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Original article

Conformity and robustness of gated rescanned carbon ion pencil beam scanning of liver tumors at NIRS

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ABSTRACT

Purpose: Pencil beam scanning offers excellent conformity, but is sensitive to organ motion. We conducted a simulation study to validate our rescanning approach in combination with gating in the irradiation of liver tumors.

Materials and methods: 4DCT imaging was performed under free-breathing conditions in 30 patients with hepatocellular carcinoma. Dose distributions for a two-field approach were calculated for layered phase controlled rescannings (PCR) under organ motion conditions. A total dose of 45 Gy(RBE) was delivered to respective field-specific target volumes (FTVs) in two fractions, each composed of two orthogonal uniform fields of 11.25 Gy(RBE) at beam angles of either 0° and 90° or 0° and 270°. The number of rescannings was changed from 1 to 10.

Results: Good dose conformity was achieved with 4× PCR or more, and over 95% of the prescribed dose was delivered to the CTV independent of the use of gating. D95, Dmax/min and dose homogeneity were similar with or without gating, whereas V10 dose to the liver as well as maximal doses to healthy tissue (esophagus and cord) were about 40% lower with gating. However, total time increased by about 50% with gating.

Conclusions: Gated rescanning provides good target coverage and homogeneity with maximal sparing of healthy tissue. Our results suggest that carbon-ion pencil beam scanning may soon be available for the safe treatment of liver tumors.

More than 30 particle treatment centers are currently using or undergoing construction to use passive scattering or active scanning irradiation techniques [1]. Our institution has treated tumors at most anatomical sites (including thoracic and abdominal regions) using passive scattering irradiation for carbon ions for almost 20 years. In 2011, we successfully completed the first clinical trials in our new carbon ion beam scanning facility [2]. Pencil beam scanning (PBS) and its associated dose distribution are more sensitive to motion than passive scattering, however, and its use remains limited to anatomical sites not requiring respiratory gating. Further, although PBS and its associated dose distribution are superior to passive delivery in sparing excessive doses to normal tissues, such as rectum in prostate treatment, they are inferior to passive delivery in lateral fall-off with a patient collimator. Moreover, they are more sensitive to motion than passive scattering and could be affected by an interplay effect, which causes hot and/or cold spots within the target due to inconsistency between beam motion and target motion [3,4]. To benefit from the superior dose distribution of PBS, we have sought to extend its use to anatomical sites, which are affected by organ motion. The dose conformity and dose homogeneity of PBS were investigated prior to clinical trials in simulation studies, which used 4D dose calculations under organ motion conditions and usage of respiratory gating. In a previous study using a numeric lung phantom, we concluded that four or more layered phase controlled rescannings (PCR) provide sufficiently good dose homogeneity and dose conformity for our irradiation system [3]. However, because tumors in the upper liver region (close to the diaphragm) can be affected by substantial respiration-induced beam range variation, resulting from replacement of liver tissue by lung tissue, which has lower electron density and stopping power, a separate study for liver tumors is required prior to the start of clinical treatment to ensure the robustness of PBS.

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Materials and methods

Patients and imaging

A total of 30 patients were randomly selected from our patients undergoing conventional carbon beam radiotherapy for hepatocellular carcinoma (HCC) or metastases. All patients were informed of the contents of the study and gave consent to participate, and the study was approved by the Institutional Review Board of our institution. Relevant patient demographics, tumor pathology, size, location and GTV 3-dimensional center of mass (COM) displacement are listed in Table A1. All tumors were located close to the diaphragm, in the middle liver region in 23 patients and in the lower regions in 7.

4DCT data sets were obtained with an area detector CT (ADCT) [5] under free breathing conditions with monitoring of respiration using a respiratory sensing system (Toyonaka Kenkyujo, Osaka, Japan). Since the scan range of the ADCT is insufficient to cover the whole liver (approximately 13 cm in a single rotation), a second 4DCT scan was acquired after completion of the first and movement of the couch to the next position. An image overlap of approximately 2 cm was used. A resorting process was adopted for the first and second 4DCT scans, although resorting as a function of respiratory phase was simpler than for a conventional multi-slice CT because there were only two resorting data sets. This process produced a total scan region of approximately 24 cm with a slice collimation of 128 × 1.0 mm at a rotation time of 0.5 s. The 4DCT data sets were subdivided into 10 phases (T00 = peak inhalation, T50 = peak exhalation). Since our treatment center uses orthogonal fixed beam ports, patient require rotation to irradiate the treatment beam at oblique beam angles. Patient position was accordingly changed from supine or prone to minimize excessive dose to normal tissues between the beam entrance surface of the patient and the tumor.

Target definition

Radiation oncologists delineated the target and normal tissue contours on the mid-exhalation CT data (T30) manually. The choice of mid-exhalation phase, which corresponds to the average tumor position during a respiratory cycle, was motivated by the need to minimize deformable image registration (DIR) errors. To evaluate registration errors, 30-point landmarks were marked on the CT data at peak mid-exhalation, inhalation and peak exhalation in the same coordinate system. Warping of the landmarks was done and the statistics for vector differences were calculated. These contours were transferred to other phases via B-Spline-based DIR [6]. Registration accuracy was an approximate mean distance of 1.4 ± 0.3 mm. The clinical target volume (CTV) was defined with a 10 mm margin to the gross tumor volume (GTV). To consider intrafractional beam range variation, field-specific target volume (FTV) was calculated from the respective 4DCT respiratory phases by selecting maximum and minimum water equivalent pathlength (WEPL) values at the distal and proximal sides, respectively, along the same ray line at respective phases [3,7]. An ungated and gated (T40–T60) irradiation scenario was simulated.

Simulation of the treatment delivery system

PBS irradiation at our hospital is performed by delivering the dose in spots of the same energy (iso-energy layers), on the basis that magnetic scanning is much faster than variation in energy, respectively range. For this study, range was varied using a hybrid depth scanning technique, which consists of a combination of the synchrotron with 11 distinct energies for WEPL steps of 30 mm (time = 150 ms) and a range shifter (time = 420 ms) for WEPL steps of 3 mm in between [8,9]. Since the carbon-ion Bragg peak is rather thin, we further used a mini ridge filter to obtain a flat Spread out Bragg Peak (SOBP) at a 3 mm spacing. We used the same spot size (lateral scatter (P80-20) of 5.0 mm) and spacing of 2 mm in all iso-energy layers. Scanning spot speed is 100 mm/ms and 50 mm/ms for the SI and LR directions, respectively. The maximum beam intensity was set to 1.5×10^8 particles per second (pps).

Treatment planning

Layered phase controlled rescanning (PCR) was applied. In this method, the dose rate for each iso-energy layer is changed to allow the rescanned irradiation of a layer to be completed within one respiratory cycle, or within the gating window if gating is applied [10]. If PCR is not completed within a single gating window due to the particular irradiation specifications selected in advance (dose rate and scan speed) and/or layer sizes, the iso-energy layer is completed by extending the beam delivery to the next gating window. For the present study, scan path was optimized to minimize total pathlength, and sweep direction (irradiation direction of respective spots) was in the superior–inferior direction. The number of PCRs was varied between 1 and 10. Beam weight maps for the FTV were calculated with beam spot spacing of 2.0 mm in the lateral beam direction and 3 mm in depth. A total dose of 45 Gy(RBE) was delivered to the respective FTVs in two fractions, each composed of two orthogonal uniform fields of 11.25 Gy(RBE) at beam angles of either 0° and 90° or 0° and 270°. Starting respiratory phase for irradiation was T00 for the ungated and T40 for the gated scenarios; that is, the beam irradiation was paused until T00 and T40 in the respective iso-energy layers. Overall accumulated dose distribution was calculated by registering the dose distributions at respective phases to that at the reference phase, T30, by applying DIR based on the respiratory signal obtained during 4DCT acquisition. Dose distribution for carbon ion PBS under motion conditions was calculated using our in-house software, Aqualyzer [11].

Results

Accumulated dose distributions of a single field with a different number of rescannings under the ungated scenario are shown in Figs. 1a and A1 (Patient No. 16). This patient received transcatheter arterial chemoembolization before particle therapy, and showed the presence of a high HU region (>600 HU) within the GTV. Beam overshoot due to the associated density variation was observed around the diaphragm region. Although this overshoot reached the esophagus, it was less than 16 Gy(RBE) in respective number of rescannings and thus not particularly large compared to the total tumor dose. A single PCR leads to a significant degradation in dose distribution and hot/cold spots. This degradation is due to interplay effects, which are emphasized by the PCR-induced slow scanning speed (Movie 1). Four or more rescannings improved dose conformity and the whole CTV received a dose larger than 95% of the prescribed dose. In contrast, the improvement in dose homogeneity from four to eight rescannings was small. Dose distribution differences calculated relative to 8× PCR are shown in Fig. 1b (Movie 2).

Accumulated dose distribution with two beam fields with respective rescanning numbers is shown in Figs. 2 and A2 in the ungated and gated scenarios for the same patient. In the ungated case, hot/cold spots within the CTV are observed for a single rescanning whereas these are largely absent in the gated case. This is because scanning speed with the gated case is faster than for the ungated case due to the different time available to deliver the layer dose. The increase in layer size with the ungated scenario due to the larger FTV is not significant enough to negate this effect.

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