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PHYSICS CONTRIBUTION

ADAPTIVE RADIOTHERAPY PLANNING ON DECREASING GROSS TUMOR VOLUMES AS SEEN ON MEGAVOLTAGE COMPUTED TOMOGRAPHY IMAGES

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Purpose: To evaluate gross tumor volume (GTV) changes for patients with non–small-cell lung cancer by using daily megavoltage (MV) computed tomography (CT) studies acquired before each treatment fraction on helical tomotherapy and to relate the potential benefit of adaptive image-guided radiotherapy to changes in GTV.
Methods and Materials: Seventeen patients were prescribed 30 fractions of radiotherapy on helical tomotherapy for non–small-cell lung cancer at London Regional Cancer Program from Dec 2005 to March 2007. The GTV was contoured on the daily MVCT studies of each patient. Adapted plans were created using merged MVCT–kilovoltage CT image sets to investigate the advantages of replanning for patients with differing GTV regression characteristics.
Results: Average GTV change observed over 30 fractions was −38%, ranging from −12 to −87%. No significant correlation was observed between GTV change and patient's physical or tumor features. Patterns of GTV changes in the 17 patients could be divided broadly into three groups with distinctive potential for benefit from adaptive planning.
Conclusions: Changes in GTV are difficult to predict quantitatively based on patient or tumor characteristics. If changes occur, there are points in time during the treatment course when it may be appropriate to adapt the plan to improve sparing of normal tissues. If GTV decreases by greater than 30% at any point in the first 20 fractions of treatment, adaptive planning is appropriate to further improve the therapeutic ratio. © 2007 Elsevier Inc.

Helical tomotherapy, Lung cancer, Plan reoptimization, Adaptive planning.

INTRODUCTION

The megavoltage (MV) computed tomography (CT) acquisition capability of helical tomotherapy has proved very effective for pretreatment patient positioning to decrease setup errors (1, 2). The MVCT image sets depict the patient's anatomy with image contrast and resolution that is slightly inferior to a kilovoltage CT (kVCT) study, but has enough soft-tissue contrast to reliably contour organs or lesions in many areas of the body (3, 4). In particular, peripheral-lung tumors can be easily detected and delineated on MVCT image sets. However, significant uncertainty in target delineation may be associated with tumors partially abutting or primarily contained in the mediastinum (5, 6). If treatment for patients with non–small-cell lung cancer (NSCLC) on helical tomotherapy involves regular MVCT imaging, the gross tumor volume (GTV) response to radiotherapy can potentially be assessed on a daily basis.

Tumor control predictions based on pretreatment measurements are well studied, and most investigators used the criterion of tumor size measured by largest tumor dimension, bidimensional product, or tumor volume for a local control predictor. Usefulness of tumor size/volume as an overall prognostic factor for survival is still under discussion (7–9). Correlation of pretreatment tumor size with local control suggests that such tumor characteristics as size could possibly be used to anticipate the amount of GTV regression during a course of treatment. Generally, NSCLC tumor response to radiotherapy is believed to be a slow process because tumors reach their maximum response (minimum volume) an average of 11 months after radiotherapy completion (9). Kupelian *et al.* (10) and Siker *et al.* (11) used measurements of tumor volume on serial MVCT image sets generated by helical tomotherapy to document interfractional radiation responses during a shorter period, whereas Ramsey *et al.* (12) focused on adaptive dosimetric planning as tumor

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volume changes. Others used multiple kVCT scans to evaluate tumor volume changes during radiotherapy (13–16) or portal images to monitor tumor position, size, and movement (17). All these investigators observed tumor volume shrinkage to varying degrees during the course of fractionated treatment, suggesting tumor volume changes during shorter periods may be clinically relevant. The aim of this report is to evaluate GTV changes in 17 patients treated for NSCLC on helical tomotherapy, characterize GTV variation, and model the potential benefit of adaptive planning during a course of fractionated radiotherapy.

METHODS AND MATERIALS

Seventeen patients were treated for NSCLC on the Hi-Art helical tomotherapy (TomoTherapy, Inc., Madison, WI) unit at the London Regional Cancer Program, Ontario, Canada, from December 2005 to March 2007. All patients received cisplatin and vinorelbine as neoadjuvant chemotherapy, finishing treatment 4–6 weeks before the start of radiotherapy. Chemotherapy is not expected to affect relative GTV changes from radiotherapy in patients because all patients were treated using the same regimen. The CT simulation and tomotherapy treatment planning (Hi-ART, version 2.2.2) occurred approximately 3 weeks before starting treatment, with delivery quality assurance performed to ensure proper dose distributions and absolute dose delivery. One initial mock treatment that included an MVCT study was performed for each patient, after which they began treatment with daily MVCT acquisitions for setup verification. A prescription dose of 60–64 Gy in 2 Gy/fraction was used for patients in this study, all of whom had locally advanced (Stage $\geq$ IIIA) disease. Elective nodal radiation was included for some patients, with doses of 50 or 60 Gy delivered to adjacent radiographically uninvolved nodal regions. The MVCT scans on the Hi-Art system were acquired with photon beam energy of 3.5 MV, field of view of 40 cm, fan beam width of 5 mm at the isocenter, and pitch factor of 2.4 for coarse (6-mm) slices (3). The reconstruction matrix was 512×512 in the axial plane, yielding a $0.78 \times 0.78 \times 6\text{-mm}^3$ voxel size. For this patient population, Planned Adaptive (TomoTherapy, Inc.) software was not available at the time of treatment. For this reason, an additional kVCT study was performed for 6 patients to construct an adapted plan at the request of the treating radiation oncologist for patients with local anatomy changes deemed clinically significant on serial MVCTs during the actual treatment course.

For this report, GTV volume changes were calculated retrospectively based on the serial MVCTs obtained daily during treatment. For calculation of GTV changes during the course of treatment, GTV was contoured after transferring the daily MVCT studies for each patient from the helical tomotherapy unit to a treatment planning system (either Pinnacle[3] version 8.0d; Philips, Fitchburg, WI, or Oncentra Treatment Planning, version 1.3.1.13; Nucletron, Veenendaal, The Netherlands). The MVCT images were contoured with a window/level setting of 1600/−300 for tumor bounded by parenchyma and 400/800 for tumor abutting the mediastinum. The kVCT studies for each patient were available to provide guidance to the investigator (C.W.) who did the MVCT contouring. Involved nodes were excluded from the GTV; only primary tumor volume was measured for the purpose of calculating response in this report.

The MVCT images generated by using helical tomotherapy can also be used to create adapted plans when significant changes in the patient's GTV are observed as treatment progresses. In our study, Planned Adaptive software was used to create merged images for 3 patients in which the 40-cm field of view of the pretreatment MVCT replaced the corresponding section of the full planning kVCT. The registration values used to position patients for treatment were also used to adjust the position of the MVCT study relative to the kVCT study when creating the merged kVCT-MVCT images. These registration values were determined by using semiautomated registration software on the helical tomotherapy treatment console. The 6-mm slices of the MVCT studies were changed to 3-mm slices by interpolation to correspond with the slice spacing of the kVCT studies. The original contours used for planning on the kVCT studies were overlaid on the merged images, and they were altered by the investigators to reflect changes in target and lung volumes based on the merged kVCT-MVCT images. The only structures that typically required modification on the merged images were the lungs (to account for changes in atelectasis or pleural effusion) and the GTVs and planning target volumes (PTVs; to account for target volume changes). A three-dimensional (3D) margin of 12 mm (corresponding to the original margins for the initial plans) was added to the GTVs to generate the PTVs. Although 4D-CT was not performed on these patients to quantify respiratory motion, Schwarz *et al.* (18) recommended a 10-mm GTV-PTV margin for patients with breathing amplitudes of up to 10 mm undergoing intensity-modulated radiotherapy. Because GTV-PTV margins are anatomy and patient specific, a margin of 12 mm was chosen to ensure target coverage beyond that provided by a 10-mm margin.

The merged images created with the MVCT scans from 3 patients were transferred to the TomoTherapy planning station to create adapted plans. Using a merged image for planning radiation delivery assumes the patient's anatomy outside the region of interest covered by the MVCT has not changed since planning and that the dose calculation using merged images is accurate.

At the London Regional Cancer Program, we have planned and treated prostate cancer patients with hip prostheses using merged images. Accuracy of dose calculation with merged image plans previously was confirmed for sites in the head and neck, lung, and prostate by creating a merged image plan and testing the delivery of the plan on tomotherapy by using three ion chamber measurements and one film exposure in a cylindrical phantom as quality assurance.

Three patients were investigated with this adaptive planning method using merged images to find out whether plan improvements can be significant for the patient and distinguish between clinically insignificant or significant anatomy changes based on their adaptive planning potential. To evaluate the quality of the adapted plans, the cumulative doses to the PTV and lungs are reported. The cumulative dose, D_c, is defined as the total dose delivered to a region of interest during the course of treatment. When using multiple adapted plans, where i is the plan number (i = 1, 2, 3, …), d_i is the planned dose to the region of interest, n_i is the number of fractions for which plan i was used, and n_t is the prescribed number of fractions, cumulative dose:

$$D_c = \frac{\sum_i d_i n_i}{n_t} \tag{1}$$

Cumulative doses were calculated for the 3 patients based on the adapted plans using merged images as the planning image set. The adapted plans (APs) are referred to by the fraction number of the MVCT used to create the merged image, so AP_{10} is an adapted plan created using the MVCT from the tenth fraction of treatment. Doses to 99% and 1% of the PTV, along with mean lung dose (MLD) and volume of lung tissue that receives more than 20 Gy (V_{20}), were compared (19, 20).