Investigation of the Therapeutic Ratio for Cancer Treatment with Carbon Ions

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GSI Biophysics
Motivation

- Complex dependence of RBE on energy, ion species, cell type and dose

- Biophysical RBE modelling is required for Heavy Ion Therapy

- Validation of models with experimental data

- Implications for Treatment planning
**Local Effect Model (LEM)**

**Physics**

Radial Dose Distribution:
Monte-Carlo (Krämer), Experimental Data

\[
D(r) \propto \frac{1}{r^2}
\]

**Biology**

Photon Survival Curve:
additional assumptions for large doses

\[
S = e^{-\left(\alpha D + \beta D^2\right)}, \quad D < D_t
\]

\[
S = e^{-s_{\text{max}} \eta (D-D_t)}, \quad D \geq D_t
\]

**Geometry**

Target (cell nucleus):
Experimental Data

Local Effect (Ions) = Local Effect (Photons)


Jacksonville, 23.05.2008

PTCOG 47
High Dose Cluster Effects

Experiments with plasmid DNA

- Non-linear yield of DSB
- Clustered SSBs reason for non-linearity
- Stagger size between 5 bp and 60 bp


larger damage at high local dose
In condensed media (liquid water):

track center depends on particle energy

=>

\[ r_{\text{min}} = 40 \text{nm} \cdot \beta \quad \beta = \frac{v}{c} \]

40nm - empirically adjusted for best agreement with ion data

Elsässer et al., *IJROBP 2008*
Accuracy of LEM

Different human cell lines of tumor and normal tissue

\[ \text{RBE}_{\alpha} \]

\[ (\beta/\alpha)_{Y} \text{ [Gy}^{-1}] \]

- 13 keV/\mu m, Data
- 77 keV/\mu m, Data
- 13 keV/\mu m, Cluster-LEM
- 77 keV/\mu m, Cluster-LEM
- 13 keV/\mu m, LEM III
- 77 keV/\mu m, LEM III

RBE(\alpha/\beta \text{ low}) > RBE(\alpha/\beta \text{ high})

Exp. Data: Suzuki et al., IJROBP 2000

distal SOBP (77 keV/\mu m)

Plateau (13 keV/\mu m)
Radiation tolerance – rat spinal cord

Experimental data
Karger et al. 2006
Conclusions for Model Versions

Generally, good agreement of key features

Improvement due to cluster extension

Intriguing agreement with exp. data for LEM III

Benchmark: radiation tolerance of rat spinal cord

comprehensive study of survival

Model improvements give more realistic therapeutic ratio
Typical treatment scenario

Chordoma $\alpha/\beta=2$, two-field irradiation, 5cm SOBP in 10cm depth
Comparison Proton vs. Carbon

RBE = 1.1

protons, redrawn from Wilkens 2007
Influence of Tissue Composition


α/β large

α/β small
Summary - Conclusions

- Local Effect Model
- Cluster extension, Track structure ($r_{\text{min}}$)
- Good agreement with a large set of \textit{in vitro} and \textit{in vivo} data
- Clinically relevant scenario
- Comparison of protons and carbon ions

- Deviations for low $Z$ -> Further model improvement necessary
- Consideration of different tissues in treatment planning

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