OncoRay – National Center for Radiation Research in Oncology, Medizinische Fakultät Carl Gustav Carus, TU Dresden, Fetscherstrasse 74, 01307 Dresden



Does the relative biological effectiveness depend on LET and ion type?



Armin Lühr¹⁻³, Cläre von Neubeck^{2,3}, Michael Baumann¹⁻⁴, Wolfgang Enghardt¹⁻⁴, Mechthild Krause¹⁻⁴

¹Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiation Oncology; ²OncoRay – National Center for Radiation Research in Oncology; ³German Cancer Consortium (DKTK), Dresden and German Cancer Research Center (DKFZ); ⁴Department of Radiation Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden



Background and Motivation

RBE is considered constant in proton therapy: **RBE** = 1.1

- But, in vitro data show: proton RBE is not constant (Fig. 1).
- Proton RBE modeling: often simple function of LET (**Fig. 1**).



Radiation Effect of lons: LET vs Z^2/E

RBE and α_{p} increase (linearly) with Z^{2}/E – ion-independent

- LET & ion species seem to be surrogates for Z^2/E (Fig. 4 & 5).
- Holds for different cell lines and clinically relevant LET range.
- **Explanation:** dose distribution around ion track is very similar for different ions with the same Z^2/E (**Fig. 6**).

Fig. 1: In vitro RBE experiment [Chaudhary et al. 2014] for U87 cells. (A) Proton spread-out Bragg-peak (SOBP). (B) Cell colony formation essay after irradiation. (C) Survival curves for different depths positions in SOBP as denoted in (A). (D) Comparison: constant RBE = 1.1 vs RBE as function of LET based on data in (C).

- RBE clearly variable for heavier ions, e.g., He, C, Ne (Fig. 4).
- Plenty of **experience** with **variable RBE** for **C-ions therapy**:
- In vitro: many cell lines & variation of microenvironment,
- Preclinical: tumor & normal tissue (e.g., spinal cord, Fig. 2),
- Clinical: experience (15.000 pts.) with variable RBE (Fig. 3).

Translate C-ion RBE to proton therapy

Assumption: RBE is independent of ion species (Fig. 4 & 5)

- Radiation effect depends on Z^2/E (Z: ion charge, E: energy)
- Ion species & LET appear to be surrogates.
- See right column of poster for details.



Relative biological effectiveness (RBE)

Z²/E



Fig 4: RBE as function of LET (left) or Z^2/E (right) for various ions: HSG and V79 cells in upper and lower row.

Linear LQ-model parameter α_p for particles

Approach:

- Take (pre-) clinical RBE for C-ions with certain Z^2/E and assign it to proton irradiation with the same Z^2/E (Fig. 2 & 4).
- RBE obtained for He- or C-ions equal RBE for protons that have energies E smaller by a factor of 4 or 36, respectively.

Example: C-ion RBE rat spinal cord

- High-quality preclinical RBE data (Fig. 2A)
- Transfer C-ion to proton RBE (Fig. 2B)
- Apply proton RBE to proton SOBP (Fig. 2C)

Conclusions

RBE depends on microscopic dose pattern

- RBE depends on Z^2/E – not directly on ion type.





Radial dose distribution around ion tracks



- Ion species & LET are surrogates for Z^2/E . **Use empirical C-ion RBE for protons**
- Ample experience on variable RBE for C-ions.
- C-ion RBE experimentally better accessible.

Outlook

Enhance proton therapy with variable RBE

- Provide RBE as simple function of depth.
- Consider effect of variable RBE for proton therapy planning as for C-ions (Fig. 3).

Fig 3: Treatment plans meningioma C-ions with patient: (A) RBE and (B) variable with constant Taken from RBE [Kosaki et al. 2012].

Fig 6: Radial dose distribution for H-, He-, and C-ions. Left: same LET = 26 keV/ μ m, right: same $Z^2/E = 1$ AMeV⁻¹.

Literature data for RBE and α_{p} are taken from: Furusawa et al. 2000, Folkard et al. 1996, Belli et al. 1998.



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Contact: Armin.Luehr@OncoRay.de