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Practical Biological Spread-out Bragg Peak Design for a Carbon Beam

Chang Hyeuk Kim, Hwa-Ryun Lee, Seduk Chang, Hong Suk Jang, Jeong Hwan Kim, Dong Wook Park, Won Taek Hwang and Tea-Keun Yang*

Korea Institute of Radiological and Medical Science, Seoul 01812, Korea

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In radiation therapy, the carbon beams has more advantages with respect to biological properties then a proton beam. The carbon beam has a high linear energy transfer (LET) to the medium and a higher relative biological effectiveness (RBE). To design the spread-out Bragg peak (SOBP) of biological dose for a carbon beam, we propose a practical method using the linear-quadratic (LQ) model and the Geant4-based Monte Carlo simulation code. Various Bragg peak profiles and LETs were calculated for each slice in the target region. To generate an appropriate biological SOBP, we applied a set of weighting factors, which are power functions in terms of energy steps, to each obtained physical dose. The designed biological SOBP showed a uniformity of 1.34%.

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I. INTRODUCTION

The way of protons and heavier ions for medical treatment was purposed by Robert Wilson in 1946 [1], and the first patient was treated with proton at the University of California at Berkeley in 1954 [2]. Patient treatments using carbon beams have been performed mainly at the Gesellschaft für Schwerionenforschung mbH (GSI) in Germany and the Heavy Ion Medical Accelerator in Chiba (HIMAC) in Japan. The current statistics shows 122,449 patients have been treated by using particle therapy worldwide, with 86.3% (105,743) of the patients being treated with protons and 10.7% (13,119) with carbon [3].

Energetic ion beams generate Bragg peaks while they transferring energy to the medium [4]. The characteristics of ion beams is a good advantage for radiation therapy. The radiation dose at entrance region is low while the maximum dose is delivered to the target region. Compared with other light ions, carbon is classified as a high linear-energy-transfer (LET) radiation. A high LET radiation has a higher relative biological effectiveness (RBE) than low LET radiation such as photons and protons [5]. In addition, the carbon beam generates a steep distal fall-off shape of the Bragg peak, which can provide conformal dose delivery and avoid unwanted doses to critical organs.

Two different groups have mainly performed the research regarding the calculation of carbon's RBE. One group developed the linear quadratic (LQ) model, which is based on the experimental results for a reference cell line [6]. The other group suggested the local element model (LEM), which simulates and calculates the effects of radiation from the spatial distribution of DNA double strand breaks (DSB) [7,8]. However, the RBE is affected by the LET, the biological endpoint, the type of tissue or cell, etc. Therefore, we can infer that simulation models might have some difficulties in representing all possible options. The way of experiment data could be considered to be a more practical way to calculate the RBE value.

If the spread-out Bragg peak (SOBP) of carbon is to be designed, the experimented target cell response, which is the dependence of the survival curve on the LET, is required. Because of the absence of actual carbon beams in Korea, in this study the HIMAC experiment data, which was human salivary grand (HSG) cell results, were adopted [9], and the LQ model was used for the RBE calculation.

II. METHOD

1. Dose and LET Calculation

For the design of a spread-out Bragg peak, the depth-dose profiles of various carbon beam energies as well as the LET, should be calculated. In this study, the Geant4 hadron therapy example was adopted [10]. The example code could be used to simulate a passive beam line, as well as an active scanning beam line. The code is used the model for the eye-therapy line at Istituto

*E-mail: changkim@kirams.re.kr; Fax: +82-2-970-1978

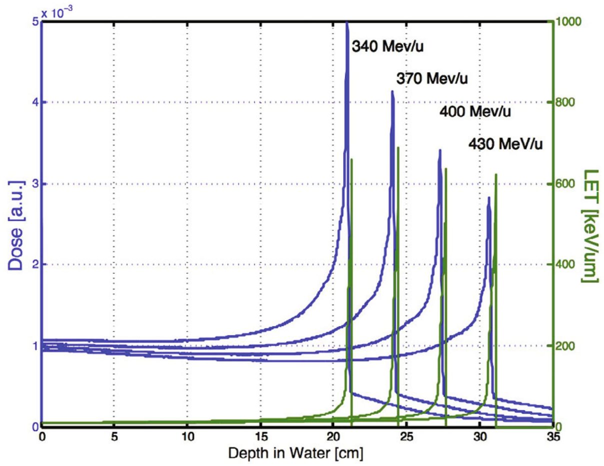

Fig. 1. (Color online) Depth dose profile and LET obtained at various carbon energies.

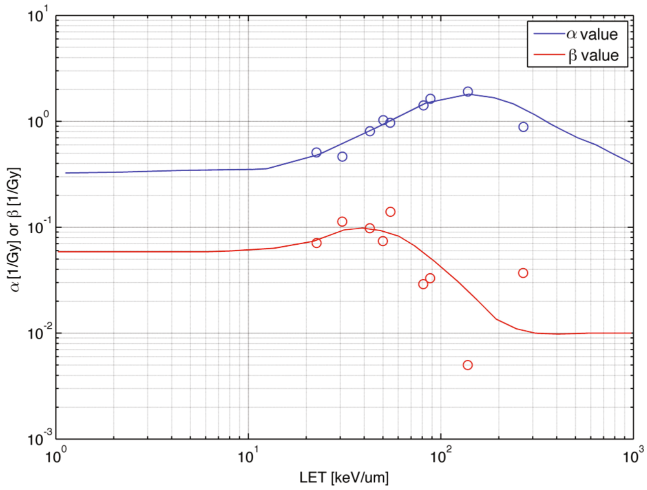

Fig. 2. (Color online) LQ Parameters α and β as functions of the LET [13].

Nazionale di Fisica Nucleare (INFN) in Italy. In this study, the response from a water phantom was the focus. The best physics model in this hardron-therapy example is QGSP_BIC_EMY as the reference physics list. The quark gluon string pre-compound (QGSP) defines the hadronic models for nucleons. The binary ion cascade (BIC) defines the inelastic models for ions, and electromagnetic Y (EMY) defines the electromagnetic models for all particles [11]. The beam energies were selected as 340, 370, 400, 430 MeV/u for carbon. The water phantom had transverse area of 40 × 40 cm^2 and longitudinal length of 40 cm. The output data of simulations was collected each 0.1 mm of spacing in the longitudinal direction of the phantom. The code generates two outputs: the depth dose profile and the LET of carbon. The incident beam was defined as a pencil beam with a 3-mm radius and a 2-mm sigma. The beam energy was set to 0.1% of the energy variation dE/E. The output of the simulation is shown in Fig. 1.

2. LQ Model and RBE Calculation

Cell killing effects are induced by several physical and bio-chemical processes. The LQ model is a mechanistic model for the cell killing effects [12], which are related to the DNA repair process for DSB and binary mis-repair of DSB from different radiation tracks. Simply, the effects based on direct radiation will be shown to be directly proportion to the dose, which is indicated as the parameter. However, the effect of indirect radiation is shown to be proportional to the square of the dose, which is represented by the parameter. Therefore, for the LQ formulation, the yield (Y) of lethal lesion can be expressed as

$$Y \propto \alpha D + \beta D^2. \quad (1)$$

When D is the radiation dose in the region. If a Poisson distribution of lethal lesions is assumed, the survival fraction S can be expressed as

$$S = \exp(-Y) = \exp[-(\alpha D + \beta D^2)]. \quad (2)$$

Therefore, the key problem of the LQ model is the define α and β as functions of LET. In this study, the LQ model parameters were referred from the National Institute of Radiological Science (NIRS) in Japan. The data were obtained based on the experimental result for the human salivary gland (HSG) case. The fitted LQ parameters are shown in Fig. 2 [13]. This LQ model was used for the RBE calculation. The definition of the RBE is well known to be the ratio between two absorbed doses delivered with two radiation qualities, one of which is a 'reference radiation'. The gamma ray of ^{60}Co is used as the reference in general [14].

3. Spread-out Bragg Peak Design Procedure

In the case of using the spread-out Bragg peak (SOBP) in beam delivery, the dose at a position is overlapped by the different depth dose distributions caused by the varying incident energy. Therefore, the LET generated by using a monochromatic carbon energy cannot use to the RBE calculation. Therefore, the concept of a dose-averaged LET is used [13]. The dose, $D_{SOBP}(x)$, and the dose-averaged LET, $LET_{SOBP}(x)$, at the position x in the SOBP can be calculated by using the following equations:

$$D_{SOBP}(x) = \sum_i \omega_j d_j(x), \quad (3)$$

$$LET_{SOBP}(x) = \frac{\Sigma_j LET_j(x)\omega_j d_j(x)}{D_{SOBP}(x)}. \quad (4)$$

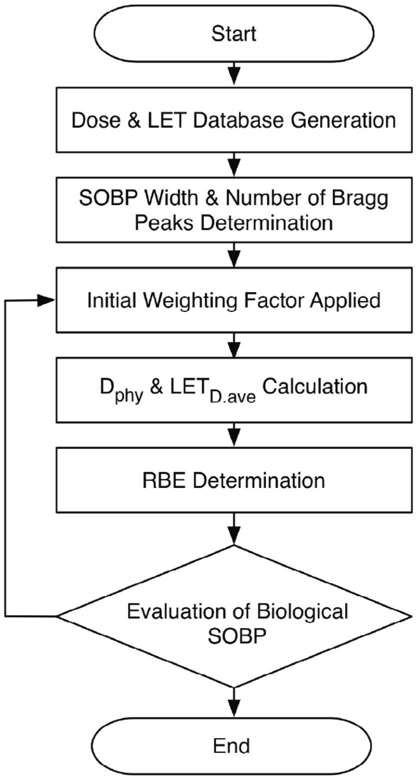

Fig. 3. Work flow for the design a biological SOBP.

Where $d_j(x)$, $w_j(x)$ and $LET_j(x)$ represent the dose profile, the weighting factor and the linear energy transfer value from the jth incident beam energy at position x. After the dose average LET has been obtained, it can be used to determine α and β for the parameters, as shown in Fig. 2. Also, the dose for a 10% cell survival fraction, D_{10}, can be generated by using

$$0.1 = \exp(-\alpha D_{10} - \beta D_{10}^2). \quad (5)$$

Then, the RBE based on a 10% survival fraction, RBE_{10}, can be expressed by using the ratio of the 10% survival fraction from the reference radiation, $D_{10 \cdot ref}$. Also, the D_{10} can be expressed by using the LQ parameters as follow:

$$RBE_{10} = \frac{D_{10 \cdot ref}}{D_{10}} = \frac{4.08 \times 2\beta}{-\alpha + \sqrt{\alpha^2 - 4\beta \ln 0.1}}. \quad (6)$$

Then, the biological dose can be determined by multiplying the physical dose by the calculated RBE_{10}. This calculation should be completed over the entire longitudinal distance. In this study, the determination of the weighting factor for the jth dose profile, d_j, was a key parameter for determining the appropriate SOBP of the biological dose. Based on this calculation, the biological SOBP design followed the work flow diagram shown in Fig. 3.

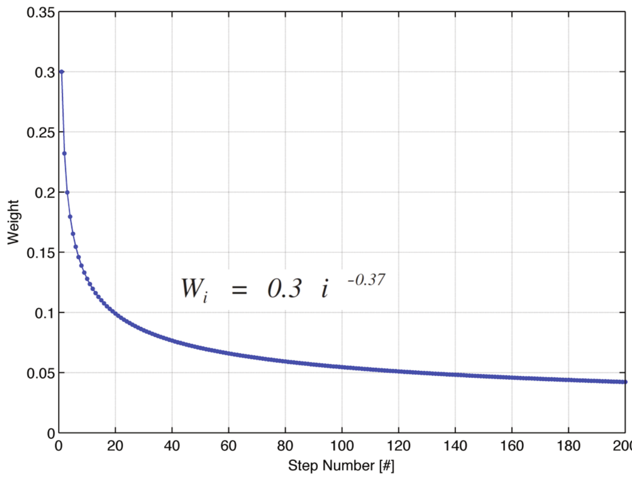

Fig. 4. (Color online) Weighting factors as a function of the number of steps.

III. RESULTS

The physical dose and the dose-averaged LET were calculated from maximum energies from 340 MeV/u to 250 MeV/u for carbon beam. For the biological SOBP generation, a set of 200 weighting factors, which can be determined the shape of ridge filter, was considered [15]. The target SOBP was 10 cm from the maximum Bragg peak position of 20.96 cm.

The weighting factors were applied in several ways to meet the uniformity requirement of the biological SOBP (2.5%). In this study, a set of weighting factors, which are power functions in terms of the energy step, was used. The applied weighting factors are shown in Fig. 4.

As described above, the weighting factors were applied to the physical dose at each slice, and the LQ parameters were extracted based on the dose-averaged LET, and the RBE for each slice position was determined. Then, the biological dose profile could be generated by applying the RBE to the physical dose profile at each position. The biological dose profile uniformity at the SOBP region was 1.34%. The physical dose with the weighting factor applied, which is indicated as a blue line, and and the biological dose with the RBE applied, which is drawn as red line, are shown in Fig. 5.

IV. CONCLUSION

The carbon beam is classified as high-LET radiation, and as such it causes higher cell killing effects compared to proton and photon beams. Therefore, the concept of the RBE is one of an important issue in determining the biological dose on the target. The physical SOBP is generated by overlapping several depth dose profiles. If uniformity is to be achieved at SOBP region, appropriate

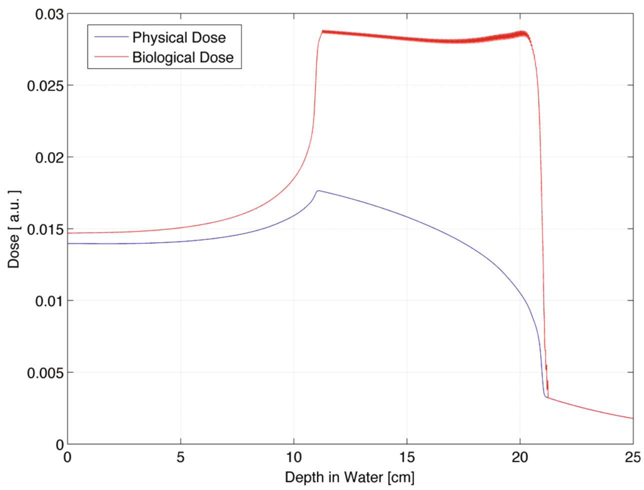

Fig. 5. (Color online) The biological SOBP and weighted applied physical dose obtained as a function of the depth in water.

weighting factors must be applied to each depth dose profile. In case of the biological SOBP, the calculated RBE based on the depth dose profiles and the dose-averaged LETs should be applied to the physical SOBP.

In this study, to determine the RBE at the SOBP region, we used the LQ model based on the NIRS experimental data and performed Monte Carlo simulations for the carbon beam. The simulation study was focused on obtaining the response of a water phantom to the carbon beam. The maximum energy of the carbon beam was set to 340 MeV/u for the simulation. The depth dose profile and the LET were obtained in the longitudinal direction for 200 different energies corresponding to 10-mm SOBP width by modifying the Geant4 hadron-therapy example code. If an appropriate biological SOBP is to be generated at the target region, power-function-based weighting factors for each depth dose profile can be determined through an iteration method. The uniformity of the biological SOBP was shown to be 1.34%, which met the uniformity requirement [16].

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