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PHYSICS CONTRIBUTION

4D PROTON TREATMENT PLANNING STRATEGY FOR MOBILE LUNG TUMORS

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Purpose: To investigate strategies for designing compensator-based 3D proton treatment plans for mobile lung tumors using four-dimensional computed tomography (4DCT) images.

Methods and Materials: Four-dimensional CT sets for 10 lung cancer patients were used in this study. The internal gross tumor volume (IGTV) was obtained by combining the tumor volumes at different phases of the respiratory cycle. For each patient, we evaluated four planning strategies based on the following dose calculations: (1) the average (AVE) CT; (2) the free-breathing (FB) CT; (3) the maximum intensity projection (MIP) CT; and (4) the AVE CT in which the CT voxel values inside the IGTV were replaced by a constant density (AVE_RIGTV). For each strategy, the resulting cumulative dose distribution in a respiratory cycle was determined using a deformable image registration method.

Results: There were dosimetric differences between the apparent dose distribution, calculated on a single CT dataset, and the motion-corrected 4D dose distribution, calculated by combining dose distributions delivered to each phase of the 4DCT. The AVE_RIGTV plan using a 1-cm smearing parameter had the best overall target coverage and critical structure sparing. The MIP plan approach resulted in an unnecessarily large treatment volume. The AVE and FB plans using 1-cm smearing did not provide adequate 4D target coverage in all patients. By using a larger smearing value, adequate 4D target coverage could be achieved; however, critical organ doses were increased.

Conclusion: The AVE_RIGTV approach is an effective strategy for designing proton treatment plans for mobile lung tumors. © 2007 Elsevier Inc.

Proton therapy, 4D treatment planning, Lung cancer, 4DCT.

INTRODUCTION

Several centers have been evaluating the use of proton beam therapy for lung cancer, with early indications that this treatment modality may hold promise for improving local control and overall disease-free survival (1–4). Bush *et al.* (1) followed up 37 patients with early-stage, medically inoperable nonsmall-cell lung cancer (NSCLC) who were treated by proton beams at Loma Linda University and reported that the patients' disease-free survival and local control appeared to be good and compared favorably with those of patients treated by conventional photon irradiation. The study also suggested that dose escalation might be possible using proton beams. A study of 51 NSCLC patients treated with proton beams at the University of Tsukuba (2) also showed that proton therapy is safe and effective, especially in patients with early-stage disease. Chang *et al.* (3) compared compensator-based 3D proton treatment plans with photon 3D conformal or intensity-modulated radiation therapy (IMRT) plans in patients with Stage I or Stage III NSCLC; the results indicated that proton treatment could reduce the dose to normal tissues significantly, even with dose escalation.

Protons are sensitive to variations in tissue density in the beam path. This is particularly important when the tissue

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moves, as in the case of tumors in the lung. To aid treatment planning, technological advances in imaging have emerged, especially the use of 4D computed tomography (4DCT) to measure internal organ motion (5–9). It is therefore essential to determine how to best implement 4DCT in proton therapy treatment planning for lung cancer.

Because proton beams have a finite range with a distinct Bragg peak, the radiation dose can be better localized to the target and normal tissues beyond the range of the proton beam better spared from irradiation. To provide sufficient coverage to the tumor target and a low dose to normal tissues, Moyers *et al.* (10) suggested formulas to estimate proton treatment planning parameters, such as aperture margins, margins proximal and distal to the target, and bolus expansion. The latter parameter is similar to the compensator smearing parameter proposed by Urie *et al.* (11) to compensate for target underdose caused by setup uncertainties and internal target motion. In that study, the treatment plan was designed using a single free-breathing (FB) CT image set, in which each slice in a CT image was from a random snapshot of a breathing phase. The free-breathing CT scan can be very unpredictable. The interplay between CT scanning (couch movement) and the breathing motion can distort anatomy after CT image reconstruction. Free-breathing is usually not equal to any one of the phases, although it is generally closer to the end-expiration phase because patients spent a longer time at the end-of-expiration phase.

The variations in spatial density in the beam path can cause changes in proton dose distributions. Thus, respiratory motion can cause difficulties in evaluating or designing proton treatment plans because of the differences in the "apparent" dose distribution designed on a single CT dataset and the "actual" (cumulative) dose distributions calculated based on 4DCT. Therefore, it is important to evaluate this relationship between the "apparent" and the "actual" dose distribution as a result of organ motion.

Engelsman *et al.* (12) proposed treatment planning strategies for lung tumors using 4DCT by planning on several 4DCT phases and combining the plans to cover the target throughout a respiratory cycle. However, they did not show the composite dose distribution of the plans. In addition, planning on multiple CT sets can be time consuming.

As 4DCT techniques have evolved, they have begun to take into account the fact that tissues (the tumor, the affected organ, and nearby organs) may be deformed as they move. Calculation of doses using deformable image registration is a relatively new approach in 4DCT treatment planning (13–18). With the availability of 4DCT and deformable image registration methods, dose distributions for the tumor target and critical organs can be calculated more accurately because it is possible to sum the doses received by a volume during different phases of the breathing cycle, including the effects of organ motion and deformation. In this process, deformable image registration plays a crucial role in mapping and combining doses received by the same volume in each phase of the respiratory cycle, relative to a reference phase. Therefore, deformable image registration provides a means of evaluating the actual dose distribution.

Unfortunately, current 4D dose calculation methods using deformable image registration are still time consuming and impractical in practice. Thus, it is desirable to develop effective treatment planning approaches that can adequately account for internal organ motion. The goal of this study was to evaluate the effectiveness of four 3D proton treatment planning strategies in designing treatment plans for mobile lung tumors using a single CT dataset derived from a set of 4DCT images; these strategies were evaluated by comparing the dose distribution with those of 4D dose calculations made using a deformable image registration method developed at our institution (17). Target coverage and critical organ sparing were used as the main metrics for the dosimetric evaluation.

METHODS AND MATERIALS

Patient selection

Ten patients with NSCLC that had been found to be subject to a large amount of tumor motion during respiration ($\geq$0.5 cm) were randomly selected for this study. These patients were typical of those who had these types of cancers, and all had received conventional photon treatment at The University of Texas M. D. Anderson Cancer Center between 2004 and 2005. Data used in developing the photon treatment plans were applied to the current analysis of proton planning strategies. Table 1 lists the amount of tumor motion, the tumor's size, and the prescribed radiation dose for each patient. Tumor motion predominantly occurred in the superior–inferior direction, with a magnitude ranging from 0.5 cm to 2.5 cm.

4D computed tomography

In this group of patients, a fast FB CT scan was acquired, in addition to the 4DCT scan for treatment planning. The 4DCT imaging protocol was similar to that described by Rietzel *et al.* (7–9). The fast FB CT scans were acquired on a multislice helical CT scanner. The average (AVE) CT and maximum intensity projection (MIP) CT values were calculated respectively using the mean and maximum CT numbers of the 10 CT datasets at each pixel location. The MIP CT scan represents the highest density in space in the path of all moving tissues among the 10 phases of the breathing cycle.

As an alternative CT set for proton treatment planning, we also constructed a CT set called AVE_RIGTV (average replacement of the internal gross tumor volume) CT, which was an AVE CT in which the CT voxels within the internal gross tumor volume (IGTV) volume had been replaced (overridden) by a higher-density value. This gave a conservative estimation of the densities within the IGTV volume for treatment planning purposes. The Hounsfeld unit (HU) value chosen to replace the IGTV volume was empirically chosen to be 100 because it provided a value slightly higher (more conservative) than the average HU value measured inside the IGTV using the MIP CT (approximately 40 HU in soft tissue). Outside of the IGTV volume, AVE_RIGTV CT has the same HU as that of the AVE CT.

The phase 0% CT was referred to as T0 CT and represented the end-of-inspiration CT; the phase 50% CT was referred to as T50 CT and represented the end-of-expiration CT. All other phases