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PHYSICS CONTRIBUTION

DIRECT COMPARISON OF BIOLOGICALLY OPTIMIZED SPREAD-OUT BRAGG PEAKS FOR PROTONS AND CARBON IONS

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Purpose: In radiotherapy with hadrons, it is anticipated that carbon ions are superior to protons, mainly because of their biological properties: the relative biological effectiveness (RBE) for carbon ions is supposedly higher in the target than in the surrounding normal tissue, leading to a therapeutic advantage over protons. The purpose of this report is to investigate this effect by using biological model calculations.
Methods and Materials: We compared spread-out Bragg peaks for protons and carbon ions by using physical and biological optimization. The RBE for protons and carbon ions was calculated according to published biological models. These models predict increased RBE values in regions of high linear energy transfer (LET) and an inverse dependency of the RBE on dose.
Results: For pure physical optimization, protons yield a better dose distribution along the central axis. In biologically optimized plans, RBE variations for protons were relatively small. For carbon ions, high RBE values were found in the high-LET target region, as well as in the low-dose region outside the target. This means that the LET dependency and dose dependency of the RBE can cancel each other. We show this for radioresistant tissues treated with two opposing beams, for which the predicted carbon RBE within the target volume was lower than outside.
Conclusions: For tissue parameters used in this study, the model used does not predict a biologic advantage of carbon ions. More reliable model parameters and clinical trials are necessary to explore the true potential of radiotherapy with carbon ions.

Protons, Carbon ions, Relative biologic effectiveness, Spread-out Bragg peak, Optimization.

INTRODUCTION

It is often stated that radiotherapy with carbon ions is superior to conventional radiotherapy with photons because of better dose conformation and higher biological efficiency. However, when comparing carbon ions with protons, the situation is more difficult because active scanning systems for protons and carbon ions yield a similar quality of dose conformation, and the differences are mainly given by the biological effects. The aim of this study therefore is to compare physically and biologically optimized spread-out Bragg peaks (SOBPs) for protons and carbon ions on the basis of published physical and biological models.

Carbon ions show a sharper Bragg peak and less lateral scattering than protons, but also a significant dose in the fragmentation tail behind the peak. The physical dose distributions achievable with scanned carbon beams are only slightly better than those for scanned proton beams (1). The main advantage of carbon ions is believed to originate from their enhanced relative biological effectiveness (RBE). However, a clinical gain can be anticipated only if high RBE values are confined to the target volume, with significantly lower RBE in the surrounding normal tissue. Increased RBE values can be expected in regions of high linear energy transfer (LET), which are frequently applied within the target volume.

However, RBE also depends on the tissue type/end point and, for most RBE models, is inversely dependent on dose level. The latter is caused mainly by the shoulder of the photon dose–effect curve used as reference and works against the therapeutic objective because the dose in normal tissue is smaller than that in the target. According to these models, it therefore is not granted that the biological effects of carbon ions are favorable in all cases, and as we note in this report, the LET dependency and dose dependency can more or less cancel each other.

METHODS AND MATERIALS

Physical beam model

In this report, we explored broad fields consisting of a large number of individual beam spots delivered by using a scanning system. We restricted ourselves to the depth–dose curve along the central axis (where we could investigate the different biological effects of

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carbon ions and protons) and did not consider lateral dose distributions. We assumed that we had a synchrotron available that could deliver nearly monoenergetic beams of protons or carbon ions of any desired initial energy. To build an SOBP, several beam spots with distinct initial energies have to be superimposed. To keep the present study as simple as possible, we did not use separate depth–dose curves for each initial energy. Instead, we picked one energy (corresponding to the distal edge of the SOBP) and used a virtual continuous range shifter to obtain depth–dose curves for the lower initial energies needed to build the SOBP. For protons, a beam with initial energy of 145 MeV was chosen (Fig. 1), which was calculated according to an analytical model (2) using an initial energy spread of $\sigma_E = 0.3$ MeV. This method was shown to agree well with measured depth–dose curves (2). For carbon ions, straggling effects are smaller and pristine Bragg peaks are too sharp for clinical applications in scanning systems with active energy variation. We therefore chose a 276-MeV beam that was degraded with a 3-mm ripple filter (3), as used for therapy at the Gesellschaft für Schwerionenforschung (GSI) in Darmstadt, Germany. The method to calculate the depth–dose curve for this carbon beam was described in (4). The degraded carbon peak was only slightly narrower than the proton peak, and the peak-to-entrance ratio was similar (Fig. 1).

Biological beam model

To calculate the biological effect, we followed the formalism described in (5) and associated with the depth–dose curve a corresponding curve of the α parameter of the linear quadratic model and a fixed value for β. For the superposition of many beam spots, the total effect at depth z was then given by $\alpha(z)D(z) + \beta D(z)^2$, where $D(z)$ is total dose and $\alpha(z)$ is the dose-averaged mean of the α values of the constituent spots. Because carbon ions are supposed to be best suited for tumors with a low α_x/β_x ratio for photons, we took the α curve shown in (5) for chordoma tissue (α_x = 0.1 Gy^{-1}, β_x = 0.05 Gy^{-2}, α_x/β_x = 2 Gy), which, in turn, represents the biological model used clinically for base-of-skull chordoma treatments with carbon ions at GSI (6). This effective α curve includes effects of secondary particles and fragments generated in the carbon beam (5). The same biological parameters were also used to estimate late effects in normal brain tissue (6), so that we applied the same tissue characteristics (and just a single biological end point) to the target and normal tissue. This approach corresponded to the current clinical practice at GSI (6, 7). Note that for carbon ion treatments at the National Institute of Radiological Sciences in Japan, a different method was used to obtain clinical RBE values (8).

For protons, we calculate α as a function of the LET according to (9) as $\alpha(\text{LET}) = \alpha_x + \lambda \cdot \text{LET}$, using $\lambda = 0.15\ \mu\text{m keV}^{-1} \cdot \alpha_x$ for $\alpha_x/\beta_x = 2$ Gy (10). Alternatively, the biological effect for protons is also computed assuming a constant RBE of 1.1, in agreement with common clinical practice.

Optimization of SOBPs

To form an SOBP with a range of 146 mm and modulation width of 51 mm in a water phantom, 18 pristine peaks were placed between depths of 95 and 146 mm with a distance of 3 mm, as typically used in active scanning systems. Individual weights were obtained by using an iterative quasi-Newton optimization algorithm. For physical optimization, a standard quadratic objective function to minimize the deviations between actual dose values in the SOBP and the prescribed dose was used. Biologic optimization was performed by using a quadratic objective function for the biological effect, as described in (5). Resolution of the calculation grid was 0.6 mm.

RESULTS

Results of pure physical dose optimization are shown in Fig. 2 for a prescribed dose of 1 Gy. Here, carbon ions showed a higher entrance dose than protons and a higher dose behind the target because of the fragmentation tail. Biologically optimized SOBPs for protons and carbon ions are shown in Fig. 3 for a typical clinical prescription of 3 Cobalt Gray Equivalent (CGE) per fraction. For protons, a variable RBE, as well as a fixed RBE of 1.1, was used. In all three cases, the biological effects were similar in the region proximal to the target and in the target itself. Beyond the target, protons were superior because of the missing fragmentation tail. For carbon ions, the dose dependency of the RBE was much more important than for protons, and it was especially pronounced for tissues with a low α_x/β_x ratio. To show the

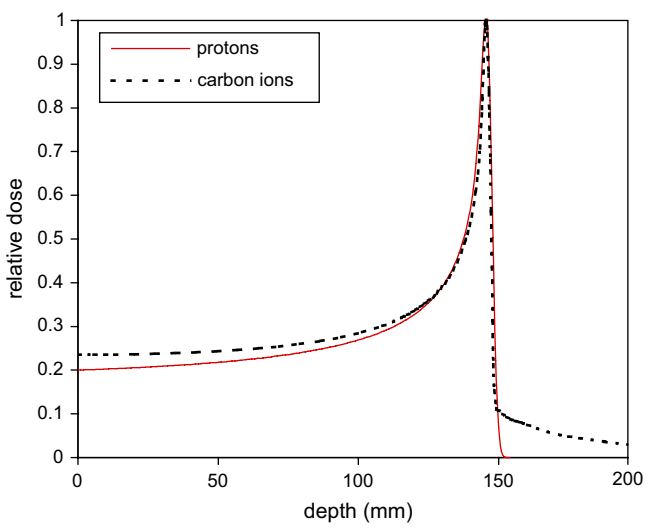

Fig. 1. Pristine Bragg peaks for a 145-MeV proton beam and a 276-MeV carbon beam (degraded with 3-mm ripple filter).

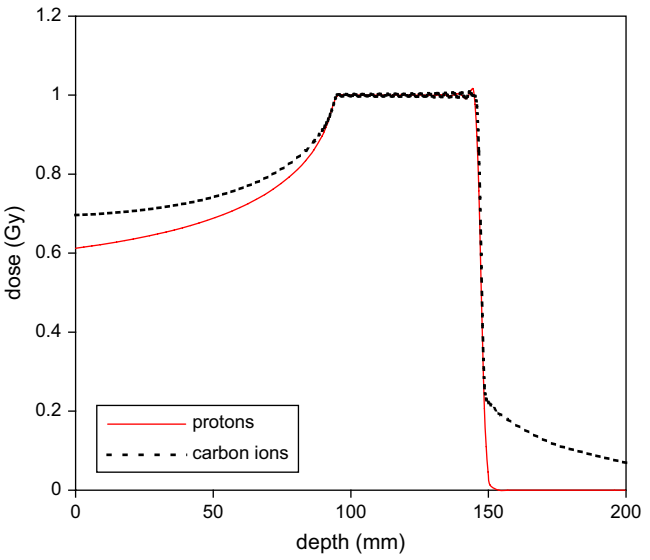

Fig. 2. Dose distribution for spread-out Bragg peaks that were optimized to yield a physical dose of 1 Gy in the target volume.