Radiotherapy and Oncology 96 (2010) 73–77

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

3-D CT in lung cancer

Feasibility of using intravenous contrast-enhanced computed tomography (CT) scans in lung cancer treatment planning

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ARTICLE INFO

Article history:
Received 5 October 2009
Received in revised form 16 February 2010
Accepted 21 February 2010
Available online 27 March 2010

Keywords:
Contrast agent
Active breathing control
Treatment planning
Dose calculation
Lung cancer

ABSTRACT

Background and purpose: To investigate the feasibility of using intravenous contrast-enhanced computed tomography (CT) scans in 3-dimensional conformal radiotherapy (3D-CRT), stereotactic body radiation therapy (SBRT) and intensity-modulated radiotherapy (IMRT) treatment planning for lung cancers, respectively.

Materials and methods: Twelve patients with bulky lung tumors and 14 patients with small lung tumors were retrospectively analyzed. Each patient took two sets of CT in the same position with active breathing control (ABC) technique before and after intravenous contrast agent (CA) injections. Bulky tumors were planned with 3D-CRT, while SBRT plans were generated for patients with small tumors based on CT scans with intravenous CA. In addition, IMRT plans were generated for patients with bulky tumors to continue on a planning study. All plans were copied and replaced on the scans without intravenous CA. The radiation doses calculated from the two sets of CTs were compared with regard to planning volumes (PTV), the organ at-risk (OAR) and the lungs using Wilcoxon's signed rank test.

Results: In comparisons for 3D-CRT plans, CT scans with intravenous CA reduced the mean dose and the maximum dose of PTV with significant differences ($p < 0.05$) that were within 1.0%. Comparing IMRT and SBRT plans, CT scans with intravenous CA obviously increased the minimum irradiation dose and dose of 95% volume of target received (D_{95}) for targets, respectively ($p < 0.05$). There was no statistical significance for lung parameters between two sets of scans in SBRT plans and IMRT plans.

Conclusions: The enhanced CT scans can be used for both target delineation and treatment planning in 3D-CRT. The dose difference caused by intravenous CA is small. But for SBRT and IMRT, the minimum irradiation dose in targets may be estimated to be increased up to 2.71% while the maximum dose may be estimated to be decreased up to 1.36%. However, the difference in dose distribution in most cases were found to be clinical tolerable.

Lung cancer continues to be one of the principal causes of death in industrialized countries. Non-small-cell lung cancer (NSCLC) constitutes near 85% of all lung cancers, and almost 40% of them have non-operable stage IIIA or IIIB at time of diagnosis [1]. For patients with inoperable locally advanced NSCLC, standard treatment is concurrent chemo-radiotherapy. For patients with early stage NSCLC, stereotactic body radiation therapy (SBRT) has shown at least as effective as a definitive surgical resection. Therefore, it appears that radiotherapy has an important position in multidisciplinary treatment strategies for NSCLC. In order to obtain an accurate delivery of radiotherapy, the accurate delineation of the treatment target is essential. However, studies have shown that the definition of the gross tumor volume (GTV) might vary significantly among professionals, centers and levels of experiences [2,3].

Intravenous contrast-enhanced computed tomography (CT) could be utilized in radiotherapy lung treatment planning to improve the delineation of the tumor volume and lymph nodal areas, as reported by McGibney et al. that contrast agent (CA) reduced GTVs by a range of 22–34% [4]. But the use of contrast-enhanced CT scans for treatment planning where heterogeneities are accounted for could adversely influence the dose distribution because the CA will not be present at the time of treatment. This may be the reason why some treatment centers have not used contrast agents CT for treatment planning. For example, a Spanish

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doi:10.1016/j.radonc.2010.02.029

patterns-of-care study for thoracic radiotherapy in patients with NSCLC indicated that intravenous CA was never used in 81.5% of the cases [5].

There have been two kinds of investigation on the effect of contrast-enhanced CT scans on dose computations until now. Studies carried out on phantoms or mathematical calculations belonged to the first group. Ulla Ramm et al. investigated influence of CT contrast agents on dose calculations in a 3D treatment planning system with a water phantom [6]. And James L. Robar et al. examined the magnitude of tumor dose enhancement achieved by injection of gadolinium or iodine contrast media (CM) by Monte Carlo modeling and a phantom [7]. Their results have shown that contrast media does enhance the dose significantly and depends on photon beam energies, molarity and expansion of the CAs. Influences of iodinated contrast media on dose calculation for tumors at various anatomical regions in patients were investigated in another group [8–11]. It was obvious that the effect on dose calculation in treatment planning is negligible for some regions where the CA concentration and its expansion were relatively low. For lung cancer, the study results indicated that the introduction of CA had a minimal dosimetric impact upon treatment plans if a density correction strategy was applied [9,11]. Due to the absence of synchronizing of diagnostic and treatment procedures with breathing in these studies, it is hard to evaluate the effect of using CA-enhanced CT scans in the planning stage actually. There has been no report on this with regard to the breathing synchrony. Therefore, we undertook the present study to examine the effect of intravenous CA on dose distribution of radiation treatment plans for lung cancer patients who were irradiated with a respiration control technique, which is called active breathing control (ABC) [12–16].

Methods and materials

A treatment planning study was performed to examine the effect of intravenous CA for planning CTs on the radiation dose distribution of SBRT and conventionally-fractionated radiation therapy (CFRT, including 3-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT)) plans for lung cancers, respectively. In this study, 14 lung cancer patients who received SBRT and 12 lung cancer patients who received 3D-CRT at West China hospital, Sichuan University in Chengdu, PR China between March 2008 and March 2009 were included. The patient characteristics were listed in Table 1. All patients were staged according to the modified 1997 AJCC staging system [17] and could tolerate ABC in the treatment process.

Table 1
Basic and clinical characteristics of selected patients in present study.

	SBRT (n = 14)	CFRT and IMRT (n = 12)
Age (years)		
Median	53	47
Range	35–75	39–66
Sex		
Male	10	9
Female	4	3
Pathology		
Primary NSCLC	4	12
Metastatic lung tumors	10	0
Location of tumor		
Right upper lung	3	3
Right lower lung	5	5
Left upper lung	3	2
Left lower lung	3	2
PTV volume (cm^3)		
10–30	5	Median: 348.68
31–50	5	Range: 237.98–540.88
51–70	4	

Acquisition of CT

All patients were immobilized with their arms raised above the head on a lung board designed to support the elbows with an individualized thermoplastic mask. The ABC device which consisted of a mouthpiece connected to a transducer turbine air-flow meter coupled to a balloon valve was used both in CT scanning and beam delivering for every patient. The resting tidal volume and maximum inspiratory volume (MIV) for patients were recorded. Patients were trained beforehand to adapt at moderate deep inspiration breath-hold (mDIBH) set at 75% of MIV up to a maximum of 35 s depending on individual tolerance. The average length of the breath holding for all patients was 28.35 ± 5.63 s. Radiation treatment would only be delivered when a patient was at this breath-holding condition. Two sets of planning CTs (Siemens, Somatom Plus 4) which had sufficient coverage to include the total lung volume were initially taken with and without intravenous CA in the same position and coordinates at 3 mm slice thickness with ABC for each patient. The enhanced scan (120 kVp, 90 mA) was started about 5 s after a bolus injection of 90 ml CA (Iopamiro370, BraccoS.P.A., Italy) with a power injector, and performed for approximately 15 s. The CA contained 370 mg/ml of iodine. After the acquisition of the CT, the two sets of CTs were transferred to a radiotherapy planning system (Pinnacle^3 8.0, Philips Inc., USA) via DICOM through network. An example of the difference between the two scans is shown in Fig. 1. An accurate registration between the CT scans with and without intravenous CA could be obtained by using the image fusion option in the Pinnacle^3 software. Essentially the setup of the patient for the two scans was the same in terms of breathing protocol, arm position and couch position. In order to compare the density difference between the two sets of CT scans, the mediastinum, lung and heart in radiation fields were outlined in each set of CT scans. The mean Hounsfield units (HU) for each of them was obtained from the Pinnacle^3 planning system.

Treatment planning

The target lesions were delineated by radiation oncologists on the enhanced CTs. The heart, mediastinum, lungs and spinal cord were contoured as the organs at-risk (OAR), respectively.

For 14 patients undergoing SBRT, the GTVs which were defined only as the solid abnormality on CT were generally contoured at pulmonary window levels. While soft tissue window levels might be used to avoid inclusion of adjacent vessels or chest wall structures within the GTVs. A 10 mm margin was added isotropically to the GTVs to generate the planning target volumes (PTV). The PTVs were modified to avoid overlapping with the mediastinum and chest wall. Seven equiangular beams and a fractionation scheme of 4 fractions of 12 Gy were applied in the present study. The aperture size and shape of each field corresponded near identical to the projection of the PTV along a beam's eye view. The request for all plans was that 90% of the prescribed dose covered 100% of the PTVs with the maximum dose less than 120% of the prescription.

For 12 patients undergoing 3D-CRT, the GTVs were defined as the solid abnormality on CT at pulmonary window levels. A 3 mm margin was added around the GTVs to generate planning GTV (PGTV). The CTVs were defined as the GTVs plus a 10 mm margin in which both the primary tumor site and the nodal levels to which the enlarged lymph nodes belonged were involved. The PTVs were defined as the CTVs plus a 3–5 mm margin. The prescription doses were 50 Gy in 25 fractions for PTV and 66 Gy in 33 fractions for PGTV, respectively. The planning objective was to