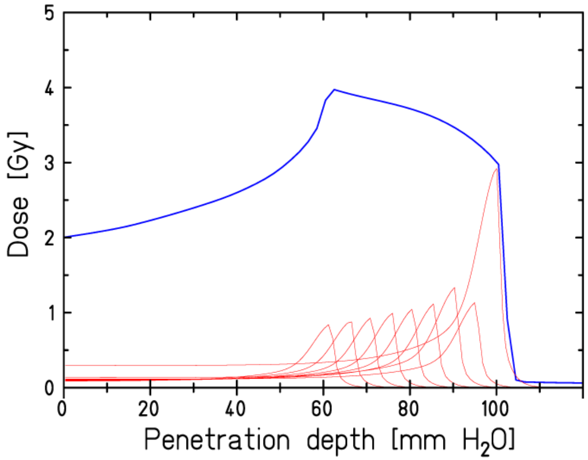
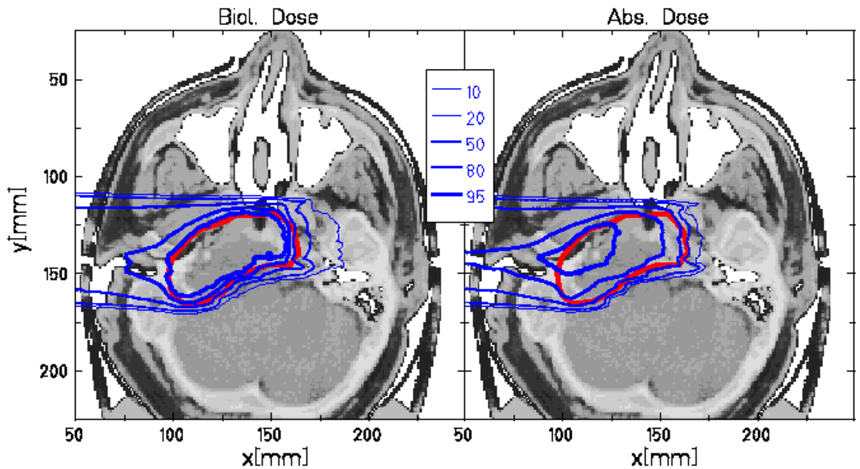
Radiobiological aspects of ion beams

Thilo Elsässer
GSI Darmstadt





Menu

- Motivation
- Relative Biological Effectiveness (RBE)
- Dependencies of RBE – Experimental Results
- Biophysical Modelling for Heavy Ion Treatment Planning
- Application to experimental data
- Consequences for Carbon Ion Therapy

Introduction

Advantage of ion beams for therapy:

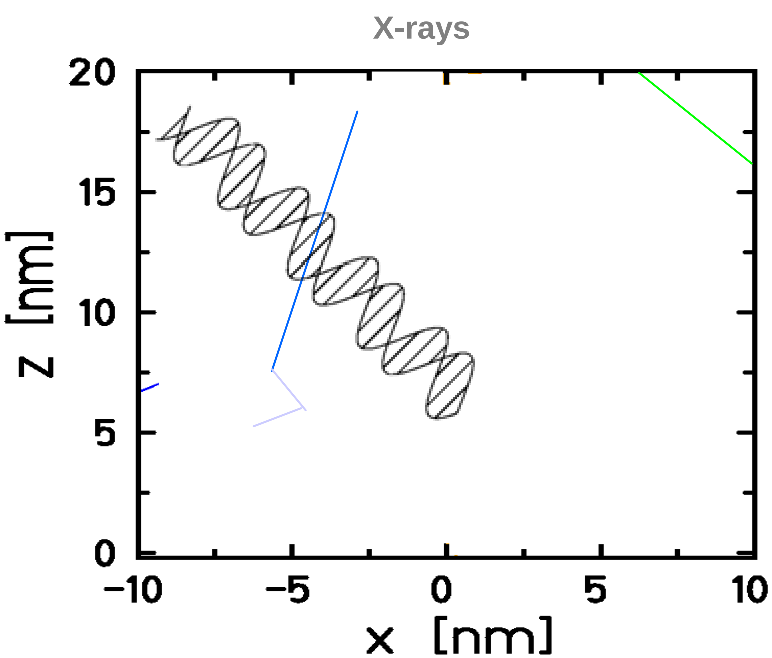
Physical aspects:

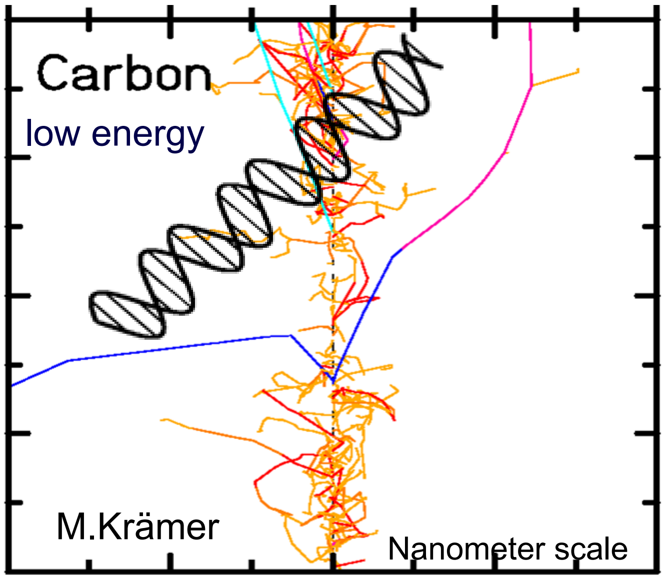
- Inverted depth dose profile
- Defined penetration depth
- Reduced lateral scattering

Biological aspects:

- Increased effectiveness
- Reduced oxygen effect

Radiation damage by heavy ions



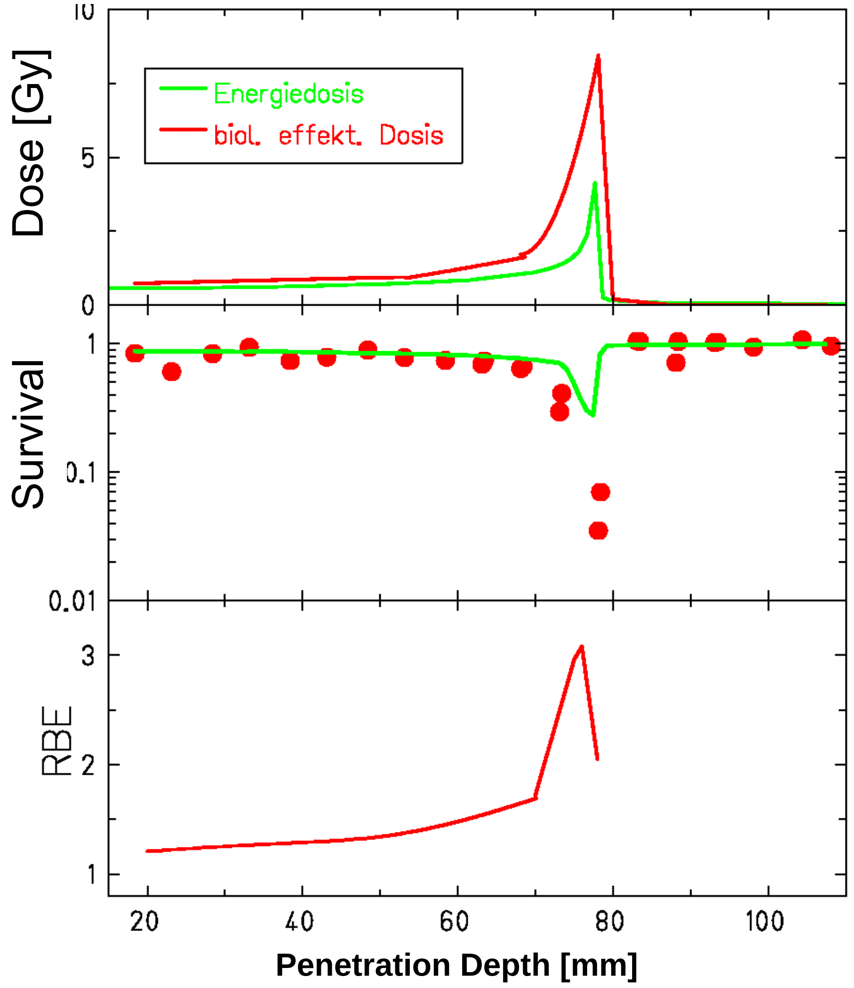


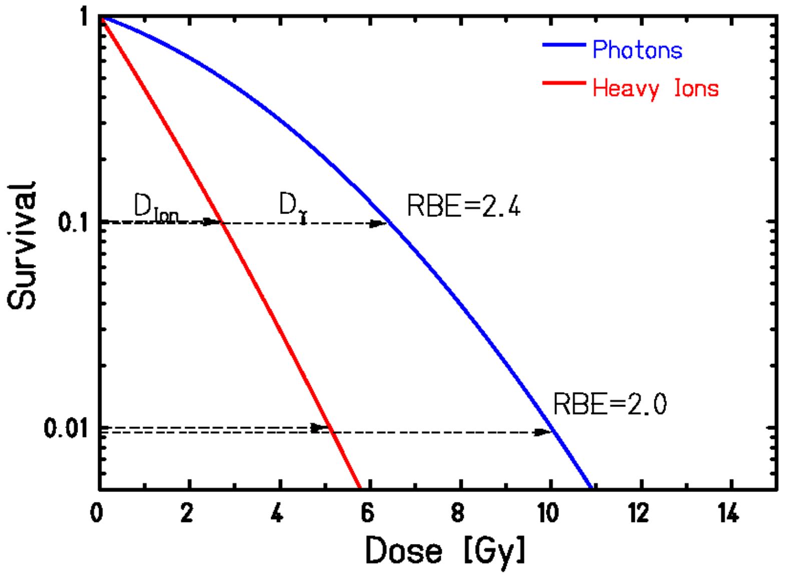
simple damage due to "homogenous" energy distribution

complex damage due to localized energy deposition

Relative Biological Effectiveness (RBE)

Carbon 195 MeV/u





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

Challenge

Challenge:

Homogenous distribution of effective dose in target volume

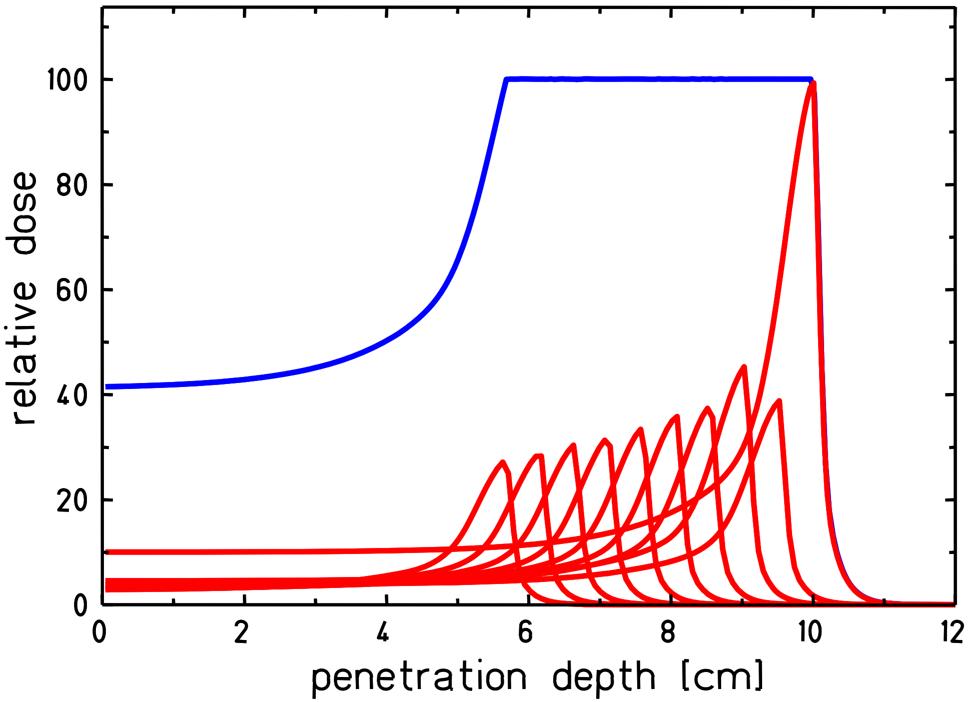
$$D_{eff} = D_{Phys} \cdot RBE$$

RBE depends on several factors:

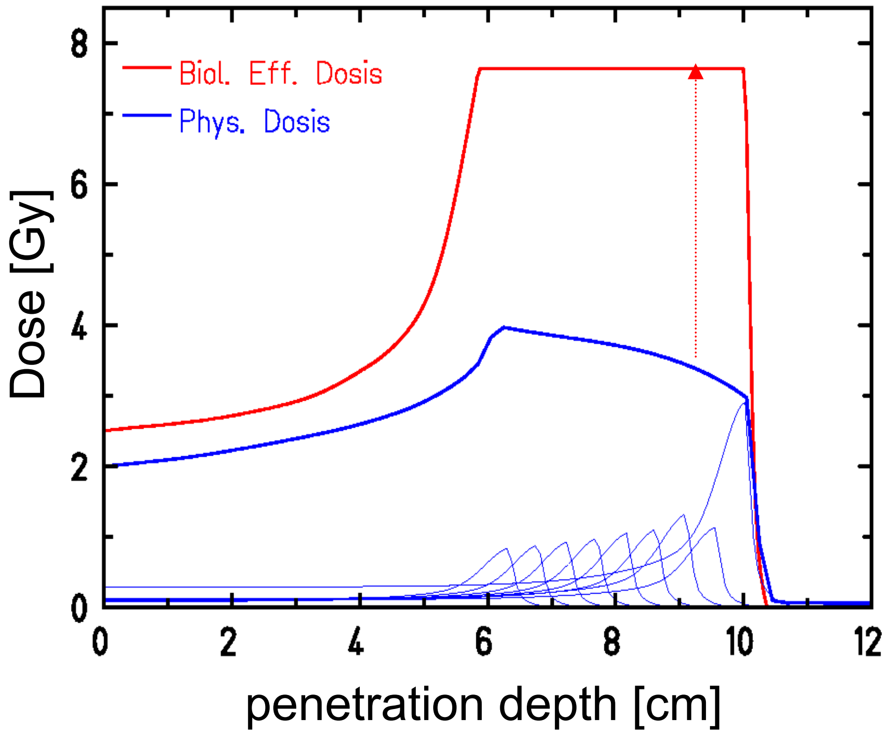
- Particle species
- Energy/ LET
- Cell / Tissue type
- Dose
- Oxygen status
- ...

Spread out Bragg peak

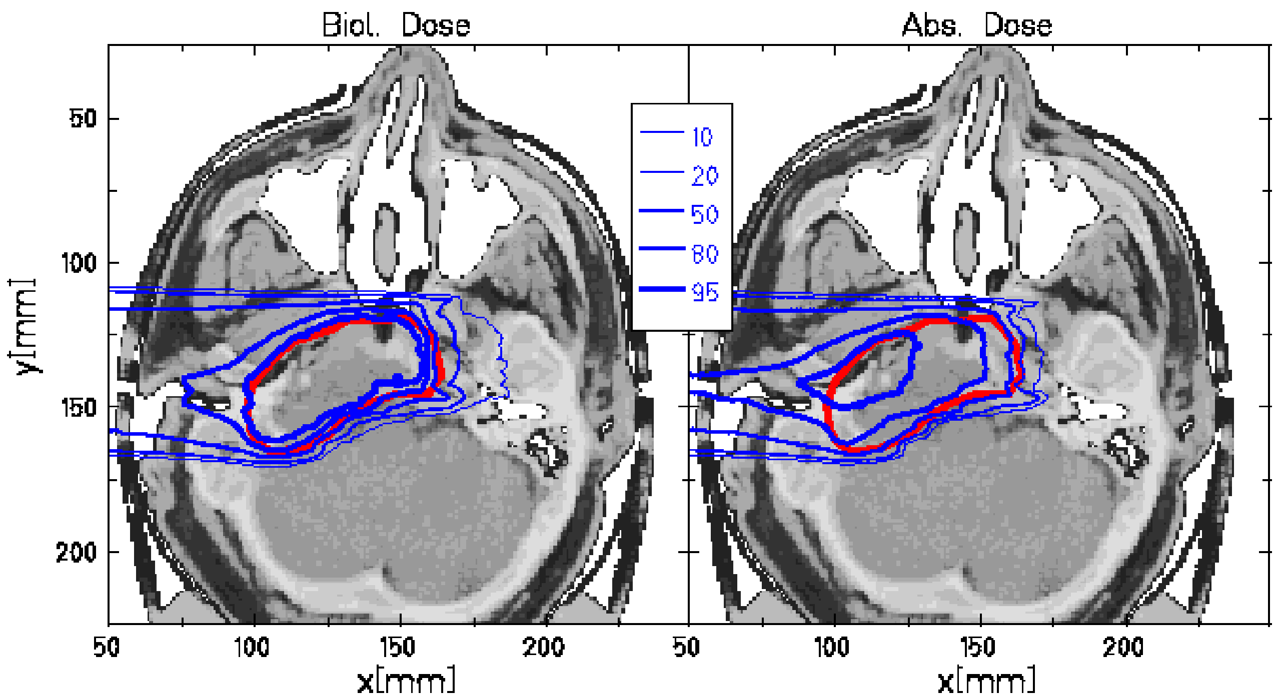
Physical Optimization

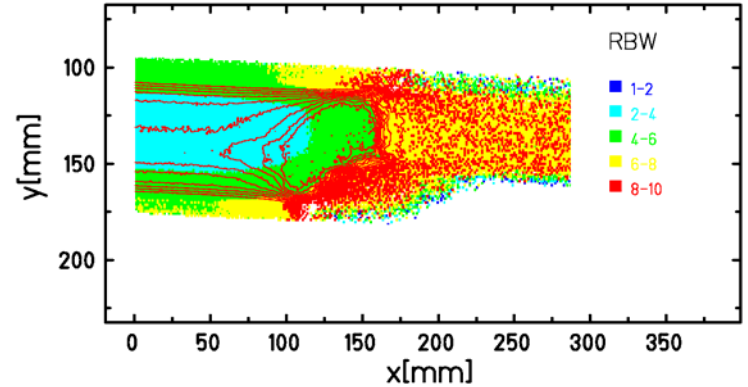


Biological Optimization



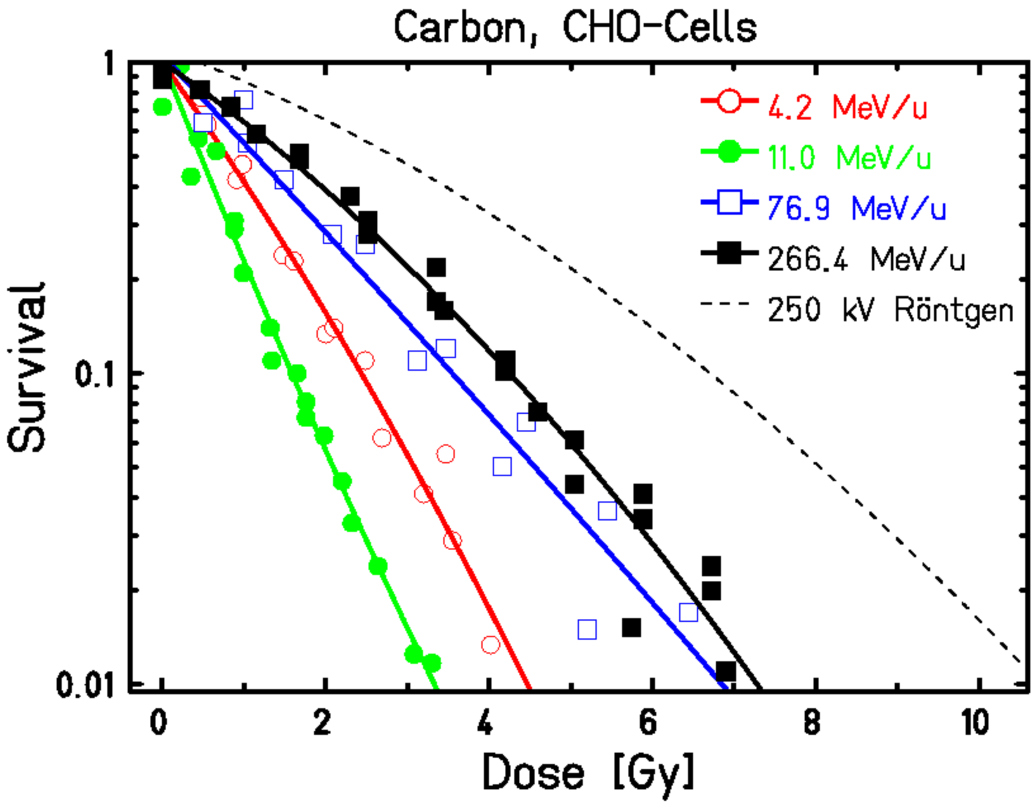
Increased biological effectiveness





Krämer et al.

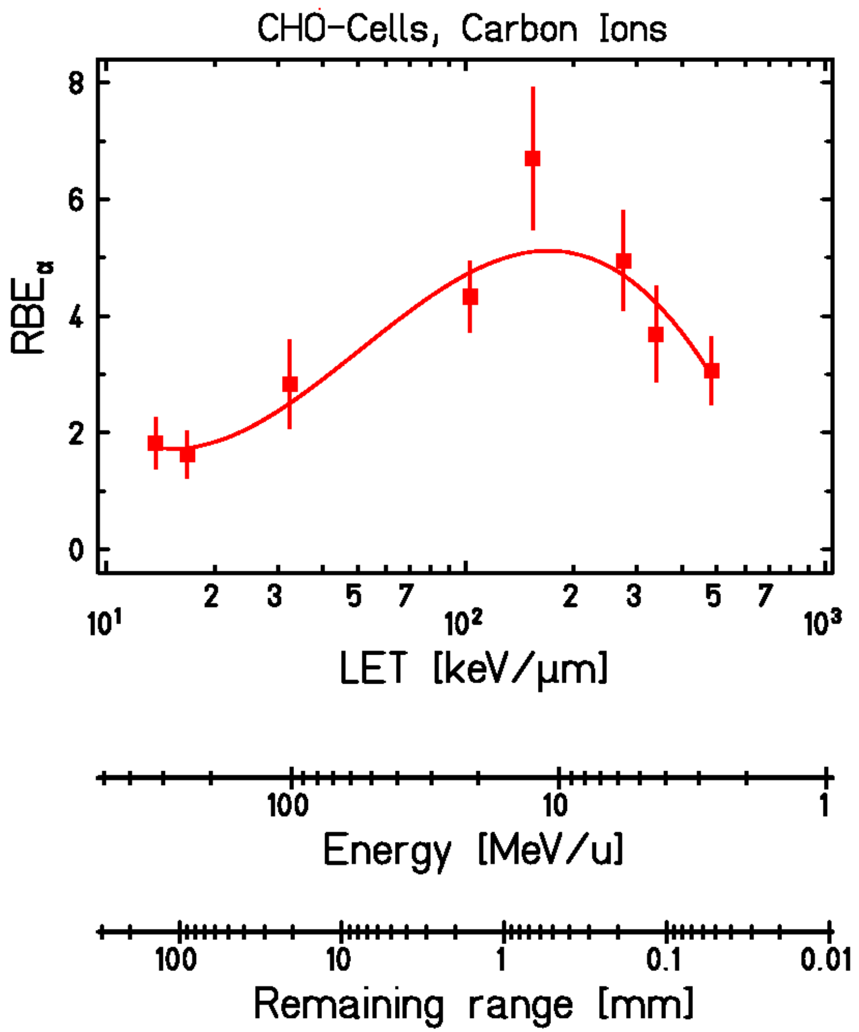
Systematic of RBE: Survival curves



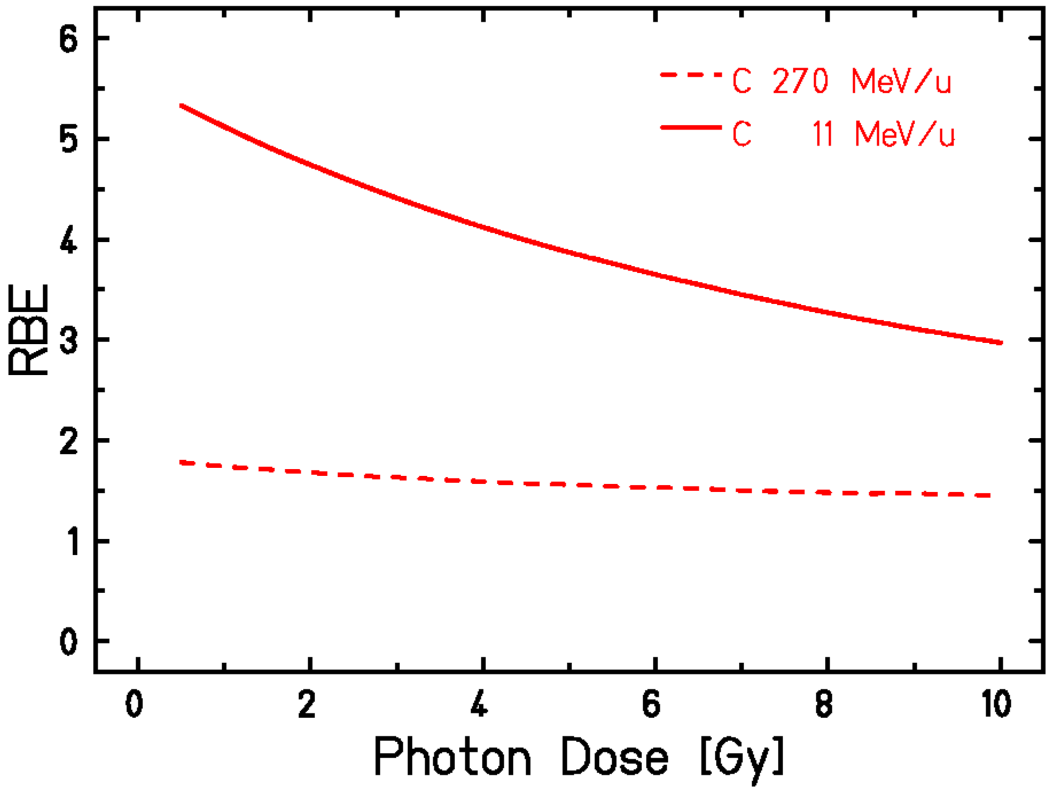
Weyrather et al.
IJRB 1999

- Increasing effectiveness with decreasing energy
- Saturation effects at very low energies (<10 MeV/u)
- Transition from shouldered to straight survival curves

RBE depends on LET



RBE depends on **Dose**

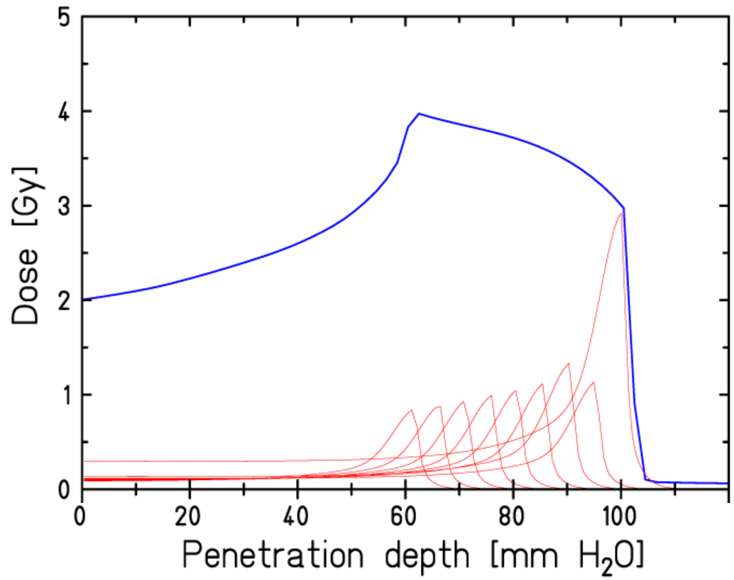


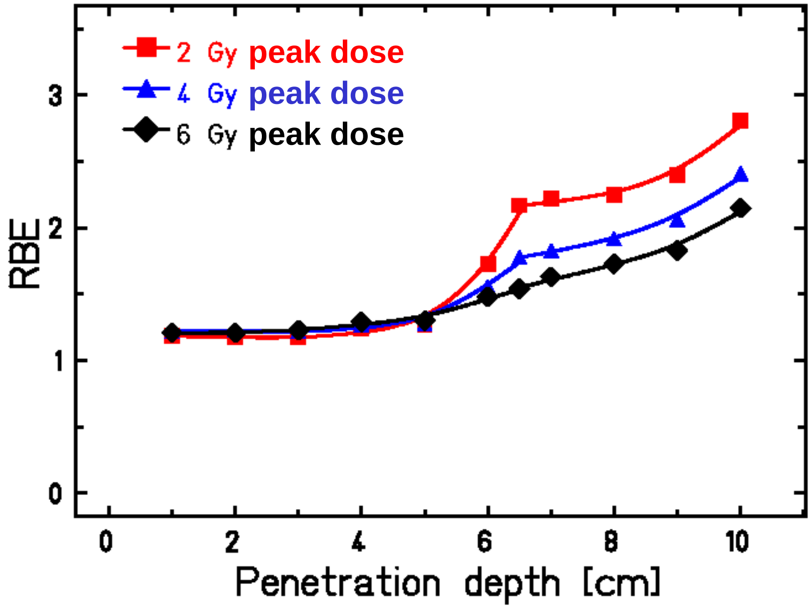
Weyrather et al.

- RBE decreases with dose
- Dose dependence more pronounced for lower energies

RBE changes with **Depth**

Carbon ion irradiation

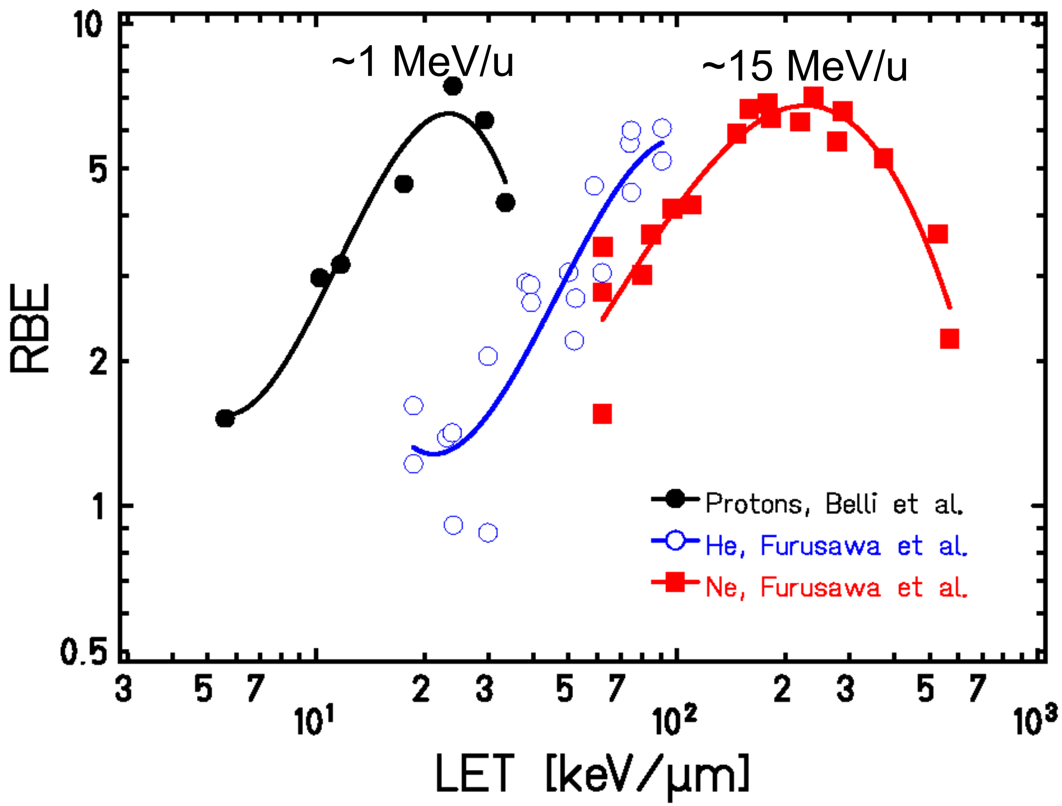




Weyrather et al.

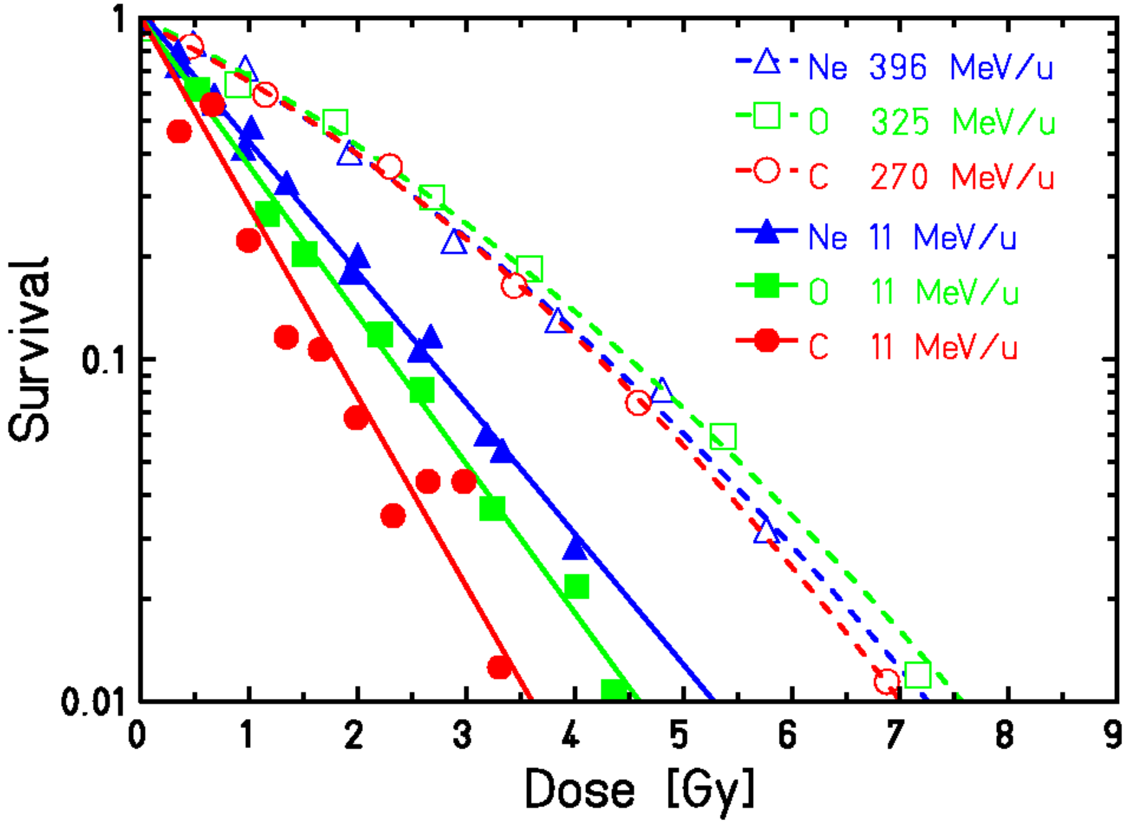
Extended Bragg peak / SOBP irradiation:
Distal part: mainly Bragg peak ions => high RBE
Proximal part: mix of Bragg peak and higher energies => moderate RBE

RBE depends on **Ion Species**



- RBE maximum is shifted to higher LET for heavier particles
- The shift corresponds to a shift to higher energies

Optimal Ion Species

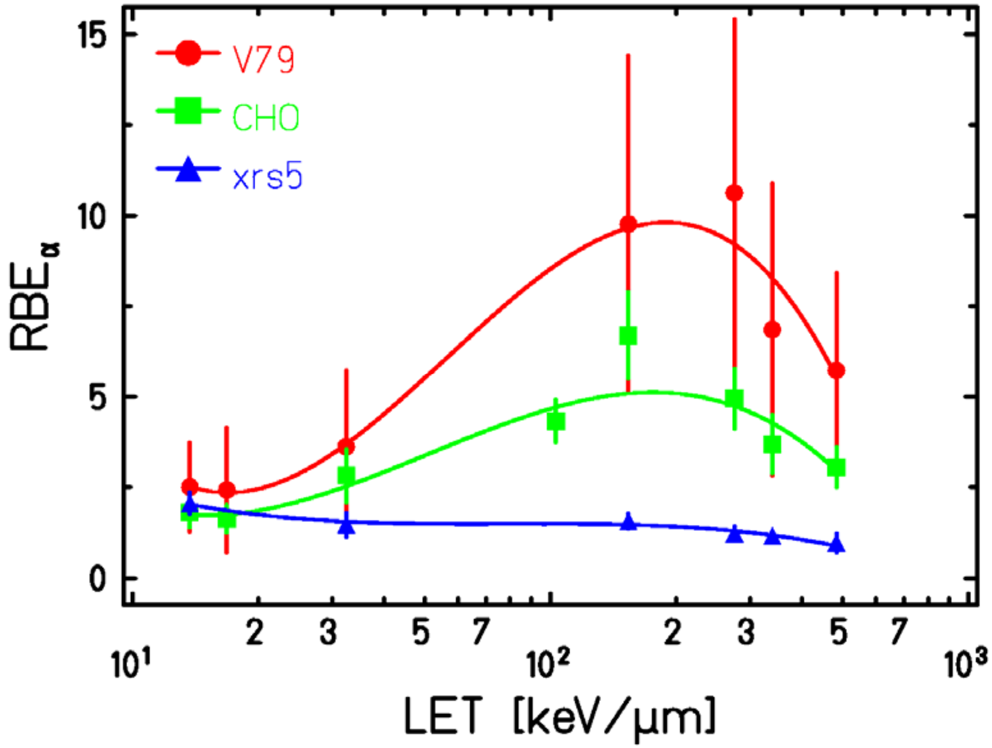


Weyrather et al.

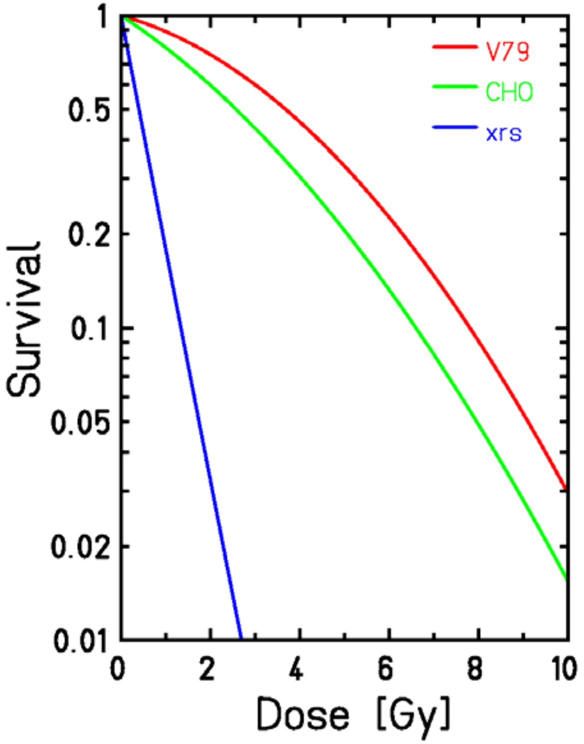
Carbon ions show most pronounced increase of RBE

RBE depends on **Cell / Tissue Type**

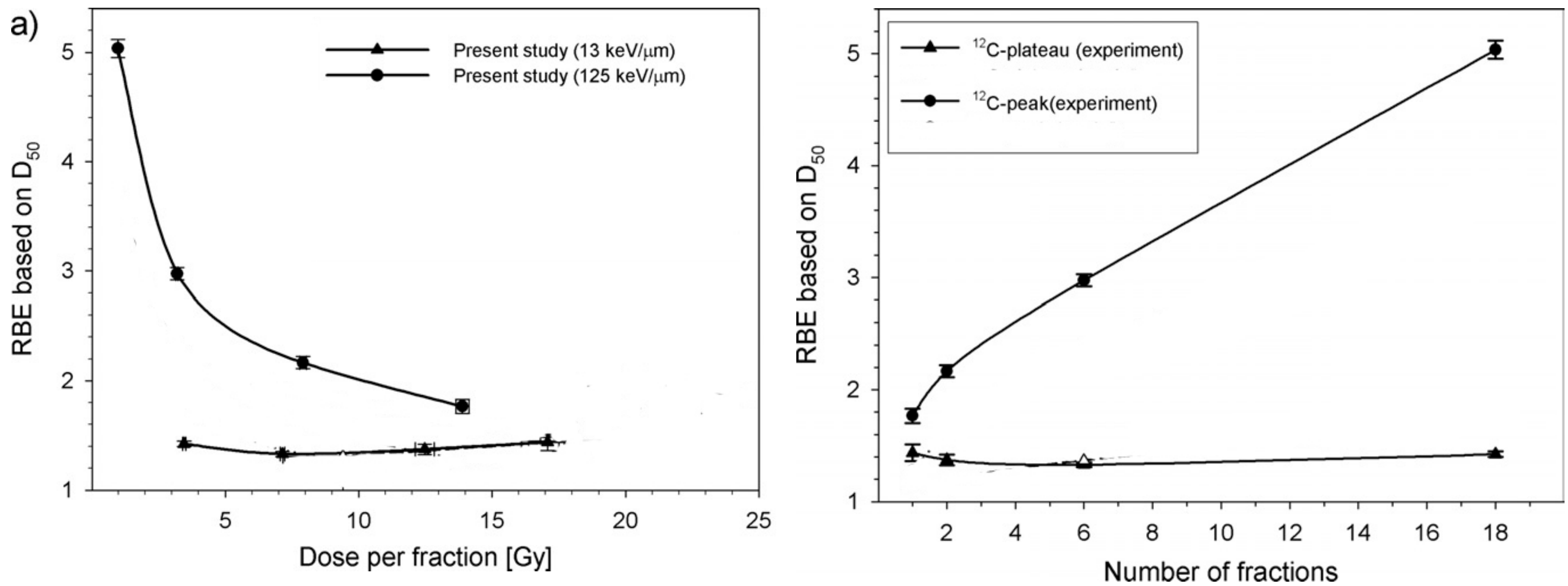
Carbon ions



Photons



In-vivo: Radiation tolerance of rat spinal cord

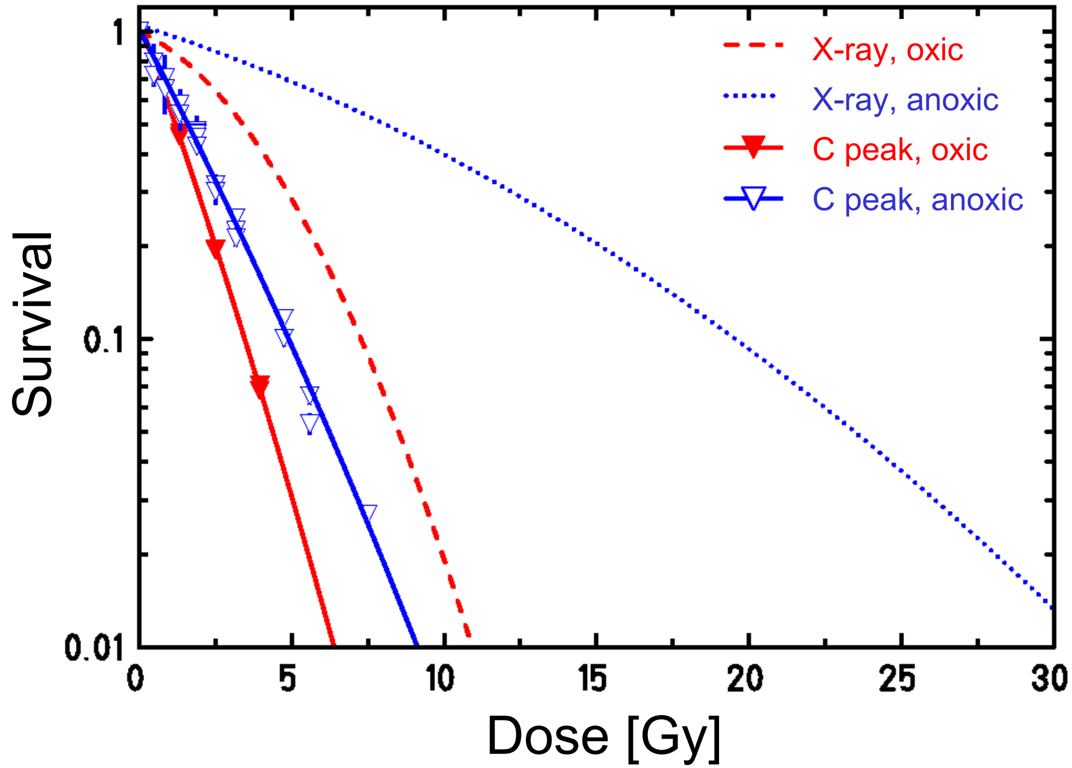


Peak: Mid of 1cm SOBP

Plateau: 270 MeV/u

Karger et al. , IJROBP 2006

RBE depends on **Oxygen status**



Staab et al.
Rad.Res. 2004

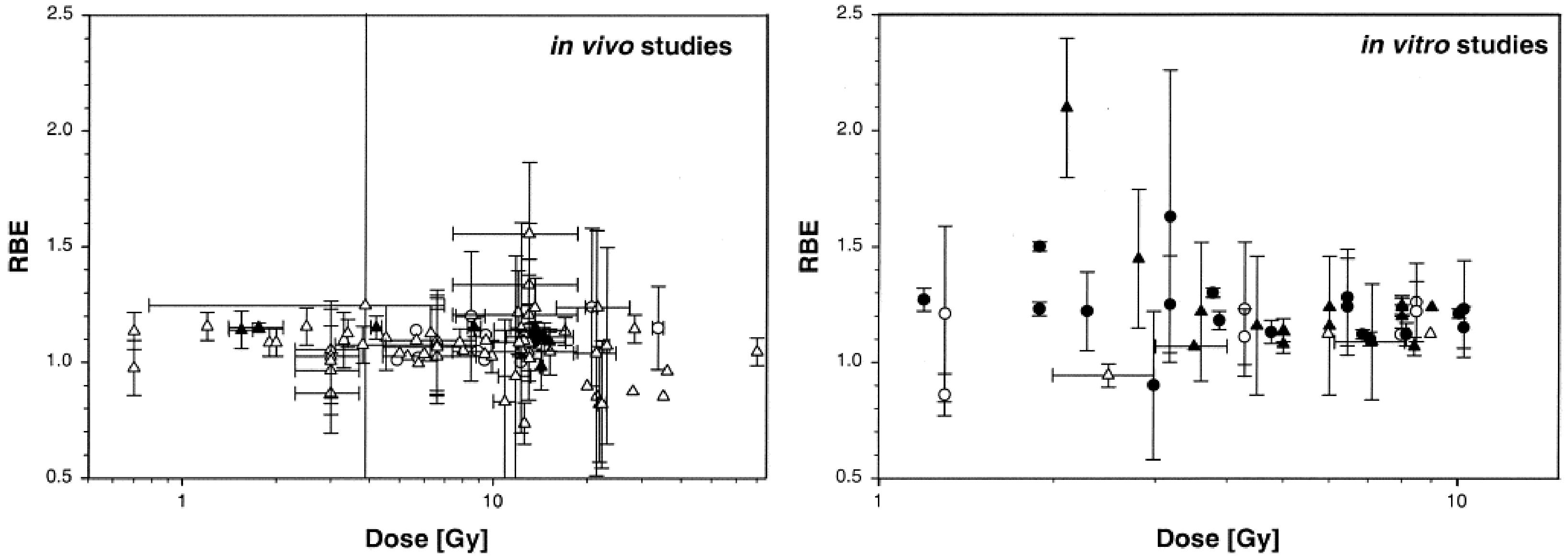
$OER_{XRAY} > OER_{ION}$ → $RBE_{ANOXIC} > RBE_{OXIC}$

How to include RBE in treatment planning?

Protons: RBE ~1.1, independent on position

↓

Simple Dose Scaling $D_{eff}=1.1xD_{Phys}$



Paganetti et al., IJROBP 2002

How to include RBE in treatment planning?

Carbon ions: RBE >>1, $RBE_{peak} \neq RBE_{entrance}$

⬇

Simple Dose Scaling not appropriate!

Treatment planning for carbon ions

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

↓

Interpolation/extrapolation required for treatment planning in HI therapy

↙ ↘

HIMAC

Experimental Data

+ Clinical Neutron Experience

GSI / HIT

Biophysical Modelling

(Local Effect Model LEM)

HIMAC - Approach

In-vitro Survival Experiments
(Monoenergetic carbon ions)
$\alpha_C(x), \beta_C(x)$

↓

Algorithm:
Dose Weighted Average

$\alpha_{Mix} = \sum f_i \alpha_i \qquad \sqrt{\beta_{Mix}} = \sum f_i \sqrt{\beta_i}$

↓

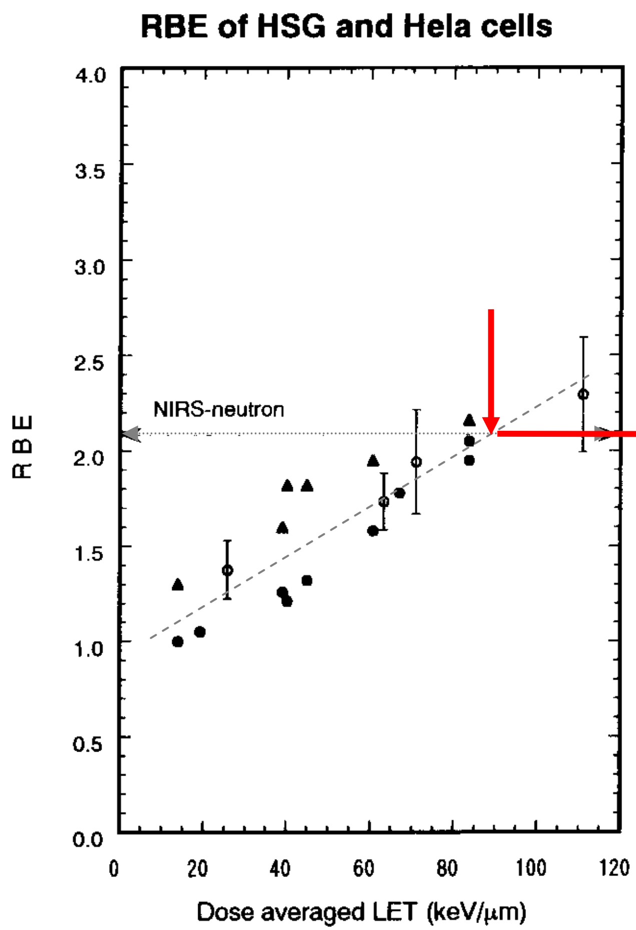
Relative Shape of
Depth Dose Distribution

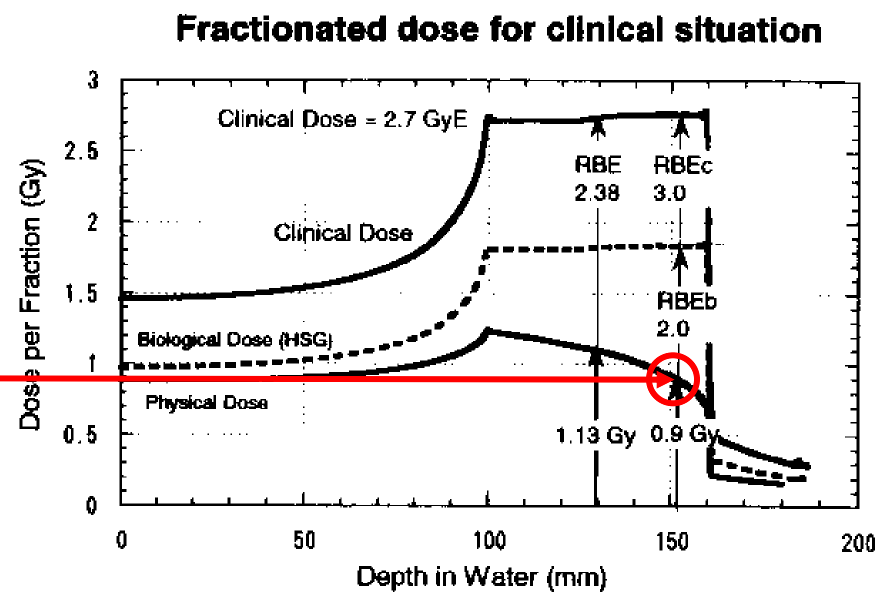
Absolute RBE:
Clinical Neutron Experience

↘ ↙

Treatment Planning

HIMAC Approach:
Link to Clinical Neutron Experience

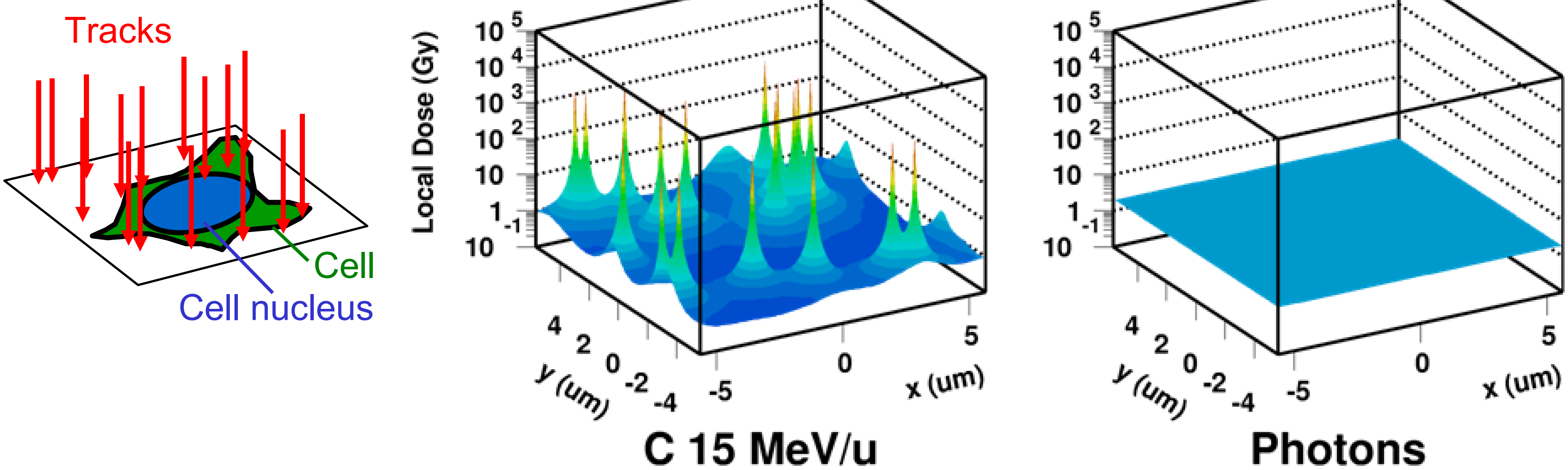




(Kanai et al. 1999)

Main assumption of GSI approach

Same average dose - different local distribution



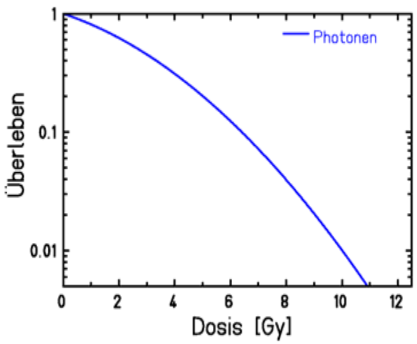
Biological damage is determined by local dose

No qualitative difference since damage is generated by ejected δ-electrons

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)



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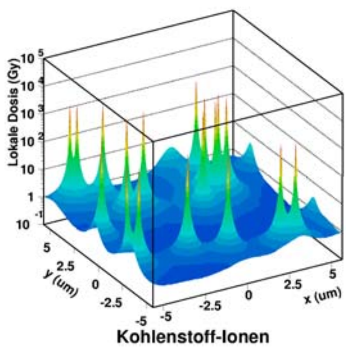
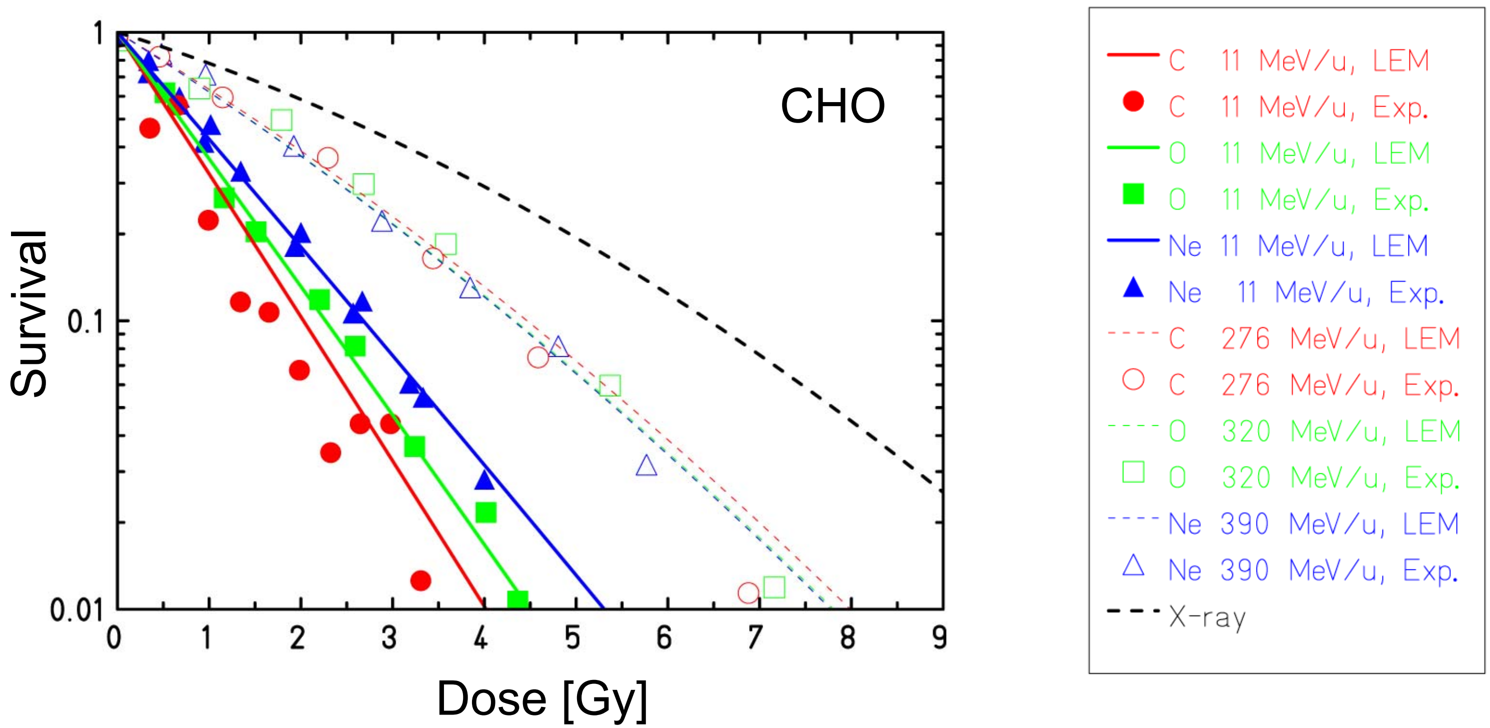


➡ RBE !

Comparison of LEM with exp. data: survival curves



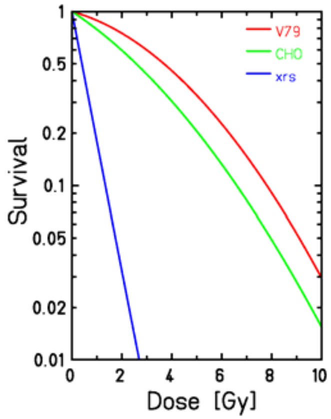
Data: Kraft-Weyrather et al.

Application to Tissue Effects

Tissues show complex response to radiation

Correlation with cell survival?

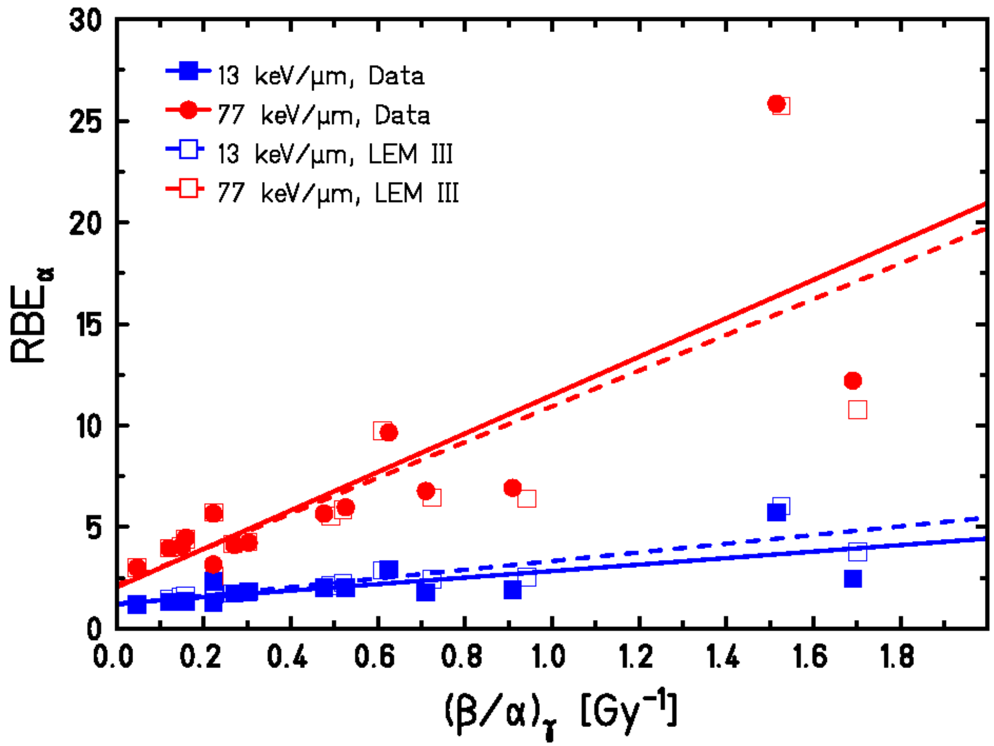
Which parameters of photon dose response define RBE?

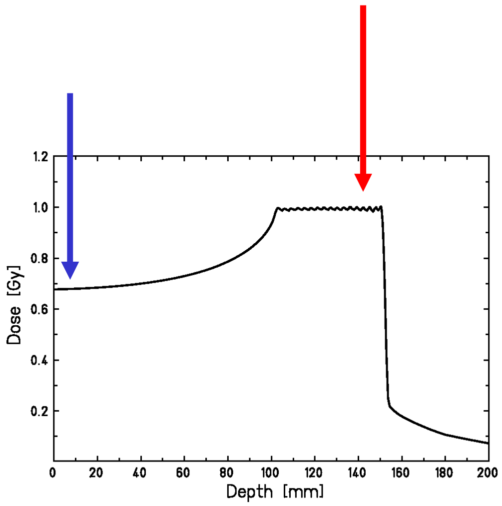


Shoulder width of photon dose response curve

LQ-model: α/β-ratio

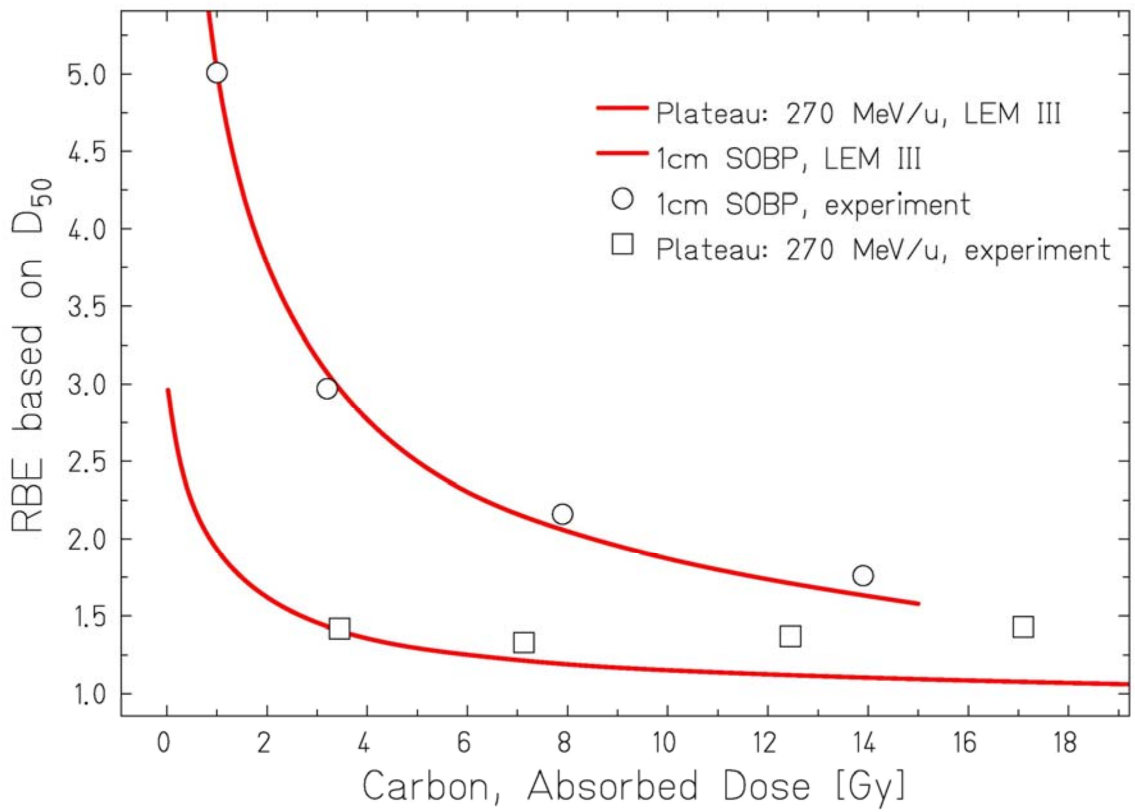
Cell type dependence





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

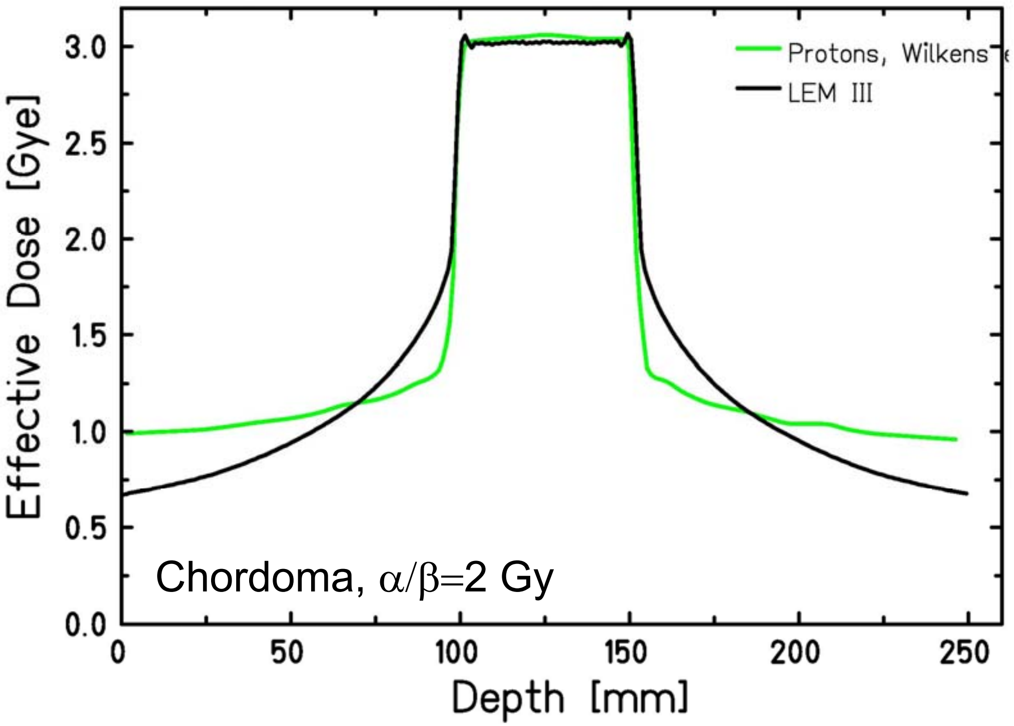
Rat Spinal Cord



Experimental data: Karger et al, *IJROBP* 2006

LEM III: Elsässer et al., IJROBP 2008

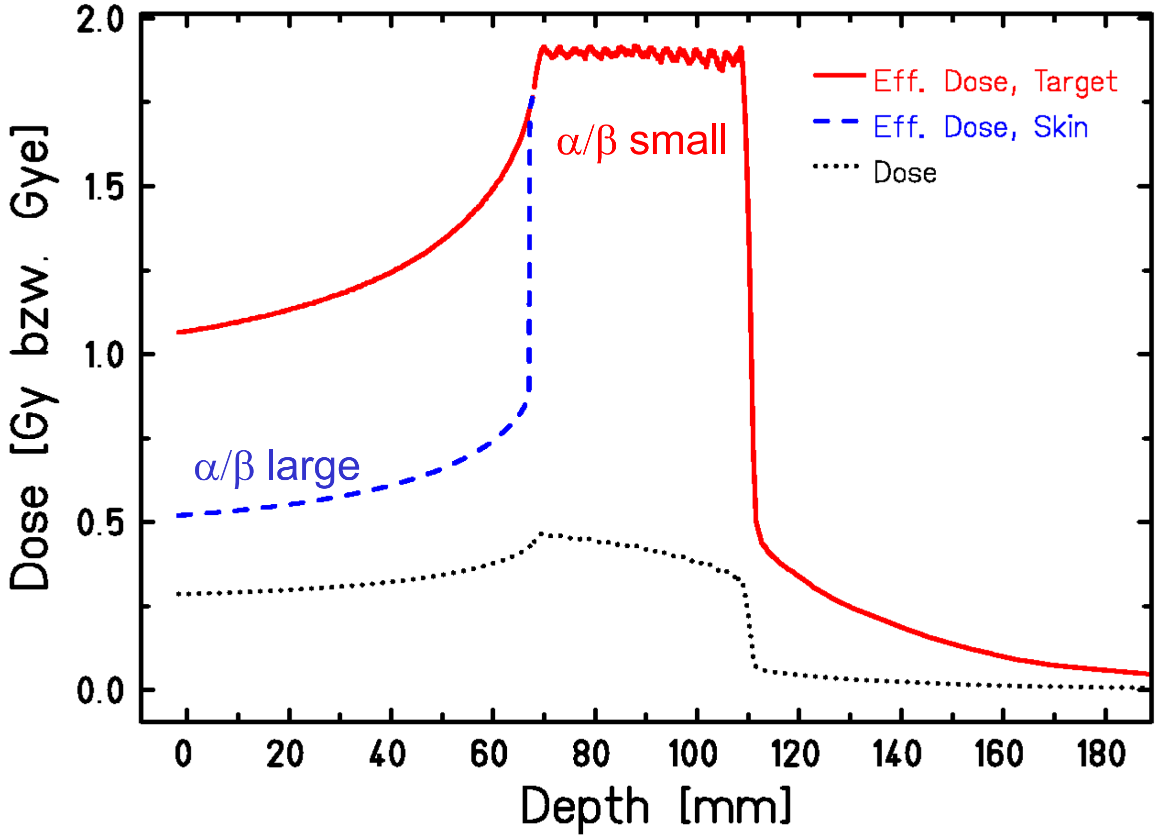
Comparison with Protons



Protons: Wilkens and Oelfke, IJROBP2008

LEM III: Elsässer et al., IJROBP2008

Influence of Tissue Composition



Krämer and Scholz, *Phys. Med. Biol.* 2000

Summary

- Advantage of carbon ions: significantly increased RBE in Bragg peak region (Protons: RBE~1.1)
- RBE dependence on several parameters has to be included in treatment planning
- RBE is cell / tissue specific
- Most significant benefit expected for (resistant) tumors characterized by small α_X/β_X-ratio
- Outlook: Additional benefit expected for hypoxic tumors (regions)

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Thanks

Michael Scholz – Local Effect Model

Michael Krämer – Treatment Planning

Wilma Kraft-Weyrather – Cell Survival studies

Entire Biophysics Group (Head: G. Kraft)