The effects of set-up errors on dose distribution in radiotherapy treatment for lung cancer

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ABSTRACT

Background: Our aim was to analyze the effects of set-up errors on dose distribution in radiotherapy treatment for lung cancer by using kilovoltage cone-beam CT (CBCT). ***Materials and Methods:*** In this study, we used a Varian IX linear accelerator system to perform CBCT scans of 30 lung cancer patients before radiotherapy. Subsequently, the image was matched with the planned CT, and the left and right (LR), top and bottom (SI), and front and back (AP) directions were set incorrectly. And in the CMS planning system, the center of the plan has been moved to the center of the actual scan. Finally, the dose distribution before the bed-moving is simulated. We want to explore the impact of the planned target volume setting error (PTV), the total tumor volume (GTV), and radiation of normal tissues. ***Results:*** The set-up errors of the LR, SI and AP directions were (-0.20±2.84), (-1.09±5.40), and (-2.61±2.08) mm, respectively. The 5mm error accounted for 97.8%, 73% and 92.6% in the three directions. Statistically significant differences were found in the distribution of 95%PTV dose, the average dose of PTV, 95% GTV dose and the average dose of GTV without bed-moving, compared with the original plan. ***Conclusions:*** In clinical lung cancer radiotherapy, the commonly used setting error is usually less than 5mm, most of which are along the AP direction. In this study, we found that the setting error is related to the patient's inherent characteristics and can significantly change the radiation treatment dose in the target area.

Keywords: *Tomography, X-ray computer, cone-beam; set-up error, lung tumor/radiation therapy, dosimetry.*

INTRODUCTION

Lung cancer is the one of the most lethal malignancies. For patients who have lost the opportunity for surgery, radiation therapy is an important choice. Precise radiotherapy of lung cancer depends on high-resolution CT, MRI, or electron emission computer tomography (positron emission tomography, PET) and other image technologies (1). Based on these instruments, integrated three-dimensional treatment techniques such as precise positioning, precise planning, precise positioning, and precise irradiation are carried out (2). Recently, kilovoltage cone-beam CT (CBCT) in three-dimensional radiotherapy has been used to make the treatment more accurate. The CBCT can image during the process of radiotherapy and clear the set-up errors by comparing the reconstructed image with the planned one.

Small setup margins are needed in order to avoid the irradiation of normal tissue. Previous studies had evaluated the effect of image-guided radiation therapy (IGRT) on the margin between the clinical target volume (CTV) and planning target volume (PTV) in lung cancer and the results showed that IGRT could reduce the

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margins by reducing the set-up errors, especially in the SI directions [3]. Moreover, an automatic 6D correction was also used to improve the accuracy [4]. CBCT-based set-up strategies had been identified to correct the set-up errors for stereotactic body radiation therapy in the liver [5]. However, the set-up error and its effects on dose distributions for CBCT guided radiotherapy were still unclear.

In this study, we used kilovolt CBCT guided radiotherapy technology to analyze and treat 30 patients with lung cancer. The purpose is to be able to study the effect of the setting error on the dose of radiation therapy in the target area. It is hoped that a suitable setting error can be explored, so that the boundary of the target area of the outgoing plan can be effectively reduced, the treatment effect can be improved, and the side effects can be reduced.

MATERIALS AND METHODS

Study design

This study was a retrospective study and approved by the medical ethics committee of the Third Hospital of Hebei Medical University.

Inclusion and exclusion criteria

Inclusion criteria: In total, 30 patients with pathological diagnosis of lung cancer were analyzed, including 18 men (mean age±standard deviation, SD, 41.8±12.9 yr; range, 24-85 yr) and 12 women (mean age±SD, 42.3±12.4 yr; range, 18-74 yr), with an overall mean age±SD of 42.6±12.5 years. These patients require radiotherapy at least once a week through CBCT scans. The dose of radiotherapy was 48-68Gy and the number of times was 8-34 times. The number of CBCT scans in each patient was at least 5 times. Exclusion criteria: Patients with insufficient scan or poor image quality. From March 2017 to December 2018, a total of 30 patients were enrolled in this study. The definition of central and peripheral lung cancer: central type was defined as lesions from the main bronchus less than 2cm and the peripheral type was defined as lesions from the main bronchus more than 2cm. The lesions were divided into upper and lower lungs according to the fifth thoracic vertebrae.

Major equipment

Varian IX Image-Directed Linear Accelerator, on board imager (OBI), airborne kilovolt-level CBCT and Eclipse treatment planning system (TPS) were purchased from Varian (U.S). Somotom-sensation Plus-16 spiral CT was purchased from Siemens, Germany.

Set-up method

All patients were placed in the supine position, and the headrest carbon fiber underframe and headrest were in a comfortable position. Then hold the head with both hands and fix it with thermoplastic body film, and select the double labeling method with reference to the coordinate labeling. Used a CT scanner to scan the chest with a layer spacing of 5 mm. From the plain scan of the cricothyroid membrane to the lower margin of the diaphragm, the CT imager told the patient to breathe calmly. The scanned image was uploaded to TPS for 3D image reconstruction.

Targeting and treatment plan

The target area was sketched according to the No. 50 report of International Commission on radiation unit and measurement (ICRU). The gross tumor volume (GTV) was the size of the tumor seen by the naked eye. The GTV was extended to obtain the clinical tumor volume (CTV) according to the lesion site and pathological type of the patient. The CTV plus motion error and 5mm set-up error was planned tumor volume (PTV). Physicists designed the treatment plan in the CMS planning system and the prescription dose was 48-68 Gy.

CBCT Image Acquisition and Matching

Varian IX Image-Directed Linear Accelerator was used for kV CBCT and Therapy. Scan parameters: low-dose chest, half-fan, reconstructed volume 512 × 512, layer spacing 2.5mm, voltage 80kV, current 25mA and image capture time was 10ms per frame. CBCT scans were performed in patients with normal divisions at the beginning and repeated 1 to 2

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times a week. Patients with large divisions underwent CBCT scans before each treatment. The pre-treatment CBCT images were automatically matched with the CT images according to the soft tissue window by on board imager (OBI).

The system automatically recorded the deviation between the center of the patient's planned target position and the center of the actual scan target in LR directions (x-axis), AP directions (y-axis) and the SI directions (z-axis). If the x, y, z axis error in either direction was >3mm, we would move the treatment bed to the correct position for further treatment. Due to directionality of the set-up error, we defined the left direction, the inferior direction, the anterior direction as positive signs and the right direction, the superior direction, the posterior direction as negative signs.

Treatment plan simulation and assessment

The images used for the dose calculation were all based on the CT images of the treatment plan and the dose parameters were 95% PTV, average PTV, 95% GTV and average GTV. In addition, the percentages of the lungs receiving ≥5, 10, 20 and 30 Gy (V5, V10, V20, V30) of the total volume, average lung volume, 1cm^3 spinal cord volume were also recorded.

Statistical methods

The values were shown as mean±standard deviation. Statistical analysis was performed by SPSS13.0 software. The effects of set-up error on dose distribution were evaluated by a paired t test and the test level α = 0.05. P <0.05 for the difference was statistically significant.

RESULTS

General clinical data

A total of 30 patients including 19 cases of left lung, 11 cases of right lung, 18 cases of central type, 12 cases of peripheral type, 15 cases of upper lung and 15 cases of lower lung were admitted and all patients were confirmed by pathological diagnosis (table 1).

Setup error and correlation analysis

All the 30 patients received 270 CBCT scans. Considering the error of direction, the errors of the x axis, the y axis and the z axis were (-0.20 ± 2.84), (-1.09 ± 5.40) and (-2.61 ± 2.08) mm, respectively. The errors less than 5 mm accounted for 97.8%, 73.0% and 92.6% in three directions respectively. The frequencies of set-up errors were shown in figure 1.

Table 1. General information of the 30 patients recruited in this study.

Items	
Patients	**30**
Age (mean age ± SD)	men 41.8±12.9 yr; women 42.3±12.4 yr;
Gender Male vs female	18:12
Weight Median (Range)	70(55-94)
Primary NSCLC (n, %)	n =26,87%
Pulmonary metastasis (n, %)	n =4,13%
Tumor size	
Diameter of tumor (cm) (mean ± SD)	5.39±2.54
Range (cm)	1.5-12
Volume(cc) (mean ± SD)	129.13±140.85
Range(cc)	2.1-520.73
tumor locations	
Left vs right	19:11
Certral vs peripheral	18:12
Upper vs lower	15:15
Lung volume(cc)	
Left volume(mean ± SD)	1249.55±470.70
Right volume (mean ± SD)	1672.70±578.26

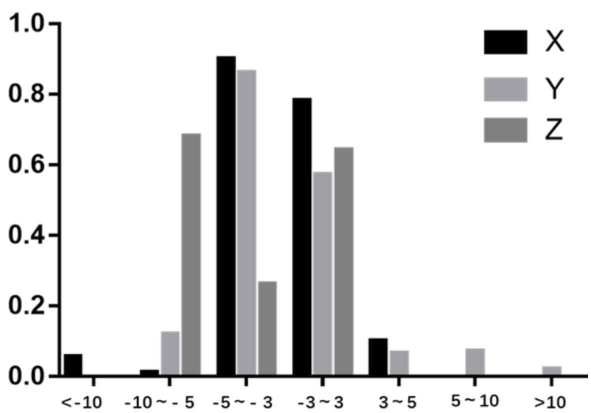

Figure 1. The frequency of the set-up errors in three axes.

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The effect of setup error on dose distribution

Next, we compared the PTV and GTV dose with the original plans. As a result, statistically significant effects were found between actual dose and planned dose in average doses of 95% PTV, PTV average, 95% GTV and GTV (table 2). The patients were further divided into three groups (error of <3mm in all directions, 3 - 5mm in either direction and> 5mm in either direction). The impact of error on dose distribution was stratifiedly analyzed (table 3). For errors of 3 - 5mm in either direction and > 5mm in either direction groups, statistically significant effects were found between actual dose and planned dose in average doses of 95% PTV, PTV average, 95% GTV and GTV. However, for error of <3mm in all directions group, statistically significant effect was found in 95% PTV.

Table 2. Dose comparisons between the original plan and no bed moving stimulation in normal tissues and target tissues.

Dose parameters	Mean± Std. Dviation	Difference Mean ± Std. Dviation	t	*p*
(Planned) lung V_5 (%)	36.62±16.38	0.064±2.959	0.118	0.907
(Actual) lung V_5 (%)	36.56±16.40			
(Planned) lung V_{10} (%)	25.92±13.37	-0.075±1.649	-0.248	0.806
Actual) lung V_{10} (%)	26.00±13.28			
(Planned) lung V_{20} (%)	14.42±7.71	-0.154±1.631	-0.516	0.610
Actual) lung V_{20} (%)	14.57±7,87			
(Planned) lung V_{30} (%)	8.97±5.19	-0.161±1.375	-0.640	0.527
Actual) lung V_{30} (%)	9.13±5.47			
(Planned)average dose of lung (cGy)	849.07±394.79	-6.900±77.649	-0.487	0.630
(Actual)average dose of lung (cGy)	855.97±401.41			
(Planned) 1cm^3 dose of spinal cord (cGy)	2778.00±1248.97	7.933±194.449	0.223	0.825
(Actual) 1cm^3 dose of spinal cord (cGy)	2770.07±1236.67			
(Planned) 95%PTV (cGy)	5399.07±829.25	537.433±621.192	4.739	0.000
(Actual) 95%PTV(cGy)	4861.63±799.17			
(Planned)average dose of PTV (cGy)	5871.80±892.67	126.000±120.491	5.728	0.000
(Actual)average dose of PTV (cGy)	5745.80±852.21			
(Planned) 95%GTV (cGy)	5750.33±874.05	271.867±326.009	4.568	0.000
(Actual) 95%GTV (cGy)	5478.47±804.95			
(Planned)average dose of GTV (cGy)	6008.60±939.62	89.400±97.421	5.026	0.000
(Actual)average dose of GTV (cGy)	5919.20±907.77			

Table 3. Stratified analysis of the effects of set-up errors on target volume.

Stratified analysis	Case	Dose parameters	Difference Mean ±Std. Dviation	t	*p*
The error in all directions <3mm	7	95%PTV (cGy)	176.286±163.478	2.853	0.029
		average dose of PTV (cGy)	41.571±51.195	2.148	0.075
		95%GTV (cGy)	99.143±112.950	2.322	0.059
		average dose of GTV (cGy)	41.429±92.862	1.180	0.283
Any direction of error at 3 - 5mm	16	95%PTV (cGy)	351.563±289.282	4.861	0.000
		average dose of PTV (cGy)	99.000±67.163	5.896	0.000
		95%GTV (cGy)	191.375±214.176	3.574	0.003
		average dose of GTV (cGy)	70.063±62.627	4.475	0.000
Any direction of error >5mm	7	95%PTV (cGy)	1323.429±814.927	4.297	0.005
		average dose of PTV (cGy)	272.143±145.242	4.957	0.003
		95%GTV (cGy)	628.571±430.965	3.859	0.008
		average dose of GTV (cGy)	181.571±117.686	4.082	0.006

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DISCUSSION

Patient setting errors are closely related to tumor radiotherapy accuracy and dose. In order to achieve the same position as the planned position of the radiotherapy patient, choose a thermoplastic body film and a vacuum pad to fix and maintain the operation procedure settings of the patient [6]. However, due to the time interval between positioning and radiotherapy, combined with radiation and indwelling needles can cause limb distortion or pain [7]. In addition, some patients will be afraid and nervous when entering the treatment room for the first time, which can cause posture twisting and produce higher setting errors [8]. Therefore, many researchers are working hard to find a suitable guidance method to reduce the positioning error and improve the positioning accuracy [9]. Image guided radiation therapy (IGRT) is a four-dimensional radiotherapy technology, which adds the concept of time factor based on three-dimensional radiotherapy technology [10]. And fully considered the movement of anatomical tissue during treatment and displacement error between fractional treatments, such as breathing and peristaltic movement [11]. Changes in the radiation dose distribution caused by daily positioning errors, shrinkage of the target area, etc. and the impact on the treatment plan [12]. Real-time monitoring of tumors and normal organs with various advanced imaging equipment before and during treatment [13]. And can adjust the treatment conditions according to the change of the organ position so that the radiation closely "follows" the target area.

In the past 24 cases of cancer patients in radiotherapy research. It was found that incorrect settings of 209 CBCT and 124 EPID can affect the final radiotherapy effect. And it is concluded that both have the same effect of correcting the setting error [14]. Another study was on the misconfiguration of 20 cases of esophageal cancer, and found that the measurement error of CBCT seems to be greater than EPID. But no statistical significance was found [15]. A total of 57 patients underwnet SBRT by using CBCT images showed that the PTV margins used to compensate for residual tumor localization errors were 3.1, 3.5 and 3.3 mm in the left-right(LR), superior-inferior(SI) and anterior-posterior(AP), respectively [4]. The results of this study showed that most of the set-up errors were less than 5mm and concentrated on the SI direction. The fixation of the body made it difficult to move at the LR and AP directions. At the same time, if the skin was loose or head posture slight changed, it would lead to deviation of the SI direction. When considering the direction of set-up error, the differences at anteroposterior direction were more significant, which might be caused by fluctuation of the thorax. Like the above findings of breast cancer patients, when we performed the first CBCT scan, we found no difference between the wrong setting in either direction and the average [16].

Moreover, set-up errors generally fluctuated around their own benchmarks, which suggested that if the set-up errors were large for several times at the beginning, the doctors needed to reduce the set-up errors by re-set-up. The set-up error has greater impact on the precise treatment compared with traditional radiotherapy [17]. The dose distributions designed by the plan was only an ideal model. In this experimental study, we found that the dose distribution of 30 patients in the simulated group was different from the planned dose distribution. The effect of setting error on the target area is statistically significant. In addition, we set the distance range of the set error to three groups (less than 3mm, 3-5mm and greater than 5mm). Further analysis showed that the effect of PTV with an error of less than 95% was statistically different. However, the effect of the less than 3mm group on the average dose of PTV, 95% GTV and the average dose of GTV was not statistically significant. And as the error increases, the effect on the dose distribution in the target area is also more obvious.

CONCLUSION

Most of the set-up errors in radiotherapy for lung cancer were less than 5mm and

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concentrated on the SI direction. The size of position errors was related to the inherent characteristics of the patients. It is necessary to correct set-up errors by CBCT before radiotherapy.

Ethical approve

This study was approved by the medical ethics committee of the third hospital of hebei medical university.

Conflicts of interest: *Declared none.*

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