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Technical note

Physical parameter optimization scheme for radiobiological studies of charged particle therapy

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ABSTRACT

We have developed an easy-to-implement method to optimize the spatial distribution of a desired physical quantity for charged particle therapy. The basic methodology requires finding the optimal solutions for the weights of the constituent particle beams that together form the desired spatial distribution of the specified physical quantity, e.g., dose or dose-averaged linear energy transfer (LET_d), within the target region. We selected proton, ^{4}He ion, and ^{12}C ion beams to demonstrate the feasibility and flexibility of our method. The pristine dose Bragg curves in water for all ion beams and the LET_d for proton beams were generated from Geant4 Monte Carlo simulations. The optimization algorithms were implemented using the Python programming language. High-accuracy optimization results of the spatial distribution of the desired physical quantity were then obtained for different cases. The relative difference between the real value and the expected value of a given quantity was approximately within ± 1.0% in the whole target region. The optimization examples include a flat dose spread-out Bragg peak (SOBP) for the three selected ions, an upslope dose SOBP for protons, and a downslope dose SOBP for protons. The relative difference was approximately within ± 2.0% for the case with a flat LET_d (target value = 4 keV/μm) distribution for protons. These one-dimensional optimization algorithms can be extended to two or three dimensions if the corresponding physical data are available. In addition, this physical quantity optimization strategy can be conveniently extended to encompass biological dose optimization if appropriate biophysical models are invoked.

1. Introduction

The number of proton and heavy ion therapy centers has dramatically increased in recent years around the world [1]. This can be attributed to many factors. First, from a physics perspective, the characteristics of a well-defined penetration range of ions can enable the delivery of a highly conformal dose to the tumor volumes while sparing the surrounding normal tissues [2]. In addition, for some specific disease sites, clinical trials have shown promising results in regards to the effectiveness of ion therapy compared with photon-based radiotherapy [3,4]. Moreover, the total cost of building a proton or heavy ion center keeps decreasing with the development of new techniques [5–7].

In clinical applications, a sharp dose Bragg peak from a mono-energetic ion beam is usually not wide enough to cover the volumetric target tumor. Instead, a spread-out Bragg peak (SOBP[2]) formed by multi-energetic beams with appropriate modulations can be used to cover the large volume of a tumor. An SOBP can be delivered by either passively scattered particle beams with range modulations or actively scanned beams with intensity modulations [8,9]. Nevertheless, the scanning technique is becoming routine and nearly all new particle therapy centers have been equipped with scanning nozzles because of the unique advantages it offers [9]. In a radiation field generated by scanned particle beams, the weight of each Bragg curve can be modulated to deliver a desired shape of dose distribution to the target tumor. This flexibility in dose delivery forms the physical basis for multi-field optimized intensity-modulated ion (or proton) therapy.

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[3] Usually, a dose SOBP refers to a uniform dose distribution longitudinally within the target, but in the current study, we do not restrict it to be a uniform dose. As long as multiple modulated beams contribute to the desired shape of the dose distribution within the target, we treat it as a dose SOBP.

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Different approaches and algorithms to optimize the spatial dose distributions of scanned particle beamlets have been developed for years [10–15]. A beam delivery strategy can be optimized using a treatment planning system (TPS) for particle therapy. However, for some radiobiologic studies, the treatment planning system may not meet all of the unique requirements for designing a cell or animal irradiation experiment. For example, a TPS is usually designed to process objects with large dimensions such as human cancer patients, and it may not be suitable to handle small geometries such as those for animals and cells. In addition, a TPS is usually limited to performing dose optimization only and may not be able to calculate other physical quantities such as linear energy transfer (LET) and particle energy spectra, which are needed to interpret the biological effects in particle radiobiology experiments. Given these limitations, it is imperative to develop a convenient and effective tool that can facilitate the use of scanned beams for particle radiobiology experiments to correlate the observed biological effects with physical parameters.

For the desired spatial distribution of a specified physical quantity, the following two steps are usually needed: (1) obtain the raw data of the physical quantity for all beams with different energies, and (2) perform the optimization procedure to solve the beam weights. In many previous studies [16–20], an analytical method was adopted to rapidly generate the Bragg curves and then the optimization procedure was performed to generate a dose SOBP. Although the analytical method has advantages in the calculation speed, systematic uncertainties exist owing to the approximated expression of Bragg peaks in the dose calculations. Using the measured data of the physical quantity may improve the accuracy of the input data for optimizations. However, in some conditions, the measured data are not easily obtained. Using benchmarked Monte Carlo systems to generate the physical data can be an effective alternative to save time in obtaining measurements while maintaining the accuracy of the optimization results.

In addition to the dose optimizations, many other respects have been optimized in charged particle therapy. For example, Dias et al. have analyzed the impact of different optimization methods in the charged particle therapy scanning paths by assessing the possibility to deflect the beam out of the extraction line during irradiation [21]. Austin et al. have developed a Monte Carlo Markov model for assisting proton therapy referral decision making [22]. Kanematsu has developed a dose calculation algorithm of fast fine-heterogeneity correction for heavy charged particle radiotherapy [23]. Trott has investigated special radiobiological features of second cancer risk after particle radiotherapy and concluded that it is unlikely that modern particle therapy has higher risk than photon therapy [24]. Bassler et al. have investigated the LET painting technique to place more high-LET particles in target tumors [25,26].

Although various approaches for optimizing particle beams have been available for years, our work has its unique novelties. First, the current study aimed to develop a general and easy-to-implement methodology to generate an optimized beam delivery strategy in terms of commonly used physical quantities such as dose and dose-averaged LET (LET_d) for radiobiological studies. In addition, the generated beam delivery plan can be applied to cell or animal experiments to investigate how the physical parameters influence the observed biological effects. Moreover, the methodology developed for physical quantity optimization can be conveniently extended to relative biological effect (RBE)-weighted dose optimization if appropriate biophysical models are invoked. The results of such efforts will be reported in future work.

2. Materials and methods

2.1. Basic settings in Monte Carlo simulations

The general-purpose Monte Carlo toolkit Geant4 [27,28] (version 10.3.p03) was used to perform the particle tracking to generate the depth dose curves for different ions and the depth LET_d curves for proton beams only. In the current work, these raw data were used as the input to the physical quantity optimization process. For charged particle therapy, various physics lists are available such as “QBBC”, “FTFP_BERT” and many others, all of which contain both of the electromagnetic and hadronic physics processes. We compared the simulation results from the above two physics lists and found the dose difference is below 1% for the selected ions within the therapeutic energy ranges. In this study, we selected the “FTFP_BERT” physics list as a representative for all the simulations as we did in our previous studies [29,30].

The 94 groups of scanned proton beams used at The University of Texas MD Anderson Proton Therapy Center were selected for the calculations. The energy varies from 72.5 to 221.8 MeV with a range (depth with 90% of the peak dose in the distal falloff) of 4.0 to 30.6 cm in water. For ^{4}He ions and ^{12}C ions, the virtual beams were modelled using energies derived from publicly available databases because our institution lacks clinical facilities that utilize heavy ions. The National Institute of Standards and Technology ASTAR [31] program was used to determine the energy and range of ^{4}He ions, and 161 groups of ^{4}He ions with energies of 70–230 MeV/n and ranges of 4.1–33.1 cm in water were selected on the basis of commonly used clinical treatment depths in patients. For ^{12}C ions, the energy and range data were obtained from the Errata and Addenda: ICRU Report 73 [32]. A total of 161 groups of energies with energies of 120 to 440 MeV/n and ranges of 3.6 to 32.0 cm in water were selected. All of the beams were assumed to have a Gaussian-shaped energy spread and a Gaussian-shaped spot profile in both of the classic x and y directions where the beam direction is assumed to be along a central z axis.

An $80 \times 80 \times 40\,cm^3$ water phantom was built as the target for scoring quantities of interest for different ion beams. A scorer with a large radius of 40 cm and thickness of 0.01 cm is built so that the simulation data with a high spatial resolution (along the z axis) could be obtained. Therefore, the scored dose can be approximately treated as the integral depth dose (IDD). Although only the simulation results along the depth were reported, the multiple Coulomb scattering processes were considered during the Monte Carlo simulations. In our radiobiology studies, a uniform radiation field at a specified depth can be easily formed by a series of equal-weight scanned beam spots with the same energy. Therefore, to form a desired 3D distribution (laterally uniform within the target) of a specified physical quantity, we only need to perform the one-dimension (depth) optimization procedure for beams with different energies. In particular, a pseudo double-layer ripple filter was modelled for carbon ions only to broaden the Bragg peak. The number of primary source particles was set as 10^7 for each beamlet to make the simulation results, e.g., total dose, meet the statistical uncertainty requirement (relative error of the mean value $<$ 1%) when the dose is larger than 5% of the peak dose. All associated simulation data were then written to ROOT histograms [33].

2.2. Dose optimization algorithm for proton and heavy ion beams

We used the Python programming language (version 3.4.3) and its NumPy and SciPy libraries to perform the physical quantity optimization procedures. The basic principle of an optimization algorithm is to find the optimal solutions for the weight of each beamlet to form the desired distribution of the specified physical quantity within the target, using an iterative scheme.

For dose optimization procedures, only the IDDs of all beamlets are needed, and these were generated from the Monte Carlo simulations. Initially, the IDD data are read into the Python program and each IDD is then normalized by its peak dose. Therefore, we can assume the peak dose is 1.0 Gy after the normalization if we assign Gy as the dose units. The normalized IDD dataset is used in seeking the optimal solutions for the beam weights. Next, the boundaries of the target region and the corresponding target dose distribution should be specified. Assuming the expected target dose at depth z is $D_t(z)$ and the real dose after