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ORIGINAL ARTICLE

Cone beam computed tomography-guided differences among registration methods for lung cancer and the effects of tumor position, treatment model, and tumor size on positioning errors*

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Abstract

Objective To explore the differences in three different registration methods of cone beam computed tomography (CBCT)-guided down-regulated intense radiation therapy for lung cancer as well as the effects of tumor location, treatment mode, and tumor size on registration.

Methods This retrospective analysis included 80 lung cancer patients undergoing radiotherapy in our hospital from November 2017 to October 2019 and compared automatic bone registration, automatic grayscale (t + r) registration, and automatic grayscale (t) positioning error on the X-, Y-, and Z-axes under three types of registration methods. The patients were also grouped according to tumor position, treatment mode, and tumor size to compare positioning errors.

Results On the X-, Y-, and Z-axes, automatic grayscale (t + r) and automatic grayscale (t) registration showed a better trend. Analysis of the different treatment modes showed differences in the three registration methods; however, these were not statistically significant. Analysis according to tumor sizes showed significant differences between the three registration methods ($P < 0.05$). Analysis according to tumor positions showed differences in the X- and Y-axes that were not significant ($P > 0.05$), while the autopsy registration in the Z-axis showed the largest difference in the mediastinal and hilar lymph nodes ($P < 0.05$).

Conclusion The treatment mode was not the main factor affecting registration error in lung cancer. Three registration methods are available for tumors in the upper and lower lungs measuring < 3 cm; among these, automatic gray registration is recommended, while any gray registration method is recommended for tumors located in the mediastinal hilar site measuring < 3 cm and in the upper and lower lungs ≥ 3 cm.

Key words: lung cancer; IMRT; positioning error; registration method; CBCT; different tumor locations; different treatment modes; tumor size

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Lung cancer is one of the most common malignant tumors worldwide, ranking first in incidence and mortality [1], with men significantly more affected than women. Radiotherapy is the primary treatment for patients with lung cancer [2–4]. However, in chest tumor radiotherapy, the target area is easily affected by organ movement, resulting in reduced radiotherapy accuracy, which has become the main reason for radiotherapy failure in lung cancer in recent years [5]. Therefore, accurate positioning is an important part of the radiotherapy process, as this directly affects the therapeutic efficacy of tumor radiotherapy [6]. The implementation of precise radiotherapy includes increased requirements for accuracy and positioning repeatability. At present,

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it is mainly solved and verified using a medical image registration strategy before performing radiotherapy [7–8]. In clinical practice, cone beam computed tomography (CBCT)-guided automatic registration is mainly used, in which the fusion registration of CBCT is generally performed by doctors and technicians in the radiotherapy room, who randomly choose among bone, gray-scale, or manual registration according to their clinical experience. Finally, the error in patient body position is adjusted based on the results of fusion registration; the disadvantage lies in the randomization of the registration mode during the precise radiotherapy process and the lack of unified and fixed standards or norms, which inevitably lead to inconsistent registration results in the same patient and ultimately affect the overall treatment effects. The present study retrospectively analyzed differences between the three registration methods used for intensity-modulated radiotherapy in 80 lung cancer patients as well as the effects of tumor positions, treatment modes, and tumor lengths on registration, to provide a scientific basis for the clinical selection of appropriate and reasonable registration modes.

Materials and methods

Clinical data

This study included a total of 80 lung cancer patients who received radiotherapy in the Department of Radiotherapy of the Affiliated Hospital of North Sichuan Medical College between November 2017 and October 2019. Among them, 70 and 10 patients received radical radiotherapy and postoperative adjuvant radiotherapy, respectively, including 68 male and 12 female patients, 48 upper lungs, 13 middle lungs, and 19 lower lungs. The median age of the patients was 61 years. All patients were confirmed to have lung cancer by histopathological examination, including squamous cell carcinoma (n = 26), adenocarcinoma (n = 27), small cell (n = 26), and atypical carcinoid (n = 1).

Patient fixation and CT positioning

Our hospital currently uses the SIEMENS SOMATOM Emotion CT scanning thermoplastic positioning system. When positioned under the CT scan simulation machine, all patients were placed in the supine position, with both hands clasping their elbows to cross to the forehead. This position is comfortable and easily repeated. A thermoplastic positioning film was used to fix it on the carbon fiber board. The "+" mark on the upper front centerline and the left and right body sides of the patient's thermoplastic film was positioned to coincide with the laser lead bead mold and a lead bead with a diameter of approximately 2 mm was placed as the body surface mark for the reference coordinate system. A CT scan was performed after all the molds were cooled and shaped. The scanning layer thickness was 5 mm. Conventional reconstruction images were used to obtain image data from the positioning CT. After the scan, the image was transmitted to the Monaco radiotherapy planning system to delineate and plan the target area.

Patient positioning and CBCT registration

Two experienced technicians positioned the patient on a linear accelerator treatment bed (Elekta Synergy) in a fixed. The patient position was adjusted so that the body membrane marker line coincided with the indoor laser at the axial, coronal, and sagittal intersection, which was used as the basis for positioning. CBCT images were collected by the Elekta XVI registration system and registered with the target images transmitted by the planning system. The registration and verification were performed by two deputy chief physicians and doctors with professional titles. The two physicians unanimously identified them as effective registrations and used the average value of each registration error as the registration error data. The left and right directions were defined as the X-axis, the head and foot directions were defined as the Y-axis, and the front and back directions were defined as the Z-axis to determine the translation and rotation errors in each of these axes, respectively. All patients underwent all three registration methods (bone, gray-scale [translation + rotation] (t + r), and gray-scale [translation] (t)) to compare the differences among the three registration methods in all three axes.

Grouping of patients

The patients were grouped according to tumor location (upper, middle, and lower lung), treatment mode (radical or postoperative radiotherapy), and tumor length (≥ 3 cm and < 3 cm) and the errors in each group under different registration methods were compared.

Data processing

Analysis was performed using IBM SPSS for Windows, version 22.0. The errors in measurement data between the three registration methods were assessed by analysis of variance (ANOVA), with post hoc tests used for pairwise comparison between groups. T-tests were used to compare the data between groups. The positioning errors of patients according to tumor location, treatment mode, and tumor size under the three registration modes were compared using two-factor ANOVA and multiple comparisons, with linear regression used to determine the quantitative relationship of interdependence between two variables. A P value < 0.05 indicated that the sample difference was statistically significant.

Results

Basic patient information

This study included a total of 80 patients (68 males and 12 females) with a median age of 61 years. Ten and 70 patients received postoperative radiotherapy and radical radiotherapy, respectively. There were 48 cases of upper lung cancer, 13 cases of middle lung cancer, and 19 cases of lower lung cancer. Thirty-three patients had tumors tumor measuring ≥ 3 cm and 47 patients had tumors measuring < 3 cm (Table 1).

Comparisons of the differences among automatic bone, automatic gray-scale (t + r) and automatic gray-scale (t) registration on the X-, Y-, and Z-axes

Automatic bone, automatic gray-scale (t + r), and automatic gray-scale (t) registration were used for each patient. The results showed no significant differences between the three registration methods on the X-, Y-, and Z-axes; however, automatic gray-scale (t + r) and automatic gray-scale (t) registration showed a better trend (Fig. 1).

Table 1 Basic conditions of patients and general characteristics of tumors

Feature		No. of patients
Age (years)	61	
Gender		
Male		68
Female		12
Treatment		
Radical radiotherapy		70
Postoperative radiotherapy		10
Tumor site		
Upper lung		48
Middle lung		13
Lower lung		19
Tumor length (cm)		
≥ 3		33
< 3		47

Comparisons of positioning errors on the X-, Y-, and Z-axes among lung cancer patients with different tumor locations under the three registration modes

There were no significant differences among the registration errors of the three registration methods on the X- and Y-axes according to tumor location ($P > 0.05$). On the Z-axis, there were no significant differences in registration error between lung cancer tumor sites using automatic gray-scale and automatic gray-scale (t) matching, but there was a significant difference using automatic bone matching ($P < 0.05$). The difference in the values of the middle lung was the highest, while those of the upper and lower lungs were low (Fig. 2).

Comparisons of positioning errors on the X-, Y-, and Z-axes among patients receiving different treatment modes for lung cancer under the three registration methods

There were no significant differences in registration errors among automatic bone, automatic gray-scale (t + r), and automatic gray-scale (t) registration on the X-, Y-, and Z-axes. Moreover, different treatment methods for lung cancer showed no significant effect on the choice of registration methods for patients with lung cancer.

Comparisons of the positioning errors on the X-, Y-, and Z-axes among patients with different lung cancer tumor sizes under the three registration methods

For tumors < 3 cm, there were no significant differences in the registration errors among automatic bone, automatic gray-scale (t + r), and automatic gray-scale (t) registration methods on the X-, Y-, and Z-axes ($P > 0.05$). For tumors ≥3 cm, there was no significant difference in errors between automatic bone, automatic gray-scale (t + r), and automatic gray-scale (t) registration on the X- and Z-axes ($P > 0.05$). However, on the Y-axis, the positioning error of automatic bone registration was

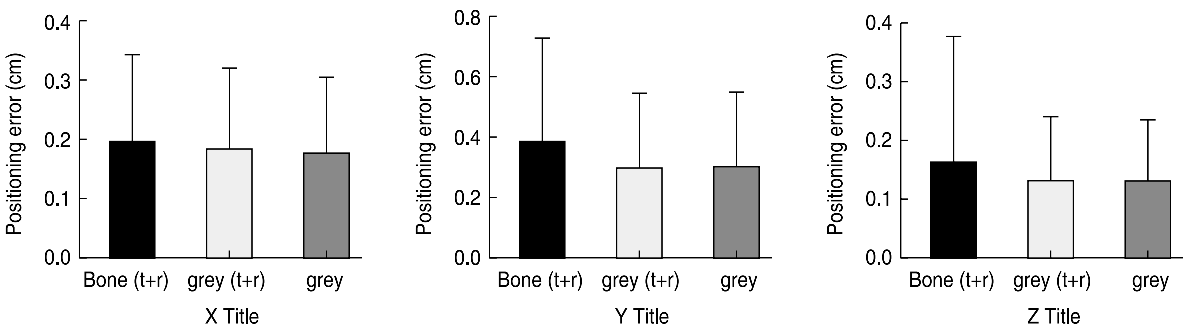

Fig. 1 Analysis of the difference of the positioning errors in the X, Y, and Z axis directions under the three registration methods

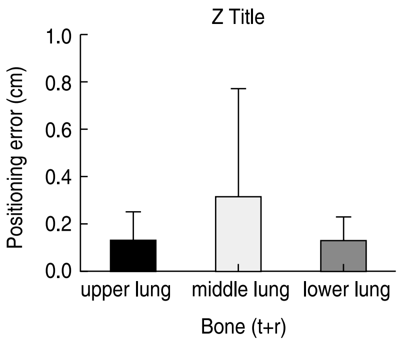

Fig. 2 The difference analysis of the positioning error in the Z-axis direction under the automatic bone registration method between different tumor sites

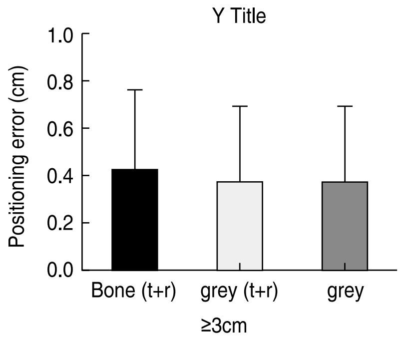

Fig. 3 Analysis of the difference in positioning errors in the Y-axis direction in the tumor ≥ 3 cm group under different registration methods

significantly larger than that of automatic gray-scale (t + r), and automatic gray-scale (t) registration ($P < 0.05$) (Fig. 3).

Discussion

Lung cancer is a common malignant tumor in the clinic and also ranks first for deaths among malignant tumors [9]. Radiotherapy is one of the main treatment methods for patients with lung cancer and can effectively prevent local recurrence in patients. This treatment also plays a very important role in many aspects, such as improving the local control rate and improving the overall survival rate of patients [10–11]. With the continuous development of radiotherapy equipment and technology, radiotherapy has entered the era of intensity-modulated radiotherapy for "accurate positioning, accurate planning, and accurate positioning" [12]. Accurate measurement and correction of the target location and intra-fractional errors in tumor radiotherapy have gradually become the focus of domestic oncology and radiotherapy physicians, physicists, and technicians [13]. Several studies [14–16] have shown that movement of the centers of GTV95 and CTV95 by 5 mm can result in a dose change to the tumor as high as 21%. Thus, pre-radiotherapy positioning verification is critical. In the current postural standard of tumor radiotherapy: the allowable range of translation error is < 5 mm, the allowable range of rotation error is < 3 mm, and CBCT is an important means of positioning verification before radiotherapy. In the clinic, automatic registration is routinely used under CBCT guidance, with manual registration performed in individual special cases. Automatic registration is fast and simple, which not only saves time but also has high precision and has been unanimously adopted in the clinic. The two types of automatic registration methods—automatic bone registration and automatic grayscale registration—can be subdivided into automatic grayscale (t) registration and automatic grayscale registration.

At present, there is no guideline for choosing the appropriate registration method in the clinic. This selection mainly depends on the experience and habits of radiotherapy doctors and physicists, and the registration method is randomized. To address this problem and provide a basis for a standardized registration model of lung cancer, we retrospectively analyzed the registration data of 80 patients with lung cancer undergoing radiotherapy. Our results showed that there was no statistical difference among the three registration methods in the X-, Y-, and Z-axes, but that automatic grayscale registration and automatic grayscale registration (t) showed a better trend than automatic bone registration. This result is consistent with the results reported by Li *et al.* [17–18]. The reason for this finding may be related to the anatomical structure of chest tumors as lung cancer tissue is rich in soft tissue, the tissue is closely connected, and the relative position is relatively fixed, while the bony markers around the lung cancer tissue are less available for reference and have a large degree of displacement, are easily affected by posture and breathing, and are not fixed. In this study, considering the mediastinal anatomy, the use of grayscale registration appears to be more reasonable, and manual registration can be combined with manual registration if necessary [19].

Domestic and foreign studies have identified tumor location as an important factor affecting the positioning error in patients undergoing radiotherapy for lung cancer [20–22]. Our analysis of the influence of different tumor positions on positioning showed that a tumor location on the X-stroke Y-axis was not the key factor affecting positioning error. On the Z-axis, we observed no significant differences in registration errors between groups with different tumor sites using automatic gray level (t + r) and automatic gray (t) registration; however, for automatic bony registration, the difference in the value of the middle lung was the highest, while that of the upper and lower lung was low. This is consistent with the findings reported by Tan [21]. The explanation for this observation may be that tumors in the middle lung are affected by respiratory mobility to a certain extent; moreover, those adjacent to the heart are also affected by the heartbeat [20–22]. Thus, the difference in the registration phase based on bony markers was greater than that of grayscale registration. Therefore, all three registration methods can be used for tumors of the upper and lower lung, while automatic bony registration should not be used if it can be avoided for tumors in the middle lung.

Furthermore, regarding the effects of tumor size on positioning, in the group with tumor size <3 cm, all three registration methods were available on the X-, Y-, and Z-axes; in contrast, in the group with tumor size > 3 cm group, both automatic gray (t + r) and automatic gray (t) registration on the Y-axis showed better results. Sarudis [22] reported a correlation between tumor size and respiratory movement. The reason for this finding may be that the larger the tumor, the more likely it is to be affected by posture, respiratory degree, heartbeat, and diaphragm contraction. Moreover, the chest bone marks are less and easily affected; thus, the automatic bone matching error is larger. Therefore, the use of automatic grayscale registration is appropriate [24–25].

The results of the present study showed that in lung cancer, automatic bony, automatic grayscale, and automatic grayscale (t) registration are recommended for tumors in the upper and lower lung measuring <3 cm, especially the latter two methods. For tumors located in the middle lung measuring <3 cm and tumors in the upper and lower lung measuring ≥3 cm, either automatic grayscale or automatic grayscale (t) registration can be used. This study included only two patients with middle lung tumors measuring ≥ 3 cm; thus, additional studies with larger sample sizes are needed.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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