



# Technical note: improved positioning protocol for patient setup accuracy in conventional radiotherapy for lung cancer

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## Abstract

This study aimed to investigate an improved setup protocol for maintaining patient setup accuracy, with minimal or no use of image-guided radiation therapy in conventional radiotherapy for lung cancer. A coordinate value for the treatment couch in the anterior–posterior (AP) direction was obtained from the first fraction using bony anatomy image guidance. The coordinate value was invariably used for patient positioning in the second and subsequent treatment fractions. The errors of 2410 setup image sets (anterior and lateral) from 105 patients with lung cancer were analyzed. The systematic and random patient positioning errors in the AP direction were  $0.6 \pm 1.0$  mm. Such errors accounted for 97% of all fractions within  $\pm 2$  mm. The protocol resulted in minimal patient setup errors in the AP direction using only one image for guidance; therefore, it may be applied to conventional radiotherapy for lung cancer in case of insufficient image guidance.

**Keywords** Image-guided radiation therapy · Patient setup error · Lung cancer · Conventional radiotherapy

## 1 Introduction

Image-guided radiation therapy (IGRT) is a method used in treatment planning to identify the location of anatomical structures with high accuracy. This is accomplished by comparing two- or three-dimensional positioning images of a patient with a reference image (a simulation of positioning or planning image). IGRT also corrects setup errors in real time for each fractionated treatment [1]. The image guidance includes a two-orthogonal direction scan imaging system for the bones or matching metal markers (kV radiography), and a rotational scan imaging system (cone-beam computed tomography [CBCT]) for soft-tissue matching [1, 2]. The use of image guidance reduces setup errors, and such errors can be divided into patient setup errors obtained via bony

anatomy verification and tumor position errors obtained via tumor verification [3]. CBCT is frequently used for tumor verification during high-precision radiotherapy for lung cancer, such as stereotactic body radiation therapy (SBRT). A bony structure, such as the vertebra, is an important verification factor that maintains the reproducible accuracy of a patient's position during SBRT [4]. The vertebra is also an important reference standard for conventional radiotherapy in advanced lung cancer cases, because soft-tissue registration has contrast resolution limitations and high interobserver variability [5]. Tumor verification is also not possible with conventional radiotherapy due to anatomical changes during the treatment period [6]. Moreover, additional treatment times and exposures can be generated in conventional radiotherapy with the use of excessive image guidance [7–9]. The most common setup for conventional radiotherapy for advanced lung cancer is online verification for the first few fractions, followed by offline verification for all subsequent fractions [10]. Representative setup protocols that use less image guidance to assure positioning accuracy, such as shrinking action level (SAL) and no action level (NAL), have been effectively used to reduce systematic setup errors in radiation therapy for prostate cancer and for head and neck tumors in clinical practice [11, 12]. However, protocols were unable to reduce the random error, and the systematic errors may increase throughout the course of treatment

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with conventional radiotherapy in advanced lung cancer [13]. Another protocol that uses less image guidance can effectively reduce systematic and random setup errors in AP direction using a fixed couch height [14]. Although this protocol is only effective in the AP direction, it can reduce setup errors from the initial fraction, because the couch height can be obtained by planning and simulation [15]. The efficacy of this protocol has been demonstrated clinically in radiotherapy for pelvic tumors, abdominal tumors, and whole breast, but there are still few reports about its application in conventional radiotherapy for lung cancer [14–18].

This study aimed to present a protocol that uses a fixed couch height to maintain interfractional patient setup accuracy. The protocol was used for lung tumors treated with conventional dose fractionations, based on our center’s clinical experience since 2013. For this protocol to be utilized as early as possible from the initial fractions of the treatment process, we only used results of the imaging registration in the first IGRT fraction and analyzed the maintenance of setup accuracy.

## 2 Materials and methods

### 2.1 Patient data

This study included 105 patients with lung cancer who received multidirectional (4–6 fields) conventional radiotherapy using 6 and 10 MV photon beams from a linear accelerator (Clinac iX; Varian Medical Systems, Inc., Palo Alto, CA, USA). Each patient underwent positioning verification via daily orthogonal two-dimensional kV radiography (on-board imaging [OBI]; version 1.5.15; Varian Medical Systems, Inc.) [19]. A total of 2410 image sets were obtained for the 112 targets in 105 patients (range = 20–30 image sets per target, mean = 22 image sets). Patient and treatment characteristics are summarized in Table 1.

### 2.2 Planning and reference image sets

In treatment planning for each patient, a computed tomography (CT) scan (Optima; GE Healthcare, Milwaukee, WI, the USA) was performed using a 1.25-mm imaging slice thickness with free breathing. To validate the respiratory movement track of the target, a four-dimensional CT scan (AdvantageSim; GE Healthcare) was conducted before planning. The respiratory movements of the lower lung field targets were reconfirmed using a fluoroscopic apparatus before treatment planning. A three-dimensional treatment planning system (Eclipse version 11.0; Varian Medical Systems, Inc.) was used for dose calculation, using the anisotropic analytical algorithm (AAA) method [20]. The gross tumor volume was contoured by a radiation oncologist using the inhale and

**Table 1** Characteristics of the patients

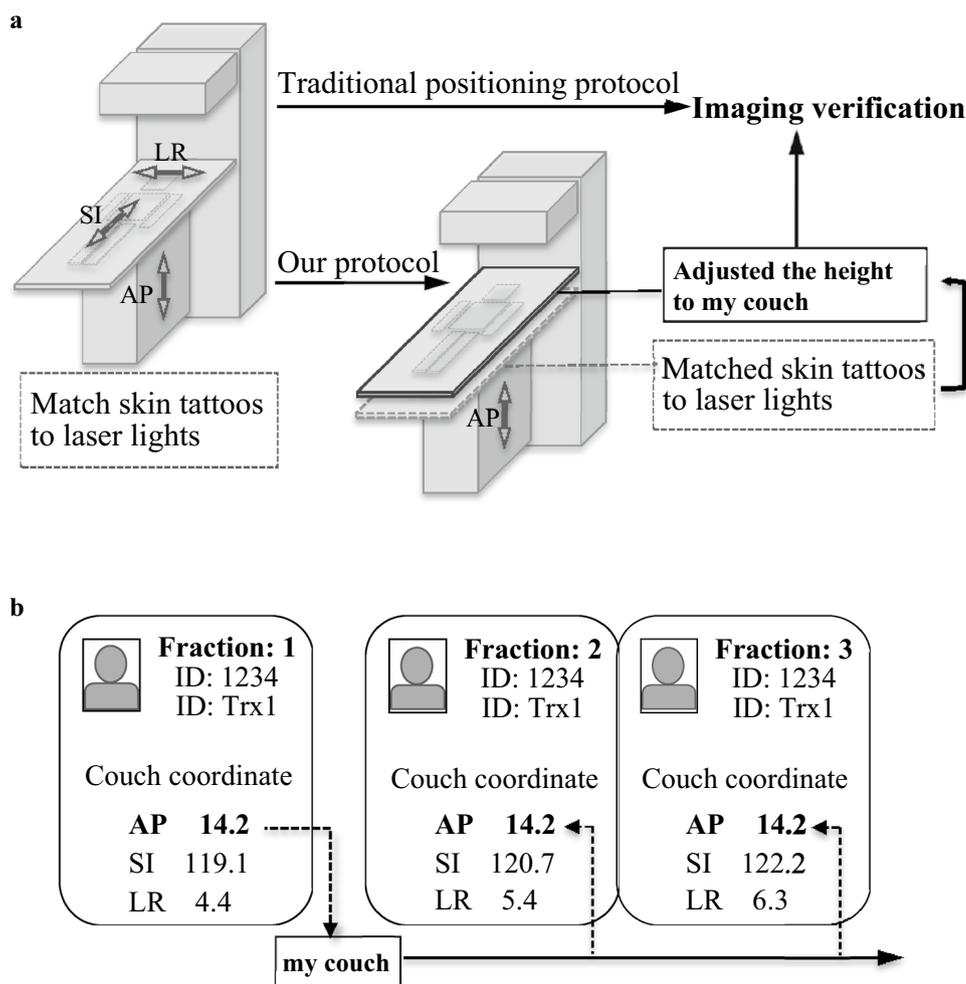
Age	
Range	53–90
Mean	76
Gender	
Male	n = 82
Female	n = 23
Target volumes	
GTV range	0.72–248.8 cm <sup>3</sup>
Mean	42.7 cm <sup>3</sup>
Tumor location	
Left upper lobe	n = 24
Left lower lobe	n = 20
Right upper lobe	n = 28
Right lower lobe	n = 19
Mediastinum	n = 21
Fractionation	
20 × 3 Gy	n = 88
25 × 2 Gy	n = 13
30 × 2 Gy	n = 11

exhale data sets. Next, 5 mm margins (respecting the anatomic boundaries) were added to the inhale and exhale gross tumor volumes to generate the corresponding clinical target volumes (CTVs). The fusion of the inhale and exhale CTV datasets generated the internal target volume (ITV), which accounted for the respiratory excursion, and an additional 5 mm setup margin expansion around the ITV provided the planning target volume (PTV), according to the International Commission on Radiation Units and Measurements report 62 guidelines [21]. A 60 or 50 Gy dose was prescribed at the reference point for the PTV. The digitally reconstructed radiographs (DRRs) were reconstructed from CT images with Eclipse and were used for planning. The DRRs were used as reference images for position verification.

### 2.3 Patient positioning protocol

The patient was placed in a supine position on the treatment couch, and no immobilization device was used except when the target was in the lower lobe, which required the technician to raise the arms on the homemade platform. The traditional positioning method was performed with the four skin tattoos matched to the laser lights: two-orthogonal midlines for the superior–inferior (SI) and left–right (LR) directions and two lateral points on either side of the thorax for the anterior–posterior (AP) direction. The patient’s body position was adjusted until the skin tattoos and laser lights matched completely (Fig. 1a). Next, localization images were acquired with the kV radiography system using 75 kVp, 200 mA, and 25 ms or 90 kVp, 200 mA,

**Fig. 1** Patient positioning protocol for radiotherapy. **a** Conventional positioning protocol and our protocol. Our method adjusted the height of the treatment couch to a specific coordinate value (“my couch”) after the conventional positioning. The setup errors were measured in three directions: superior–inferior, left–right, and anterior–posterior. **b** Method for obtaining “my couch”, which was derived using the coordinate values of the treatment couch in the first fraction with vertebral bony anatomy verification



and 200 ms for the anterior and lateral images, respectively. The imaging dose ranged from 0.3 to 0.5 mGy and from 2 to 4 mGy for the anterior and lateral images, respectively. For the setup error evaluation, an automatic registration of the bony anatomy in the DRR and kV radiography images was performed online, and the region of interest included as many thoracic vertebrae as possible. The setup errors, which could be expressed in terms of translational (AP, SI, and LR) displacements, were measured and presented on the review console. The patient’s position was corrected by automatically translating the couch according to the image registration results. After correcting the patient’s position, verification image sets were taken to confirm the accuracy of the automatic correction, and it measured the residual setup error. The first treatment session was started after the bony anatomy was completely matched with DRR, and the residual errors were confirmed within margin set in planning. The coordinate value of the treatment couch position in the AP direction was recorded and described as “my couch”. Figure 1b shows an example of the acquisition and application of “my couch”.

For the second fraction and subsequent treatments, the position of the patient was similar to that of the first fraction, with corresponding laser lights and skin tattoos. Next, the treatment couch was manually adjusted to the “my couch” position in the AP direction. Image registration was performed similar to that in the first fraction. If a setup error between the localization images and DRRs exceeded  $\pm 2$  mm in any direction, the patient’s position was corrected by automatically translating the couch according to the image registration results. During planning, our  $\pm 2$ -mm threshold was initially established to reflect the safety margins used clinically around the organs at risk, such as the spinal cord. The treatment was not initiated until the therapists were sure that the patient’s position was within the  $\pm 2$ -mm threshold.

## 2.4 Statistical analysis

The three-direction registration results of all fractions for the 105 patients were retrospectively analyzed, and the mean shifts and standard deviations (SDs) were calculated per patient. The random error was calculated using the root

mean square of all SDs, and systematic error was calculated using the SDs of the means [22]. The van Herk margin equation ( $2.5\Sigma + 0.7\sigma$ ) was used as an approximation of the required setup margins using the setup data, where  $\Sigma$  and  $\sigma$  are the systematic and random errors, respectively [22]. Because it is our practice to use four-dimensional CT to define an ITV that accounts for respiratory motion, this margin estimate represents the setup margin only. Data analysis was conducted using Microsoft Office Excel 2011 (Microsoft, Redmond, WA, the USA), and statistical analysis was performed using the Statistical Package for the Social Sciences software for Windows version 22.0 (IBM Corp., Armonk, NY, the USA). The level of significance ( $P$ ) was set to 0.01.

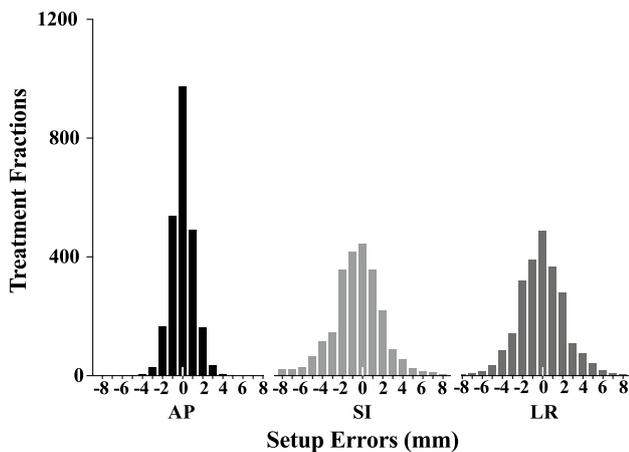
### 3 Results

All patients successfully completed their treatments while using our positioning protocol. The total treatment time, including the kV radiography guidance, setup error correction, and beam delivery, ranged from 15 to 20 min. The systematic and random patient positioning errors were  $0.6 \pm 1.0$  mm in the AP direction,  $1.1 \pm 2.4$  mm in the SI direction, and  $1.0 \pm 2.3$  mm in the LR direction. Figure 2 shows the patient setup error distribution in the three directions. Patient setup errors < 1 mm accounted for 83%, 51%, and 52% of all fractions in the AP, SI, and LR directions, respectively. The AP direction setup errors comprised 97% of all fractions,  $\pm 2$  mm of our tolerance. The setup errors were significantly smaller in the AP direction than in the other directions (Tukey’s multiple comparisons

test,  $P < 0.01$ ). Setup margins were calculated and were 2 mm, 4 mm and 4 mm for the AP, SI, and LR directions, respectively.

### 4 Discussion

In this study, we analyzed patient setup errors via online kV radiography verification in daily IGRT for lung cancer, and we investigated the efficacy of a clinical experimental protocol in reducing patient setup errors. The results showed that the treatment couch fixed height at “my couch” in all fractions resulted in minimal patient setup errors in the AP direction (Fig. 2). The results for systematic and random errors in all three directions are presented in Table 2. This is followed by a comparison with results found in the literature [3, 23–28]. Although there are no comparisons available for parameters such as patient conditions, treatment devices, and image-guided methods, systematic errors in the AP direction are fewer in the present study than in the previous studies. Our protocol is superior, because it maintains minimal systematic errors and random errors in the AP direction without image guidance from the second fraction. The traditional protocol was used for positioning in the SI and LR directions. Perhaps, due to the daily image guidance, the number of systematic errors was maintained at a lower level; however, the number of random errors was obviously higher than in the AP direction (Table 2). Therefore, daily image guidance and online correction may still be the ideal method for ensuring positioning accuracy in the SI and LR directions. The van Herk margin equation ( $2.5\Sigma + 0.7\sigma$ ) was used to derive setup margins for patient positioning error. If a high-precision setup protocol is reflected in the PTV margin decision, it may cause reduction of the PTV margin, thereby not only decreasing the mean heart, lung, and esophageal dose, but also providing a dose-escalation opportunity



**Fig. 2** Histogram for the setup errors in all fractions. The setup error distribution in the three directions is shown, according to the proposed positioning protocol. Statistical analysis showed that the setup errors in the anterior–posterior direction were significantly less than those in the superior–inferior and left–right directions (Tukey’s multiple comparisons test,  $P < 0.01$ )

**Table 2** Systematic ( $\Sigma$ ) and random ( $\sigma$ ) patient setup errors and comparison with published data

	$n$	Systematic error ( $\Sigma$ ) $\pm$ Random error ( $\sigma$ )		
		AP (mm)	SI (mm)	LR (mm)
Present study	112	$0.6 \pm 1.0$	$1.1 \pm 2.4$	$1.0 \pm 2.3$
GR. Borst et al. [23]	62	$1.2 \pm 1.4$	$1.9 \pm 3.8$	$1.7 \pm 3.1$
IS. Grills et al. [24]	24	$5.8 \pm 2.0$	$2.9 \pm 3.5$	$2.0 \pm 2.7$
AR. Yeung et al. [25]	13	$3.2 \pm 4.0$	$5.6 \pm 4.6$	$3.5 \pm 3.7$
ES. Worm et al. [26]	19	$1.6 \pm 1.4$	$4.5 \pm 2.8$	$2.3 \pm 1.9$
JP. Bissonnette et al. [27]	48	$1.9 \pm 2.3$	$2.6 \pm 3.8$	$1.9 \pm 2.6$
M. Guckenberger et al. [3]	25	$2.6 \pm 1.1$	$3.2 \pm 2.1$	$1.8 \pm 2.0$
MC. Mesias et al. [28]	53	$3.5 \pm 2.6$	$3.3 \pm 4.1$	$2.6 \pm 3.1$

AP anterior–posterior, SI anterior–posterior, LR left–right

[13]. Yeung et al. reported possible setup margin reductions after applying daily CBCT image guidance in advanced lung cancer patients [25]. Our data showed a 2 mm setup margin in the AP direction and 4 mm setup margin in the SI and LR directions. Using our protocol, the setup margin in the AP direction may be reduced.

When the patients were positioned on the flat carbon treatment couch, the kyphotic thoracic vertebrae may have been fixed in the AP direction by compression due to body weight on the spinous processes of the thoracic spine. The relative variation between the thoracic vertebrae and treatment couch in the AP direction was extremely poor. Therefore, the coordinate values in the AP direction may be an effective alternative for patient setup by matching bony anatomy such as vertebrae. The variation range, based on our clinical outcome of the couch coordinate values (data not shown), was wide in the SI and LR directions. For the SI and LR directions that should be applied in this manner as well, the same degree of pressure may be required to fix the spine. In clinical biomechanics, the spinal column consists of the cervical, thoracic, lumbar, and sacral vertebrae, and it can exhibit flexion, extension, side curvature, and rotation movements based on the associations between the vertebral bodies. In particular, the thoracic vertebrae have special bony structures such as the upper and lower vertebral articular surfaces which are predominantly parallel to the coronal plane. The thoracic vertebrae are also tightly wrapped in ligaments such as the anterior longitudinal ligament, posterior longitudinal ligament, and ligamenta flava [29]. The collision of the bony structures and tightness of the ligaments limit the flexion and extension of the thoracic vertebrae more than the lumbar or cervical vertebrae [30]. Moreover, when a patient is in a supine position, it is challenging to fit the cervical and lumbar vertebrae to a horizontal couch, due to physiological lordosis. Based on these anatomical features, the efficacy of our proposed patient setup protocol must be treated with caution when applied to cervical and abdominal tumors.

Guckenberger et al. demonstrated the importance of tumor intrafractional motion via respiration. They recommended the use of CBCT for the image registration of the tumor position in the SBRT of early stage lung cancer [3]. Daily CBCT has become the reference standard in SBRT because of the small targets, short fraction regimens, high doses per fraction, and risk of treatment-related toxicities [24, 31]. In conventional radiotherapy for advanced lung cancer, direct target registration is different with SBRT, because the potential lung target deformation and migration during a treatment course could affect the accuracy of the registrations, as the CBCT target begins to differ from the planning CT target. In addition, the limited image contrast of CBCT restricts mediastinal disease assessment; therefore, vertebral bony anatomy registration, followed by

visual inspection of the tumor and carina, seems a reasonable method to identify all misalignments [13]. Because a correlation of  $R^2 = 0.5$  was found between the tumor setup errors and patient positioning errors, it is clear that vertebral bony anatomy registration is important in SBRT [3]. However, this factor is of greater importance in conventional radiotherapy of advanced lung cancer. In a previous study, registration using the spine provided complete target coverage for advanced lung cancer when using a 5 mm setup margin [5]. Both CBCT and orthogonal kV–kV can provide satisfactory registration for vertebral bony anatomy [32, 33], but there is a significant difference in the imaging effective dose. The effective dose per fraction in phantoms using the Varian kV CBCT was  $5.00 \pm 0.30$  mSv for the standard low-dose thorax protocol, while it was  $1.14 \pm 0.16$  mSv for the orthogonal kV–kV protocol [34]. In the orthogonal kV–kV protocol, the lateral imaging dose was larger than the dose used in the anterior protocol [35]. However, lateral image guidance may also be omitted from the second fraction using “my couch,” which obtained vertebral bony anatomy registration in the first fraction only. Our protocol may provide a beneficial technique for reducing the imaging effective dose for patients who receive daily image guidance in conventional radiotherapy for lung cases.

Fixed couch height protocols have been reported in several studies and have been used clinically. A common finding between these studies and ours is that an accurate position may be achieved by ignoring the interfractional skin marker movement in the AP direction. However, we found differences in the method for determining couch height compared to previous studies. Greer et al. determined the couch height by measuring the distance between the couch top and the isocenter in a simulation system, and then measuring the same distance again in the first fraction, to keep the couch height the same as that in the simulation [14]. Observational errors may be easily triggered by such frequent measurement procedures in clinical practice. Van Lin et al. used the digital couch height readout from the simulator, but inaccuracies were created by sag between the accelerator system couch and the digital readout [15]. It may be ideal to obtain the couch height alone in the accelerator system. In a recent study, couch height was calculated alone in the accelerator system by analyzing the setup error of the initial five fractions [18]. Our setup protocol may be more easily applied to clinical practice using “my couch” obtained from the vertebral bony anatomy registration in the first fraction only. Although IGRT can be easily implemented due to improvements in radiation therapy equipment and software, the combination of clinical experience and research for effective use of these devices may provide the greatest benefit to patients and reduce the burden on patients during the treatment process.

## 5 Conclusion

We validated whether the patient positioning protocol in this study can be used as an alternative to thoracic vertebral bony anatomy with a treatment couch coordinate value in radiotherapy for lung cancer. The couch coordinate value was obtained from the first fraction image guidance alone. This protocol resulted in minimal patient setup errors in the AP direction, and, therefore, may be applied to conventional radiotherapy for lung cancer with insufficient image guidance.

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## Compliance with ethical standards

**Conflict of interest** The authors declare no conflicts of interest associated with this study.

**Ethical approval** The IRB was obtained without patients' informed consent.

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