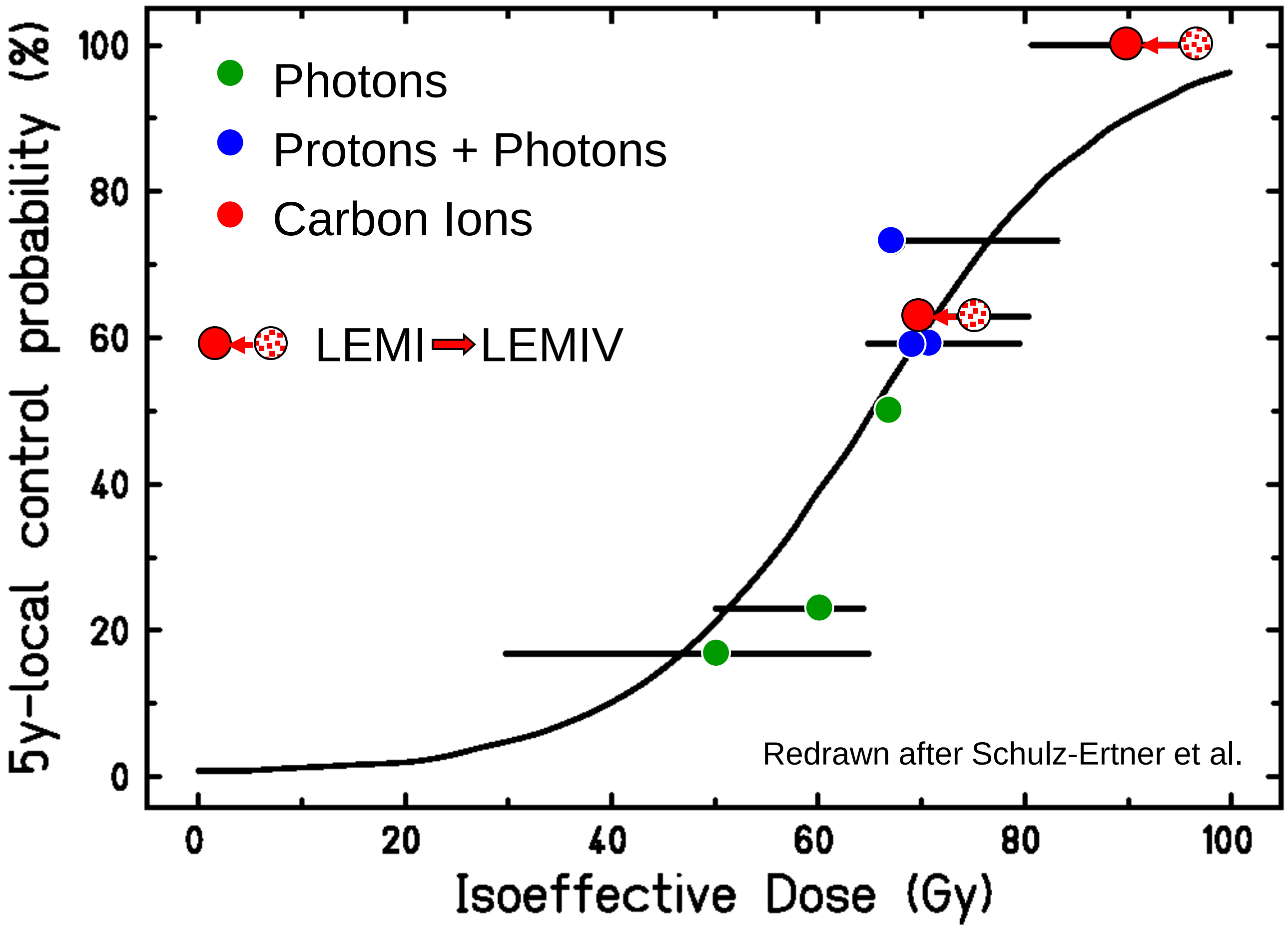
Normal 2

Normal 3

Tissue dependence of RBE might lead to discontinuities of the RBE-weighted dose distribution!

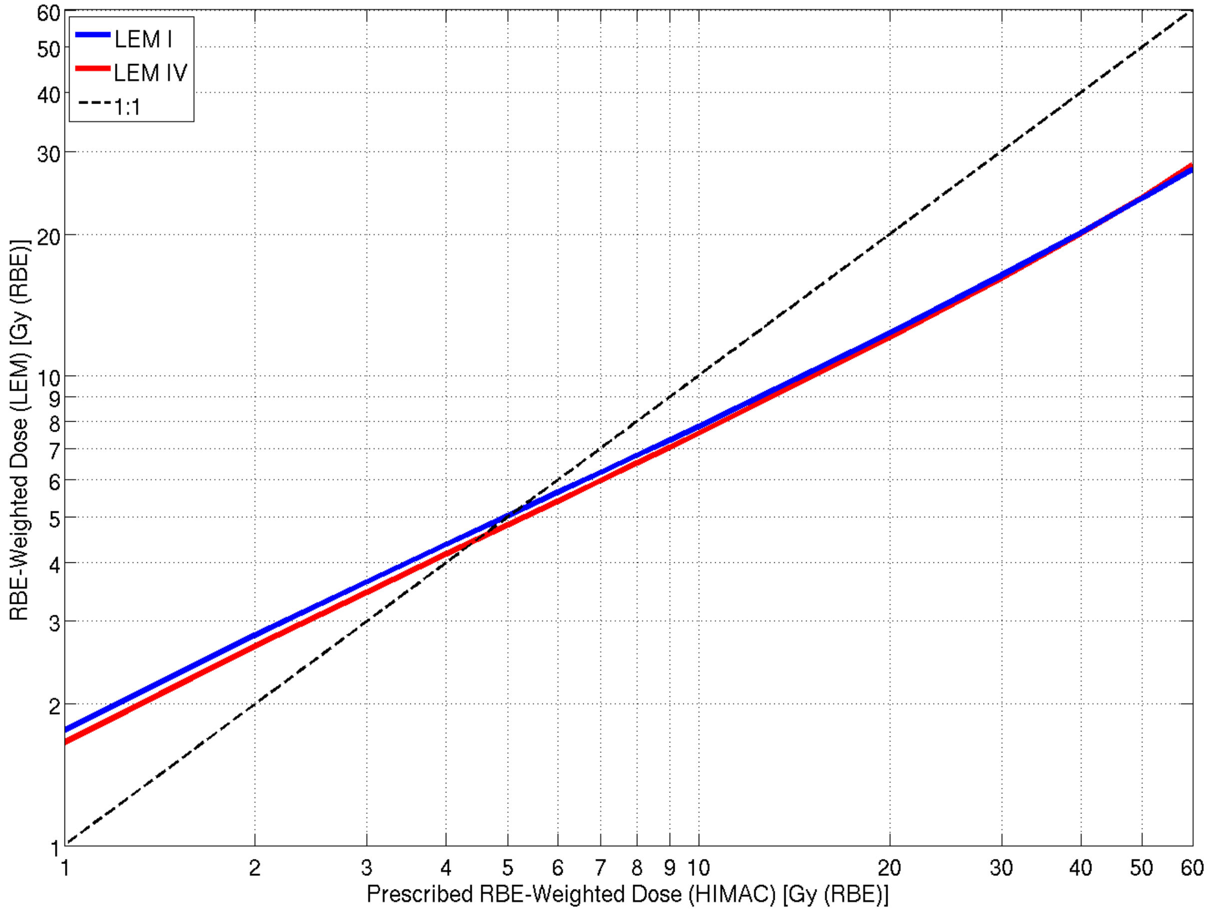


Comparison with clinical data: tumor control



R. Grün et al., PMB 2012

Comparison LEM – HIMAC approach



Comparison

LEM I / LEM IV

Conversion

HIMAC based

RBE-weighted dose

vs.

LEM based

RBE-weighted dose

O. Steinsträter et al., IJROBP 2012

Summary

- RBE depends on position in SOBP, dose level and biological system
- Interpolation / extrapolation of experimental data and/or modelling are required to represent these dependencies in treatment planning
- LEM has been implemented in the TRiP treatment planning environment for the GSI pilot project and in the Siemens TPS
- Consideration of dose dependent and tissue specific RBE values is crucial e.g. for hypofractionation studies
- Differences between HIMAC and GSI/HIT approach need to be taken into account when interpreting RBE-weighted dose values