ORIGINAL ARTICLE

Incidence of Setup Errors in Patients Treated with Radiotherapy in the Faculty of Medicine, Vajira Hospital

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Objective: To study incidents of radiation therapy setup errors and factors affecting patients treated with radiation therapy to assess treatment effectiveness and provide fundamental data for the continued care of future patients at the Faculty of Medicine, Vajira Hospital.

Materials and Methods: The retrospective study was conducted from December 2023 to March 2024 on 39 patients who underwent radiation therapy in the TrueBeam linear accelerator, receiving MV-kV and CBCT images before each treatment session. These images were compared with CT images obtained from the treatment simulation process to determine the positional setup errors in all three directions. Subsequently, the values obtained were used to calculate systematic and random errors. The statistical analysis was performed using percentages and univariate analysis to assess statistical correlations.

Results: A total of 434 MV-kV and CBCT images were collected. It was found that the cumulative incidence of radiation therapy setup errors was 0.65, with systematic and random errors in the vertical (Vrt.), longitudinal (Lng.), and lateral (Lat.) directions of patients being 0.23, 0.22, 017, and 0.20, 0.21, and 0.21 cm, respectively. Moreover, the use of different patient immobilization devices significantly impacted the setup errors, particularly in the Vrt. direction. Conversely, other factors, such as gender, radiation technique, treatment site, and bladder preparation did not show significant correlation with setup errors values.

Conclusion: Setup errors were detected in every treatment session, and the measurement and correction of these errors before treatment using MV-kV and CBCT images significantly improve the accuracy and precision of radiotherapy. The choice of immobilization devices plays a crucial role in minimizing setup errors. This approach can reduce the PTV margin and increase the radiation dose to the cancerous tumor. Therefore, it is essential to determine the setup errors and appropriate radiation margins specific to each institution.

Keywords: Radiotherapy; Setup error; Systematic error; Random error

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Cancer is a significant public health concern worldwide. In Thailand, cancer is the leading cause of continuous and increasing mortality, showing an age-standardized incidence rate of approximately 137.6 people per 100,000 population per year; liver cancer and cholangiocarcinoma are the most common types of cancer in males, whereas breast cancer in females(1).

Currently, cancer treatment involves a combination of various methods, including surgery, chemotherapy, hormone therapy, radiation therapy, targeted therapy, and symptom management by multidisciplinary teams. The choice of treatment depends on prognostic factors and treatment responses that enhance the effectiveness of disease management and patients' quality of life.

Radiation therapy utilizes electromagnetic radiation and particle to treat cancer(2,3). It plays a crucial role in 40% of patients requiring curative treatment(4) and used to treat loco regional diseases or provide palliation for metastatic diseases. Radiation induces ionizing radiation, which interacts with cancer cells' DNA, causing damage and leading to cell death(5).

The objective of radiation therapy is to deliver high-energy radiation that controls or eradicates cancer cells while minimizing radiation exposure to surrounding normal tissues or vital organs within their tolerance limits. This process involves simulation, treatment planning, treatment verification, and actual radiation delivery.

Accuracy in radiation beam alignment is crucial. Setup errors may occur during treatment, stemming from either systematic (SEs) or random errors (REs)(6-8). Systematic errors arise from differences between the actual radiation

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delivery and planned positions, and Random errors occur unpredictably. Image-guided radiation therapy (IGRT) is employed to verify and correct positioning errors before treatment, ensuring accuracy and facilitating treatment adjustments[9,10].

Factors contributing to setup errors include equipment malfunctions, particularly those in radiation delivery machines and treatment couch and immobilization devices; patient-positioning changes; anxiety; radiation setup; and internal organ motion during treatment.

The accuracy of positioning for radiation therapy using IGRT can be verified by using radiographic images, which indicate the position of radiation delivery each day during treatment. This procedure allows the adjustment of positions before actual treatment, ensuring the precision of radiation delivery. Additionally, it is used for evaluating the adaptation of treatment area boundaries[11-13].

Setup verification entails acquiring two-dimensional (2D) kV or MV portal images, which are subsequently matched with digitally reconstructed radiographs from computed tomography (CT) scans. The advent of cone-beam computed tomography (CBCT), a volumetric imaging technique, has transformed IGRT, elevating it from mere 2D verification and bony landmark matching to 3D assessment of target volume positioning and organ-at-risk localization and thereby enhancing overall treatment quality[14,15].

Researchers aim to study the incidence of setup errors in radiation therapy and factors influencing them in patients receiving radiation treatment at the Faculty of Medicine, Vajira Hospital. The present study intends to evaluate treatment effectiveness and provide fundamental data for the care of future patients.

Materials and Methods

The present study was approved by the ethics committee of the institute (COA165/2562). It identified patients undergoing radiation treatment in the TrueBeam linear accelerator at the Department of Radiation Oncology, Faculty of Medicine, Vajira Hospital, from December 2023 to March 2024. The inclusion criteria comprised treatment verification using MV electronic portal imaging device guidance, kV on-board imaging, and CBCT images. Patients lacking treatment information were excluded. Data on patient characteristics, tumor profiles, and treatment specifics were gathered from the patients' medical records.

All patients underwent CT simulation, wherein the planning isocenter was established as the registration reference point, invariably coinciding with the center of the planning target volume (PTV). The setup errors were collected with this reference point. Radiation treatments were verified using MV-kV and CBCT images, which were automatically aligned with CT simulator images for the detection of shifts in the initial tumor position across the vertical (Vrt.), longitudinal (Lng.), and lateral (Lat.) directions. After verification, the radiation oncologist conducted a final review before radiation therapy.

Analysis of setup errors was conducted using ARIA version 17 (Varian Medical Systems Inc., Palo Alto, CA). By comparing MV-kV (MV image in AP position and kV image in Lateral position) and CBCT images acquired before each treatment with the CT images, positional errors of the tumor in three directions were assessed. The setup error was considered when the measured value greater than 5 mm in three-dimensional conformal radiation therapy (3D-CRT) technique, 3 mm in volumetric -modulated arc therapy (VMAT)/intensity-modulated radiation therapy (IMRT) technique. The average of the displacements of the Vrt., Lng., and Lat. directions were calculated. Systematic error was estimated by determining the standard deviation of the averages for each direction. The random error was calculated as the square root of the average of the sum of the squared SDs per axis.

For statistical analysis, the authors employed SPSS statistical software (version 22.0, IBM Corp., Armonk, NY). Data were summarized using frequency distributions, measures of central tendency, and dispersion. In the univariate analyses, all risk factor variables were considered. All p-values were two-sided, with values below 0.05 indicating statistical significance.

Results

A total of 434 MV-kV and CBCT images were meticulously acquired for thorough analysis, encompassing data from 39 patients. These images comprised 25 (5.8%) brain scans, 79 (18.2%) head and neck (H&N) scans, 33 (7.6%) thoracic scans, 7 (1.6%) breast scans, and 290 (66.8%) lower abdomen (pelvic) scans. Patient demographics and treatment characteristics are succinctly summarized in Table 1.

The patient predominantly comprised males, accounting for 70.3% of the total. Body mass index (BMI) across the patients ranged from 14.7 kg/m^2 to 31.0 kg/m^2, with a median BMI of 23.3 kg/m^2. Notably, only 34.1% of patients had a BMI exceeding 25 kg/m^2, indicating overweight status.

VMAT and IMRT have emerged as predominant treatment modalities, collectively accounting for 84.3% of cases (366 images). By contrast, the utilization of the 3D-CRT technique was relatively less common, comprising only 15.7% (68 images).

For patients undergoing radiation therapy targeting the lower abdominal region, various techniques were employed to optimize treatment accuracy and minimize side effects. These strategies included optimizing bladder filling with protocols for empty bladder (49.66%), full bladder

Table 1. Patient-treatment characteristics, systematic-random error and p-value

Factor	Systematic error (cm)			Random error (cm)			Univariate analysis (p-value) for systematic error		
	Vrt.	Lng.	Lat.	Vrt.	Lng.	Lat.	Vrt.	Lng.	Lat.
Sex							0.651	0.157	0.174
Male (70.3%)	0.34	0.08	0.13	0.21±0.17	0.16±0.07	0.21±0.11			
Female (29.7%)	0.11	0.28	0.20	0.19±0.13	0.25±0.38	0.22±0.18			
BMI							0.366	0.386	0.760
<25 kg/m² (65,9%)	0.25	0.10	0.16	0.17±0.14	0.16±0.08	0.18±0.15			
≥25 kg/m² (34.1%)	0.18	0.37	0.20	0.26±0.16	0.32±0.50	0.28±0.21			
Treatment region							0.212	0.526	0.244
Brain (5.8%)	0.05	0.07	0.05	0.10±0.03	0.14±0.04	0.10±0.04			
H&N (18.2%)	0.06	0.08	0.07	0.12±0.05	0.11±0.05	0.14±0.06			
Thorax (7.6%)	0.24	0.52	0.17	0.35±0.22	0.53±0.75	0.26±0.08			
Breast (1.6%)	0.02	0.03	0.41	0.27±0.29	0.22±0.01	0.37±0.20			
Lower abdomen (Pelvis) (66.8%)	0.29	0.14	0.15	0.21±0.15	0.19±0.10	0.24±0.22			
Technique							0.350	0.081	0.697
3D-CRT (15.7%)	0.12	0.31	0.22	0.20±0.15	0.28±0.08	0.22±0.16			
VMAT/IMRT (84.3%)	0.29	0.13	0.12	0.21±0.15	0.16±0.45	0.19±0.14			
Immobilization							<0.001	0.147	0.800
Short mask (3.2%)	0.03	0.13	0.01	0.11±0.04	0.14±0.04	0.11±0.04			
Long mask (27.6%)	0.06	0.06	0.07	0.12±0.05	0.10±0.03	0.14±0.07			
Wing board (3.7%)	0.20	0.85	0.10	0.26±0.22	1.03±1.02	0.28±0.13			
Vac lock (2.5%)	0.49	0.01	0.21	0.34±0.48	0.26±0.12	0.48±0.42			
Breast board (1.6%)	0.02	0.03	0.41	0.27±0.09	0.22±0.01	0.37±0.20			
Pillow with ankle support (56.2%)	0.29	0.14	0.16	0.23±0.14	0.18±0.09	0.22±0.18			
Headrest with ankle support (5.1%)	0.04	0.01	0.13	0.16±0.08	0.20±0.03	0.21±0.07			
Pelvic area							0.617	0.350	0.730
Empty bladder (49.6%)	0.49	0.20	0.17	0.36±0.16	0.22±0.12	0.29±0.31			
Full bladder (38.97)	0.12	0.07	0.05	0.16±0.08	0.20±0.06	0.18±0.06			
Full bladder and empty rectum (11.38%)	0.03	0.04	0.01	0.21±0.01	0.17±0.25	0.14±0.02			

Systematic error was the standard deviation of the averages of each direction

(38.97%), and full bladder with empty rectum (11.38%). Additionally, patient positioning and immobilization were crucial. Pillow and ankle support are the most frequently utilized form of immobilization (56.2%), followed by long masks with s-type (27.6%).

In this research, the cumulative incidence of set up errors (setup errors of more than 5 mm for 3D-CRT technique and 3 mm for VMAT/IMRT technique) were 0.65. Systematic errors in the Vrt., Lng., and Lat. directions were 0.23, 0.22, and 0.17 cm, respectively, and Random errors in the Vrt., Lng., and Lat. directions were 0.20±0.14, 0.21±0.29, and 0.21±0.17 cm, respectively (Table 2). The range of setup errors was 0 to 2.6 cm in the Vrt. direction, 0 to 2.5 cm in the Lng. direction, and 0 to 2.5 cm in the Lat. direction.

Each factor was considered a potential risk factor for setup errors in Table 1. Only difference in patients' immobilization considerably affected setup errors in the Vrt. direction. Conversely, other factors such as gender, radiation therapy technique, radiation treatment area, and bladder preparation did not show significant correlation with setup error values (Table 1).

Table 2. Analysis of setup errors

Type	Deviation (cm)		
	Vrt.	Lng.	Lat.
Systematic error	0.23	0.22	0.17
Random error	0.20±0.14	0.21±0.29	0.21±0.17

Discussion

The study found that the cumulative incidence of setup errors (defined as errors exceeding 5 mm for 3D-CRT and 3 mm for VMAT/IMRT) was 0.65. The systematic setup errors in all three directions ranged from 0.17 cm to 0.23 cm. whereas random setup errors ranged from 0.20 cm to 0.21 cm. These findings indicated that systematic and random setup errors in all directions were less than 3 mm, consistent with the findings of Xu et al.[16] in their prospective study analyzing 201 CBCT scans of 30 nasopharyngeal carcinoma patients. Xu et al. reported that translational setup errors in the X, Y, and Z directions were 1.2±0.9, 1.2±1.1, and 1.0±0.8 mm, respectively, and suggested adding a 3 mm margin in all directions from the clinical target volume (CTV) to obtain the PTVs and to manage setup errors.

Hurkmans et al.[17] reported in routine clinical practice that systematic and random errors can be less than 2 mm for the H&N, 3 mm for the pelvic, and 2.5 mm for the prostate. Additionally, Chung MJ et al.[18] examined patients with breast cancer and on IGRT with MVCT and revealed that systematic and random setup errors in all directions were within 3 mm. In a prospective study comparing setup errors in patients with H&N cancer treated with IMRT, setup errors before corrections were less than 3 mm in any direction in 762 CBCT scans[19]. These results were similar and comparable to the findings of our study.

Consistent with the studies conducted by Murthy et al.[20] and Ghaffari et al.[21], systematic and random errors were minimal in the H&N and brain regions compared with those in the thoracic and pelvic regions. This discrepancy was due to the rigid treatment sites in the H&N and brain, leading to minimal day-to-day variations in setup geometry.

In the evaluation of setup errors in immobilization devices, a statistically significant difference was observed ($p<0.001$). Notably, the vac lock, pillow, and ankle support exhibited the highest degree of setup errors. This finding is inconsistent with a previous study[22] that compared head support pillows combined with foot support and air-filled cushion immobilization devices, focusing on the pelvic and proximal leg bone areas in patients with prostate cancer. Interestingly, the prior study showed no statistically significant difference between the two devices. The discrepancy in study results may be due to the smaller number of cases using this device in the current study, which presents a limitation.

Numerous dosimetry studies have recommended the necessity of large CTV-to-PTV margins in the absence of IGRT to counteract setup errors[23,24]. Nevertheless, reducing PTV margins in the H&N region with IGRT is feasible. This procedure potentially minimizes toxicity while maintaining tumor control. Chen et al.[23] demonstrated that small PTV margins obtained through IGRT are safe and do compromise clinical outcomes. Utilizing IGRT for setup verification may enhance the precision of dose delivery to target volumes while preserving normal tissue structures.

The assessment of setup errors is crucial for each institution and depends on various factors, such as the availability of immobilization devices, imaging techniques, and the clinical expertise of staff members. However, high radiation therapy setup errors must be restricted within the setup margin for the PTV during treatment planning.

The present study did not account for intrafraction setup errors. Intrafraction organ motion and variations within each patient during treatment are crucial for the accurate assessment of uncertainties in setup. Hence, further studies are needed to enhance the comprehensiveness of the current findings.

Conclusion

Setup errors were detected in every treatment session. The detection and correction of setup errors play an important role in ensuring the accurate and precise delivery of radiotherapy. Utilizing image guidance facilitates the verification of patient positioning prior to treatment and enables the correction of setup errors, thereby enhancing the precision of patient repositioning. This approach offers the potential to reduce PTV margins, mitigate risks to organs at risk, and potentially escalate radiation doses. It is essential for each radiotherapy department to assess setup variations to calculate institution-specific margins effectively.

What is already known on this topic?

Image guidance enhances the verification of patient positioning before treatment, allowing for the correction of set-up errors. This, in turn, boosts the precision of patient repositioning and helps mitigate risks to organs at risk and potentially escalate radiation doses, thereby maximizing treatment efficacy while minimizing adverse effects.

What this study adds?

A 5 mm PTV margin beyond the CTV is considered safe to accommodate setup errors. Employing appropriate immobilization equipment significantly reduces the occurrence of setup errors, thus further enhancing treatment accuracy and patient safety.

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Conflict of interest

The authors declare no conflict of interest.

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