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# Evaluation of the Effect of Patient-Specific Factors on Setup Errors in Different Patient Groups Treated with Image-Guided Radiotherapy

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## ABSTRACT

Purpose: In contrast to conventional techniques, modern radiotherapy systems integrate imaging technologies such as Image-Guided Radiotherapy (IGRT) to detect and correct setup uncertainties during treatment, enabling precise target localization, improved geometric accuracy and conformality, enhanced normal tissue sparing, and safe dose escalation with reduced margins. The aim of this study was to evaluate patient-specific factors associated with setup errors in various patient groups undergoing IGRT.

Methodology: This study was conducted at the Department of Radiation Oncology, University of Health Sciences Gülhane Training and Research Hospital, and imaging data obtained from different patient groups treated with the Elekta Synergy IGRT system were evaluated to calculate setup errors. For statistical analysis of these setup errors, SPSS (Statistical Package for the Social Sciences version 20.0) was used.

Findings: Mean setup errors were −0.59 mm (X), −0.87 mm (Y), and −0.49 mm (Z), with wide variability across all directions. Positional correction was required in ~90% of patients, decreasing to 80% in the abdominal group. Importantly, statistical analyses demonstrated that patient-specific factors, including gender, body mass index (BMI), age, and treatment site, did not have a statistically significant impact on setup errors. Conclusion: In conclusion, patient-specific factors, including age, gender, BMI, and treatment region, were not significantly associated with setup errors, indicating that setup uncertainties cannot be reliably predicted based solely on individual characteristics. These findings underscore the critical role of IGRT in ensuring accurate patient positioning and treatment safety.

***Keywords:*** *Patient Positioning, Setup Errors, Geometrical Uncertainties, BMI, Patient Specific Factors.*

## INTRODUCTION

Recent advances in radiotherapy technology have enabled the development of sophisticated treatment delivery systems and planning platforms that significantly improve geometric accuracy and dosimetric conformity. These systems enable highly conformal dose delivery, allowing dose escalation to the target volume while maintaining acceptable dose levels to the organs at risk.

Geometric uncertainties associated with patient anatomy and positioning during treatment represent a major source of error in radiotherapy and commonly consist of systematic and random components. Systematic errors originate from discrepancies between the target position defined on planning images and the mean target position during treatment delivery, whereas random errors arise from day-to-day variations in patient setup and internal organ motion during fractionated radiotherapy [1,2].

Systematic uncertainties are of particular clinical relevance, as they persist throughout the entire treatment course if uncorrected and can substantially compromise target coverage and local tumor control. Consequently, systematic errors play a dominant role in margin determination and directly influence Planning Target Volume (PTV) expansion, potentially increasing radiation exposure to surrounding normal tissues and associated toxicity.

Since the introduction of X-ray–based imaging in radiotherapy, image-guided technologies have advanced to allow real-time or near real-time visualization of both target volumes and adjacent normal tissues. IGRT systems integrate on-board imaging into the treatment workflow and employ dedicated image registration algorithms to accurately match reference planning images with images acquired immediately prior to or during treatment delivery, thereby enabling precise quantification and correction of setup deviations [3,4,5,6].

Setup errors were determined through image registration between IGRT-acquired images and planning Computed Tomography (CT) reference images. In this study, patient positioning accuracy was assessed using both two-dimensional (2D) portal imaging and three-dimensional (3D) volumetric imaging, with setup deviations calculated by the treatment system's dedicated image registration software.

Setup errors represent an important source of geometric uncertainty in radiotherapy and are defined as deviations between the planned patient position and the actual treatment position during treatment fractions. These positioning deviations may compromise target coverage and alter radiation dose delivery to surrounding organs at risk. Image-guided radiotherapy (IGRT) enables the detection and correction of such deviations by comparing planning images with images acquired during treatment. Recent studies have emphasized the importance of daily image-guided verification in reducing positioning uncertainties and improving treatment accuracy [7,8].

Previous studies have explored the relationship between set-up errors and patient-specific factors such as height, weight, body mass index (BMI), and treatment-related weight loss. Although these parameters have generally not been shown to exert a significant direct effect on set-up errors, they remain relevant when determining appropriate target volume margins [9, 10]. Furthermore, Mandal et al. reported that set-up uncertainties may vary depending on the anatomical treatment region and emphasized that planning target volume (PTV) margins should therefore be defined according to the treated anatomical site [9]. More recently, surface-guided radiotherapy (SGRT) has emerged as a promising technology for patient positioning and has demonstrated high set-up accuracy across multiple anatomical regions, supporting region-specific margin optimization [9,11] Despite these technological advances, geometric uncertainties related to patient positioning remain an important challenge in modern radiotherapy, and the influence of patient-specific characteristics on set-up errors has not yet been fully clarified. Therefore, further investigation is required to better understand how these factors may contribute to positioning uncertainties and margin determination in clinical practice.

In this context, this study aims to evaluate the effect of patient-specific factors such as BMI on setup errors in different patient groups using appropriate statistical analysis, and to contribute to margin optimization and improvement of treatment accuracy in routine clinical practice.

## MATERIAL AND METHODS

### Clinical Data

Ethical approval for this study was obtained from the University of Health Sciences (SBÜ) Gülhane Interventional Research Ethics Committee. In this study, demographic and treatment-related data of 133 patients with a total of 205 images were acquired and evaluated at the Department of Radiation Oncology, SBÜ Gülhane Training and Research Hospital (GEAH), retrospectively. Patients aged 18 years and older who received external beam radiotherapy were included in this study. Patients treated with stereotactic radiosurgery (SRS) or stereotactic body radiotherapy (SBRT), in whom specialized immobilization techniques and different setup criteria are applied, as well as patients younger than 18 years of age, were excluded from the study.

Patients were categorized into four groups according to the treatment site: head and neck, thoracic, abdominal, and pelvic regions. Appropriate immobilization devices were used for all patient groups to ensure reproducible positioning.

For each patient, a CT scan images were initially used for treatment planning in the TPS and subsequently employed as reference datasets for image registration and setup verification within the IGRT workflow. Following completion of treatment planning, all planning and delivery parameters were transferred to the Elekta Synergy IGRT linear accelerator.

Pre-treatment imaging was performed for all patients, and setup errors were calculated using the manufacturer-provided image guidance software integrated within the treatment system. These data were acquired in a three-dimensional, isocenter-based coordinate system defined relative to bony landmarks along the X (lateral; left-right [LR]), Y (anterior-posterior [AP]), and Z (superior-inferior [SI]) axes.

Patient age, sex, BMI, and treatment site were evaluated as potential determinants of setup errors. The associations between these patient-specific factors and setup errors along the X, Y, and Z axes were subsequently analyzed using appropriate statistical methods. Statistical analyses were performed using SPSS software version 20.0. Descriptive statistics were calculated according to patient characteristics. Given the non-normal distribution of setup error data, non-parametric statistical methods were employed to ensure robust analysis. The Mann–Whitney U test was used to evaluate differences in setup errors between two independent groups (sex and age), while the Kruskal–Wallis test was applied for variables comprising more than two categories (BMI and treatment site) across the X, Y, and Z directions. A p-value of < 0.05 was considered statistically significant.

## RESULTS

Patients were dichotomized according to the mean age of 61 years into two groups (<61 years and ≥61 years). BMI values were classified as normal (<24.99 kg/m²), overweight (25.00–29.99 kg/m²), and obese (≥30.00 kg/m²). For patients with setup errors ≥ 2 mm, positional corrections were performed and treatment was delivered following re-imaging verification. The results of the distribution of data by groups are given in Table 1. Our study analyzed a relatively large and heterogeneous patient cohort, enabling the identification of statistically significant findings across multiple patient groups. The cohort included patients with diverse physical characteristics. The median age was 61 years (range: 19–87 years). The median body weight was 76 kg (range: 44–116 kg), and the median height was 170 cm (range: 137–189 cm). Accordingly, the median BMI was 26.04, with values ranging from 17.54 to 40.49. Based on BMI classification, 55 patients were categorized as normal weight, 49 as overweight, and 29 as obese. This wide distribution allowed for the evaluation of the influence of patient-specific physical characteristics on setup errors across different subgroups and enhanced the clinical workflow of the study. The calculated setup errors showed a mean value of −0.59 mm in the X direction, with minimum and maximum values ranging from −33.90 to 17.10 mm; −0.87 mm in the Y direction, with values ranging from −31.00 to 24.80 mm; and −0.49 mm in the Z direction, with values ranging from −41.00 to 47.50 mm. Statistical comparisons of setup errors according to patient-specific characteristics were performed, and the distribution of setup error determinants across these variables is presented in Table 2. Regarding the treatment area, the need for positional adjustment was observed in approximately 90% of most subgroups, such as the thoracic and pelvic regions, while this rate was lower, at around 80%, in the abdominal region (Table 3.).

Statistical analyses revealed no significant differences in setup errors among gender (p=0.339, 0.407, and 0.736 for X, Y, and Z directions, respectively), BMI categories (p=0.153, 0.157, and 0.456, respectively), treatment areas (p=0.700, 0.073, and 0.430, respectively), or age groups (p=0.651, 0.361, and 0.934, respectively) (Table 2). Although the Y-axis variation among treatment areas approached borderline significance (p=0.073), it did not reach statistical significance. These findings indicate that neither anatomical region nor patient-specific characteristics are primary determinants of setup accuracy.

Shift corrections were observed in the majority of patients across all subgroups. Specifically, shifts were required in 91.7% (n=77) of male patients and 91.8% (n=45) of female patients. According to BMI categories, shifts were observed in 42.6% (n=52) of normal-weight, 36.9% (n=45) of overweight, and 20.5% (n=25) of obese patients. In terms of treatment regions, shift occurrence rates were 86.7% (n=26) in head and neck, 96.1% (n=49) in thoracic, 80% (n=8) in abdominal, and 92.9% (n=39) in pelvic cases. Additionally, shifts were detected in 92.5% (n=62) of patients aged 61 years and under and 90.9% (n=60) of those over 61 years (Table 3). No statistically significant association was found between shift occurrence and gender (p=0.973), BMI (p=0.419), treatment area (p=0.244), or age (p=0.733).

**Table 1.** Numerical and Percentage Distributions of Set-up Error Determinants.

| | | n | % |
|---|---|---|---|
| **Gender** | Male | 84 | 63,2 |
| | Female | 49 | 36,8 |
| **BMI** | Normal (BMI≤24,99) | 55 | 41,4 |
| | Overweight(25≤BMI≤29,99) | 49 | 36,8 |
| | Obese (BMI≥30) | 29 | 21,8 |
| **Treatment Area** | Head and Neck | 30 | 22,6 |
| | Thoracic Abdomen | 51 | 38,3 |
| | Pelvic | 10 | 7,5 |
| | | 42 | 31,6 |
| **Age** | 61 and under | 66 | 50,4 |
| | Over 61 | 67 | 49,6 |

**Table 2.** Changes in gender, BMI, treatment area, and age determinants in the X, Y, and Z directions.

| | | X | Y | Z |
|---|---|---|---|---|
| **Gender** | Male | 0,0 (-19,5-14,5) | 0,0(-31,0-24,8) | -0,3 (-41,0-15,9) |
| | Female | -0,2 (-33,9-17,1) | -2,0 (-16,6-23,0) | 0,0 (-18,4;47,5) |
| **P*** | | 0,339 | 0,407 | 0,736 |
| **BMI** | Normal(BMI≤24,99) | -0,7 (-19,5-17,1) | 0,7 (-31,0-24,8) | 1,4 (-18,4-15,9) |
| | Overweight (25≤BMI≤29,99) | -0,0 (-33,9-12,0) | -2,0 (-25,0-23,0) | 0,0 (-41,0-47,5) |
| | Obese (BMI≥30) | 0,4 (-14,9-9,5) | -0,5 (-6,3-11,5) | -0,2 (-8,3-11,0) |
| **P**** | | 0,153 | 0,157 | 0,456 |
| **Treatment Area** | Head and Neck | -0,1 (-14,9-3,2) | 0,75 (-7,0-4,5) | 0,95 (-5,9-47,5) |
| | Thoracic | -0,5 (-33,9-17,1) | -2,5 (-31,0-17,5) | 0,0(-41,0-15,9) |
| | Abdomen | -0,1 (-2,9-7,3) | 0,7 (-7,8-23,0) | 0,0 (-5,0-17,5) |
| | Pelvic | 0,5 (-10,5-12,0) | 0,0 (-13,5-24,8) | -0,35 (-9,1-11,5) |
| **P**** | | 0,7 | 0,073 | 0,43 |

| | | | | |
|---|---|---|---|---|
| **Age** | 61 under | 0,0 (-33,9-17,1) | 0,0 (-31,0-23,0) | 0,0 (-18,4-13,5) |
| | Over 61 | -0,3 (-14,9-9,5) | -0,8 (-25,0-24,8) | 0,5 (-41,0-47,5) |
| **P*** | | 0,651 | 0,361 | 0,934 |

* Mann-Whitney U Analysis Result

** Kruskal-Wallis Analysis Result

**Table 3.** Comparison of patients' shift values according to setup determinants

| | | **Shift** | | |
|---|---|---|---|---|
| | | **Exists n (%)** | **No n (%)** | **P (Chi-Square Test )** |
| **Gender** | Male | 77 (91,7) | 7 (8,3) | 0,973 |
| | Female | 45 (91,8) | 4(8,2) | |
| **BMI** | Normal (BMI≤24,99) | 52 (42,6) | 3 (27,3) | 0,419 |
| | Overweight (25≤BMI≤29,99) | 45 (36,9) | 4 (36,4) | |
| | Obese (BMI≥30) | 25 (20,5) | 4 (36,4) | |
| **Treatment Area** | Head and Neck | 26 (86,7) | 4 (13,3) | 0,244 |
| | Thoracic | 49 (96,1) | 2(3,9) | |
| | Abdomen | 8(80) | 2(22) | |
| | Pelvic | 39(92,9) | 31 (7,1) | |
| **Age** | 61 and under | 62 (92,5) | 5 (7,5) | 0,733 |
| | Over 61 | 60 (90,9) | 6 (9,1) | |

## DISCUSSION

The present study systematically evaluated setup errors across multiple anatomical regions in a relatively large and clinically heterogeneous cohort, while also examining the influence of patient-specific factors. The cohort demonstrated a balanced distribution in terms of age and gender, together with variability across BMI categories and treatment regions. Although the mean translational deviations were minimal in all directions, a considerable degree of variability was observed, highlighting the persistence of clinically relevant geometric uncertainties despite the routine implementation of IGRT. This variability may partly reflect region-specific characteristics, such as larger treatment field sizes in abdominal radiotherapy and the limited number of abdominal cases included in the cohort. Notably, the head and neck subgroup exhibited a high positional correction rate (86.7%), likely attributable to the use of dedicated immobilization systems that enhance setup reproducibility. However, despite these numerical differences and patient-related variations, no statistically significant differences were identified in setup errors among subgroups, indicating that neither anatomical region nor basic patient-specific characteristics constitute primary determinants of setup accuracy. Collectively, these findings reinforce the dominant role of IGRT in mitigating geometric uncertainties and ensuring consistent and reproducible treatment accuracy across diverse clinical scenarios.

Previous studies have generally investigated setup errors in region-specific cohorts with limited sample sizes. In contrast, the present study included a relatively large patient population and evaluated multiple treatment sites. Overall, no statistically significant effect of patient-specific characteristics on setup errors was identified. In agreement with the literature, setup displacements along the X, Y, and Z axes did not follow a normal distribution and were not statistically significant. These findings support the robustness of the current results and suggest that patient-specific factors alone may not be sufficient predictors of setup errors in routine clinical practice.

In conclusion, no statistically significant association was identified between patient-specific factors and setup errors in the present study. Setup errors were found to be independent of age, sex, treatment site, and BMI, indicating that patient positioning accuracy cannot be reliably improved through setup adjustments based solely on these variables. Similar findings have been reported in previous studies, including investigations in gynecological patients [6], head and neck cancer patients [12], and the quantitative analysis by Johansen et al. evaluating the relationship between setup errors and anthropometric parameters such as height, weight, BMI, and treatment-related weight loss [13]. The absence of statistically significant differences across treatment sites supports the notion that, under standardized immobilization and IGRT protocols, setup uncertainties are not predominantly driven by anatomical treatment region. Overall, these findings suggest that setup errors are multifactorial and cannot reliably be predicted based on individual demographic or anthropometric parameters alone. Consequently, reliance on patient-specific characteristics for selective setup correction strategies may be insufficient, reinforcing the clinical importance of routine image-guided verification for all patients.

From a clinical workflow perspective, these results further emphasize the necessity of IGRT for accurate patient positioning, irrespective of patient-specific physical characteristics. While Zhao et al. demonstrated a BMI-dependent increase in setup errors in thoracic tumor patients and suggested BMI-based margin adaptation [9], and Mandal et al. highlighted the importance of treatment-site–specific PTV margin definition [14,15], the findings of the present study support the concept that demographic and anthropometric parameters alone are insufficient predictors of setup uncertainties. Accordingly, routine pre-treatment imaging and verification should be maintained as a fundamental component of daily clinical practice rather than being selectively applied to specific patient subgroups.

Several recent studies have investigated the influence of patient-specific factors on setup uncertainties across various treatment sites. For example, pelvic treatments showed that patient anthropometric characteristics, including BMI, may correlate with setup variations [15,16]. Similarly, Costin and Marcu [16] observed a positive association between BMI and setup deviations in breast radiotherapy. However, other analyses, such as the quantitative IGRT assessment by Johansen et al. [17], found no significant link between setup errors and demographic or anthropometric parameters, aligning with our findings. Investigations in thoracic tumors also suggest a BMI-dependent trend in setup deviations and support margin adaptations [18], while Mandal et al. [19] emphasize the importance of treatment-site–specific PTV margin definitions rather than patient characteristics alone. Moreover, immobilization and daily imaging protocols, as demonstrated by Ruan et al. [7] and Rudat et al. [8], play a major role in reducing geometric uncertainties regardless of patient factors. Taken together, these studies highlight that although certain cohorts may exhibit variations linked to BMI or treatment site, demographic and anthropometric parameters alone do not consistently predict setup uncertainties.

Numerous literature studies have examined the impact of patient-specific factors such as body mass index (BMI), age, sex, and treatment site on setup errors, yielding largely inconsistent findings. Several studies in the pelvic and head-neck regions have reported no significant association between setup errors and parameters such as BMI or age, suggesting that these factors may have limited predictive value for positioning accuracy under routine clinical conditions [12,13]. Similarly, comprehensive analyses including variables such as height, weight, BMI, and treatment-related weight loss have failed to demonstrate a significant effect on setup deviations [9]. In contrast to these studies, other research has highlighted potential site- and patient-dependent effects. For example, Zhao et al. found a significant association between BMI and setup errors in thoracic tumor patients and highlighted its importance for defining the target volume margin [9]. Furthermore, Mandal et al. reported that setup uncertainties vary between anatomical regions and suggested that planning target volume (PTV) margins should be adapted accordingly [15]. In addition to conventional IGRT, advanced image-guided techniques such as surface-guided radiotherapy (SGRT) can further improve setup accuracy. In particular, Rudat et al.

demonstrated that SGRT provides high positioning accuracy in multiple anatomical regions and facilitates region-specific margin optimization [9].

As a result these findings indicate that while patient-specific factors alone may not consistently predict setup errors, anatomical region and imaging strategy remain critical determinants of geometric accuracy, underscoring the importance of robust image-guidance protocols in modern radiotherapy practice.

## CONCLUSION

In conclusion, patient-specific factors, including age, sex, BMI, and treatment site, were not significantly associated with setup errors. These findings indicate that setup uncertainties cannot be reliably predicted based solely on demographic or anthropometric characteristics, highlighting their inherently multifactorial nature. From a clinical standpoint, this underscores the critical importance of routine image-guided verification in ensuring accurate and reproducible patient positioning.

These findings indicate that setup uncertainties cannot be reliably predicted based solely on individual patient characteristics. Therefore, the routine use of IGRT remains essential to ensure accurate patient positioning and safe treatment delivery across all patient groups. Furthermore, accumulating evidence from surface-guided radiotherapy (SGRT) supports the role of advanced image-guidance techniques in enhancing setup precision and optimizing margin strategies across multiple anatomical regions. The integration of IGRT with SGRT-based approaches therefore represents a robust and clinically effective framework for minimizing geometric uncertainties and improving treatment accuracy in contemporary radiotherapy practice.

## Conflict of Interest

There are no conflicts of interest and no acknowledgements.

## ETHICS STATEMENT

Ethical approval for this retrospective study was obtained from the Health Sciences University GülhaneScientific Research Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki. Informed consent was waived due to its retrospective design.

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