Original Article

Presentation of a New Averaging Method for Improvement of Systematic and Random Errors in Radiotherapy of Chest and Abdomen Cancer Using Electronic Portal Imaging Device

Abstract

Background: This study aims to introduce and evaluate a new averaging method to decrease systematic and random errors using an electronic portal imaging device (EPID) in radiotherapy of chest and abdomen cancers. **Methods:** Thirty-three patients with tumors in different chest and abdominal organs were evaluated. A novel averaging method for decreasing systematic and random errors was introduced and compared with conventional methods in radiotherapy of chest and abdomen cancers. In method 1, averaging by EPID was not performed. While in method 2, EPID sessions that had outlier data were also included in the averaging. The new method (method 3) included, removing the EPID sessions that had high random errors, increasing the number of EPID sessions, and averaging from more accurate data. Pair-sample *t*- and Chi-square tests were used for comparisons of results from the three methods. **Results:** For comparison between optimized averaging (method 3) and 3-first fraction averaging (method 2) in terms of individual mean set-up error, the $P = 0.00$, which indicates a significant difference between these two methods. In the method 3, the three-dimensional displacement vector individual mean set-up errors were lower than the other methods. Moreover, in this method, only one patient has a systematic error greater than the gross error, whereas that of methods 2 and 3 accounted for 4 and 10 patients, respectively. **Conclusion:** The optimized averaging method introduces a great improvement in chest and abdomen cancers radiotherapy by decreasing systematic errors and increasing treatment accuracy.

Keywords: *Abdomen cancer, chest cancer, electronic portal imaging device, radiotherapy, random error, systematic error*

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Mohammad Reza Asgari[1], Mahdi Ghorbani[1], Mehdi Khosravi[2], Ahmad Shakeri[2], Mohamad Pursamimi[1], Meysam Tavakoli[3]

[1]Department of Biomedical Engineering and Medical Physics, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [2]Department of Radiotherapy, Shahid Beheshti Hospital, Qom, Iran, [3]Department of Radiation Oncology, Winship Cancer Institute, Emory University, Atlanta, GA, USA

Introduction

Radiotherapy increasingly employs advanced techniques like intensity-modulated radiotherapy (IMRT), which is recommended for more than half of cancer patients independently or in combination with other treatment modalities.[1] This approach utilizes optimized, modulated two-dimensional fluency distributions for each beam direction, enabling the dose distribution to conform more precisely to the tumor volume compared to conventional methods, particularly for targets with concave shapes. Moreover, it allows for sharper dose gradients beyond the target area, minimizing exposure to nearby critical organs and healthy tissues.[2,3] To ensure the safe and effective use of these methods, which often involve delivering high doses to tumors, most of the clinics are developing a patient-specific quality assurance program. This program primarily relies on electronic portal imaging devices (EPIDs) to verify patient positioning and monitor dose delivery both before and during treatment.[4]

There are different treatment sites, such as breast, lung, head, and neck that we can use EPID to perform quality control in every step of the treatment process to reduce the overall uncertainty to the required level.[5] One critical source of uncertainty arises from interfractional adjustment errors during patient positioning, which lead to spatial discrepancies between the tumor's position during computed tomography (CT) simulation and its location during radiotherapy sessions. These errors are

Address for correspondence:
Dr. Mahdi Ghorbani, Department of Biomedical Engineering and Medical Physics, School of Medicine, Shahid Beheshti University of Medical Sciences, Velenjak, Tehran, Iran.
E-mail: mhdghorbani@gmail.com

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classified into two categories: systematic and random. Systematic errors are consistent, predictable deviations that occur in the same size and direction across all treatment sessions, whereas random errors vary in magnitude and direction, making them unpredictable.[6]

Previous research underscores the effectiveness of EPID in reducing setup errors and ensuring the quality of complex treatments.[7] The digital nature of EPIDs provides quantitative tools for analyzing systematic and random errors based on population or individual patients.[8] In a retrospective study, Kanakavelu and Jebaseelan Samuel[9] evaluated errors in patient positioning in three different directions for brain, head, neck, and prostate tumors. For this purpose, 60 patients who were treated with the IMRT technique were evaluated, and systematic and random errors and optimal margins were calculated. The results of that study showed that the use of image-guided radiotherapy (IGRT) system and the creation of an optimal margin cause accurate dose delivery to the clinical target volume (CTV).[9] Noghreiyan and Naseri[10] examined 15 patients with head-and-neck cancers underwent daily EPID imaging. Then, they measured the systematic and random errors in three directions (x, y, and z). The results indicated that a margin of 6.5–10.5 mm in CTV for head-and-neck tumors delivers 90% of the cumulative dose and 95% of the prescribed dose to the target organ. Hanley *et al*.[11] measured patient positioning errors in three-dimensional (3D) conformal radiotherapy of the prostate. The results show that the setup verification protocol appears to minimize systematic setup errors to a level that approaches the sensitivity of the image registration technique. There are several studies in this subject related to the setup verification protocol, which can be reviewed.[6,12-15]

Consideration of previously performed studies illustrates that any differences between the shape and the mean shape of the organ during radiotherapy sessions due to a change in the volume of the organ can cause a systematic error.[16] In those studies that measured and reduced the systematic error using EPID, the maximum number of EPID was three sessions, and data were included in the averaging method.[2] However, in the proposed study, we aimed to resolve these defects to obtain more accurate results. Previous studies have some limitations. First, rotational errors could not be considered because there were portal images in the anterior-posterior (AP) and lateral projections; therefore, rotational shifts were not captured. Second, portal images did not provide information about organ motion. Consequently, it is essential to decrease these errors in order to have more accuracy in radiotherapy sessions.[8] This study aims to introduce and evaluate a new averaging method to decrease systematic and random errors using EPID in the radiotherapy of chest and abdomen cancers.

Methods

First, from all patients with chest and abdominal tumors who were treated at the Radiotherapy Center of Shahid Beheshti Hospital (Qom, Iran), 33 patients were selected. The selection criteria were a treatment regimen of 50 Gy in 25 fractions and having at least 5 EPID sessions. The CT scans were taken by Siemens Somatom scanner and transferred to the PACS system, then the images were imported to the Monaco treatment planning system (TPS). EPID compared the isocenter images of the patient with the digital reconstructed radiography (DRR) image (Elekta Synergy Platform, United Kingdom, West Sussex) of the plane, and then the displacements were obtained and collected in three directions: x, y, and z. There are three methods: (1) the no-averaging method, in which the EPID system was not used to reduce errors, so the EPID displacement was corrected only for the related fraction and had no impact on other fractions; (2) the three-first-fraction averaging method, in which the EPID displacement results from the first three fractions were used for averaging; and (3) the optimized averaging method, in which the EPID results from the first three fractions were reviewed by a qualified physicist. If the inaccuracies were found in the data (for example, an outlier with a very large displacement or a displacement in the opposite direction of others), the data point was removed based on the physicist's judgment. In such cases, the fourth or fifth EPID sessions were added if needed, and then the data were averaged. If the correction exceeded the action level, the next fraction was checked with EPID, followed by weekly EPID monitoring. The results were compared with two methods of taking EPID in three sessions and the method without performing EPID. The number of reducing errors and the number of patients who had displacement more than gross error were compared.

Patients' characteristics

The study was performed at the Radiotherapy Center of Shahid Beheshti Hospital (Qom, Iran), starting from August 2020 to July 2022. Data from all patients who affected with tumors in different chest or abdominal organs were included. The age range of the studied patients was from 33 to 75 years for men and from 35 to 72 years for women. The type and number of patients for each tumor type are presented in Table 1.

Treatment planning

As part of their routine treatment, patients were positioned supine on the wing step and put their hands placed above the heads. As their routine treatment, all patients were treated using an Elekta Synergy linear accelerator (Elekta, Stockholm, Sweden) with photon energies of 6, 10, and 15 MV, based on the IGRT plans. Five radio-opaque markers were used for both chest and abdominal tumors. For both regions, one marker was placed on the suprasternal notch, a marker was placed on the xiphoid process, and another marker was placed below the navel on the patient's abdomen. These three markers were aligned parallel to each other in the sagittal direction. Two additional markers were placed on either side of the xiphoid marker, parallel to it. For patient immobilization, a pad was placed under the patient's knee to make the patient feel comfortable and fix the patient's lumbar spine curve. Furthermore, the wing step was used with hand grips for repeating the patient's hands positioning.

CT scans of the patients with a slice thickness of 5 mm were performed using a Siemens Somatom CT simulator scanner (Siemens, Munich, Germany). The resulting CT scan images were then imported into the Monaco TPS (Elekta Company, Stockholm, Sweden). The prescribed dose and the number of fractions for each type of tumor are presented in Table 1.

Electronic portal imaging device setup

As shown in Figure 1, two EPID images were acquired in AP (anterior/posterior) and lateral directions, respectively, with zero and 90 gantry degrees, field size of 26 cm × 26 cm, and 6 MV photon beam energy. Then, the treatment plan was seamlessly transmitted to the Modular Oncology Information System for Adaptive Intelligence in Quality system, which is an interface between TPS and the treatment linac. The isocenter image was matched with the DRR image of the treatment plan in order to obtain the displacements in the three x, y, and z axes [Figure 2].

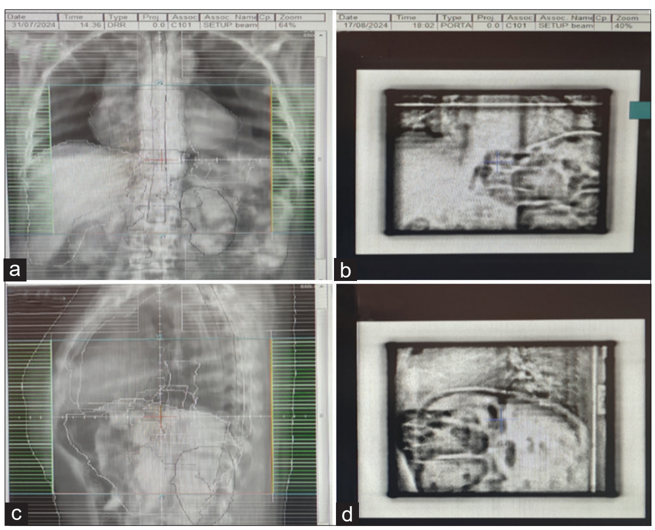

Figure 1: Image from MOSAIC system obtained from treatment planning system (TPS), (a) Anterior to posterior digital reconstructed radiography (DRR) image, (b) anterior to posterior portal image, (c) lateral DRR image, and (d) lateral portal image. DRR images were exported from Monaco TPS, and portal images were taken by Elekta Synergy linear accelerator

Data collection and averaging

In this study, systematic errors were assessed through an in-depth evaluation of three distinct methods. In the first method, involving one EPID session (fractions where orthogonal images were taken from the patient), EPID was not used to average errors. Instead, the displacements in different directions were determined for that session and applied only to the same fraction. The second method used the first three EPID sessions, where the displacement results were averaged and then applied to subsequent treatment sessions to reduce systematic error. In the optimized averaging method (method 3), after three EPID sessions, the data were reviewed by a physicist. If any extraneous data were identified (e.g., outliers or inconsistencies), they were excluded, and additional sessions were performed as replacements. For all patients, displacements in the x, y, and z directions were measured using all three methods. The 3D displacement vector (RMS) (Equation 1) was then calculated using the following formula for each method.

Parameters compared across all three methods included individual setup errors in the x, y, and z axes, population setup errors, and the proportion of patients with setup errors exceeding predefined thresholds of 2 mm.[11] This complete comparison aimed to determine whether method 3 could be a more effective and reliable treatment plan in comparison to methods 1 and 2.

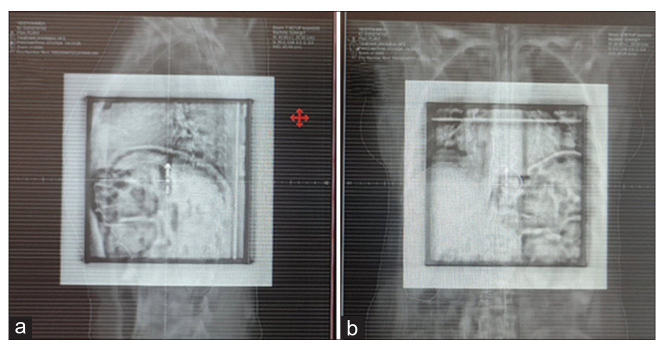

Figure 2: Image from the MOSAIC system obtained from treatment planning system (TPS), (a) Matched anterior to posterior digital reconstructed radiography (DRR) and portal images, (b) Matched lateral DRR and portal images. Image matching was performed by considering the bony structures

Table 1: The prescribed dose (Gy) and the number of fractions for each type of tumor based on Perez and Brady's book[17] and the number of patients for each tumor

	Prescribed dose (Gy)			Number of patients
Cancer type	Whole pelvic	Boost to tumor	Total dose in Gy	
Esophagus	45 Gy in 25 fractions	5.4 Gy in 3 fractions	50.4	5 women, 5 men
Stomach	45 Gy in 25 fractions	5.4 Gy in 3 fractions	50.4	5 women, 7 men
Lung	50 Gy in 25 fractions	10 Gy in 5 fractions	60	3 women, 7 men
Lymphoma	36 Gy in 20 fractions	-	36	2 women, 3 men

Statistical analysis

To validate the data, statistical analyses were performed by the statistical package for the social sciences (SPSS) software (version 28, SPSS Inc., Chicago, USA). The normality of data distribution was assessed using the Kolmogorov–Smirnov test. For variables that exhibited a normal distribution, a paired-sample *t*-test was used, putting the threshold for statistical importance at $P < 0.05$ level. Categorical variables were subjected to analysis using the Chi-square test. It provides a rigorous statistical evaluation to aid the findings.

Results

In Table 2, the systematic and random errors for 3D displacement vector (RMS) (in mm) of all three methods are listed. For all patients, displacements in the x, y, and z directions were measured with all three methods. The RMS or square root (R) was calculated by the following formula for each method:

$$R = \sqrt{x^2 + y^2 + z^2} \quad (1)$$

In Table 2, the confidence intervals were calculated using the following formula:

$$\text{Confidence interval} = 1.96 \times \frac{\text{Standard deviation}}{\sqrt{33}} \quad (2)$$

Where 33 is the sample size (number of patients), and the confidence level is 95%.

The percentage of patients whose systematic error was lower than that from the other methods for each method is presented in Table 3. The purpose of introducing the new method was to better estimation and reduce the systematic error. For this reason, an important factor in comparing two methods was that the averaging results (systematic error) are lower than others, so every method that have higher percentage of patients whose 3D displacement vector (RMS) of systematic error is closer to zero is accounted as a better method. The number of patients with displacement more than the gross error for all three methods is presented in Table 4.

Table 2: Systematic error (±confidence interval) and random errors for the 3D displacement vector root mean square of *x*, *y*, and *z* displacements for all three methods, including: No averaging, 3 sessions averaging, and optimized averaging

	Mean (systematic error, in terms of mm)	SD (random error, in terms of mm)	*P*
Method 1	0.36±0.07	0.20	0.12 (method 1 vs. 2)
Method 2	0.46±0.09	0.26	0.03 (method 1 vs. 3)
Method 3	0.27±0.05	0.15	0.00 (method 2 vs. 3)

SD – Standard deviation

Table 3: The number and overall percentage of patients whose systematic error 3D displacement vector root mean square was closer to zero in each method

	Number of patients (%)	Optimized method
Method 1	12 (36.34)	Method 2
Method 2	21 (63.63)	
Method 1	11 (33.33)	Method 3
Method 3	22 (66.67)	
Method 2	4 (12.12)	Method 3
Method 3	29 (87.88)	

Table 4: Number of patients with displacement more than the gross error (1 cm) for all three methods including: No averaging, 3 sessions averaging, and optimized averaging

	No averaging (method 1)	3 sessions averaging (method 2)	Optimized averaging (method 3)
Number of patients	10	4	1

Discussion

In this study, an optimized averaging method of patient displacement during EPID imaging was introduced for chest and abdominal tumors. Table 2 shows that there was no significant difference in systematic error between methods 2 and 1, with $P = 0.12$. A comparison between optimized averaging (method 3) and no averaging (method 1) shows $P = 0.03$, indicating a significant difference in the 3D displacement vector (RMS) of systematic error. For the comparison between optimized averaging (method 3) and the three-first-fraction averaging (method 2), the $P = 0.00$, confirming a statistically significant difference between these two methods.

As mentioned in the method section, after patient setup and acquisition of two orthogonal images (anterior to posterior and lateral), the set-up isocenter on the EPID images was matched with the DRR isocenter, and displacement was obtained in the x, y, and z axes. After data collection and averaging data for each axis, the obtained findings were used to optimize the setup isocenter. The imaging process was then performed once per week, and the displacements for those fractions were recorded. To ensure a fair comparison, the results of the methods were compared rather than the data from all fractions. For methods 2 and 3, the fraction data that were used to calculate the systematic error were excluded.

The aim of presenting the proposed method is to decrease the systematic error. For this reason, an important factor in comparing two methods, which is the percentage of patients whose RMS of systematic error is closer to zero; therefore, any methods that closer to zero is a more efficient method in reducing systematic error. Table 4 illustrates that this is clearly lower in the 3-first fraction, averaging (method 2) comparing to the no average method (method 1). In the method 1, the percentage of patients whose RMS of systematic error is closer to zero is 36.34%, and for method 2, it is 63.63%, respectively. With comparison of method 1 and method 3, this is 33.33% for method 1 and 66.67 for method 3, clearly the optimized averaging method (method 3) in more patients, the 3D displacement vector (RMS) of systematic error is closer to zero, which means the new method reduces the systematic error more. Furthermore, in the last row, methods 2 and 3 were compared, indicating that the percentage of patients whose RMS of systematic error is closer to zero is 12.12% for method 2 and 87.88% for method 3. Clearly, the optimized averaging method in almost all patients, the RMS or root mean square of systematic error is closer to zero, which means the new method reduced the systematic error (mean set-up error) better. In other words, based on the statistics in Table 4, the allowed gross error for all patients was 1 cm. For displacements greater than this level, CT imaging and treatment planning were repeated. Among the 33 patients, in method 3, only one patient had a systematic error greater than the gross error, while in methods 2 and 1, the numbers were 4 and 10 patients, respectively. These data show that method 3 significantly reduced errors compared with the other methods. Specifically, method 3, which included more EPID measurement sessions and review of the results by a physicist and exclusion of large positioning error data from averaging, resulted in less positioning error and lower patient displacement across treatment sessions. Patient setup error in radiotherapy can be influenced by several factors, including the immobilization device used, the verification system, and the treatment position. These factors should be carefully considered when evaluating patient setup error with EPID or other IGRT systems.

An important factor that should be mentioned for comparing the performance of the three methods is the comparison of the fractions' data, which were used after the fractions were averaged. Because the method affects these sessions and the better the method, the closer the displacement is to zero. The data of fractions that were used for averaging were excluded.

In this study, the new averaging method significantly enhances the accuracy of chest and abdomen cancer radiotherapy by decreasing systematic error. These findings align with previous research by Noghreiyan and Naseri[10] which emphasized the significance of EPID in improving patient positioning accuracy and reducing setup uncertainties, albeit in the context of head-and-neck radiation therapy. While this study focused specifically on chest and abdomen cancer radiotherapy, the utilization of EPID technology underscores its versatility across various cancer sites. In addition, this new averaging method offers a different method to decrease setup errors compared to the setup verification method explored by Noghreiyan and Naseri[10] highlighting the innovation and potential impact of these findings in enhancing treatment accuracy. Prabhakar *et al*.[18] considered the importance of accurate patient positioning in tangential breast radiotherapy to minimize risks related to setup errors. Although their study focused on assessing the implications of setup errors, the current study goes a step further by proposing a new method, utilizing EPID technology, to actively reduce these errors. Similarly, Topolnjak *et al*.[19] demonstrated the effectiveness of EPID in assessing setup errors in breast cancer radiotherapy, but their study did not introduce techniques for error reduction. Whereas the current study suggests a new averaging method specifically tailored to enhance accuracy and reduce systematic error in chest and abdomen cancer radiotherapy, therefore, addressing a critical gap in the current approaches. Deantonio *et al*.[20] and Kanakavelu and Jebaseelan Samuel[9] also explored methods for setup uncertainty detection and introducing optimal treatment margins in breast cancer radiotherapy by different imaging and IGRT. While their studies contributed valuable insights into setup detection and treatment optimization, the approach in the present study offers a contribution by introducing a new averaging method leveraging EPID technology. By comparing and contrasting these studies, these data underscore the innovative potential of EPID-based approaches in enhancing treatment accuracy in chest–abdomen cancer radiotherapy.

By reducing patient setup errors, the implementation of the new averaging method in clinical settings holds promising implications for chest–abdomen cancer radiotherapy. Accurate patient positioning is essential in radiotherapy to ensure that the planning target volume (PTV) receives the maximum dose and the dose to organs at risks (OARs) is minimized. Because OARs are located close to the tumor, margins must be defined around the PTV. Setup margins directly affect the total dose delivered to the target and OARs. Systematic errors, which can be accumulated across treatment sessions, may lead to tumor recurrence or severe organ injury, whereas random errors occur less frequently.[21] Evaluating and reducing both systematic and random errors can significantly improve radiotherapy outcomes. By reducing treatment-related side effects and improving overall patient quality of life, radiologists and oncologists may observe enhanced treatment efficiency.

Limitations of the study include the time-consuming data collection process and offline review of all images by an experienced physicist to reduce the impact of different physicists' attitudes in matching EPID and DRR images, and the limited number of patients with 5 or more EPID sessions. To add enhancement in treatment accuracy and solve the limitations identified in this study, future research needs to be performed. Integration of the new averaging method with other advanced imaging techniques could offer synergistic benefits and improve overall treatment accuracy. Research into the cost-effectiveness of widespread implementation is necessary to ensure the feasibility and accessibility of the method in diverse healthcare settings.

Furthermore, it is beneficial if this method is performed for other organs in order to understand the accuracy of this method in other organs.

The findings from this study underscore the significant effect of employing advanced EPID-based methods in improving the accuracy of chest–abdomen cancer radiotherapy. Method 3, with its optimized five-session EPID approach, emerges as the preferred method for decreasing both systematic and random errors, thereby increasing treatment efficacy and patient safety. Future research could explore further refinements to EPID technology integration or investigate its application in other types of cancer sites to broaden its clinical utility.

Conclusion

All in all, the optimized averaging method is an effective way to reduce systematic errors. The new averaging method introduces an advancement in chest and abdomen cancer radiotherapy by decreasing systematic errors and increasing treatment accuracy. The implementation of this method creates promising results for chest and abdomen cancer patients in radiation therapy centers which do not have cone beam CT by reducing systematic errors and more important preventing PTV from getting under-dose and OARs from getting over-dose.

Ethical approval

The study was performed based on the guidelines by Shahid Beheshti University of Medical Sciences, and it was approved by the Etchics Committee of the university with ethical code of IR. SBMU. MSP. REC.1403.443.

Availability of data and materials

The data from this study can be available upon request from the corresponding authors.

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Conflicts of interest

There are no conflicts of interest.

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