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CLINICAL INVESTIGATION **Gastrointestinal Cancer**

INVESTIGATION OF THE GEOMETRIC ACCURACY OF PROTON BEAM IRRADIATION IN THE LIVER

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Purpose: To investigate the geometric accuracy of proton beam irradiation to the liver by measuring the change in Hounsfield units (HUs) after irradiation.
Methods and Materials: We examined 21 patients with liver tumors who were treated with respiratory-gated proton beam therapy (PBT). The radiation dose was 66 GyE in 12 patients and 72.6 GyE in 9 patients. Image registration and reslicing of the computed tomography (CT) results obtained within 1 month before and 3 months after PBT was performed, referring to the planning CT image. The resliced CT images obtained after PBT were subtracted from the images obtained before PBT. We investigated whether the area of the large HU change was consistent with the high-dose distribution area using the location of the largest change in HU around the tumor (peak) on the subtracted CT image and the 90% dose distribution area of the planning CT image.
Results: The number of patients (n = 20) whose left–right peaks were within the 90% dose distribution area was significantly larger than the number of patients whose anterior–posterior peaks and superior–inferior peaks were within the 90% dose distribution area (n = 14, n = 13, p = 0.034, and p = 0.02, respectively). Twelve patients exhibited a peak within the 90% dose distribution area in all directions. Nine of the 11 patients with smaller 90% confidence intervals of the percent normalization of the beam cycle (BC; 90% BC) showed a peak within the 90% dose distribution area in six directions, and this percentage was higher than that among the patients with larger 90% BC (3/10, p = 0.03).
Conclusion: The geometric accuracy of proton beam irradiation to the liver was higher in the left–right direction than in the other directions. Patients with an irregular respiratory rhythm have a greater risk of a reduced geometric accuracy of PBT in the liver. © 2012 Elsevier Inc.

Proton beam therapy, Liver tumor, Image analysis software, Respiratory-gated therapy.

INTRODUCTION

To increase the precision of radiotherapy, reducing geometric uncertainties induced by interfraction setup variations and intrafraction breathing movements that lead to differences between the planned dose distribution and the actually delivered radiation dose are essential. Many methods have been investigated and clinically used to improve the geometric accuracy of irradiation. Methods of managing the interfraction setup variation include the use of daily portal images (1), fiducial markers (2), computed tomography (CT) simulation (3), and video cameras (4). Methods of managing intrafraction breathing movements include the use of breath control (5), respiratory-gated radiotherapy (6), and a tumor-tracking system (7).

A variety of methods have been reported for monitoring the interfraction setup variation including the isocenter dose reproducibility (8), repeated radiographs (9), and repeated CT examinations (10). A variety of methods have also been reported for monitoring intrafraction breathing movements, such as diaphragm movements during fluoroscopy (11), tumor movement from CT (12), dose–volume histograms (13), and calculation of the geometric error based on respiratory motion data (14). Moreover, not only interfraction setup variations and intrafraction breathing movements, but also the changes in Hounsfield units (HU) during

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breathing (15), mechanical response delays (14), and tumor volume changes during the treatment course may change the dose distributions. Hence, the accuracy of the dose delivery is too complex to be confirmed or predicted based solely on an evaluation of the setup or breathing movements only. To our knowledge, radiographic investigation of the geometric accuracy for quantitatively assessing the radiation dose delivery to the tumor has not been previously reported.

Hypoattenuation of the irradiated areas on CT images occur after hepatic irradiation (16). In proton beam therapy (PBT), the proton beam allows a rapidly increasing dose at the end of the beam range (17). Excellent dose localization of the proton beam causes a clearly distinguishable hypoattenuation area in and surrounding the tumor after irradiation (18). Hence, the HU of the liver tissue surrounding the tumor should be markedly reduced after PBT. In contrast, the HU inside the liver tumor should not be as markedly reduced, as it was relatively low before treatment. Consequently, if a CT image obtained after PBT is subtracted from that obtained before PBT, the profile curve of the reduction in HU should appear as two high peaks with a low-value zone in between, representing the periphery and the inside of the tumor during proton beam exposure, respectively. We hypothesized that the localization of the high-value zones and the low-value zone on the profile curve of the reduction in HU should represent the boundary of the tumor and the surrounding normal liver tissue during radiation exposure, enabling the geometric accuracy of the actual irradiation to be verified.

The aim of this study was to investigate the geometric accuracy of proton irradiation to the liver by examining the locations of the areas with large HU changes on a subtraction CT image.

METHODS AND MATERIALS

Patients and procedures

We analyzed data for 21 liver tumor patients (mean age, 65.0 years; range, 48–78 years; 15 men and 6 women) who underwent PBT between July of 2005 and December of 2007 at the University of Tsukuba (Tsukuba, Japan). The selection criteria included patients with a constant irradiation field and any field size or beam angle that was not changed during the course of treatment. Patients with any other prior or concomitant irradiation were excluded. A CT examination was performed within 1 month before and 3 months after PBT using the same CT scanner (IDT16; Philips Electronics Japan Medical Systems, Bothell, WA). The diagnosis was hepatocellular carcinoma (HCC) in 20 patients and liver metastasis in 1 patient.

Before the start of treatment, metallic fiducial markers were implanted percutaneously into the hepatic parenchyma adjacent to the tumor in 18 patients. A drainage tube, gallstone, and the diaphragm were used as substitute markers in 3 patients in whom metallic fiducial markers were not implanted. Custom-made body casts (ESFORM; Engineering Systems, Matsumoto, Japan) were created to ensure adequate immobilization of each patient during radiotherapy. A treatment planning CT examination (CT [plan]) was performed 1 week before PBT using a CT scanner (W3000AD; Hitachi Medical Corporation, Tokyo, Japan). An abdominal CT scan was obtained using a respiratory-gated acquisition protocol. The respiratory waveform was obtained from a laser displacement sensor that could be focused on an area around the patient's navel. A gate signal was given to enable exposure once the respiratory waveform dropped below a certain threshold. The start of exposure was triggered by the gate signal (Fig. 1). To achieve this, the CT table was moved to the next slice position after scanning. All of the slices (5-mm thick) were scanned downward from the top of the diaphragm. The pitch was 0.5.

A clinical target volume (CTV) was contoured as the gross tumor volume plus a 5- to 10-mm margin on serial CT images. An additional 4- to 6-mm margin in the inferior direction was added to the CTV as an internal margin for respiratory movement. The planning target volume was defined as an internal target volume plus a 7- to 13-mm margin (7 mm, 2 patients; 8 mm, 11 patients; 10 mm, 7 patients; 13 mm, 1 patient) in all directions.

Proton beams of 155 to 250 MeV were generated using a synchrotron accelerator at the Proton Medical Research Center, University of Tsukuba. The beams were delivered under respiratory gating through one to three ports using a rotational gantry. During each treatment session, the positional relationship between the isocenter and the fiducial markers was examined using the orthogonal fluoroscopy unit attached to the treatment unit. The dose distribution was calculated using a pencil beam algorithm. The beam delivery devices, including a ridge filter and a fine degrader, were selected automatically by the treatment planning system. A collimator to shape the lateral edge of the field was produced using a brass array.

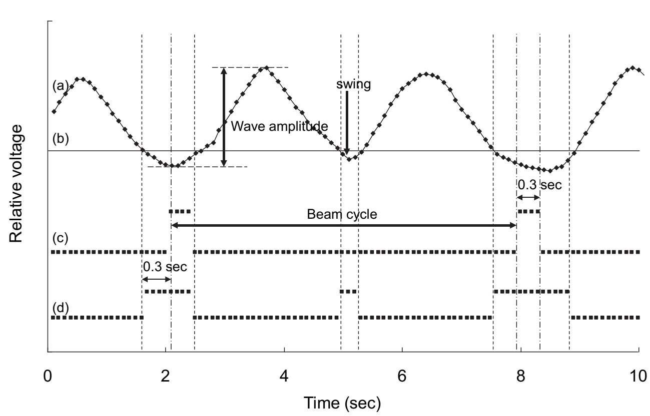

Fig. 1. Time chart of respiratory gated proton beam therapy (PBT). (a) Respiratory waveform. (b) Threshold level of gating. (c) Timing of proton beam exposure. (d) Gate signal. Proton beam is delivered 0.3 s after waveform drops below threshold for 0.3 s.