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# A novel averaging method for reducing systematic and random errors in breast cancer radiotherapy using electronic portal imaging device

**M. Khosravi[1#], A. Shakeri[2#], M. Khosroabadi[3], S.M. Hosseini[4], G. Mehri-Kakavand[5], M. Pursamimi[5*], W. Parwaie[6], M. Shafiee[2], M. Ghorbani[1*], M. Tavakoli[7]**

*[1]Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
*[2]Radiotherapy Center, Shahid Beheshti Hospital, Qom, Iran*
*[3]Medical Physics Department, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
*[4]Department of Medical Physics and Medical Engineering, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran*
*[5]Department of Anatomy and Medical Imaging, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand*
*[6]Department of Medical Physics, Faculty of Paramedical Sciences, Ilam University of Medical Sciences, Ilam, Iran*
*[7]Department of Radiation Oncology, Winship Cancer Institute, Emory University, Atlanta, GA, USA*

► ***Original article***

***Corresponding author:***
*Mohamad Pursamimi, Ph.D.,*
*Mahdi Ghorbani, Ph.D.,*
***E-mail:***
*mohamadpursamimi65@gmail.com, mhdghorbani@gmail.com*

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[#]The first two authors contributed equally to this study

## ABSTRACT

***Background:*** The aim of this study is to introduce a novel averaging method to reduce systematic and random errors using electronic portal imaging device (EPID) in breast cancer radiotherapy. ***Materials and methods:*** Data from 78 female breast cancer patients, treated with photons beams of an Elekta Synergy linac were retrospectively analyzed. A novel five-session EPID averaging method (Optimized Five Session Averaging Method) was compared with a traditional three-session approach (Three Session Averaging Method) and a no-averaging approach (No Averaging Method). Statistical analysis was performed to compare the accuracy of the three methods. ***Results:*** The Optimized Five-Session Averaging Method demonstrated superior accuracy in minimizing individual mean set up errors compared to the Three-Session Averaging Method. Specifically, in the x direction, 71.80 of patients in the Optimized Five-Session Averaging Method had errors closer to zero, as opposed to 28.21 in the 2 Three-Session Averaging Method. In the y direction, 67.94 and 32.05 were closer to zero in the Optimized Five-Session Averaging Method and Three-Session Averaging Method, respectively. In the z direction, 70.51 and 29.49 achieved this in the Optimized Five-Session Averaging Method and Three-Session Averaging Method. Statistical analysis confirmed the significant difference between the two methods (p=0.00). ***Conclusion:*** The novel averaging method effectively enhanced the accuracy and reduced errors in breast cancer radiotherapy compared to the two conventional methods. This study provides a significant advancement in reducing patient set up error in breast cancer radiotherapy and highlights the potential of the Optimized Five-Session Averaging Method for optimization in diverse clinical contexts.

## INTRODUCTION

Breast cancer is a leading global health concern, with an estimated incidence rate of 37 per 100,000 women [(1)]. The primary treatment approach for breast cancer typically involves surgery, complemented by adjuvant therapies such as chemotherapy, and radiotherapy, to ensure comprehensive care [(2, 3)]. Among these, radiotherapy stands as a pivotal component of comprehensive cancer care [(4)]. In this situation, quality control of the treatment plan is an essential step to guarantee the safety of radiotherapy before a patient begins treatment. This process involves various techniques and equipment to verify both the accuracy of the treatment plan and the consistency of the delivered dose [(5)]. The need for precise dose delivery is paramount in all forms of radiation therapy, whether it is external beam radiotherapy or brachytherapy, where radioactive sources are placed internally [(6)].

The introduction of Image-Guided Radiotherapy (IGRT) complements Intensity-Modulated Radiotherapy (IMRT) by enhancing the accuracy of radiation delivery. IGRT utilizes imaging techniques during treatment sessions to account for daily variations in tumor position and patient anatomy. This precise localization of the clinical target volume (CTV) and organs at risk (OAR) throughout the treatment course helps to ensure that radiation is accurately delivered to the intended areas. By

correcting for inter-fraction anatomical changes, IGRT can reduce the need for large planning target volume (PTV) margins, thereby minimizing radiation exposure to healthy tissues [7-10]. Despite these advancements, a significant challenge in radiotherapy remains the interfractional setup errors during patient positioning, defined as the difference between the patient's anatomy in the computational tomography (CT) planning scan and during treatment [11]. These errors, categorized into systematic and random ones, can impact treatment accuracy and outcomes [12]. Minimizing these errors and establishing safety margins around the CTV to compensate for geometric uncertainties is crucial in radiotherapy [11].

Electronic portal imaging device (EPID) has emerged as a versatile tool to address this challenge, initially developed for pre-treatment position verification [13, 14]. When combined with bone markers, EPID enhances patient alignment, quality assurance, and treatment verification, offering superior image quality and an analytical tool that aid clinical decision-making. Previous research underscores the effectiveness of EPID in reducing setup errors and ensuring the quality of complex treatments [15-19]. The digital nature of EPIDs provides quantitative tools for analyzing systematic and random errors based on population or individual patients [11].

There are several influential studies that have investigated the role of EPID and other imaging methods in radiotherapy setup verification. Noghreiyan *et al*. [17] highlighted EPID's effectiveness in improving setup accuracy for head and neck radiation therapy, though their study on breast cancer treatments. However, their study did not explore methods to actively reduce errors or apply their findings to breast cancer treatments. Prabhakar *et al*. [20] underscored the impact of setup errors in tangential breast radiotherapy but noted the study's limited cohort size, which may not fully represent the variability in setup errors crucial for comprehensive breast cancer treatment planning. In 2025, Dong *et al*. [21] explored EPID-based dose verification for breast IMRT, using Edose software for pre-treatment and dose reconstruction. They found that while pre-treatment verification showed high gamma pass rates, *in-vivo* verification was significantly lower and revealed under-coverage of the chest wall target, despite meeting medical physics standards. The study highlights the value of *in-vivo* 3D dose reconstruction for understanding actual patient dose, considering motion and anatomical changes. Topolnjak *et al*. [22] compared EPID with CBCT for setup error assessment, revealing differences in accuracy and clinical relevance, particularly in understanding static setup errors in breast cancer radiotherapy. Their work was limited to error detection without introducing or evaluating a multi-session error-reduction model. Zhang *et al*. [23] explored EPID's radiomics analysis for detecting positioning errors in thyroid-associated ophthalmopathy, highlighting challenges such as small sample sizes that may hinder direct application to breast cancer radiotherapy. Deantonio *et al*. [19] evaluated EPID for setup verification in head and neck radiation therapy, noting limitations in spatial resolution and imaging frequency relevant to dynamic breast cancer treatments. Kanakavelo *et al*. [24] determined optimal treatment margins using image guidance systems, offering insights that differ from EPID-based approaches in breast cancer radiotherapy. However, they did not utilize EPID's unique capabilities for precision error reduction.

Unlike these studies, our research introduces a novel five-session EPID-based averaging method specifically designed for breast cancer radiotherapy, addressing systematic and random errors comprehensively and offering enhanced accuracy and clinical applicability.

This study introduces a novel five-session EPID averaging method designed specifically for breast cancer radiotherapy to address the limitations of conventional approaches that typically use only the first few treatment sessions for EPID data acquisition. These limited datasets can hinder accurate setup error analysis and correction, potentially compromising treatment efficacy. Unlike previous studies that primarily focused on error detection or single-session verification, this research proposes a comprehensive solution to reduce both systematic and random errors through an optimized multi-session averaging technique. By averaging data from five sessions, including a physicist's review and correction after the initial three sessions, this method aims to enhance setup precision, improve treatment accuracy, minimize the need for large planning target volume margins, and ultimately reduce radiation exposure to healthy tissues.

This approach is, to the best of our knowledge, the first to address both systematic and random errors in breast cancer radiotherapy through such an enhanced multi-session EPID averaging method.

## MATERIALS AND METHODS

### *Patient characteristics*

The study was performed at Radiotherapy Center, starting from August 2020 to July 2022. Here data from 78 female patients were evaluated in this study, comprising 41 patients (53%) with left breast cancer and 37 patients (47%) with right breast cancer. As their routine treatment, the patients were treated using an Elekta Synergy linear accelerator (Elekta, Stockholm, Sweden) at varying energy levels of 6, 10, and 15 MV, based on their IMRT plans. Patients characteristics in this study are presented in table 1.

**Table 1.** Patients characteristics in this study.

| Characteristics | Number |
|---|---|
| Age (year) (average (range)) | 50 (35-74) |
| Number of femail patients | 78 |
| Stage 2 | 23 |
| Stage 3 | 36 |
| Stage 4 | 19 |
| Prescribed dose in the fisrt phase (Gy) | 50 |
| Number of fractions in the first phase | 25 |
| Prescribed dose in the second phase (Gy) | 12 |
| Number of fractions in the second phase | 6 |

Patients diagnosed with breast cancer within the past two years were included in this analysis. The focus was specifically on those who underwent a treatment regimen involving the administration of 50 Gy in 25 fractions (for the first phase) and 12 Gy in 6 fractions (for the second phase) and had completed a minimum of 5 EPID sessions. EPID images were acquired and evaluated by assessing the shifts along the *x*, *y*, and *z* axes. Set-up errors and random positioning errors were estimated for all 78 patients along the *x*-, *y*- and *z*-axes directions. Patients were excluded from the study if their displacement, as assessed by EPID, exceeded 1 cm, as this required re-simulation with a new CT scan. Additionally, patients who were retrospectively analyzed or had fewer than five EPID sessions were also excluded from the study.

### *Treatment planning*

The treatment procedure commenced with patients being placed in supine position, with their arms extended alongside their bodies. To facilitate precise alignment and data collection, nine distinct points were marked on each patient's body. These markers included three along the central axis (one above the supra-sternal notch, one at the midpoint between the breasts, and one beneath each breast). Three markers were placed parallel to these markers on the right side, and three markers parallel to them on the left side.

Following the positioning and marking, computed tomography (CT) scans of the patients were acquired. This scan, with slice thickness of 3.5 millimeter, was performed using a NeuViz 16 scanner (Neusoft Medical Systems in PR, China). The resulting CT scan images were then introduced in the Monaco Treatment Planning System (TPS) (Elekta in Stockholm, Sweden). Treatment plans were meticulously designed, taking into account by a physicist the involvement of breast lymph nodes. Sample treatment plans for a patient with right breast cancer (a), and a patient with left breast cancer (b) are presented in figure 1.

### *EPID setup*

To optimize radiation delivery, two distinct EPID fields were established for the right breast (at 0 degrees and 290 degrees) and two for the left breast (at 0 degrees and 70 degrees). Subsequently, the treatment plan was seamlessly transmitted to the Modular Oncology Information System for Adaptive Intelligence in Quality (MOSAIQ) system (Elekta Medical Systems, Stockholm, Sweden), which served as a critical bridge between treatment plan and the treatment linac. EPIDs played a pivotal role in ensuring precise alignment of patients. They facilitated the accurate alignment of the patient's isocenter image with the digitally reconstructed radiograph (DRR) image, allowing for meticulous measurements of displacements in three dimensions of *x*, *y*, and *z*. DRR and portal images for a sample breast cancer patient which were exported from the TPS and mosaic systems are presented in figure 2. Sample images for registration and matching of DRR and EPID images are also presented in figure 3.

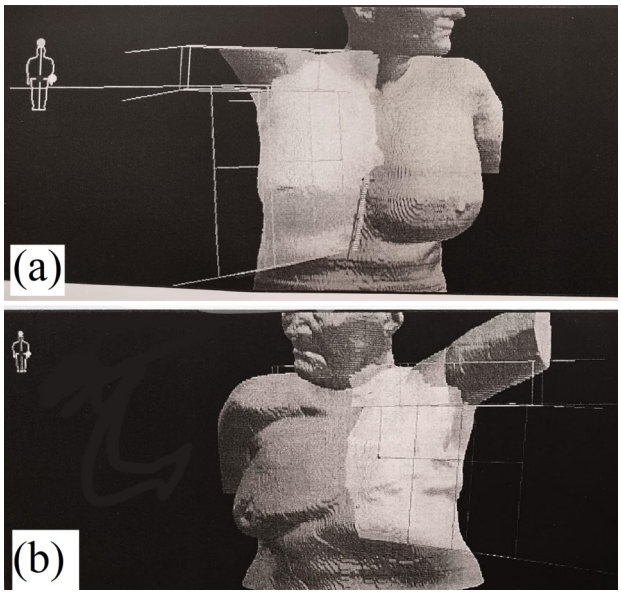



**Figure 1.** Sample treatment plans for a patient with right breast cancer **(a)**, and a patient with left breast cancer **(b)**.

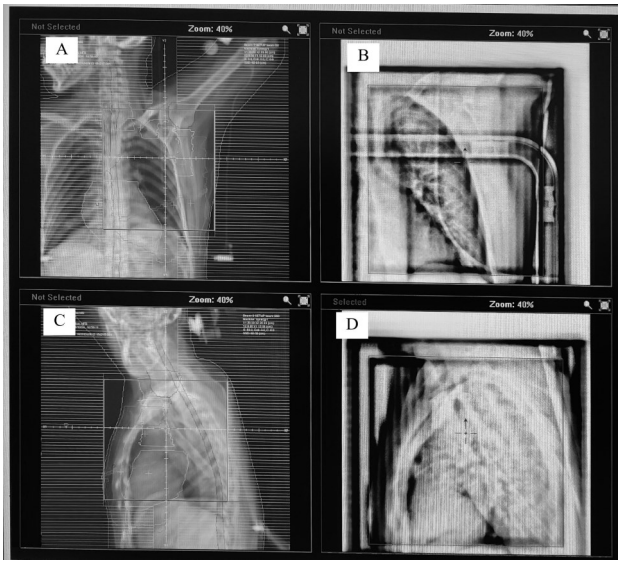



**Figure 2.** DRR (Digitally Reconstructed Radiograph) and portal images which were exported from the TPS (Treatment Planning System) and mosaic systems, respectively: AP DRR image **(A)**, AP EPID (Electronic Portal Imaging Device) image **(B)**, lateral DRR image **(C)**, lateral EPID image **(D)**.

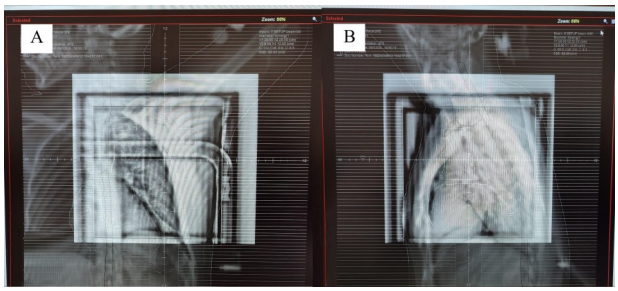



**Figure 3.** 2D image registration of DRR (Digitally Reconstructed Radiograph) and EPID (Electronic Portal Imaging Device) images by mosaic system indicating matching lateral DRR and EPID images **(A)**, and matching AP DRR and EPID images **(B)**.

### *Data collection and averaging*

Data collection began with three initial EPID sessions to assess patient positioning. After these sessions, the acquired data was reviewed by a physicist to identify and correct any discrepancies or errors in patient positioning assessment. Following this data adjustment phase, two additional EPID sessions were conducted to further refine the data. To ensure more accurate and stable measurements, the data from all five EPID sessions were averaged, reducing the impact of outliers and random variations.

The "data adjustment" phase involved a review of the initial three EPID images by a qualified medical physicist. If the review showed a systematic error in patient setup, the patient's position was adjusted before the next session. This adjustment was not part of the averaging process but a correction step to minimize setup errors before the additional two sessions. In addition, the data from each EPID was reviewed for any artifacts or abnormalities that could skew the results. If such an artifact was found, the data was excluded and the session was repeated.

In this study, the results were evaluated through a detailed comparison involving three distinct methods. The first method No Averaging Method excluded EPID acquisition, acknowledging its limitations in averaging and detecting systematic errors. The second method Three-Session Averaging Method utilized the conventional approach of averaging data from the initial three treatment sessions using EPID, assessing setup errors in three dimensions $x$, $y$, and $z$. The third method, Optimized Five-Session Averaging Method, aimed to improve accuracy beyond the conventional method by averaging data from five treatment sessions. This averaging process was specifically designed to reduce systematic errors by incorporating data across multiple treatment sessions, thereby enhancing the reliability of setup error estimation.

The averaging process for the Three-Session Averaging Method can be represented by the following equations (1 and 2). For each direction ($x$, $y$, and $z$), the average error ($E_{avg}$) is calculated as:

$$E_{avg} = (E_1 + E_2 + E_3) / 3 \quad (1)$$

Where; $E_1$, $E_2$, and $E_3$ are the setup errors measured in the first, second, and third EPID sessions, respectively.

Similarly, the averaging process for the Optimized Five-Session Averaging Method can be represented as:

$$E_{avg} = (E_1 + E_2 + E_3 + E_4 + E_5) / 5 \quad (2)$$

Where; $E_1$, $E_2$, $E_3$, $E_4$, and $E_5$ are the setup errors measured in the first, second, third, fourth, and fifth EPID sessions, respectively.

Parameters compared across all three methods included individual mean setup errors in the $x$, $y$, and $z$ directions, population setup errors, and the percentage of patients with setup errors exceeding predefined thresholds. These errors were measured by acquiring and analyzing EPID images for each treatment session. For Three-Session Averaging Method and Optimized Five-Session Averaging Method, the systematic error reduction was achieved by calculating the mean setup error across three or five EPID acquired images, respectively, taken during the initial sessions of treatment. By increasing the number of EPID acquisitions in the Optimized Five-Session Averaging Method, the study demonstrated improved precision and a reduction in gross setup errors compared to the No Averaging Method and Three-Session Averaging Method. This step by step comparison, illustrated in figure 4, highlights the potential of the Optimized Five-Session Averaging Method in achieving more accurate and reliable treatment planning outcomes.

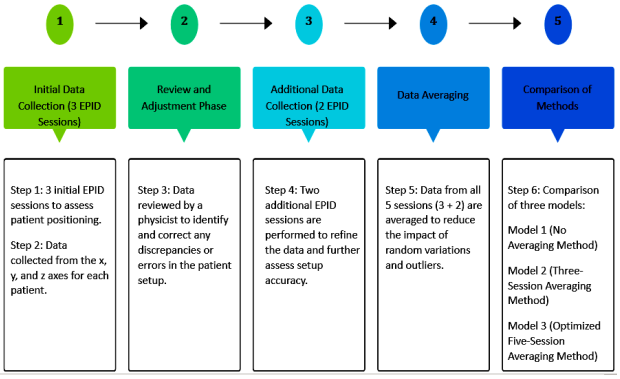



**Figure 4.** Steps of method of this study.

### *Statistical analysis*

To validate the findings, statistical evaluations were performed by the use of 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, while the threshold for statistical significance was set at $p$-*value*<0.05 level. Categorical variables were subjected to analysis using the Chi-square test.

## RESULTS

The comparison of the three treatment methods (No Averaging Method, Three-Session Averaging Method and Optimized Five-Session Averaging Method) revealed significant improvements in patient set up accuracy with the use of averaging techniques. As shown in Table 2, Optimized Five-Session Averaging Method demonstrated the smallest mean set up errors in all three directions, with values of 0.11 mm SD 0.14 mm in the x direction, 0.13 mm SD 0.16 mm in the y direction, and 0.13 mm SD 0.16 mm in the z direction, outperforming both No Averaging Method and Three-Session Averaging Method. Statistically significant differences *p-value* 0.05 were observed. Statistically significant differences ($p<0.05$) were observed between all models in each direction, confirming the superior accuracy of the five-session averaging approach.

Further analysis in table 3 showed the number and percentage of patients with individual mean set up errors closer to zero. In Three-Session Averaging Method, %82.05 of patients in the x direction, %80.77 in the y direction, and %84.62 in the z direction had minimal errors, while Optimized Five-Session Averaging Method also demonstrated high percentages, with %71.79 in the x direction, %67.95 in the y direction, and %70.51 in the z direction. Although Optimized Five-Session Averaging Method yielded thesmallest errors, Three-Session Averaging Method had the highest percentage of patients with errors closer to zero, indicating that the three session averaging method is highly effective, but the five session method offers slightly greater consistency and accuracy. The statistical analysis further supported the efficacy of both averaging methods, with Optimized Five-Session Averaging Method providing the most reliable treatment outcomes.

**Table 2.** Comparison of individual mean set-up error between all three methods in x, y and z directions (in mm).

| | | Right to left (*x*) | | | | | Superior to posterior (*y*) | | | | | Anterior to posterior (*z*) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean (mm) | SD (mm) | ð² (mm²) | SD (mm) | p-value | Mean (mm) | SD (mm) | ð² (mm²) | SD (mm) | *p*-value | Mean (mm) | SD (mm) | ð² (mm²) | SD (mm) | *p-value* |
| **Model 1 and model 2** | Model 1 | 0.20 | 0.25 | 0.02 | 0.03 | 0.00 | 0.21 | 0.25 | 0.03 | 0.05 | 0.00 | 0.24 | 0.30 | 0.04 | 0.05 | |
| | Model 2 | 0.17 | 0.20 | 0.01 | 0.02 | | 0. 20 | 0.25 | 0.02 | 0.06 | | 0.20 | 0.23 | 0.02 | 0.03 | |
| **Model 1 and model 3** | Model 1 | 0.20 | 0.25 | 0.02 | 0.03 | 0.00 | 0.21 | 0.25 | 0.03 | 0.05 | 0.00 | 0.24 | 0.30 | 0.04 | 0.05 | |
| | Model 3 | 0.11 | 0.14 | 0.01 | 0.01 | | 0.13 | 0.16 | 0.01 | 0.04 | | 0.13 | 0.16 | 0.01 | 0.02 | |
| **Model 2 and model 3** | Model 2 | 0.17 | 0.20 | 0.01 | 0.02 | 0.00 | 0. 20 | 0.25 | 0.02 | 0.06 | 0.01 | 0.20 | 0.23 | 0.02 | 0.03 | |
| | Model 3 | 0.11 | 0.14 | 0.01 | 0.01 | | 0.13 | 0.16 | 0.01 | 0.04 | | 0.13 | 0.16 | 0.01 | 0.02 | |

ð2= variance

**Table 3.** The number and overall percentage of patients whose individual mean set-up error was closer to zero in each technique and in x, y and z direction.

| | | Right to left (*x*) | | Superior to posterior (*y*) | | Anterior to posterior (*z*) | |
|---|---|---|---|---|---|---|---|
| | | Number | Percent | Number | Percent | Number | Percent |
| **No Averaging Method and Three-Session Averaging Method** | No Averaging Method | 14 | 17.95 | 15 | 19.23 | 12 | 15.38 |
| | Three-Session Averaging Method | 64 | 82.05 | 63 | 80.77 | 66 | 84.62 |
| **Three-Session Averaging Method and Optimized Five-Session Averaging Method** | Three-Session Averaging Method | 22 | 28.21 | 25 | 32.05 | 23 | 29.49 |
| | Optimized Five-Session Averaging Method | 56 | 71.79 | 53 | 67.95 | 55 | 70.51 |

In this study, the number of patients exhibiting displacement greater than the gross error varied across the different models. A 'gross error' refers to a significant deviation in patient setup or positioning that exceeds a predefined threshold, typically large enough to impact the accuracy of radiation delivery and potentially compromise treatment outcomes. For the method with no averaging No Averaging Method 25 patients demonstrated such displacement. When utilizing the three first fraction averaging method Three-Session Averaging Method this number decreased to 16 patients. The Optimized Five-Session Averaging Method showed a further reduction, with only 4 patients presenting displacement greater than the gross error.

## DISCUSSION

The efficacy of an Optimized Five-Session Averaging Method for enhancing treatment planning accuracy in breast cancer radiotherapy, utilizing EPIDs, was investigated in this study. It was demonstrated that the Optimized Five-Session Averaging Method significantly reduces both systematic and random setup errors compared to the conventional Three-Session Averaging Method and the No Averaging Method. This improvement is evident across all three spatial directions (x, y, and z), as indicated by the statistically significant reductions in mean setup errors ($p<0.05$) presented in table 2. Specifically, the smallest mean setup errors were yielded by the Optimized Five-Session Averaging Method: 0.11 mm (SD 0.14 mm) in the x-direction, 0.13 mm (SD 0.16 mm) in the y-direction, and 0.13 mm (SD 0.16 mm) in the z-direction.

A significant reduction in systematic errors with the Three-Session Averaging Method, which aligns with the established utility of EPIDs for setup

verification, was revealed by the comparison between the No Averaging Method and the Three-Session Averaging Method. However, this study advances beyond mere error assessment through the introduction of an active error reduction strategy. The statistically significant reduction in setup errors with both the three-session and five-session averaging approaches ($p<0.05$) underscores the importance of these methods in enhancing treatment precision. Furthermore, the Optimized Five-Session Averaging Method was shown to consistently outperform the Three-Session Averaging Method, indicating a more refined approach to minimizing setup uncertainties.

The superiority of the Optimized Five-Session Averaging Method is further highlighted by its comparison with the No Averaging Method. Statistically significant reductions in systematic errors were demonstrated by the *p-values* of 0.00 in all directions (table 2), confirming its superior accuracy. This addresses the limitations of studies like Prabhakar *et al*. [20], where the significance of accurate positioning was emphasized, but a method for active error reduction was not proposed. While EPID and cone-beam computed tomography (CBCT) were compared for error assessment by Topolnjak *et al*. [22], a method for active error reduction using EPID data is introduced in this study.

The use of five EPID sessions, incorporating a physicist review after the first three sessions to correct systematic errors, is a key element of the approach taken. This multi-session strategy is crucial because systematic errors can vary throughout treatment. By averaging over five sessions, these variations are captured and corrected more effectively, which contrasts with conventional approaches that often rely on only the first few sessions for EPID data acquisition. This is further supported by recent research emphasizing the need for correction methods for radiotherapy verification plans, as highlighted by Guo *et al*. [5]. The correction of EPID data when the device itself is displaced, which is a different but related problem to the setup errors addressed here, was the focus of their study.

The correction of EPID data when the device itself is displaced from its calibration position, a scenario that can occur in complex treatments, was explored by Guo *et al*. [5]. A correction model and specific correction matrices were proposed to revise the data obtained from displaced EPIDs. It was shown by their findings that both methods could correct the data, with specific correction matrices yielding results closely resembling those from non-displaced EPIDs. While patient setup errors, rather than EPID displacement, are the focus of this study, both studies underscore the importance of addressing systematic errors in EPID-based measurements. The work of Guo *et al*. [5] is particularly relevant because it highlights the potential for EPID data to be affected by various factors, necessitating robust correction methods. This study complements this work by demonstrating the efficacy of a multi-session averaging method in reducing patient setup errors, which are a distinct but equally critical source of uncertainty in radiotherapy.

It is also important to notice that while this study illustrates significant error reduction in all directions, other studies have highlighted the importance of minimizing errors in specific directions. For example, Cao *et al*. [25] found that setup errors in the superior-inferior (SI) direction were particularly problematic in lung cancer radiotherapy, underscoring the need for robust methods to address these specific errors.

The effectiveness of the Optimized Five-Session Averaging Method is further emphasized by the data presented in Table 3. While a higher percentage of patients with errors closer to zero was shown by the Three-Session Averaging Method compared to the No Averaging Method, the Optimized Five-Session Averaging Method consistently outperformed both methods in all directions (x, y, and z). This indicates that the optimized approach not only reduces systematic errors more effectively but also provides more accurate and reliable treatment planning results by better aligning the patient setup. This improvement was statistically significant ($p<0.05$), as evidenced by the p-values reported in table 2, further underscoring the enhanced accuracy of the five-session averaging method in minimizing patient setup errors.

The efficacy of the Optimized Five-Session Averaging Method is further supported by the analysis of patient displacements exceeding gross errors across the three methods. This method demonstrated the lowest number of patients with displacements exceeding gross errors, indicating its superior ability to mitigate setup uncertainties compared to the No Averaging Method and Three-Session Averaging Method. This finding underscores the importance of employing an optimized averaging method to ensure that treatment margins adequately encompass the target volume while minimizing the risk of underdosing or overdosing.

Alignment with previous research by Noghreiyan *et al*. [17], where the significance of EPID in improving patient positioning accuracy and reducing setup uncertainties was emphasized, is also found in this study. However, their study focused on head and neck radiation therapy, while breast cancer radiotherapy is specifically addressed in this study. This distinction highlights the versatility of EPID technology across various cancer treatments. Furthermore, a distinct approach to addressing setup errors is offered by the novel averaging method used here compared to the setup verification method explored by Noghreiyan *et al*. [17], highlighting the innovation and potential impact of these findings in enhancing treatment precision. While optimal treatment margins using

image guidance systems have been explored in studies like Kanakavelu *et al*. [24], the unique advantages of EPID for error reduction are emphasized in this study. EPID is readily available on most linacs, making the method used here more accessible and cost-effective than other advanced imaging techniques. Furthermore, alignment with the recent trend in radiotherapy towards more personalized and adaptive treatment approaches is found in these findings. By reducing both systematic and random errors, this method contributes to more precise radiation delivery, potentially leading to better treatment outcomes and less radiation side effects.

A detailed comparison of three distinct methods, the No Averaging Method, the Three-Session Averaging Method, and the Optimized Five-Session Averaging Method, was involved in the methodology of this study. The averaging process for the Three-Session Averaging Method involved calculating the average error ($E_{avg}$) for each direction ($x$, $y$, and $z$) using the setup errors measured in the first three EPID sessions ($E_1$, $E_2$, and $E_3$): $E_{avg} = (E_1 + E_2 + E_3) / 3$. Similarly, for the Optimized Five-Session Averaging Method, the average error was calculated using the setup errors from the first five EPID sessions ($E_1$, $E_2$, $E_3$, $E_4$, and $E_5$): $E_{avg} = (E_1 + E_2 + E_3 + E_4 + E_5) / 5$. This multi-session approach, combined with a physicist review after the initial three sessions, is a key innovation of the method.

In contrast to our study, Mahdavi *et al*. [26] used implanted gold markers in the prostate to track its position during treatment, demonstrating another method for setup correction using EPID. While our approach focuses on multi-session averaging, both studies highlight the importance of EPID in improving treatment accuracy.

The clinical implications of these findings are significant. The implementation of the Optimized Five-Session Averaging Method in clinical settings holds promise for improving treatment efficacy and overall patient quality of life. By reducing setup errors, this method can potentially minimize radiation related side effects and improve the accuracy of radiation delivery. Moreover, the compatibility of the method with existing EPID systems facilitates its adoption without requiring substantial additional investments, making it a feasible option for routine clinical practice.

To further enhance treatment accuracy and address the limitations identified in this study, several avenues should be explored in future research. Integrating this averaging method with other advanced imaging techniques could offer synergistic benefits and improve overall treatment precision. The application of this method in other types of cancer and radiotherapy modalities may provide valuable insights into its broader clinical utility. Furthermore, research into the cost-effectiveness of widespread implementation is essential to ensure the feasibility and accessibility of the method in diverse healthcare settings.

In conclusion, it is demonstrated in this study that the Optimized Five-Session Averaging Method offers a significant advancement in breast cancer radiotherapy by effectively reducing both systematic and random errors. A more robust and accurate approach to patient setup is provided by this method compared to conventional methods, potentially leading to improved patient outcomes and a reduction in treatment-related side effects. The findings of this study is accounted as evidence supporting data on the use of EPID-based methods for enhancing treatment precision in breast cancer radiotherapy.

## CONCLUSION

In conclusion, this study demonstrates that the novel averaging method presents a significant advancement in breast cancer radiotherapy by reducing systematic errors and enhancing treatment precision. These findings hold the potential to improve patient outcomes and mark a significant step forward in cancer care. The implementation of this method in clinical practice has promising implications for enhancing treatment efficacy and quality of life for breast cancer patients.

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***Conflict of Interest***: The authors declare that they have no conflicts of interest.

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***Ethical Consideration***: This study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki and was approved by Etchics Committee of Shahid Beheshti University of Medical Sciences with the approval number of IR.SBMU.CRC.REC.1402.040. Informed consent was not required as this was a retrospective study using anonymized patient data.

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