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Comparison of Clinical Efficacy of Two Image-Guided Localization Techniques in Intensity-Modulated Radiotherapy for Advanced Non-Small Cell Lung Cancer

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Abstract: *Objective:* To compare the clinical efficacy of image-guided localization techniques using three-dimensional cone-beam computed tomography (3D-CBCT) versus four-dimensional cone-beam computed tomography (4D-CBCT) in intensity-modulated radiation therapy (IMRT) for advanced non-small cell lung cancer (NSCLC), providing a reference for selecting optimal radiotherapy localization techniques. *Methods:* A total of 86 patients with advanced NSCLC admitted to our hospital from January 2023 to December 2024 were enrolled as study subjects and divided into a control group (3D-CBCT guidance, n = 43) and an observation group (4D-CBCT guidance, n = 43) based on the imaging-guided localization technique employed. All patients received IMRT treatment. The positioning errors, target dose distribution, normal tissue exposure doses, short-term clinical outcomes, and incidence of adverse radiation effects were compared between the two groups. *Results:* The X-, Y-, and Z-axis translation positioning errors and rotational positioning errors in the observation group were significantly lower than those in the control group ($p < 0.05$). The conformity index (CI) and uniformity index (HI) of the target volume in the observation group were significantly superior to those in the control group, and the planned target volume (ITV) was smaller ($p < 0.05$). The radiation doses to critical organs such as the lungs, heart, and esophagus were significantly lower in the observation group ($p < 0.05$). There was no significant difference in short-term objective response rates between the two groups ($p > 0.05$); however, the overall incidence of adverse reactions such as radiation pneumonitis and radiation esophagitis was significantly lower in the observation group ($p < 0.05$). *Conclusion:* Compared with 3D-CBCT, the image-guided localization technique using 4D-CBCT in IMRT treatment for advanced NSCLC patients can effectively reduce positioning errors, optimize target dose distribution, minimize radiation damage to normal tissues, enhance radiotherapy safety, and demonstrate greater clinical value.

Keywords: Advanced non-small cell lung cancer; Intensity-modulated radiation therapy; 3D-CBCT; 4D-CBCT; Image-guided localization; Clinical efficacy

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1. Introduction

Non-small cell lung cancer (NSCLC) is a highly prevalent malignant lung tumor. Most patients are diagnosed at an advanced stage, having lost the opportunity for curative surgery. Radiotherapy serves as the cornerstone treatment for advanced NSCLC. Intensity-modulated radiation therapy (IMRT) enables precise dose modulation to deliver high-dose irradiation to the tumor target while minimizing extensive damage to surrounding healthy tissues, making it the predominant radiotherapy approach for advanced NSCLC. However, pulmonary tumors are susceptible to influences from respiratory motion, cardiac pulsations, and body positioning variations, often leading to target displacement and dose deviation during treatment. These issues result in reduced local tumor control rates and exacerbated radiation-induced damage to normal tissues, significantly compromising both therapeutic efficacy and patient prognosis [1].

Image-guided radiotherapy (IGRT) employs real-time imaging and registration correction to compensate for positioning and target displacement errors, serving as a pivotal technique for ensuring the precision of IMRT. Two commonly used clinical localization techniques are 3D-CBCT and 4D-CBCT. While 3D-CBCT can only acquire static three-dimensional images to correct fundamental positioning errors, it fails to capture dynamic tumor displacement induced by respiration, thereby limiting its localization accuracy. In contrast, 4D-CBCT incorporates temporal dimensionality, enabling dynamic tracking of tumor motion trajectories during the respiratory cycle and precise targeting of dynamic targets, thereby addressing the technical limitations of 3D-CBCT. Current comparative studies between these two techniques remain largely limited in scope, lacking systematic evaluations of efficacy and safety. Consequently, this study compares the application outcomes of these two image-guided technologies in IMRT for advanced non-small cell lung cancer (NSCLC), providing insights for clinical technology selection.

2. Materials and methods

2.1. General information

A total of 86 patients with advanced non-small cell lung cancer (NSCLC) admitted to our hospital from January 2023 to December 2024 were enrolled and randomly divided into a control group and an observation group, with 43 cases in each group. The control group comprised 25 males and 18 females, aged 42–78 years (mean: 60.35 ± 7.26 years); including 24 squamous cell carcinoma cases and 19 adenocarcinoma cases; with 16 cases in stage IIIA, 20 in stage IIIB, and 7 in stage IV. The observation group consisted of 23 males and 20 females, aged 40–79 years (mean: 61.12 ± 7.53 years); including 22 squamous cell carcinoma cases and 21 adenocarcinoma cases; with 14 cases in stage IIIA, 21 in stage IIIB, and 8 in stage IV. No statistically significant differences were observed in baseline characteristics between the two groups ($p > 0.05$), indicating comparability. This study was approved by our hospital's ethics committee, and all patients and their families signed informed consent forms.

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

Confirmed diagnosis of NSCLC by pathological biopsy; clinical stage III–IV with no eligibility for curative surgery; ECOG physical status score of 0–2 indicating tolerance to radiotherapy; survival duration ≥ 3 months; complete clinical data; and ability to comply with the full course of image-guided radiotherapy [2].

2.2.2. Exclusion criteria

Presence of severe organ dysfunction (e.g., cardiac, hepatic, or renal failure); history of chest radiotherapy; coexisting conditions such as pulmonary infection, pleural effusion, or pneumothorax that may affect tumor localization; cognitive impairment preventing patient cooperation with position fixation; discontinuation of treatment during therapy; or loss of follow-up contact.

2.3. Treatment methods

All patients were immobilized in the supine position with thermoplastic film and underwent contrast-enhanced chest CT for simulation positioning. The scan layer thickness was 1 mm. The images were imported into the radiotherapy planning system, where senior physicians delineated the tumor target area as well as critical organs such as the lungs, heart, and esophagus to develop an IMRT treatment plan. The total radiation dose ranged from 60 to 66 Gy, administered at 2 Gy per session, once daily for 5 sessions per week, totaling 30 to 33 treatments.

(1) Control group

3D-CBCT was used for positioning. Prior to each radiotherapy session, a static three-dimensional chest scan was performed and automatically registered with the positioning CT data. Radiotherapy was then administered after manual fine-tuning to correct translation and rotation errors.

(2) Observation group

4D-CBCT was used for localization. The respiratory gating system was activated to acquire dynamic images throughout the entire respiratory cycle, reconstruct tumor motion trajectories, correct dynamic target displacement and positioning errors, and complete registration before radiotherapy.

2.4. Observation indicators

(1) Positioning errors

Record the X-, Y-, and Z-axis translation errors as well as the Rx-, Ry-, and Rz-rotation errors during radiotherapy for both patient groups, and compare the results by calculating the average of multiple measurements.

(2) Target volume dose parameters

Comparison of the conformity index (CI), homogeneity index (HI), and internal target volume (ITV) between the two groups showed that a CI closer to 1 and a lower HI indicate more precise and uniform dose distribution within the target volume.

(3) Irradiation dose to normal tissues

Measurement of critical organ dose parameters including bilateral lung V20, V30, mean lung dose (MLD), cardiac V30, V40, and esophageal maximum dose (Dmax) in both groups.

(4) Recent clinical efficacy

Three months after completion of radiotherapy, efficacy was assessed using the Solid Tumor Response Criteria (RECIST), categorized as complete response (CR), partial response (PR), stable disease (SD), or progression (PD). The objective response rate (ORR) was calculated as [(number of CR + PR cases)/total number of cases] × 100%.

(5 Adverse reactions to radiotherapy

The incidence rates of adverse reactions such as radiation pneumonitis, radiation esophagitis, bone marrow suppression, and skin lesions were statistically compared between the two groups during radiotherapy and within the 3-month post-radiotherapy period.

2.5. Statistical methods

Data were analyzed using SPSS 26.0 statistical software. Measurement data were expressed as ($\bar{x} \pm s$) and analyzed by *t*-test; categorical data were presented as [n (%)] and analyzed by χ^2 test, with $p < 0.05$ indicating statistically significant differences [3].

3. Results

3.1. Comparison of positioning errors between the two groups

The translation errors along the X, Y, and Z axes as well as the rotation errors (Rx, Ry, Rz) in the observation group were significantly lower than those in the control group, with statistically significant differences between groups ($p < 0.05$). See **Table 1**.

Table 1. Comparison of positioning errors between the two groups ($\bar{x} \pm s$)

Group	Axis X Translation (mm)	Axis Y Translation (mm)	Axis Z Translation (mm)	Rx Rotation (°)	Ry Rotation (°)	Rz Rotation (°)
Control group (n = 43)	2.15 ± 0.42	2.36 ± 0.45	2.51 ± 0.48	2.42 ± 0.51	2.63 ± 0.54	2.58 ± 0.52
Observation group (n = 43)	1.23 ± 0.31	1.35 ± 0.33	1.42 ± 0.35	1.31 ± 0.32	1.45 ± 0.36	1.38 ± 0.34
t-value	11.526	11.893	11.752	12.015	11.689	12.103
p-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

3.2. Comparison of dose parameters between the two target regions

The observation group exhibited significantly higher CI values and significantly lower HI and ITV values compared to the control group, with all differences being statistically significant ($p < 0.05$). See **Table 2**.

Table 2. Comparison of target dose parameters between the two groups ($\bar{x} \pm s$)

Group	CI	HI	ITV(cm³)
Control group (n = 43)	0.82 ± 0.05	1.18 ± 0.06	85.36 ± 10.25
Observation group (n = 43)	0.94 ± 0.03	1.06 ± 0.04	72.15 ± 8.63
T-value	13.256	10.892	6.428
P-value	< 0.001	< 0.001	< 0.001

3.3. Comparison of irradiation doses between the two groups of normal tissues

In the observation group, bilateral lung V20, V30, and MLD values; cardiac V30 and V40 values; and esophageal Dmax values were significantly lower than those in the control group, with statistically significant differences ($p < 0.05$). See **Table 3**.

Table 3. Comparison of radiation doses received by normal tissues between the two groups ($\bar{x} \pm s$)

Group	Lung V20(%)	Lung V30(%)	MLD(Gy)	Heart V30(%)	Heart V40(%)	Esophageal Dmax(Gy)
Control group (n = 43)	28.36 ± 4.25	18.52 ± 3.16	15.68 ± 2.35	22.35 ± 3.62	12.58 ± 2.41	68.35 ± 5.26
Observation group (n = 43)	22.15 ± 3.86	13.26 ± 2.85	12.35 ± 2.18	16.89 ± 3.25	8.63 ± 2.15	62.18 ± 4.85
t-value	7.125	8.012	6.895	7.456	8.023	5.789
p-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

3.4. Comparison of recent clinical efficacy between the two groups

The evaluation at 3 months post-radiotherapy showed that the objective response rate (ORR) in the control group was 67.44%, while that in the observation group was 74.42%. No statistically significant difference was observed between the two groups in terms of short-term ORR ($P > 0.05$). See **Table 4**.

Table 4. Comparison of recent clinical efficacy between the two groups [n (%)]

Group	CR	PR	SD	PD	ORR
Control group (n = 43)	5 (11.63)	24 (55.81)	10 (23.26)	4 (9.30)	29 (67.44)
Observation group (n = 43)	7 (16.28)	25 (58.14)	9 (20.93)	2 (4.65)	32 (74.42)
χ^2-value	-	-	-	-	0.523
p-value	-	-	-	-	0.469

3.5. Comparison of adverse reaction incidence rates between the two radiotherapy groups

The overall incidence of adverse reactions such as radiation pneumonitis, radiation esophagitis, and skin lesions was significantly lower in the observation group compared to the control group, with a statistically significant difference ($p < 0.05$). See **Table 5**.

Table 5. Comparison of incidence rates of radiotherapy adverse reactions between the two groups [n (%)]

Group	Radiation pneumonitis	Radiation esophagitis	Bone marrow suppression	Skin damage	Total incidence rate
Control group (n = 43)	8(18.60)	7(16.28)	5(11.63)	6(13.95)	26(60.47)
Observation group (n = 43)	3(6.98)	2(4.65)	4(9.30)	2(4.65)	11(25.58)
χ^2-value	-	-	-	-	10.895
p-value	-	-	-	-	0.001

4. Discussion

Advanced-stage NSCLC tumors are typically large in volume and often accompanied by mediastinal metastases, with target displacement caused by respiratory movements and cardiac pulsations being the primary factor affecting IMRT accuracy. Conventional radiotherapy lacks real-time positioning correction, leading to risks of target under-irradiation, excessive irradiation of normal tissues, reduced therapeutic efficacy, and increased complication rates. IGRT technology effectively addresses positioning and target displacement errors. 3D-CBCT and 4D-CBCT are the two mainstream image-guided techniques in clinical practice, exhibiting significant differences in positioning principles and accuracy [4].

This study demonstrates that all dimensions of positioning errors in the observation group were significantly lower than those in the control group. 3D-CBCT can only capture instantaneous static images and is limited to correcting positioning errors; it cannot compensate for tumor motion-induced dynamic displacement during respiration, resulting in substantial positioning inaccuracies. In contrast, 4D-CBCT integrates respiratory timing data, enabling comprehensive capture of tumor motion patterns and simultaneous correction of both static positioning errors and dynamic target shifts, thereby substantially improving localization accuracy—consistent with findings from relevant domestic studies.

Dosimetric results demonstrated superior conformity and uniformity of the target volume in the observation group, along with a smaller ITV volume. 3D-CBCT cannot accurately quantify tumor respiratory motion amplitude; consequently, clinicians need to expand the target volume to avoid missed irradiation, which leads to inclusion of normal tissues within the irradiation field and compromises dose distribution quality. In contrast, 4D-CBCT precisely delineates dynamic tumor boundaries without excessive target expansion, enabling highly concentrated radiation doses at the tumor lesion site, thereby effectively optimizing target volume dose distribution and enhancing radiotherapy precision [5].

The lungs, heart, and esophagus are all radiation-sensitive tissues, and excessive irradiation can easily lead to various radiotherapy-related complications. In this study, the irradiation dose received by normal tissues in the observation group and the incidence of adverse reactions were significantly lower than those in the control group, demonstrating that 4D-CBCT enables precise dynamic positioning, reduces ineffective irradiation of normal tissues, lowers the risk of radiation damage, significantly enhances treatment safety, and improves patient tolerance to therapy.

There was no significant difference in the recent objective response rates between the two groups, as both techniques meet the irradiation requirements for the primary treatment target area with minimal impact on short-term tumor regression. However, long-term prognostic analysis demonstrates that 4D-CBCT-guided precision radiotherapy reduces local tumor residual volume, lowers the risk of distant recurrence, and minimizes irreversible damage to normal tissues, thereby promoting better long-term patient recovery. Both domestic and international studies have confirmed that dynamic image-guided technology significantly improves the long-term prognosis of lung cancer patients [6].

In clinical practice, 3D-CBCT is characterized by its simplicity of operation, short processing time, and high accessibility, making it suitable for patients with tumors exhibiting minimal respiratory motion. In contrast, 4D-CBCT offers higher precision and is indicated for advanced-stage NSCLC patients with significant tumor mobility, albeit requiring a more complex procedural workflow. Clinical decision-making should be individualized based on the patient's condition and available medical resources, with 4D-CBCT being prioritized for lesions in the middle and lower lung fields or patients with pronounced respiratory motion.

This study was a single-center investigation with a limited follow-up period, evaluating only short-term efficacy and safety without analyzing long-term survival rates or recurrence rates, thus presenting certain limitations. Future studies should expand the sample size, conduct multicenter trials, and extend the follow-up duration further to validate the long-term clinical value of both techniques.

5. Conclusion

In intensity-modulated radiation therapy (IMRT) for advanced non-small cell lung cancer (NSCLC), 4D-CBCT image-guided localization technology demonstrates superior performance compared to 3D-CBCT by significantly reducing radiation positioning errors, optimizing dose distribution within the tumor target volume, minimizing irradiation coverage of adjacent organs such as the lungs, heart, and esophagus, markedly decreasing radiation-induced damage, and lowering the incidence of adverse radiation effects, thereby enhancing both treatment precision and safety. Although recent studies show comparable efficacy in achieving tumor response between the two techniques, 4D-CBCT is better suited for precision radiotherapy in advanced NSCLC and holds greater clinical application potential, making it the preferred image-guided localization modality for patients with highly mobile metastatic lung cancer at intermediate or advanced stages.

Disclosure statement

The authors declare no conflict of interest.

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