Consistency in assessment of relative biological effectiveness in carbon ion radiotherapy

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INTRODUCTION

There are currently several models used to evaluate relative biological effectiveness (RBE) in carbon ion therapy. The calculation of RBE values across all models (Microdosimetric Kinetic Model (MKM), the Local Effect Model I (LEM I), and the Repair Misrepair Fixation (RMF) model) are necessary to provide the basis of clinical uniformity across RBE models and therefore across institutions. This will allow direct comparison of RBE values and provide a means of assessing the consistency across carbon ion centers, a critical parameter in the proper implementation of clinical trials within this modality.

Aim:

Calculate and compare RBE values across several models to determine agreement using GEANT IV Monte Carlo generated microdosimetric and kinetic energy spectra.

METHODS

GEANT IV Monte Carlo was used to generate microdosimetric and kinetic energy spectra of a standard clinical carbon therapy beam, the parameters of which were determined by a survey sent from IROC Houston to clinical carbon facilities. Both microdosimetric and kinetic energy spectra were generated for energies ranging from 120 – 440 MeV/u in 2 MeV/u increments. In order to calculate RBE using the Linear-Quadratic (LQ) formulism implemented by each of the three models, α_c and β_c were used along with accepted reference radiation values (α_c and β_c) and MC generated physical dose to calculate RBE due to each model using the linear-quadratic formulism shown in the equation below. Accepted values for reference radiation are shown in Table 1 below.

RBE Model	Cell Line	α_x (Gy^{-1})	β_x (Gy^{-2})	α_c (Gy^{-1})	β_c (Gy^{-2})
MKM	HSG Tumor	0.19	0.05	Variable	0.05
LEM	Chordoma	0.1	0.05	Variable	Variable
RMF	NSCLC H460	0.29	0.083	Variable	Variable

Table 1. Shows published alpha and beta values of reference radiation and (if applicable) carbon ions for each RBE model.

$$ RBE = \frac{-\alpha_X + \sqrt{\alpha_X{}^2 + 4\beta_X(\alpha_C D + \beta_C D^2)}}{2\beta_X D} $$

D = absorbed dose
α_X, β_X = LQ parameters for reference radiation
α_C, β_C = LQ parameters for carbon beam

MKM and RMF:
- Microdosimetric spectra used to calculate lineal energy values (frequency-, dose-, and saturation corrected dose-mean lineal energies)
- Lineal energy values used along with model specific parameters to calculate α_c and β_c [1,2]

LEM I
- Kinetic energy spectra were extracted for each relevant fragment contributing to a therapeutic carbon beam, as detailed in Figure 1 (including C, H, He, Li, Be, B, secondary C, N, O, and F)
- KE as function of depth was used to interpolate α and β values from clinical LEM I tables for each fragment independently
- α_c and β_c calculated using α and β of each fragment along with the respective dose weighting
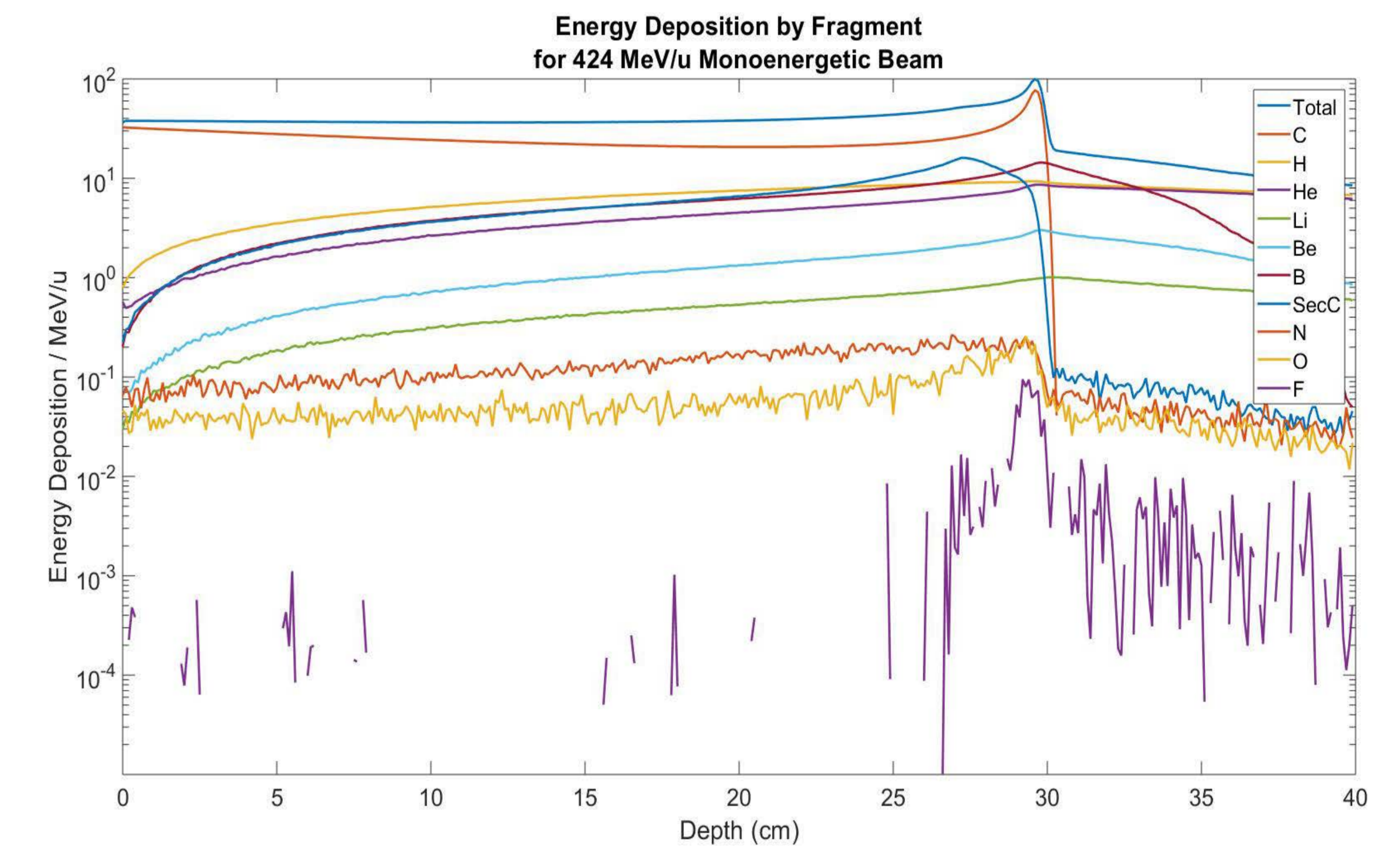

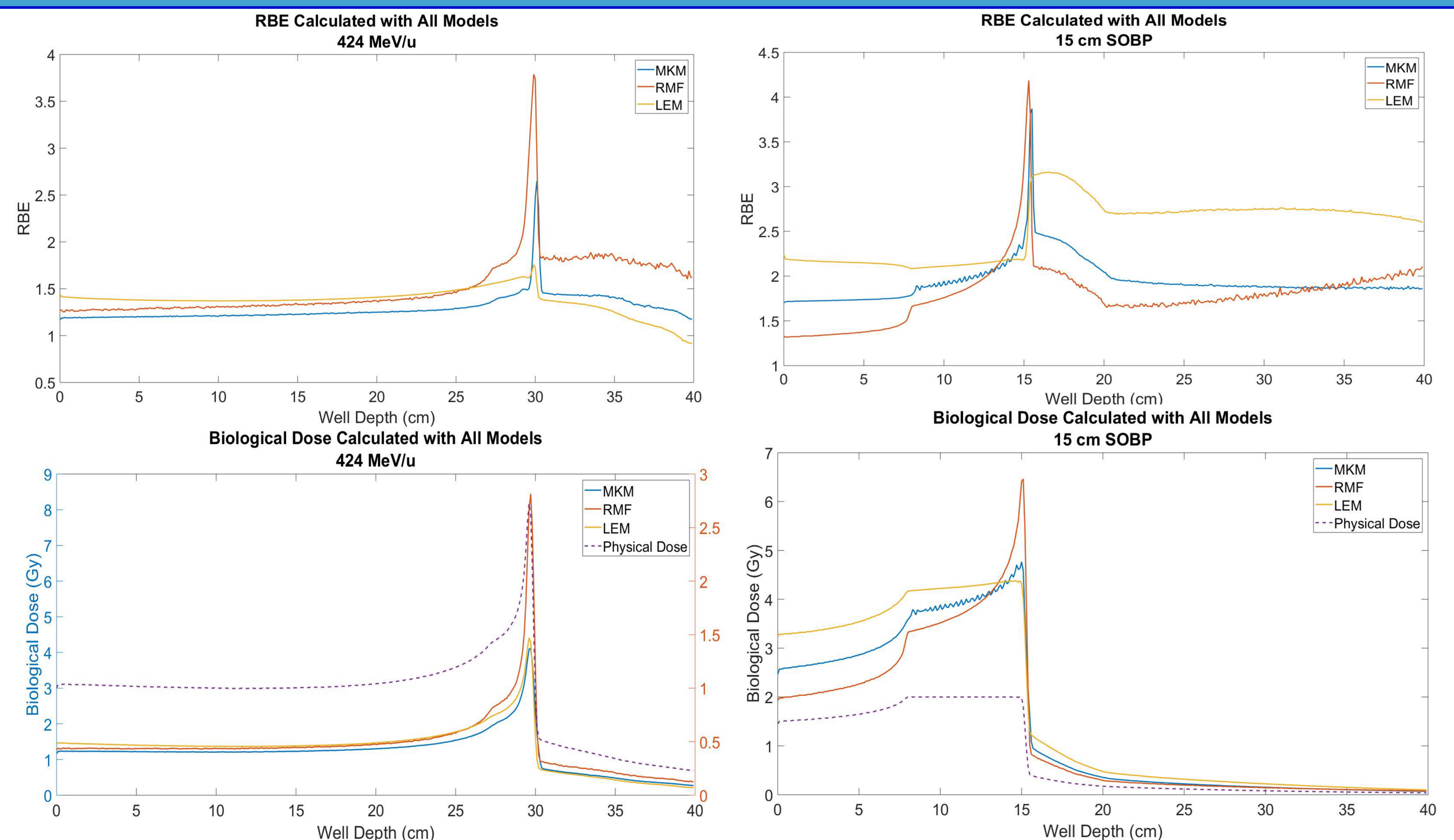Figure 1. Energy deposition by each fragment for 424 MeV/u monoenergetic beam.

RESULTS

RBE and biological dose, shown in Figure 2 to the left (top and bottom, respectively), are plotted as a function of depth for each model. Two clinical beams are shown for comparison; that for a 424 MeV/u monoenergetic beam (left), and that for a 15 cm SOBP (right). Physical dose is plotted along with biological dose for reference. As can be seen, the biological dose is similar for both MKM and LEM I, despite having very different RBE trends and magnitudes. This is due to the location of the peak with respect to the physical depth. The percent difference across models was just 15% in the entrance region of the monoenergetic beam, while differences in the Bragg peak and tail were significantly higher. However, these values showed good agreement in biological dose.

The surviving fraction was also plotted as a function of dose in Figure 3 to the right, showing strong agreement between the two clinical models, MKM and LEM I.
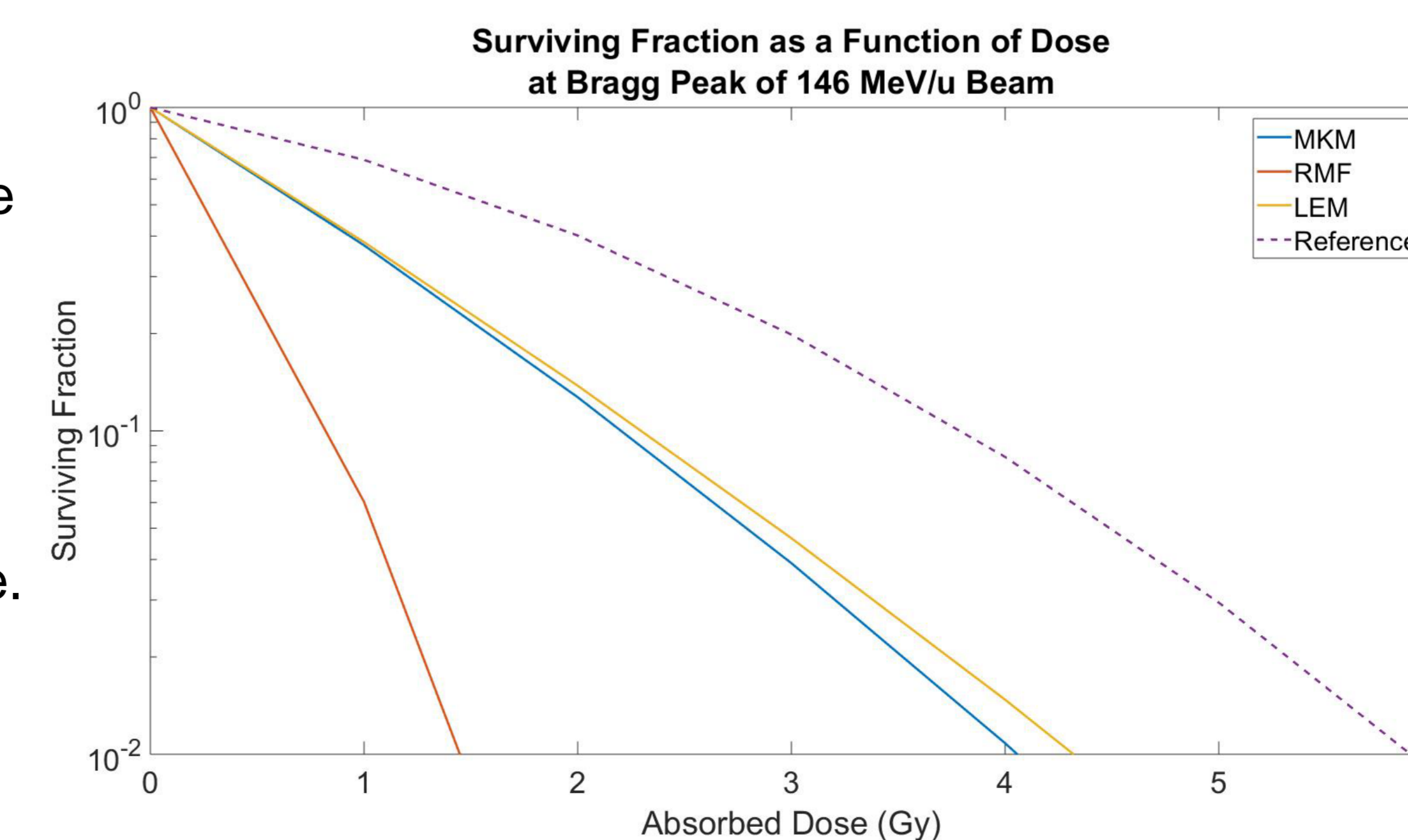

Figure 3. Surviving fraction as a function of absorbed dose calculated for carbon therapy using MKM, RMF, and LEM I and compared to that of reference x-rays.

Figure 2. RBE and biological dose plotted for each model for a 424 MeV/u monoenergetic beam and a 15 cm SOBP.

CONCLUSIONS

While no conclusions may be drawn as to the accuracy of any one model, these results emphasize the inconsistencies of each model. Though the two clinical models, MKM and LEM I, show very similar trends and magnitudes in biological dose, their RBE values are vastly different due to the peak location of each in comparison with the physical dose.

REFERENCES

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[2] Guan, F., et al., *A mechanistic relative biological effectiveness model-based biological dose optimization for charged particle radiobiology studies.* Phys. Med. Biol., 2018. **64**(1): p. 015008.