PhD Thesis Title: Modeling proton relative biological effectiveness using Monte Carlo simulations of microdosimetry

Author: Mark Newpower
Email: mark.newpower@gmail.com
Institution: University of Texas MD Anderson Cancer Center UT Health School of Biomedical Sciences
Supervisor: Radhe Mohan, PhD
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ABSTRACT:

Proton therapy is a radiotherapy modality that can offer a better physical dose distribution when compared to photon radiotherapy by taking advantage of the Bragg peak, a narrow region of rapid energy loss. Proton therapy is also known to offer an enhanced relative biological effectiveness (RBE) compared to photons. In the current clinical standard, RBE is fixed at 1.1 at all points along the proton beam, meaning protons are assumed to require 10% less dose than photons to achieve target coverage and organ at risk (OAR) sparing. However, there is mounting clinical evidence, and a significant number of in vitro experiments, that show RBE varies, typically as a function of dose averaged linear energy transfer (LET_D).

There are two goals of this work. The first is to develop a novel method to model proton RBE by using the microdosimetric kinetic model (MKM). The MKM requires a quantity called dose mean lineal energy (y_D), which is analogous to LET_D, to model RBE. In this work, a novel method to calculate y_D is proposed, based on the proton energy spectrum at a location, and Monte Carlo simulations of microdosimetry. The second goal of this work is to implement MKM into a treatment planning system to assess the theoretical clinical impact of including variable RBE during treatment plan optimization.

This work presents a method to calculate y_D and model the RBE of several proton RBE experiments. The variable RBE of these experiments was modeled more accurately by MKM than previously proposed phenomenological models. However, a clear superiority over an LET_D-based model was not demonstrated. In a treatment planning exercise, including variable RBE modeling into the optimization algorithm led to increased target coverage while maintaining the dose sparing of OARs. Based on the parameters chosen for the MKM, this led to an increase in physical dose delivered to the brainstem, and when reanalyzed assuming an RBE = 1.1, led to doses beyond tolerance. In conclusion, this work presents a novel method to compute y_D for input into the MK model, and demonstrates slight potential benefits of considering a variable RBE in treatment plan optimization.

References to author publications that relate specifically to the dissertation:

1) **Newpower, M**; Patel, D; Bronk, L; Guan, F; Chaudhary, P; McMahon, SJ; Prise, K; Schettino, G; Grosshans, D; and Mohan, R. "Using the proton energy spectrum and microdosimetry to model proton relative biological effectiveness." International Journal of Radiation Oncology Biology Phys. 2019. Volume 104, Issue 2, 316-324.