Uncertainty and influencing factors of the placement error of three-dimensional conformal intensity-modulated radiotherapy for thoracic tumors

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Abstract. – OBJECTIVE: Radiation therapy is an important method for the treatment of chest tumors. This study discussed the placement error of three-dimensional (3D) conformal intensity-modulated radiotherapy in patients with different types of chest tumors and analyzed the relevant influencing factors.

PATIENTS AND METHODS: 100 patients with chest tumors diagnosed and treated in our hospital from March 2016 to March 2018 were randomly selected as research subjects, including 42 cases of esophageal cancer, 44 cases of breast cancer, and 14 cases of lung cancer. All patients underwent 3D conformal radiotherapy. The setup errors of patients with esophageal cancer, breast cancer, and lung cancer were detected after 3D conformal radiotherapy. Besides, the influencing factors of 3D conformal for thoracic tumors were analyzed by multiple linear regression analysis.

RESULTS: After 3D conformal radiotherapy, the systematic errors of patients with esophageal cancer in X-axis, Y-axis, and Z-axis were -0.10, 1.26 and 0.07, respectively, while the random errors in X-axis, Y-axis, and Z-axis were 1.18, -1.14, and 0.97 respectively. The times for the absolute values of the positioning error with a range of ≤5 mm in X-axis, Y-axis, and Z-axis were 40 (95.24%), 2 (4.76%) and 36 (85.71%), while these with a range of >5 mm in X-axis, Y-axis, and Z-axis were 6 (14.29%), 41 (97.62%) and 1 (2.38%), respectively. For patients with breast cancer, the systematic errors and random errors in X-axis, Y-axis, and Z-axis are -0.19, 1.19, and 0.15, as well as 0.97, 0.02 and 1.29, respectively. The times for the absolute values of the positioning error with a range of ≤5 mm and >5 mm were 41 (93.18%), 3 (6.82%), and 36 (81.82%), as well as 8 (18.18%), 42 (95.45%) and 2 (4.55%), severally. For patients with lung cancer, the systematic errors and random errors in X-axis, Y-axis, and Z-axis were 0.14, 1.42, and 0.15, as well as 1.35, -0.23 and 1.12, respectively. The times for the absolute values of the positioning error with the range of ≤5 mm and >5 mm were 14 (93.33%), 1 (6.67%), and 11 (73.33%), as well as 4 (26.67%), 14 (93.33%) and 1 (6.67%) after 3D conformal radiotherapy. After multiple linear regression analyses, gender and lung volume were the influencing factors of Z-axis setup error, and the lesion location was the influence factor of Y-axis setup error ($p<0.05$).

CONCLUSIONS: There are certain positioning errors in the X-axis, Y-axis, and Z-axis directions of thoracic tumors receiving 3D conformal radiotherapy. Gender, lung volume, and lesion location are all important factors that affect the placement error. The results of this study provide a certain reference for the positioning error of radiation therapy for thoracic tumors, which is conducive to improving the accuracy of radiotherapy and better protecting the surrounding tissues.

Key Words:

Thoracic tumor, 3D conformal intensity-modulated radiotherapy, Positional error, Uncertainty, Influencing factors.

Introduction

Malignant tumors have caused serious harm to people all over the world. The incidence of malignant tumors has increased at an average annual rate of 3%-5% in the past three decades. About 75% of the new cases occur in newly industrialized and developing countries, and malignant tumors have become the leading cause of human death[1,2]. At present, more than 3 million new cases of malignant tumors have been diagnosed in China every year, with more than 1.5 million deaths[3]. Lung cancer, breast cancer, gastric cancer, liver cancer, and esophageal cancer are common thoracic tumors, but most patients have no obvious symptoms in the early stage. Thus, they have missed the best treatment time when they are diagnosed in the middle and late stages[4].

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Radiotherapy is one of the main methods for the treatment of malignant tumors. Three-dimensional (3D) conformal intensity-modulated radiotherapy is a new method developed in recent years. Its purpose is to maximize the killing of tumor cells through precise positioning, precise planning, and precise treatment. At the same time, the radiation toxicity of adjacent tissues and organs can be avoided or reduced as much as possible[5]. A study by Yu and Zhou[6] found that, compared with traditional radiotherapy, the survival rate of patients with 3D conformal intensity-modulated radiotherapy is notably increased with reduced postoperative recurrence rate. However, at present, there are few reports on the positioning error of 3D conformal radiotherapy for chest tumors. High requirements are needed for operator to process the radiotherapy. Respiratory movements can cause tumors and organs in the chest and abdomen to move at a certain frequency and amplitude. There are differences between the actual and planned positions, so 3D conformal radiotherapy has a remarkable impact on the radiotherapy dose in the lesion area, thereby affecting the disease control rate[6]. In other words, the existence of setup errors can affect the dose distribution of the target volume and surrounding normal tissues and organs, which may lead to missed irradiation of the target volume and/or increase the irradiation dose to organs at risk, thereby increasing the probability of normal tissue and organ complications. If the positioning error is too great, the irradiation dose of the surrounding normal tissues and organs may be increased, thereby damaging the normal tissues. Minimizing the positioning error plays an important role in improving the effect of radiation therapy and improving the tumor control rate. If the positioning error cannot be controlled within the allowable range, the advantages of 3D conformal radiation therapy will be difficult to reflect.

In this study, patients with chest tumors who were diagnosed and treated in our hospital from March 2016 to March 2018 were examined by measuring the error values of X-axis, Y-axis, and Z-axis, aiming to explore the uncertainty of the setup error of 3D conformal radiotherapy for thoracic tumors, and to explore and analyze their influencing factors.

Patients and Methods

General Information

A total of 100 patients with thoracic tumors who were diagnosed and treated in our hospital from March 2016 to March 2018 was randomly selected as the research subjects, including 42 cases of esophageal cancer, 44 cases of breast cancer and 14 cases of lung cancer. Among them, there were 39 males and 61 females, aged (33-92) years old, with an average age of (57.40±11.00) years old.

Inclusion criteria: (1) All study subjects were diagnosed by chest imaging examination, and all met the relevant diagnostic criteria for esophageal cancer[7], breast cancer[8] and lung cancer[9]. All patients were diagnosed by pathological examination. (2) All patients received radiotherapy for the first time. (3) All research subjects and their families gave informed consent and agreed to participate in this research. (4) The Karnofsky score test was not less than 70 points. (5) All research subjects had good mental symptoms and were able to cooperate with the corresponding research. (6) The study was approved by the hospital Ethics Committee. (7) All patients received 3D conformal radiotherapy.

Exclusion criteria: (1) patients with severe impairment of liver, kidney, or cardiac function. (2) Patients with a history of thoracic surgery combined with pulmonary insufficiency. (3) Patients who were withdrawn from the study due to personal or family reasons. (4) Patients with distant metastasis of tumor.

Methods

Positioning method

The patient was in a supine position and in a calm state with both hands on the head and fixed with a thermoplastic film and a vacuum pad. The reference center was set below the simulator and marked with a lead point about 2 mm in diameter. The patients were scanned by Siemens spiral CT (Emotion, Siemens, Munich, Germany). The scanning area ranged from the cricothyroid membrane to the lower edge of the septum. The layer spacing and layer thickness were both 5 mm. The scanned images were transmitted to the Capital Market Services (CMS) treatment planning system (CMS XIO, Thermo Fisher, Shanghai, China) to automatically generate positive and lateral digital reconstructed radiographs (DRR) after delineating the target area and designing the radiotherapy plan. Frontal (0° frame angle) and side (270° frame angle) Echo Planar Imaging (EPI) images were captured weekly using the electronic field imaging device (EPID) (D-VISION, Beijing Shimadzu Medical Equipment, Beijing, China).

The EPI shooting conditions were set as 20 cm × 20 cm, 10 cm × 10 cm, and 2-3 MU in the large field area, small field area, and the accelerator hop number, respectively. The radiant dose was 36 to 40 Gy, the image acquisition speed was 5.5 frames/s with a total of 361 frames, and the shooting was taken with dual exposure.

Measurement of placement error[10]

Manual registration function and image registration software were applied and DRR was used as the reference image. Using the trachea, carina or vertebral body, spinous process or sternum of the thoracic spine as reference marks, the anatomical structures were delineated and confirmed by two different radiotherapy physicians. The EPI was manually registered with the DRR. Then, using the coordinate system in the ICRU62 report, the left and right directions were represented by the X axis, the upper and lower directions were represented by the Y axis, and the front and back directions were represented by the Z axis, and the positioning error value was calculated.

Observation Indicators

(1) The error values in the X-axis, Y-axis, and Z-axis directions of patients with esophageal cancer, breast cancer, and lung cancer were detected, respectively. The mean and standard deviation of the placement error represented the systematic error and random error. The placement error between grades was calculated in absolute value11. Among them, the X, Y, and Z axes represented the left and right head and feet, and abdominal back, respectively.

(2) The change of lung volume in all patients was measured by a respiratory function tester.

(3) A multiple linear regression equation was established. With the patient's sex, age, tumor site, and lung volume as the independent variables, and the X, Y, and Z axes as the dependent variables, the multivariate linear regression was used to analyze the influencing factors of setup error of 3D conformal radiotherapy for thoracic tumors.

Statistical Analysis

The SPSS 22.0 (IBM Corp., Armonk, NY, USA) data statistical software package was taken to calculate the different observation indicators and data. The enumeration data such as age and gender of patients with different prognosis outcomes were expressed as [cases (%)]. Multiple linear regression analysis was used to analyze the influencing factors of the setup error of 3D conformal radiotherapy for thoracic tumor. $p<0.05$ was regarded as a significant difference.

Results

Measurement Results of Placement Error

A total of 410 frontal and lateral electron portal images were taken during the radiotherapy of 100 patients. The median position verification times were 5 times. The translation error range of the X, Y, and Z axes for the 410 treatments was -3 - 2.5 cm, -2.5 - 3 cm, and -3 - 3.3 cm, respectively. The distribution was illustrated in Figure 1.

Positioning Error After 3D Conformal Radiotherapy for Esophageal Cancer

After 3D conformal radiotherapy for patients with esophageal cancer, the systematic and random errors in X-axis, Y-axis, and Z-axis were -0.10, 1.26 and 0.07, as well as 1.18, -1.14, and 0.97, respectively. The times for absolute value of the positioning error with range of ≤5 mm and >5 mm were 40 (95.24%), 2 (4.76%), and 36 (85.71%), as well as 6 (14.29%), 41 (97.62%) and 1 (2.38%). The details were shown in Table I.

Table I. Placement error after 3D conformal radiotherapy for esophageal cancer [cases (%)].

Direction	Cases	Systematic error (mm)	Random error (mm)	Placement error (mm)			Absolute value of placement error (times)	
				Maximum	Median	Minimum	≤5 mm	>5 mm
X-axis	42	-0.10	1.26	2.50	-0.50	-2.50	40 (95.24)	2 (4.76)
Y-axis	42	0.07	1.18	2.00	0.50	-2.50	36 (85.71)	6 (14.29)
Z-axis	42	-1.14	0.97	1.00	0.35	-3.00	41 (97.62)	1 (2.38)

X-axis: left and right; Y-axis: up and down; Z-axis: front and rear.

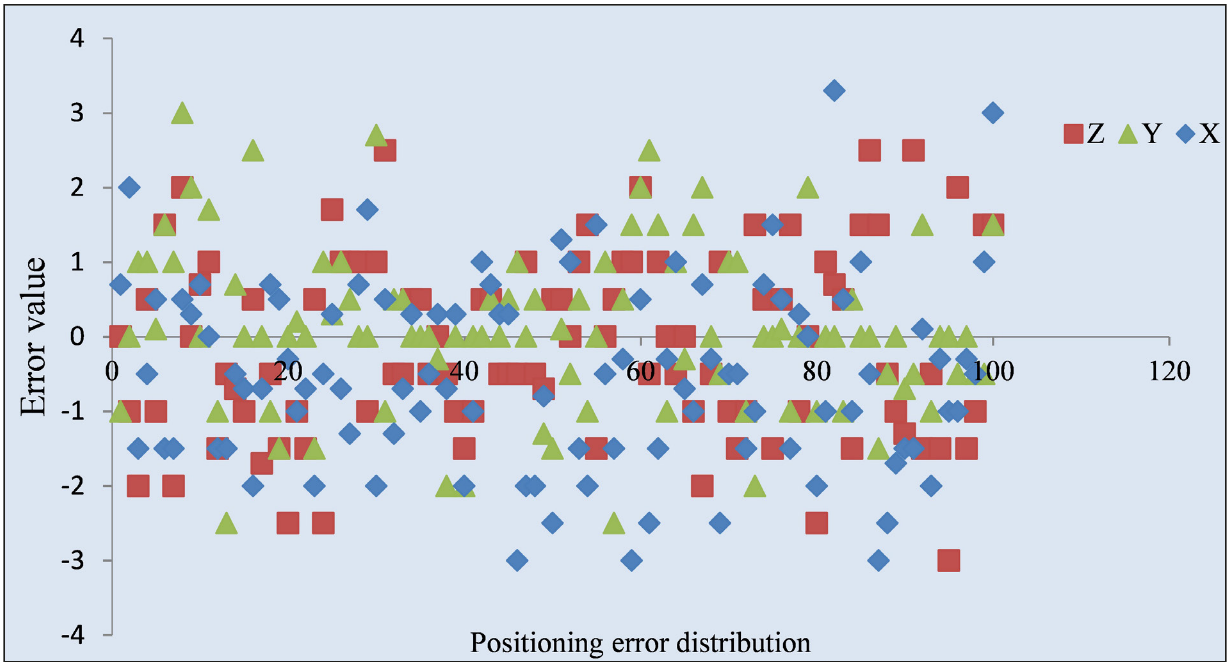

Figure 1. The distribution of the placement error.

Positioning Error After 3D Conformal Radiotherapy for Breast Cancer

After 3D conformal radiotherapy for breast cancer patients, the systematic errors and random errors of X-axis, Y-axis, and Z-axis were -0.19, 1.19, and 0.15, as well as 0.97, 0.02 and 1.29, respectively. The times for absolute value of the positioning error with range of ≤5 mm and >5 mm were 41 (93.18%), 3 (6.82%), and 36 (81.82%), as well as 8 (18.18%), 42 (95.45%) and 2 (4.55%). The details were listed in Table II.

Positioning Error After 3D Conformal Radiotherapy for Lung Cancer

After 3D conformal radiotherapy for lung cancer patients, the systematic errors and random errors in the three directions of X-axis, Y-axis, and Z-axis were 0.14, 1.42 and 0.15, as well as 1.35, -0.23 and 1.12, respectively. The times for absolute value of the positioning error with range of ≤5 mm and >5 mm were 14 (93.33%), 1 (6.67%), and 11 (73.33%), as well as 4 (26.67%), 14 (93.33%) and 1 (6.67%). The detailed results were displayed in Table III.

Relevant Factors Affecting 3D Conformal Radiotherapy of Thoracic Tumors

Gender and lung volume were the influencing factors of Z-axis positioning error. Besides, lesion location was the influencing factor of Y-axis positioning error through multiple linear regression analysis ($p<0.05$, Table IV).

Discussion

Thoracic tumors are a general term for a class of tumors including esophageal tumors, breast tumors, and lung tumors. The tumor surgery is difficult, due to the presence of many vital organs such as the heart in the chest. Besides, the treatment effect of esophageal cancer and lung cancer is poor. The 5-year survival rate of surgical treatment of esophageal cancer is about 15-24%, while the 5-year overall cure rate of lung cancer is less than 10%[12]. Many patients with advanced esophageal cancer and lung cancer have lost the opportunity for surgical treatment when they are diagnosed. Radical resection is possible in less than 20% of patients. Radiation therapy is the mainstay of treatment for patients with advanced tumors. However, the efficacy of conventional fractionated radiotherapy is not satisfactory.

Radiation therapy methods have been modified notably with the continuous progress of medical science and technology. The 3D conformal radiation therapy has gradually developed into the mainstream radiation therapy technology in

Table II. Positioning error after 3D conformal radiotherapy for breast cancer [cases (%)].

Direction	Cases	Systematic error (mm)	Random error (mm)	Placement error (mm)			Absolute value of placement error (times)	
				Maximum	Median	Minimum	≤5 mm	>5 mm
X-axis	44	-0.19	1.19	1.70	0.00	-3.00	41 (93.18)	3 (6.82)
Y-axis	44	0.15	0.97	2.70	-0.40	-2.00	36 (81.82)	8 (18.18)
Z-axis	44	0.02	1.29	3.30	0.15	-2.50	42 (95.45)	2 (4.55)

X-axis: left and right; Y-axis: up and down; Z-axis: front and rear.

Table III. Positioning error after 3D conformal radiotherapy for lung cancer [cases (%)].

Direction	Cases	Systematic error (mm)	Random error (mm)	Placement error (mm)			Absolute value of placement error (times)	
				Maximum	Median	Minimum	≤5 mm	>5 mm
X-axis	14	0.14	1.42	2.50	0.00	-1.70	14 (93.33)	1 (6.67)
Y-axis	14	0.15	1.35	3.00	-0.30	-1.00	11 (73.33)	4 (26.67)
Z-axis	14	-0.23	1.12	1.50	0.30	-2.50	14 (93.33)	1 (6.67)

X-axis: left and right; Y-axis: up and down; Z-axis: front and rear.

Table IV. Relevant factors affecting the positioning error of 3D conformal radiotherapy for thoracic tumors.

Indicators	Direction	Regression coefficient			Regression equation		Correlation coefficient
		β	t	p	F	p	
Gender	Z-axis system error	0.169	1.986	0.037	3.871	0.028	0.018
Lesion	Y-axis random error	-0.165	-2.138	0.033	4.207	0.041	0.024
Lung capacity	Z-axis random error	-0.179	-2.027	0.027	4.358	0.027	0.040

the 21st century with high accuracy. This radiation therapy can significantly reduce the normal tissue dose, increase the tumor dose, and effectively improve the local control rate of the tumor and the survival rate of patients[13]. However, 3D conformal radiation therapy requires strict quality assurance in the process of radiotherapy, and the requirements for positioning accuracy are gradually increasing. The setup error is an important part of the quality assurance in the radiotherapy process, and even a small error will have a great impact on the target volume and normal tissue[14]. Compared with traditional radiotherapy technology, positioning error has a large influence on the precise radiotherapy, so precise radiotherapy has strict requirements on the accuracy of irradiation position and irradiation field[15]. Postural fixation technology and electronic portal imaging devices can accurately measure the positioning error and improve the accuracy of the radiation dose to the tumor target area and surrounding organs. Their application not only effectively improves the effect of tumor radiotherapy, but also reduces the side effects of radiotherapy, thereby playing a certain guiding significance in the practice of clinical radiotherapy[16,17]. Reducing the setup error is one of the key quality assurances for improving the efficacy of radiotherapy and protecting organs at risk.

The positioning errors are different, due to the varying degrees of activity and movement patterns of different parts of the body, and the varying levels of machine equipment, fixed devices, and the ability of operator. The postoperative recurrence rate of patients who received 3D conformal radiation therapy was significantly lower compared with traditional two-position intracavitary brachytherapy[18]. The 3D conformal radiotherapy can significantly reduce the average dose to the heart, lungs, and the largest umbilical cord compared with traditional methods[19]. This study found that the systematic errors in the X-axis, Y-axis, and Z-axis of patients with esophageal cancer, breast cancer, and lung cancer were -0.10 mm, 0.07 mm, -1.14 mm, -0.19 mm, 0.15 mm, 0.02 mm, 0.07 mm, 0.30 mm, -0.10 mm. The random errors in the X-axis, Y-axis, and Z-axis of patients with esophageal cancer, breast cancer, and lung cancer were 1.26 mm, 1.18 mm, 0.97 mm, 1.19 mm, 0.97 mm, 1.29 mm, 1.40 mm, 1.43 mm, and 1.19 mm, respectively. The placement error of tumor patients on the Y axis was significantly higher than X and Z axes. The patient was in the supine position during the examination, thus, compared with the left and right and front and rear directions, the positioning error of the patient's chest tumor in the 3D direction was high due to the influence of the body's respiratory movement in the upper and lower directions[20]. In addition, gender and lung volume were the influencing factors of Z-axis setup error, and the lesion location was the influence factor of Y-axis setup error in this study. The reason may be that the female breast fat is thicker, and the patient's positioning error has greater uncertainty[21]. Some scholars[22] have found that the positioning and anatomical changes of patients with different anatomical sites are different between different treatments. Moreover, the uncertainty of the positioning error of patients with different lung lesions is different, resulting in clinically unacceptable target coverage loss. It may be that the patient's respiratory movement and physiological activity are different due to the difference in lung volume and different lesion sites, resulting in differences in positioning errors.

Conclusions

There are certain positioning errors in the X-axis, Y-axis, and Z-axis directions of thoracic tumors when receiving 3D conformal radiation therapy. The gender, lung volume, and lesion location are important factors that affect the positioning error. This study provides an accurate measurement method for the setup error of radiotherapy for thoracic tumors and provides a scientific basis for the margin expansion of the radiotherapy position. However, the system error and registration accuracy are relatively low, due to the different ability of operator and the influence of DRR image clarity. In the following study, the training of registration physicians should be strengthened to minimize the placement error.

Conflict of Interest

The authors declare that they have no competing interests.

Funding

This project has received support from the Research Project of Putian University (2016047).

Informed Consent

All research subjects and their families gave informed consent and agreed to participate in this research.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' Contributions

QSC: guarantor of integrity of the entire study, study concepts, study design, definition of intellectual content, literature research, clinical studies and experimental studies, data analysis, and manuscript review. JKX: clinical studies and experimental studies, data acquisition, data analysis, statistical analysis, and manuscript preparation and editing. YHZ: clinical studies and experimental studies, data acquisition, data acquisition, data analysis, statistical analysis, and manuscript preparation and editing. XC: clinical studies and experimental studies, data analysis, and manuscript preparation and editing. QG: data acquisition.

Ethics Approval

This research was approved by the Ethics Review Committee of Affiliated Hospital of Putian University (202306). Registration number of the clinical trial: ChiCTR2300072260.

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