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EASTERN TIME [GMT-4]

A Probabilistic Poisson Model to Determine RBE Changes Facilitates LET-Based Optimization in Intensity Modulated Proton Treatment

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INTRODUCTION

Protons offer therapeutic advantages over photons due to their inverted depth-dose profile, allowing for a more conformal distribution of dose and improved healthy tissue sparing. However, this nice dose deposition characteristic does not tell the full story. Densely ionising particle tracks offer an enhanced cell-killing efficiency over sparsely ionising x-rays, which may be quantified through various biological endpoints. The relative biological effectiveness (RBE) is defined as the ratio of the proton beam dose to that delivered by a photon beam that yields the same biological effect.

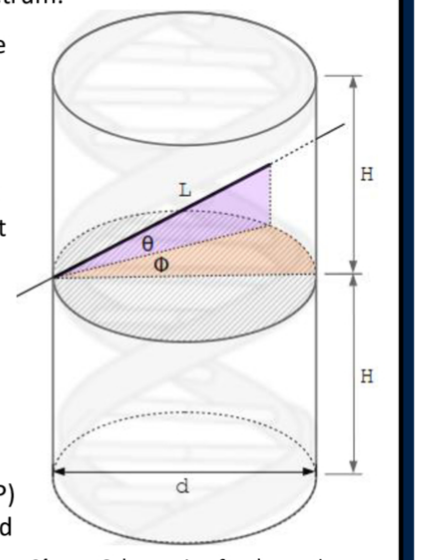
The major mechanism for cell kill is believed to be the induction of double strand breaks (DSBs) in nuclear DNA [1, 2], so we therefore define a restricted "RBE-like" measure for complex damage as the ratio of the number of DSBs in the modality of interest to the number generated in a reference modality depositing the same dose. In our formalism, DSB-induction is modelled from first principles, capturing the fundamental physical process behind the phenomenon of increased cell-killing efficiency toward the distal edge of the Bragg peak.

AIMS

- **To develop a simple biophysical DNA double-strand-break (DSB) induction model for proton therapy.**
- **To explore its possible uses in radiobiologically constrained inverse plan optimization.**

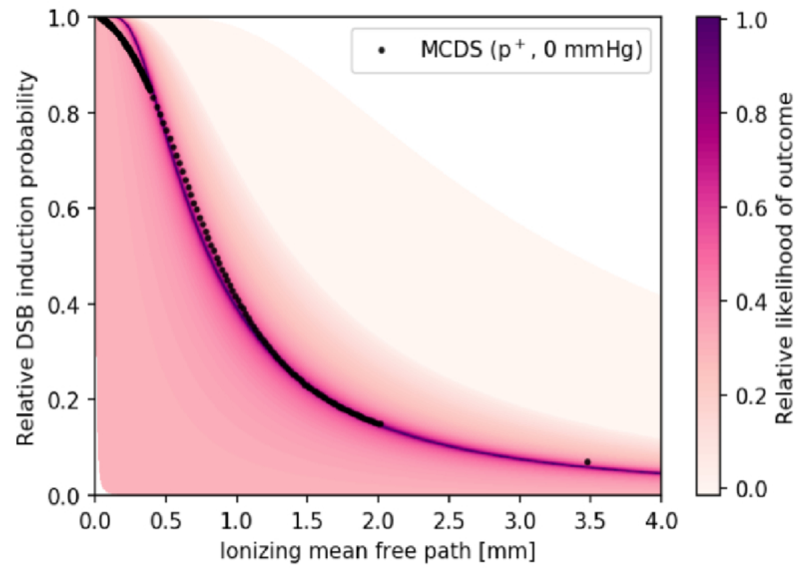
METHODS

- A probabilistic single particle interaction model was developed to quantify DSB yield for a given voxelized energy spectrum.
- Parametric fitting was performed to Monte Carlo DSB counts [3, 4] under hypoxic conditions, to limit effects of chemical repair and oxygen fixation.
- Monte Carlo simulations of 60 MeV to 120 MeV proton pencil beams were carried out in water, as well as a 10 cm^3 6 MV photon field for comparison, using TOPAS [5].
- Restricted RBE, based on DSB induction, was calculated by dividing proton beam DSB counts by photon field DSB counts.
- The spread in RBE was assessed in the middle of the spread out Bragg peak (SOBP) for maximum beam energies of 60, 100 and 180 MeV.
- A mathematical relationship was derived between RBE and linear energy transfer (LET).

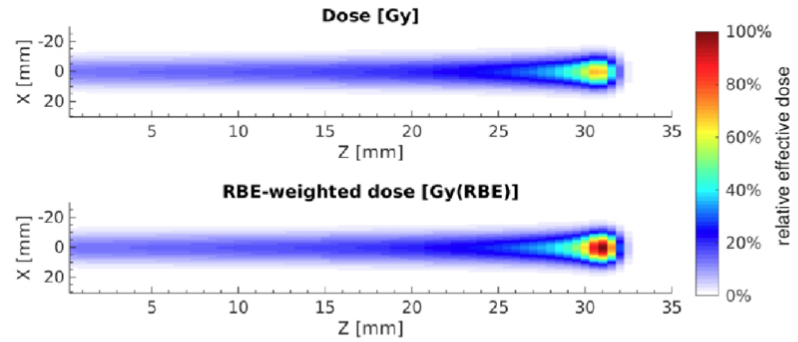


Above: Schematic of a charged particle travelling through a cylindrical section of DNA and surrounding cellular material, 10 base pairs high, with an interaction length of L.

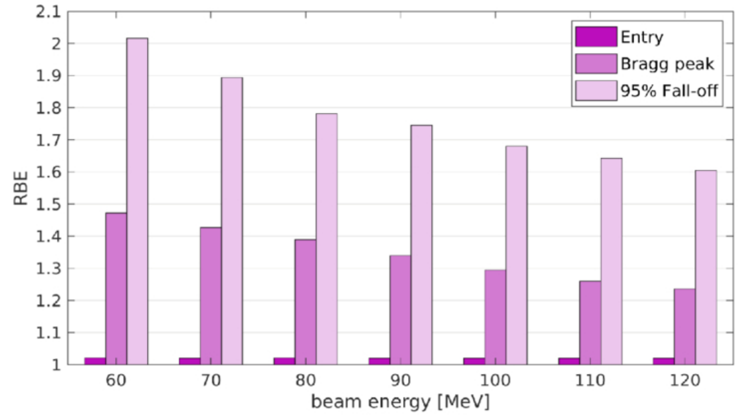
RESULTS



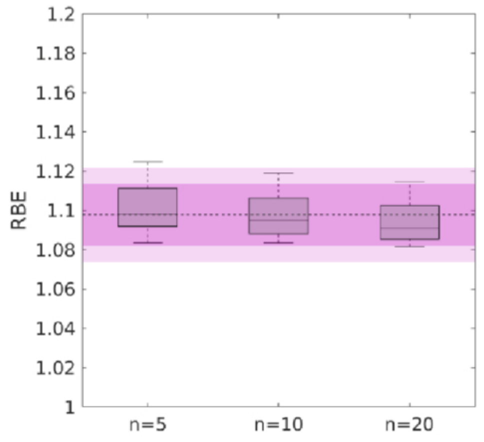
Above: Poisson-distributed relative DSB induction likelihood, or probability that a particle with ionizing mean free path generates at least two ionizing events within an interaction length of L. Contours indicate the likelihood of a given interaction length. The model has been parameterized to fit Monte Carlo MCDS [3, 4] data in hypoxic conditions.



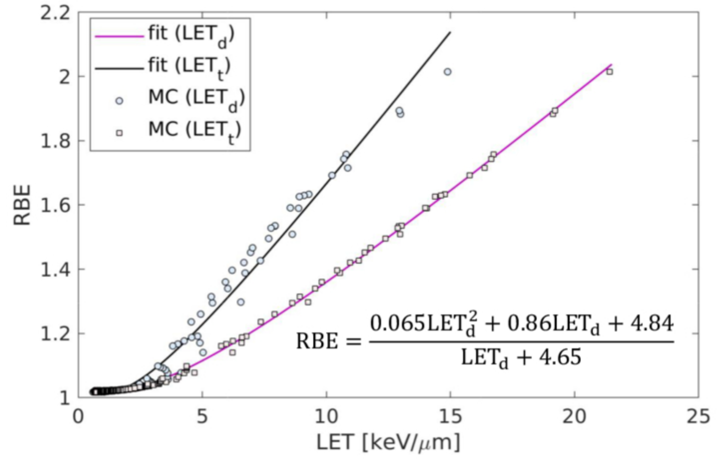
Above: Visualised dose and RBE-weighted dose scored in TOPAS for a pristine 60 MeV proton pencil beam in water.



Left: Summary of RBE calculations, using the DSB model, along the central axis of pristine proton pencil beams in water between 60 MeV and 120 MeV, simulated in TOPAS [5]. A decrease in RBE, both at the Bragg peak and at the 95% dose fall-off, is evident as the beam energy is increased.



Left: Variation in the RBE calculation in the middle 50% of the SOBP for a 100 MeV proton beam. The SOBP was constructed from n = 5, 10 or 20 energy intervals. The darker pink shaded region represents the 68% confidence interval in the mean RBE while the lighter pink region represents the 95% confidence interval.



Left: relationship between RBE and LET. Also shown is the fit of a rational function to 550 data points with both dose-averaged and track-averaged LET.

KEY POINTS & CONCLUSIONS

RBE is higher at lower energies

- Maximum RBE along the central axis showed a trend of decreasing as the pencil beam energy was increased.
- This could be considered in selecting the direction and energy of treatment fields in intensity modulated proton therapy (IMPT)

RBE of 1.1 is recovered in SOBP

- An average RBE of 1.1 was calculated for an SOBP at 100 MeV.
- This falls in line with much of the experimental evidence in literature.

RBE scales linearly with dose

- Our single particle interaction model scales linearly with dose, meaning DSB counts due to multiple pencil beams in overlapping voxels simply add.
- This leads to simple fluence-based inverse plan optimization.

REFERENCES

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[4] Semenenko, VA, Stewart, RD. *Phys. Med. Biol.* 2006; **51**(7):1693-1706

[5] Perl J, Shin J, Schumann J, Faddegon B, Paganetti H. *Med. Phys.* 2012; **39**(11):6818-37

Further reading:

Van den Heuvel, F. *PLoS One*, 2014; **9**(10): e110333.

Footnote:

Correction to abstract: please note that the original abstract for this ePoster claims that *"the RBE in the entrance region was 1.1 on average, and reached between 1.8 and 2.4 at the distal edge."* This should be corrected to read *"the RBE in the entrance region was 1.0 on average, and reached between 1.6 and 2.0 at the distal edge. An average RBE of 1.1 was calculated for a spread out Bragg peak at 100 MeV."*

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