A clinical dose prescription system for proton radiotherapy based on the Mayo Clinic Florida microdosimetric kinetic model

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BACKGROUND

- **Mayo Clinic Florida** is commissioning the **first multi-ion center in the Americas** (protons and carbon ions)
- **Clinical proton dose prescription** uses a **fixed** relative biological effectiveness (**RBE**) **factor of 1.1**
- There is **clinical evidence** that **RBE varies** with dose, radiation quality and tissue radiosensitivity, **particularly near the distal edge of treatments**
- **Numerous empirical proton-specific** RBE models **were proposed** to account for these possible RBE variations.
- **These empirical models** were shown to possess **limitations** in their **predictive capabilities and theoretical framework**
  - their applicability limited to protons only
  - reliance on purely phenomenological correlations
  - the use of the dose-averaged LET as a descriptor of radiation quality
- **The results** of these empirical models were found to be **substantially different** when compared under controlled conditions, **thus limiting the confidence in choosing a specific model for clinical implementation**

AIM OF THIS WORK

Develop a clinical dose-prescription system for proton radiotherapy that

- is **consistent** with the **clinical RBE = 1.1 for target dose definition**
- accounts for RBE variations in a framework **compatible with clinical practice in carbon ion radiotherapy**

MAYO CLINIC FLORIDA MICRODOSIMETRIC KINETIC MODEL

- **Predicts the RBE** knowing the **microdosimetric distributions** and **four cell-specific model parameters derived from**
  - the photon dose-response
  - and measurable cell characteristics (karyotype, DNA content, nuclear morphometry, cell cycle distribution)
- **Extensively validated** *in vitro* (25+ cell lines exposed to ions from ^{1}H to ^{238}U) and *in vivo* (myelopathy in rats, ^{1}H to ^{16}O) → see my other poster in this session

CLINICAL DOSE PRESCRIPTION SYSTEM

$$D_{clin} = D_{abs}\, RBE_{bio}\, F_{clin} = 1.1\, D_{abs}\, RBE_{bio}$$

- Mathematical formalism derived from the Japanese clinical prescription system for carbon ions (Inaniwa et al., 2015)
- RBE_{bio} is calculated with MCF MKM for HSG cell line
- Reference radiation: mid of reference SOBP (below)

$$\alpha = \int \left(\alpha_0 + \beta_0 \frac{y}{\rho\,\pi\, r_d^2}\right) \left\{ \frac{1 - \exp\left[-\left(\alpha_0 + \beta_0 \frac{y}{\rho\,\pi\, r_d^2}\right)\frac{y}{\rho\,\pi\, R_n^2} - \beta_0 \left(\frac{y}{\rho\,\pi\, R_n^2}\right)^2\right]}{\left(\alpha_0 + \beta_0 \frac{y}{\rho\,\pi\, r_d^2}\right)\frac{y}{\rho\,\pi\, R_n^2} + \beta_0 \left(\frac{y}{\rho\,\pi\, R_n^2}\right)^2} \right\} d(y)\, dy$$

$$\beta = \beta_0 \left[\int \left\{ \frac{1 - \exp\left[-\left(\alpha_0 + \beta_0 \frac{y}{\rho\,\pi\, r_d^2}\right)\frac{y}{\rho\,\pi\, R_n^2} - \beta_0 \left(\frac{y}{\rho\,\pi\, R_n^2}\right)^2\right]}{\left(\alpha_0 + \beta_0 \frac{y}{\rho\,\pi\, r_d^2}\right)\frac{y}{\rho\,\pi\, R_n^2} + \beta_0 \left(\frac{y}{\rho\,\pi\, R_n^2}\right)^2} \right\} d(y)\, dy \right]^2$$

METHODOLOGY

- OpenTOPAS simulations were performed for water-phantom SOBPs spanning different prescribed doses, depths, and widths
- Lineal-energy distributions were computed including primary and secondary ions for spherical water targets (0.3 μm radius)
- Results were compared with calculations based on fixed RBE = 1.1 and two LET-based proton RBE models (Beltran and McNamara)

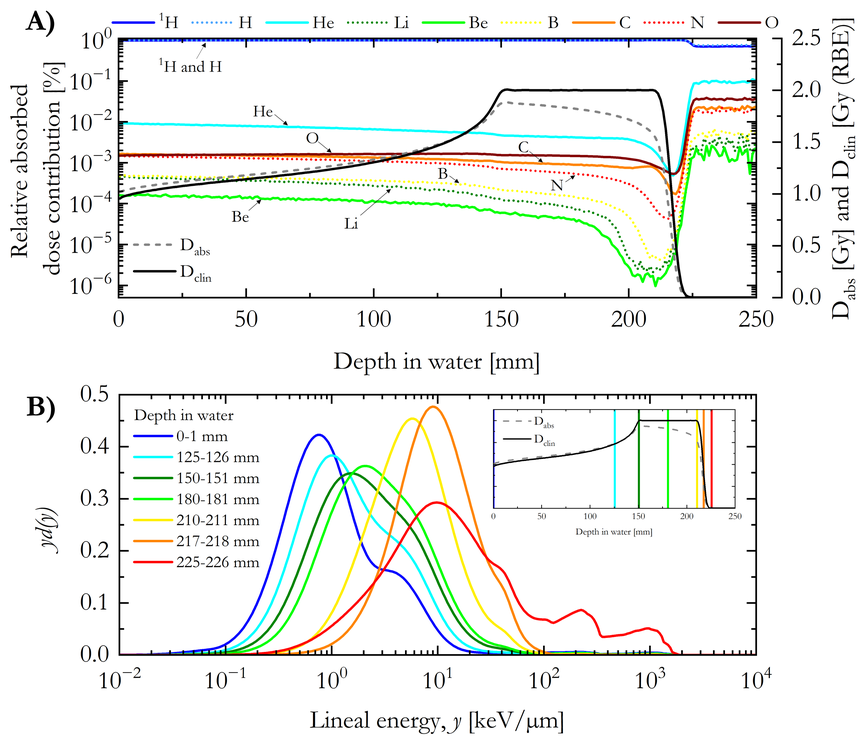

Figure 1. A): The relative contribution of different ions to the absorbed dose at the center of a 60×60 mm² field along a SOBP with a flat clinical dose profile of 2 Gy (RBE) between depths of 150 and 210 mm (reference SOBP). **B):** Lineal energy probability density distributions at seven depths in water along the reference SOBP.

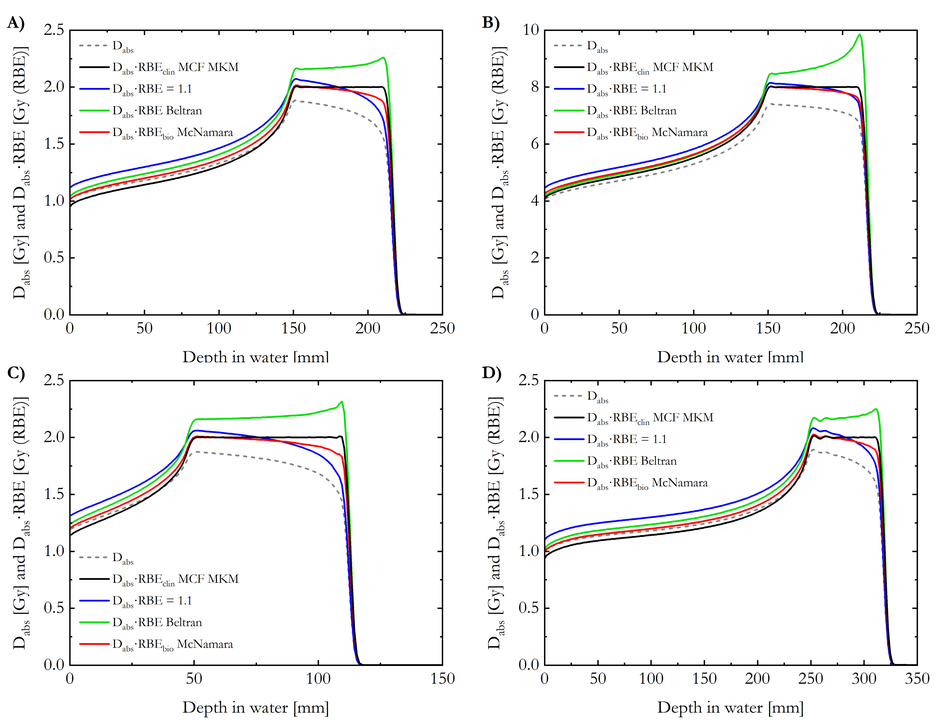

Figure 2. Comparison of the clinical dose profiles calculated using the proposed MCF MKM-based system, the fixed RBE = 1.1, the McNamara model, and the Beltran model along SOBPs with a MCF MKM-based flat clinical dose profile of 2 Gy (RBE) and 8 Gy (RBE) between depths of 150-210 mm (panels A and B), and 2 Gy (RBE) between depths of 50-110 mm (panel C) and 250-310 mm (panel D).

CONCLUSIONS

The proposed clinical dose system accounts for the variable proton RBE while remaining consistent with the current clinical standard of RBE = 1.1 in the target region and ensuring compatibility with the corresponding system for carbon ions.