EVALUATION OF SET-UP ERRORS IN 4D-DIBH THORACIC RADIOTHERAPY USING WHOLE-BODY VACLOCK AT VINMEC TIMES CITY INTERNATIONAL GENERAL HOSPITAL

Nguyen Van Nam*, Ha Ngoc Son, Nguyen Trung Hieu, Pham Tuan Anh, Phung Thi Thu Huong, Tran Ba Bach, Nguyen Dinh Long, Doan Trung Hiep

ABSTRACT

Purpose: To determine the daily initial set-up errors and the patient position reproducibility pre-irradiation with 4D-DIBH breathing control radiotherapy technique the whole-body Vac-lock immobilisation device.

Materials and methods: A total of 53 patients were assigned to the Thoracic Radiotherapy (Esophageal cancer: 31 patients; lung cancer: 15 patients; thymic tumor: 5 patients; Rib metastasis: 1 patient) at Vinmec Times City International Hospital from June 2023 to September 2024. Patients were treated by VMAT technique with 4D – DIBH (Deep Inhale Breath-Hold) using Whole Body Vac-lock immobilization devices (QFIX, PA, USA) and (CIVCO, Orange City, IA, USA). Determined the set – up error and pre-treatment repodicibility by collecting daily kV and CBCT images before treatment. A total 1027 of 3D-CBCT image serries were collected and analyzed offline on the ARIA system (Varian Medical System, CA, USA). These data were used to determined the setup margin (SM), systematic margin, and random margin errors in three directions: anterior-posterior (AP); left-right (LR); Cranial-Caudal (CC) and stored on the ARIA system (Varian Medical System, CA, USA).

Results: Innitial set - up error of 4D-DIBH radiotherapy for the thoracic tumors were: 2.4 ± 0.9 mm (in the AP direction), 3.2 ± 1.3 mm (in the Cranial-Caudal direction), and 1.9 ± 1.1 mm (in the LR direction). Average set-up error for the 4D-DIBH radiotherapy group of patients with esophageal cancer: 2.4 ± 0.9 mm, 3.4 ± 1.2 mm, and 1.8 ± 1.1 mm in the AP, CC, and LR directions, respectively; average setting error for the 4D-DIBH radiotherapy group of patients with lung cancer: 2.7 ± 0.9 mm (AP direction), 2.9 ± 1.3mm (CC direction), and 1.8 ± 0.9 mm (LR direction). Average setting error for the 4D-DIBH radiotherapy group of patients with thymic cancer and ribs metastases: 1.8 ± 0.6 mm, 3.0 ± 2.3 mm, 3.1 ± 1.4 mm in the AP, CC, LR directions respectively; Set - up error (SM) for 4D-DIBH radiotherapy using Whole – Body Vac-lock is

Vinmec Times City International Hospital

*Corresponding Author: Nguyen Van Nam
Email: v.namnv1@vinmec.com

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calculated according to the van Herk formula for the Thoracic region: 3.7 mm (AP) 4.8 mm (CC); 4.0 mm (LR); esophageal cancer: 3.9 mm (AP) 4.8 mm (CC); 3.6 mm (LR)); lung cancer: 3.5 mm (AP) 4.8 mm (CC); 4.1 mm (LR)); thymic cancer, bone metastasis: 2.9 mm (AP) 4.7 mm (CC); 4.9 mm (LR).

Conclusion: 4D-DIBH radiotherapy for the thoracic cancer using Body Vac-lock ensures well position repositioning, reduces initial set – up error to deliver accurate radiation dose to the tumors, and limits side effects on organ at risk (OAR). The results of the study and set – up error (SM) calculation is the base - evidence to help Radiation oncolosist determine the appropriate PTV - Margin for treatment in each location.

Keywords: Setup error; 2D-kV image verification; cone-beam computed tomography (CBCT); immobilization systems; esophageal cancer; lung cancer; thoracic tumours; Deep Inspirarion Breath Hold (DIBH).

1. INTRODUCTION

Thoracic malignancies such as breast cancer, esophageal cancer, lung cancer, thymoma, mediastinal tumors, or metastatic lesions of the spine and ribs are characterized by organ motion due to physiological respiratory activity and cardiac movement. Irregularities in respiratory cycles during inspiration and expiration, as well as stimuli such as coughing or swallowing due to esophageal secretion, can significantly affect the reproducibility and accuracy of treatment positioning throughout the entire course of radiotherapy. Without proper motion management strategies, these factors may result in treatment setup deviations, leading to displacement of the target volume, altered dose distribution, decreased treatment efficacy, and increased radiation exposure to surrounding organs at risk (OARs).

Respiratory-induced motion presents challenges to accurate target localization and complicates the delineation of the planning target volume (PTV) and patient immobilization. According to ICRU Report 62 [1], expansion from the clinical target volume (CTV) to PTV must consider both internal margin (IM), which accounts for physiological organ motion, and setup margin (SM), which compensates for patient positioning uncertainties: CTV–PTV margin = IM + SM. While the IM can be estimated based on prior published studies or 4D imaging data, the SM can be calculated more practically through statistical analysis of setup errors from daily image guidance data routinely collected at each center. Accurately quantifying the SM provides critical evidence for radiation oncologists to determine the optimal CTV-to-PTV expansion, thereby minimizing unnecessary radiation exposure to surrounding healthy tissues.

Given the significant motion of thoracic organs caused by respiration, the implementation of modern radiotherapy techniques such as Image-Guided Radiotherapy (IGRT), Volumetric Modulated Arc Therapy (VMAT), and 4D Deep Inspiration Breath Hold (4D-DIBH), in combination with full-body immobilization devices like Vac-Lok, has been widely adopted in clinical practice. These approaches aim to effectively control organ motion, ensure reproducible and precise patient positioning, enhance dose accuracy to the tumor, and minimize radiation-induced toxicity to critical adjacent structures.

At Vinmec Times City International Hospital, since 2017 we have systematically applied the 4D-DIBH technique for respiratory motion management, using immobilization systems such as Body Vac-Lok (QFIX, PA, USA), ProLock, and Wing Board (CIVCO, Orange City, IA, USA). Since 2022, full-body Vac-Lok systems (CIVCO, Orange

City, IA, USA) have also been introduced to further enhance control of respiratory-induced motion in thoracic radiotherapy. In this study, we aim to evaluate initial setup errors and the reproducibility of patient positioning using 4D-DIBH-controlled radiotherapy in combination with full-body Vac-Lok immobilization for thoracic malignancies.

2. SUBJECTS AND METHODS

2.1. Study subjects

A total of 53 patients diagnosed with thoracic malignancies and indicated for radiotherapy were included in this study. The cohort consisted of patients treated at Vinmec Times City International Hospital between June 2023 and September 2024. The patients were diagnosed with various thoracic cancers, including: esophageal cancer (31 patients), lung cancer (15 patients), thymic cancer (5 patients), and rib bone metastasis (1 patient). Patients were categorized into three groups based on their primary diagnosis: Group 1: 31 patients with esophageal cancer, Group 2: 15 patients with lung cancer, Group 3: 6 patients with thymic cancer or rib bone metastasis (Table 1).

Table 1. Patient characteristics and thoracic radiotherapy information

Patients		N (number)	Percentage (%)
Gender	Male	50	94.3%
	Female	3	5.7%
Pre-treatment image verification	2D-kV	-	-
	3D-CBCT	1027	100
Thoracic cancer type	Esophageal (Group 1)	31	58.4%
	Lung (Group 2)	15	28.3%
	Thymic or rib bone metastasis (Group 3)	6	13.3%
Immobilization device type	Wing board Whole - Body Vaclock	53	100
Breath-hold duration (DIBH)		15s - 30s	

2.1.1. Inclusion criteria

Patients were instructed on breath-hold training and assessed for their breath-holding capability. Inclusion criteria required patients to have good general condition, stable clinical indices, and vital signs, with no acute respiratory or airway conditions.

A breath-hold duration of ≥ 15 seconds was required to ensure comfort during treatment procedures, as well as reproducibility, amplitude stability and consistency throughout the entire radiotherapy course.

2.1.2. Exclusion criteria

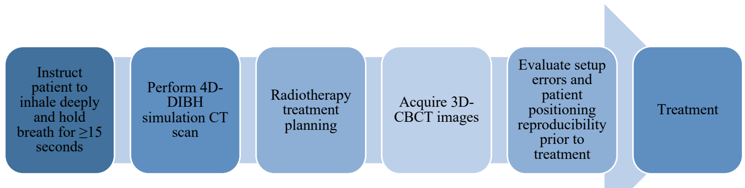
Patients were excluded if they were unable to reproduce consistent breathing patterns or breath-hold amplitudes, or if their breath-hold duration was ≤ 15 seconds.

2.2. Study methodology

This was a retrospective study.

All daily 3D-CBCT (Cone-Beam Computed Tomography) verification image datasets were collected for analysis of initial setup errors and patient position reproducibility prior to treatment. A total of 1,027 3D-CBCT image sets were collected and analyzed offline. These datasets were used to calculate: Setup margin (SM), Systematic error (Σ), Random error (σ). Measurements were analyzed along the anterior-posterior (AP), left-right (LR) and cranial-caudal (CC) directions, and stored in the treatment management system for further statistical evaluation.

2.2.1. Procedure for performing 4D-DIBH breath-hold-gated radiotherapy



2.2.2. Patient breathing training instructions

The patient lies in the supine position on the treatment couch or on the immobilization device, with both arms raised above the head. A cushion may be placed under the knees if needed. This position is identical to the treatment setup used during daily radiotherapy sessions (Figure 1).

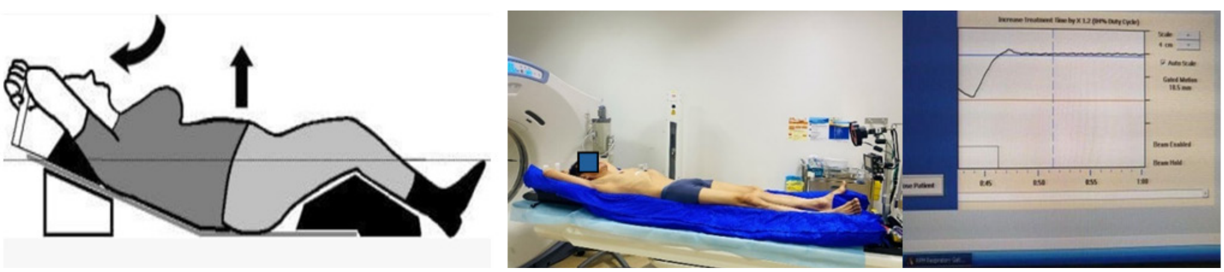


Figure 1. Patient setup position for treatment and breathing training guidance

The patient is instructed to perform several cycles of inhalation and exhalation. Inhale slowly and deeply through the nose, allowing the lungs and abdomen to fully expand, then exhale gently. Repeat this cycle 5-10 times while ensuring the body remains still, the treatment position is maintained correctly, and there is no straining or arching of the back off the treatment table or immobilization device (Figure 2).

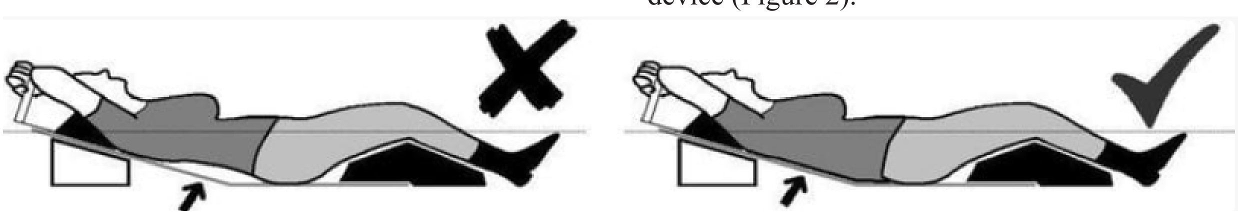


Figure 2. Standard posture for patient during DIBH breathing training

A minimum breath-hold duration of ≥ 15 seconds is required. The amplitude in the anterior-posterior (AP), cranial-caudal (CC) and lateral (LAT) directions during deep inspiration breath-hold must remain stable and consistent.

2.2.3. Patient Immobilization and positioning setup

Patients are positioned supine on a full-body Vaclock immobilization device, with both arms raised above the head using a Wing Board. The treatment origin is then marked and tattooed on the patient's skin in the CT simulation room. CT simulation is performed for the thoracic region using a 2.5 mm slice thickness protocol on a GE 16-slice CT Scanner (GE Healthcare System, USA). Following that, radiation oncologists contour the treatment volumes including GTV (Gross Tumor Volume), CTV (Clinical Target Volume), and PTV (Planning Target Volume) on the simulation CT images for treatment planning (Figure 3).

Figure 3. Patient positioning and origin marking

2.2.4. Pre-treatment 3D-CBCT image verification for setup error evaluation

All 53 patients underwent daily 3D-CBCT (Cone Beam CT) image verification prior to each radiotherapy session. A total of 1,027 3D-CBCT image sets were acquired using the OBI (On-Board Imager) system and analyzed both online and offline. The 3D-CBCT images were compared with the planning CT simulation (CT SIM) images to evaluate setup errors in three directions: anterior-posterior (AP), cranial-caudal (CC), and left-right (LR). The setup error data were recorded and managed using the ARIA software (Varian) (Figure 4).

A B C

Figure 4. Patient setup before treatment (A), breathing training (B) and pre-treatment 3D-CBCT image verification (C)

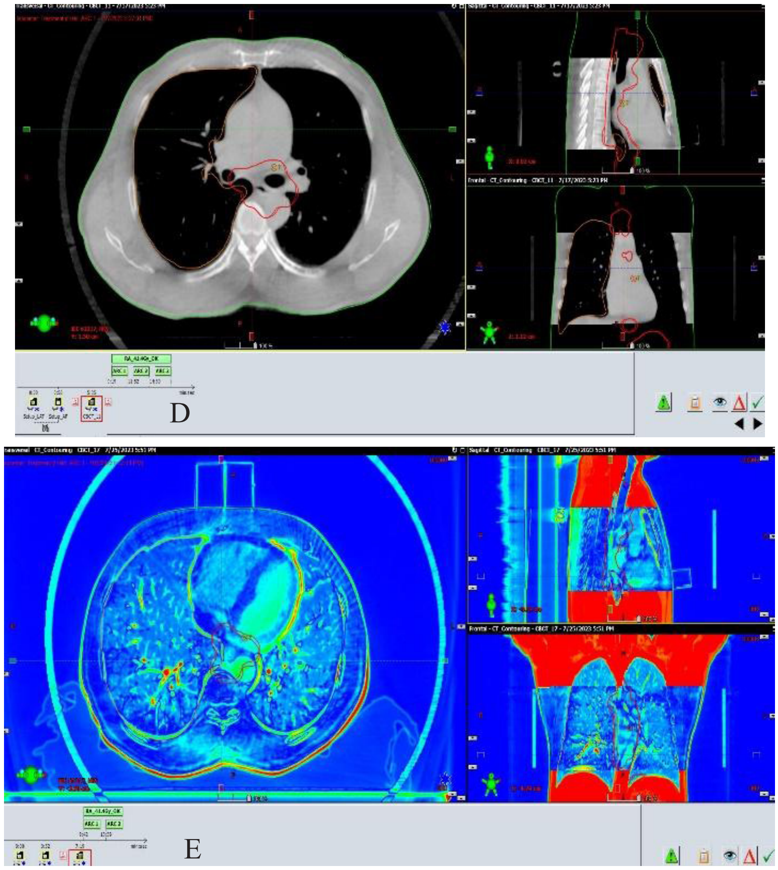


Figure 5. Evaluation of pre-treatment setup errors (D) and reproducibility of treatment position; DIBH breathing amplitude (E)

2.2.5. Analysis and evaluation of pre-treatment setup errors on 3D-CBCT images

A total of 1027 sets of 3D-CBCT images were collected to assess setup errors in three directions: anterior-posterior (AP), cranial-caudal (CC), and left-right (LR), using Bony Matching and PTV & Volume Matching methods on the ARIA Offline Review software. Initial setup errors and treatment position reproducibility were analyzed to determine the following objectives:

1. To evaluate initial setup errors in chest cancer patients undergoing 4D-DIBH radiotherapy using full-body Vaclock immobilization.

2. To assess initial setup errors in 4D-DIBH radiotherapy for esophageal cancer.

3. To assess initial setup errors in 4D-DIBH radiotherapy for lung cancer.

4. To assess initial setup errors in 4D-DIBH radiotherapy for thymic cancer and rib bone metastases.

5. To determine setup margins based on the Van Herk formula: $SM_{vanHerk} = 2{,}5\ \Sigma_{setup} + 0{,}7_{\sigma setup}$ for thoracic cancers including esophageal, lung, thymic cancers, and rib metastases [2,3], where: Setup margin ($SM_{vanHerk}$: Setup margin) represents the calculated expansion from CTV to PTV, Systematic

error (Σ) is defined as the standard deviation of the mean setup errors across all patients, Random error (σ) is defined as the average standard deviation of setup errors for each patient.

3. RESULTS AND DISCUSSION

3.1. Initial setup errors before treatment

The setup errors prior to 4D-DIBH radiotherapy for thoracic regions were: 2.5 mm ± 1.0 mm (AP), 3.2 mm ± 1.3 mm (CC), and 2.1 mm ± 1.5 mm (LR) (Table 2). In Group 1 (esophageal cancer patients receiving 4D-DIBH radiotherapy), the setup errors were: 2.4 mm ± 0.9 mm (AP), 3.4 mm ± 1.2 mm (CC), and 1.8 mm ± 1.1 mm (LR) (Table 3). For Group 2 (lung cancer patients), the corresponding errors were: 2.7 mm ± 0.9 mm (AP), 2.9 mm ± 1.3 mm (CC), and 2.3 mm ± 2.0 mm (LR) (Table 4). In Group 3 (patients with thymic cancer or rib bone metastasis), the setup errors were: 2.6 mm ± 1.6 mm (AP), 3.0 mm ± 1.3 mm (CC), and 3.1 mm ± 1.7 mm (LR) (Table 5). Setup margins (SM) calculated using the Van Herk formula for full-body Vac-lock–assisted 4D-DIBH radiotherapy were: Thoracic region overall: 3.7 mm (AP), 4.8 mm (CC), 4.0 mm (LR). Group 1 – Esophageal cancer: 3.9 mm (AP), 4.8 mm (CC), 3.6 mm (LR). Group 2 – Lung cancer: 3.5 mm (AP), 4.8 mm (CC), 6.8 mm (LR). Group 3 – Thymic cancer & rib metastases: 3.0 mm (AP), 4.7 mm (CC), 4.9 mm (LR) (Table 6).

3.2. Initial setup errors and reproducibility in 4D-DIBH thoracic radiotherapy

Table 2. Initial setup errors for 4D-DIBH radiotherapy using full-body vac-lok in thoracic cancer patients

Direction	Vrt (AP) mm	Lng (CC) mm	Lat (LR) mm
Mean Setup Error ± SD	2.4 ± 0.9	3.2 ± 1.3	1.9 ± 1.1
Systematic Error (∑SM)	2.2	3.2	2.7
Random Error (σSM)	1.5	1.6	2.0
Setup Margin (Van Herk formula)	3.7	4.8	4.0

Analysis and discussion: The results of this study indicate that the initial setup errors in thoracic radiotherapy using the 4D-DIBH technique with full-body Vac-Lok immobilization were effectively controlled, with pre-treatment setup deviations maintained at ≤ 3 mm in the anterior–posterior (AP) and lateral (LR) directions. Larger deviations (≥ 3 mm) were observed primarily in the cranial caudal (CC) direction. Both systematic and random setup errors were well-managed, ensuring accurate dose delivery to the tumor, minimizing respiratory-induced positional deviations, and optimizing radiation dose distribution to surrounding critical organs at risk (OARs). The calculated setup margins (SM) using Van Herk's formula for thoracic treatment were: 3.7 mm (AP), 4.8 mm (CC) and 4.0 mm (LR).

However, certain subjective and objective factors continue to affect positional accuracy and reproducibility, including patient fatigue, suboptimal breath-hold compliance, and insufficient breathing training. In some cases, setup deviations exceeded 3 mm in 4D-VMAT and SBRT treatments, necessitating repeat 3D-CBCT scans and extended treatment time to ensure alignment. Positional inconsistencies were most commonly observed in the diaphragm region, likely due to instability in abdominal and thoracic wall movement during deep inspiration and breath-hold. This highlights the need for improved pre-treatment respiratory coaching and patient compliance monitoring to enhance setup reproducibility and treatment efficiency.

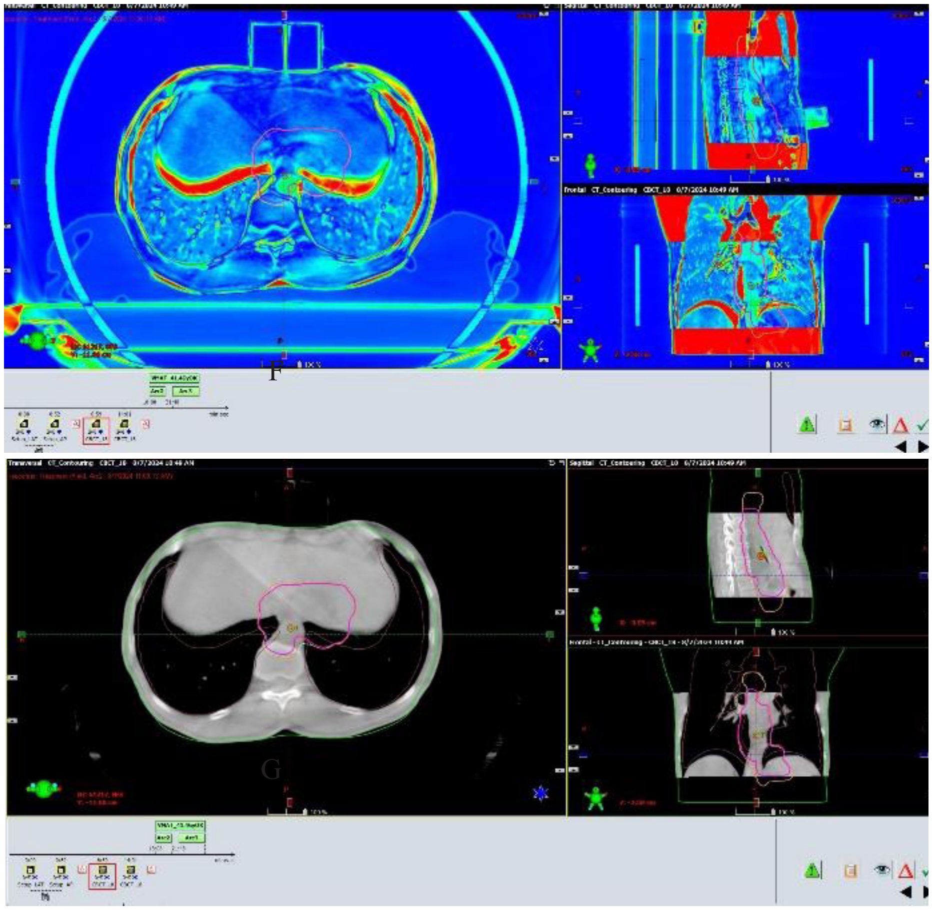


Figure 6. Positional variation due to suboptimal breath-hold reproducibility caused by excessive inhalation, resulting in non-reproducible organ volumes of the heart and lungs (F) and (G)

3.3. Initial setup error and positional reproducibility in 4D-DIBH radiotherapy for esophageal cancer

Table 3. Initial setup errors in 4D-DIBH radiotherapy using full-body vac-lok immobilization for esophageal cancer

Direction	Vrt (AP) mm	Lng (CC) mm	Lat (LR) mm
Mean setup error ± SD	2.4 ± 0.9	3.4 ± 1.2	1.8 ± 1.1
Systematic error (∑SM)	2.3	3.1	2.8
Random Error (σSM)	1.6	1.8	0.8
Setup margin (van Herk)	3.9	4.8	3.6

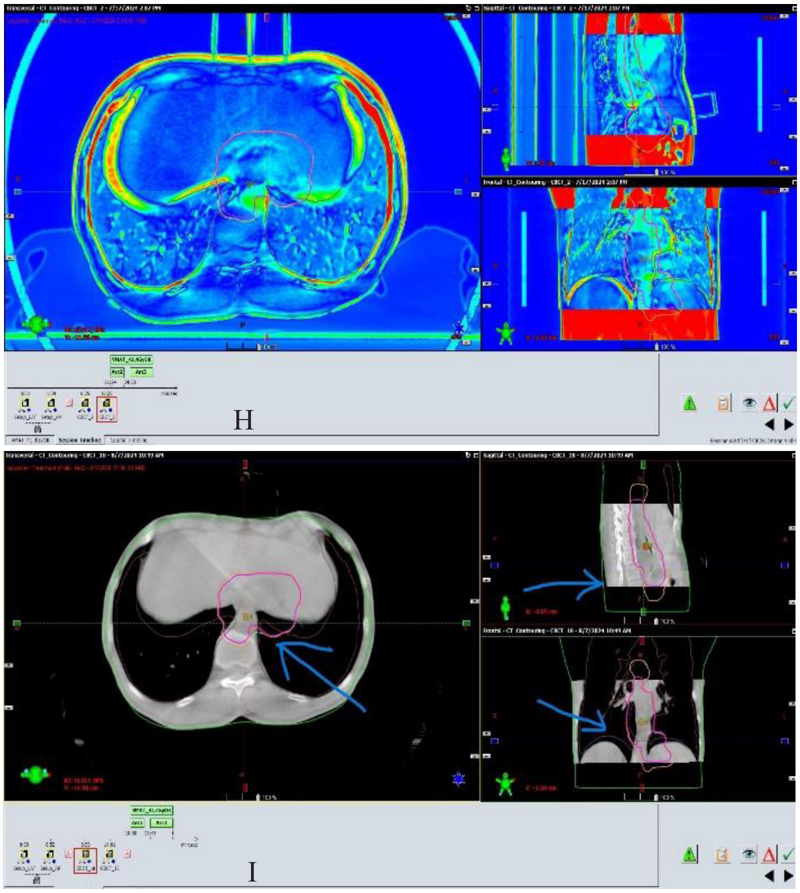


Figure 7. Positional variation due to suboptimal breath-hold reproducibility-excessive inhalation during deep inspiration breath-hold (DIBH) leads to lifting of the back off the Vac-Lok cushion, resulting in failure to reproduce the target organ volumes of the heart and lungs (H) and (I).

Analysis and discussion: The evaluation results for 4D-DIBH radiotherapy in esophageal cancer demonstrated setup errors of ≤ 3 mm in the AP and LR directions, while errors ≥ 3 mm tended to occur more frequently in the CC direction. For patients unable to reproduce the breath-hold pattern to adequately manage setup error and internal motion, breath-hold training and repeat 3D-CBCT image verification were performed to ensure accurate repositioning before irradiation. The calculated setup margins (SM) for esophageal cancer (Group 1) were: 3.9 mm (AP), 4.8 mm (CC) and 3.6 mm (LR).

Due to the anatomical characteristics of the esophagus-being a long digestive tube from the mouth to the stomach-tumor location may vary (upper, middle, or lower third), necessitating strict adherence to setup error management protocols and requiring good patient compliance during the radiotherapy process. The 4D-DIBH breath-hold technique combined with full-body Vac-Lok immobilization helps stabilize patients during treatment, minimizing positional changes caused by coughing or lifting of the back off the immobilization device during prolonged breath-hold periods.

3.4. Setup errors before treatment and position reproducibility in 4D-DIBH radiotherapy for Lung cancer

Analysis and discussion: The evaluation results for 4D-DIBH radiotherapy in lung cancer showed that the initial setup errors were ≤ 3 mm in the AP and LAT directions, while errors ≥ 3 mm tended to occur in the CC direction. The calculated setup margins (SM) for lung cancer (Group 2) were: 3.5 mm (AP), 4.8 mm (CC) and 4.1 mm (LR).

Motion management in 4D-DIBH lung radiotherapy presents significant challenges, particularly when treating small tumors located above the diaphragm-where respiratory-induced motion can be substantial if breathing is not well-controlled and patient breathing training is insufficient. Inadequate motion control during 4D-DIBH may lead to positional deviations in all three directions: AP, CC, and LAT, thereby compromising treatment accuracy and dose delivery.

Table 4. Initial setup errors in 4D-DIBH radiotherapy using whole-body vaclock for Lung cancer

Direction	Vrt (AP) mm	Lng (CC) mm	Lat (LR) mm
Mean setup error ± SD	2.7 ± 0.9	2.9 ± 1.3	1.8 ± 0.9
Systematic error (∑SM)	2.1	3.4	2.3
Random error (σSM)	1.4	1.4	1.9
Setup margin (van Herk)	3.5	4.8	4.1

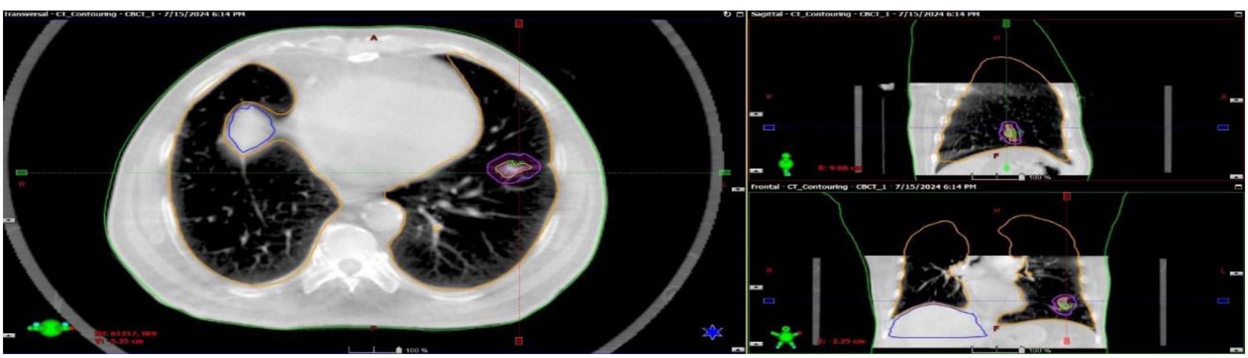


Figure 7. Accurate repositioning and reproducibility of the treatment volume for small tumors located above the diaphragm

3.5. Initial setup errors and reproducibility in 4D-DIBH radiotherapy for thymic and rib lesions

Table 5. Initial setup errors in 4D-DIBH radiotherapy using whole-body vaclock immobilization for thymic and rib metastatic tumors

Direction	Vrt (AP) mm	Lng (CC) mm	Lat (LR) mm
Mean setup error ± SD	1.8 ± 0.6	3.0 ± 1.3	2.3 ± 1.4

Direction	Vrt (AP) mm	Lng (CC) mm	Lat (LR) mm
Systematic error (∑SM)	1.5	3.3	3.4
Random error (σSM)	1.5	1.4	1.5
Setup margin (van Herk)	3.0	4.7	4.9

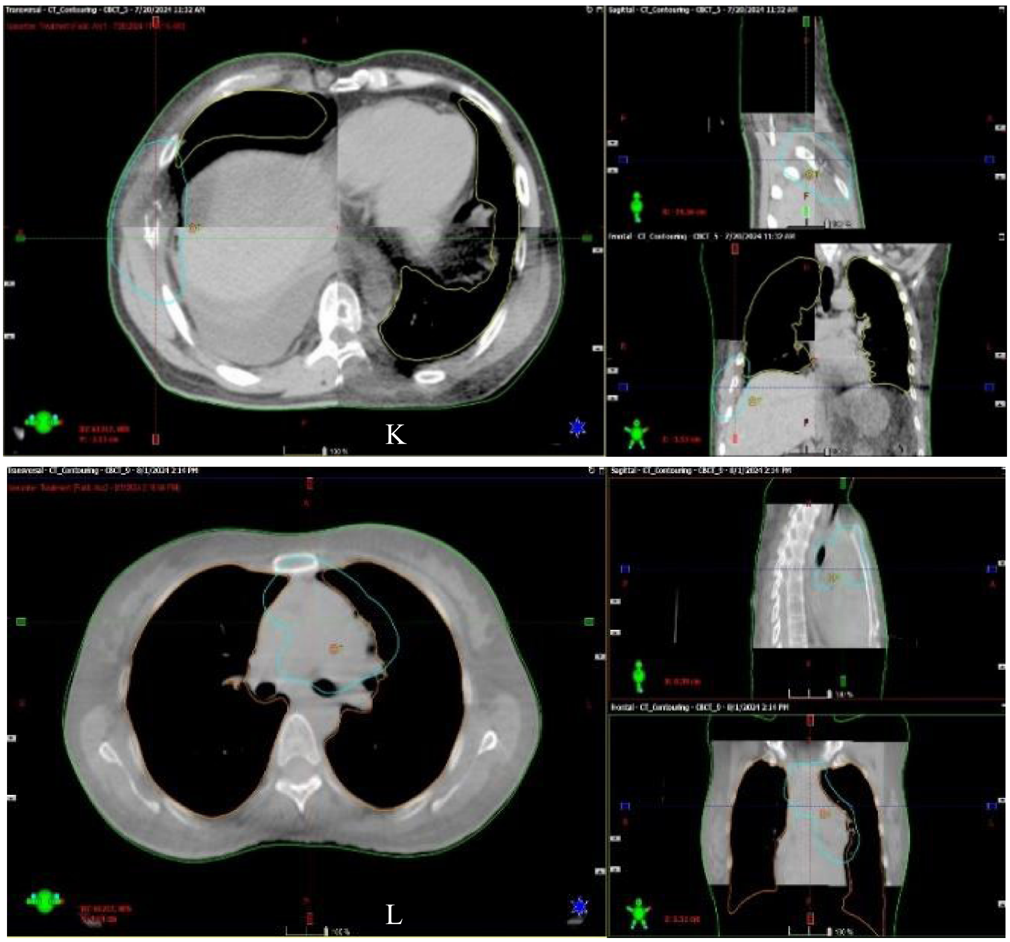


Figure 8. The accuracy of target volume repositioning for metastatic rib lesion (K) and thymic tumor (L)

Analysis and discussion: The evaluation results for 4D-DIBH radiotherapy in thymic tumors or rib metastases demonstrated initial setup errors ≤ 3 mm in the AP and LR directions, with a tendency for larger errors ≥ 3 mm in the CC direction. The calculated setup margins (SM) for Group 3 (thymic tumors and rib metastases) were 3.0 mm (AP), 4.7 mm (CC) and 4.9 mm (LR).

Based on our observations in setup error control and repositioning reproducibility, the thymus is a centrally located mediastinal organ, where the respiratory motion-induced volume and positional variations are typically minimal, allowing effective control of setup errors within ≤ 3 mm. However, for certain cases involving rib or chest wall metastases, achieving accurate target positioning and consistent patient posture, along with stable breath-hold amplitude, poses considerable challenges. These difficulties underscore the importance of tailored respiratory training protocols and strict patient compliance requirements, particularly for this patient subgroup. As a result of these findings, we have implemented enhanced breath-hold training and stricter procedural adherence for patients receiving radiotherapy for rib metastases or chest wall involvement.

3.6. Setup margins calculated using the van herk formula

Table 6. Setup margins (SM) calculated by the van herk formula in 4D-DIBH radiotherapy using Full-body vaclock immobilization

Patient Group	Vrt (AP) mm	Lng (CC) mm	Lat (LR) mm
Thoracic Region (General)	3.7	4.8	4.0
Esophageal Cancer (Mean)	3.9	4.8	3.6
Lung Cancer (Mean)	3.5	4.8	4.1
Thymic/Rib Mets	2.7	4.7	4.9
Setup Margin (Van Herk)	7.0	9.0	5.0

Analysis and discussion: The results of this study on setup errors prior to treatment and the evaluation of reproducibility of patient positioning in 4D-DIBH radiotherapy using full-body Vac-Lok immobilization demonstrated favorable outcomes. These findings meet the clinical standards for high-precision radiotherapy as practiced at Vinmec Times City International General Hospital, ensuring accurate dose distribution to the target tumor volume, high treatment efficacy, and patient safety. The setup margins (SM) calculated at the center align well with those reported in the published work by van Herk and colleagues, further validating the accuracy and consistency of our clinical workflow and positioning protocols.

4. CONCLUSION

4D-DIBH radiotherapy utilizing full-body Vac-Lok immobilization ensures daily reproducibility and positional stability during treatment. It allows for precise radiation dose delivery to the tumor target while minimizing exposure to surrounding healthy tissues. This study provides an important clinical basis for radiation oncologists to define appropriate PTV margins tailored to tumor location and pathology within the thoracic region.

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