

EPID-Based Setup Error Correction in Head and Neck Radiotherapy

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ABSTRACT

Introduction: This study introduces and evaluates a novel optimized averaging method for Electronic Portal Imaging Device (EPID)-based setup corrections, comparing it with conventional approaches.

Material and Methods: A total of 28 head and neck cancer patients undergoing conformal radiotherapy were enrolled prospectively. Three EPID-based setup correction methods were compared: no averaging (Method 1), standard three-fraction averaging (Method 2), and a new optimized averaging method (Method 3). Setup errors were quantified in three dimensions, and Clinical Target Volume to Planning Target Volume (CTV-PTV) margins were calculated. Primary outcomes included systematic and random errors, CTV-PTV margin reduction, and the proportion of patients benefiting from each method.

Results: Both averaging methods significantly reduced systematic and random errors compared to no averaging ($p < 0.05$). Mean setup errors decreased to < 1 mm in all directions for Methods 2 and 3. CTV-PTV margins were reduced from 5.7-7.9 mm to 3.6-3.7 mm, a reduction of 35-50%. The optimized method (Method 3) reduced mean errors in 64-68% of patients across all directions, compared to 68-71% for Method 2 relative to Method 1. Notably, Method 3 reduced the incidence of gross errors by 67% compared to no averaging.

Conclusion: The novel optimized averaging method for EPID-based setup corrections significantly improves setup accuracy in head and neck radiotherapy, outperforming conventional techniques. This approach substantially reduces CTV-PTV margins and the occurrence of gross errors, potentially allowing for more conformal dose distributions and reduced toxicity. These findings have important implications for improving treatment precision and outcomes in head and neck cancer radiotherapy.

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Introduction

Head and neck cancer is one of the most common types of cancer globally, with over 660,000 new cases and causing approximately 325,000 deaths each year [1, 2]. Radiation therapy plays a crucial role in the curative treatment of head and neck cancer. It can be used alone for early-stage tumors or together with surgery, radiation therapy, and chemotherapy for advanced stages, depending on the tumor stage [3]. Modern radiotherapy techniques, like 3D conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT), are being developed and used for head and neck radiotherapy treatments to effectively control tumors while minimizing damage to surrounding tissues such as the parotids, eyes, and brain tissue [4]. Fractionation is delivery of total radiation dose in multiple sessions, it helps normal tissues to be recovered and reduces the treatment complications.

Ensuring reproducibility of patient setup and avoiding setup errors in consecutive radiotherapy fractions is crucial [5]. As radiation therapy becomes more complex and technologically advanced, it is increasingly important to thoroughly assess uncertainties that may have a significant impact on treatment outcomes [6]. When the intended and actual patient positions differ during radiotherapy, the uncertainty in patient setup becomes more significant. This represents a type of geometric uncertainty that can impact radiotherapy treatment outcomes and accuracy [7]. Set-up errors refer to the difference between the intended and actual position of radiation fields delivered to the patient. They can be categorized into two main types: systematic errors (Σ) and random errors (σ) [8]. In radiotherapy treatment positioning, systematic errors are consistent deviations of the delivered dose distribution from the

intended target area, persisting in both direction and magnitude across all treatment fractions, often related to initial patient position adjustments. If uncorrected, they can lead to tumor recurrence or organ injury. Random errors cause inconsistent dose displacement, varying in direction and magnitude for each fraction, associated with day-to-day positioning variations. While random errors can displace the dose, their impact is generally less severe than systematic errors due to their inconsistent nature and less frequent occurrence [9-11].

Recent advancements in electronic portal imaging devices (EPIDs) have replaced cassette films for patient positioning verification. EPIDs can generate digital images from megavoltage beams that can be compared with reference images exported from treatment planning system to verify the accuracy of the patient's position relative to the intended treatment area [12]. As the use of advanced radiation therapy techniques grows, EPIDs are increasingly being used to maximize accuracy for radiotherapy treatment and minimize patient set-up errors [6, 13, 14]. Various studies have demonstrated the effectiveness of EPIDs for error detection compared to other error prevention tools when used at the start of treatment [14-16].

EPIDs have proven more advantageous in head and neck radiotherapy than radiography films due to their ability to provide real-time imaging of critical organs and bony landmarks during radiotherapy treatment [17]. Electronic portal images can be an invaluable tool in reducing setup errors and treatment margins, thereby contributing to enhanced local tumor control outcomes [18]. Piron et al [19] demonstrated that daily EPID image analysis can identify head and neck patients at risk of deviation from their planned treatment, supporting early re-planning decisions. These findings highlight the potential benefits of frequent imaging in improving treatment accuracy and patient outcomes [19]. Several recent studies have focused on EPID-guided setup verification and correction for head and neck cancer patients to improve treatment accuracy. These studies have highlighted the potential benefits of this approach in enhancing patient outcomes [6, 20, 21].

Most radiotherapy departments typically employ the standard approach of using EPIDs to correct setup errors by imaging in the first three treatment sessions and calculating an average of these errors in millimeters (mm). Subsequently, this average value is used to correct errors for the remaining treatment sessions. While this method is effective in reducing setup errors, it relies on a limited number of imaging sessions and may not adequately account for both systematic and random variations that can occur throughout the course of treatment. This study aims to propose a novel averaging method that utilizes data from multiple imaging sessions to enhance the correction of systematic and random errors in head

and neck cancer radiotherapy using EPID. By considering a larger dataset and employing advanced algorithms, this method seeks to derive an improved error correction strategy that accounts for both consistent trends and daily variations in patient positioning. The proposed approach aims to enhance the accuracy of treatment delivery while minimizing additional resource burden on the radiotherapy department. To the best of our knowledge, previous studies have not explored the potential benefits of this specific method in the context of head and neck radiotherapy. By investigating the effectiveness of this novel approach, we aim to contribute to the development of improved patient positioning verification techniques that can ultimately lead to better clinical outcomes for patients undergoing head and neck radiotherapy treatments.

Materials and Methods

Patient selection and CT imaging

This study included 28 patients with head and neck tumors who had previously undergone conformal radiotherapy at Shahid Beheshti Hospital (Qom, Iran). Each patient underwent a computed tomography (CT) scan using the state-of-the-art Neusoft CT scanner (NeuViz 16, Neusoft Medical System Co, China) in a supine position and wearing their personalized thermoplastic masks. The CT scans covered all areas of the head and neck with a precise slice thickness of 3 mm to ensure comprehensive imaging for treatment planning. Moreover, as part of the meticulous process to guarantee accurate treatment delivery, each patient's thermoplastic mask was adorned with either 4 or 5 strategically placed markers whose positions were scrupulously verified using the CT scan images before being securely affixed throughout each patient's treatment regimen. This thorough approach aimed to uphold precision in targeting specific areas during radiation therapy.

Treatment planning

The CT simulation images were imported to the MONACO treatment planning system. Following the delineation of the target volume and organs at risk, a radiation physicist meticulously developed the treatment plan. Each CT scan included a digitally reconstructed radiograph (DRR) serving as a reference image. The treatment plans for all 28 patients were devised by one physicist and then scrutinized by another seasoned professional to ensure exceptional quality and precision. A prescribed dose of 70 Gy was delivered to the patients by Elekta Synergy platform linear accelerator over 35 fractions (2 Gy per fraction). Elekta Synergy linear accelerator is equipped with an amorphous silicon EPID, that can generate portal images from megavoltage beams for accurate monitoring of radiotherapy delivery.

The treatment process for these patients remained consistent. Each patient was positioned on the radiotherapy couch in the same CT position using lasers and radiopaque markers attached to their thermoplastic

mask. Two images were obtained orthogonally from the patient's head at 0 and 90 degrees with EPIDs before irradiation by applying two monitor units of a similar size to the treatment field.

Subsequently, portal images obtained were matched with DRR produced from the patient's CT scans for more accurate image matching, utilizing bony landmarks such as maxillary sinus, mandible, and skull base as references.

Ideally, DRR and EPID images should overlap perfectly. However, errors can occur for various reasons, leading to systematic and random errors. Adjustments can be made if the error falls between the action level and gross error magnitude to improve image matching before proceeding with treatment. If the error value is below the action level, no shift needs to be made. Repositioning of the patient and a new portal image acquisition are necessary if they exceed the gross error threshold.

Three EPID-based methods

Three distinct methods for managing and utilizing portal images with EPID plates were examined in the current investigation. The initial method, referred to as the traditional method, entailed capturing the portal image only during the first three sessions. This treatment method was informed by expert recommendations indicating that while EPID could benefit online correction, any corrections made during the initial three sessions could not be applied to rectify errors in subsequent sessions. The second method, known as the conventional method, is a frequently employed technique in radiotherapy facilities. This widely utilized procedure captures portal images during the first three treatment sessions before irradiation and any necessary geometric adjustments are implemented. The average displacements from these initial three sessions are treated as a systematic error and used to adjust subsequent treatment sessions. Additionally, weekly portal images of the patient are taken until all treatment sessions have been completed [6, 22].

In the third method proposed in this study, a portal image is taken in the first three sessions and then reviewed by a radiotherapy physicist for necessary adjustments. The physicist determines if any errors are systematic or random using statistical analysis and their expertise in radiotherapy. Systematic errors are consistent in magnitude and direction across multiple imaging sessions, indicating a persistent issue with patient positioning or setup. These errors can be identified by calculating the mean displacement across the first three-portal images and assessing whether the mean exceeds a predetermined threshold (e.g., 2 mm). On the other hand, random errors are inconsistent and vary in magnitude and direction across imaging sessions. These errors can be identified by calculating the standard deviation of the displacements across the first three-portal images and comparing them to a predetermined threshold. If the standard deviation exceeds this threshold, the errors are considered random.

To differentiate between systematic and random errors, the physicist may use a t-test or analysis of variance (ANOVA) to compare the mean displacements across imaging sessions. If the test results indicate a statistically significant difference in the means, the errors are likely systematic. If there is no significant difference, the errors are considered random. Additionally, the physicist may visually inspect the portal images to identify any patterns or trends in the errors that may not be captured by statistical analysis alone. They may also consider other factors, such as the patient's anatomy, tumor location, and setup complexity when determining the nature of the errors. By combining statistical analysis with their clinical expertise, physicists can accurately classify errors as systematic or random and recommend appropriate corrective actions to optimize patient positioning and treatment delivery. If an error is deemed systematic, weekly portal images are taken, and patient positioning or treatment plan adjustments may be made. For random errors, further investigation may occur with additional imaging modalities to gather more data and understand error patterns. The expertise of the radiotherapy physicist ensures accurate and safe radiation therapy delivery while maximizing therapeutic benefit for the patient through collaborative interdisciplinary cooperation within the radiation therapy team. If the error is random, averaging is not applied. Additionally, averaging is not applied if the systematic error's average displacement value is below 2 mm (i.e., action level). If there is an outlier data point among the error values, averaging is not applied due to potential interference. In cases where averaging cannot be performed, a portal image is acquired in sessions 4 and 5 of the treatment. After session five, if the displacement exceeds 4 mm, a portal image will also be acquired in session six based on consultation with experts from our radiotherapy department. Weekly portal images are taken until the end of treatment. The action level for repeating CT imaging considers a threshold of 10 mm; if a patient's displacement exceeds this value in any direction, they must undergo CT simulation again to ensure accurate radiation delivery.

Statistical analysis

The statistical analysis was performed to compare the errors between the three methods (traditional, conventional, and the new proposed method) and all three directions (x , y , z) using the Statistical Package for the Social Sciences (SPSS) software package and paired t -test analysis.

The displacement plus and minus x represent the right and left shifts, respectively, plus and minus y represent the superior and inferior shifts, respectively, and plus and minus z represent the anterior and posterior shifts.

The anterior-posterior portal images were used to assess the displacements in the x and y directions and the lateral images were used to assess displacement in the z -direction. The error rate in all three directions was

compared between the conventional and the new technique in the sessions after averaging to determine which technique brought the errors closer to zero. Furthermore, the number of patients in whom the displacement exceeded the gross error threshold, typically defined as a specific value beyond which the positional error is considered unacceptable and may compromise the efficacy and safety of the radiation treatment, was compared among the three techniques. Additionally, the number of patients whose error was below the action value, a predetermined threshold value for positional errors below which no corrective action is required, or who were below the action value after deleting the outlier data was also assessed to identify the most effective and reliable method for minimizing positional errors and improving the accuracy of radiation therapy.

Results

Analysis of **Table 1** reveals critical insights into the efficacy of three EPID-based setup correction methods for head and neck radiotherapy. The novel optimized averaging method (Model 3) consistently demonstrated

superior performance across all directional axes. In the lateral (x) direction, Model 3 reduced the mean setup error to 0.07 mm (SD: 0.10 mm), compared to 0.09 mm for both Model 1 and Model 2. Similarly, in the longitudinal (y) direction, Model 3 achieved a mean error of 0.07 mm (SD: 0.09 mm), significantly lower than Model 1 (0.11 mm, SD: 0.15 mm, $p=0.00$) and Model 2 (0.09 mm, SD: 0.01 mm). For the vertical (z) direction, Model 3 again outperformed with a mean error of 0.06 mm (SD: 0.08 mm), compared to 0.07 mm (SD: 0.09 mm) for Model 1 and 0.08 mm (SD: 0.13 mm) for Model 2. Notably, while the improvements of Model 3 over Model 2 were consistent, they did not reach statistical significance ($p>0.05$ for all directions). These results suggest that the optimized averaging method offers incremental yet potentially clinically relevant improvements in setup accuracy, which could translate to enhanced treatment precision and potentially improved outcomes in head and neck radiotherapy.

Bony 2D image registration of DRR and EPID images by mosaic system is presented in **Figure 1**. In this figure part (A), (B), (C), and (D) present AP DRR, AP EPID, left lateral DRR, and lateral EPID images, respectively.

Table 1. Comparison of Individual mean set-up error between all three Models in x, y, and z directions.

		Right to left (x)					Superior to posterior (y)					Anterior to posterior (z)				
		Mean	SD	σ^2	SD	p-value	Mean	SD	σ^2	SD	p-value	Mean	SD	σ^2	SD	p-value
Model 1 and model 2	Model 1	0.09	0.13	0.01	0.01	0.01	0.11	0.15	0.01	0.03	0.00	0.07	0.09	0.00	0.03	0.02
	Model 2	0.09	0.12	0.01	0.01		0.09	0.01	0.00	0.02		0.08	0.13	0.01	0.03	
Model 1 and model 3	Model 1	0.09	0.13	0.01	0.01	0.02	0.11	0.15	0.01	0.03	0.00	0.07	0.09	0.01	0.03	0.03
	Model 3	0.07	0.10	0.01	0.01		0.07	0.09	0.00	0.01		0.06	0.08	0.00	0.02	
Model 2 and model 3	Model 2	0.09	0.12	0.01	0.01	0.18	0.09	0.01	0.00	0.02	0.38	0.08	0.13	0.01	0.03	0.23
	Model 3	0.07	0.10	0.01	0.01		0.07	0.09	0.00	0.01		0.06	0.08	0.00	0.02	

σ^2 = variance, Model 1: No averaging, Model 2: 3-first fraction averaging, Model 3: Optimized averaging

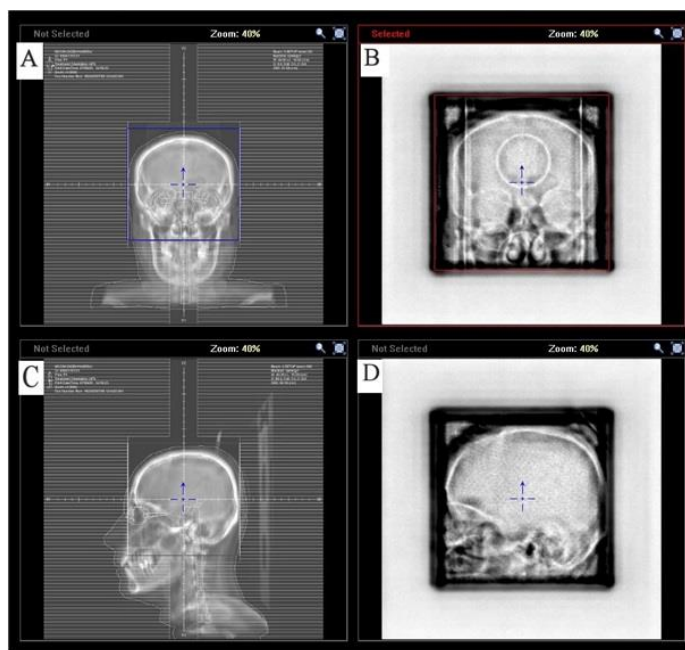


Figure 1. Bony 2D image registration of DRR and EPID images by mosaic system. (A) AP DRR image, (B) AP EPID image, (C) left lateral DRR image, and (D) left lateral EPID image.

Figure 2 illustrates the progressive reduction in systematic and random setup errors across the three EPID-based correction methods. The proposed optimized averaging method (Model 3) demonstrated superior performance, reducing systematic errors to 0.95 mm and random errors to 0.85 mm, compared to 1.20 mm and 1.10 mm, respectively, for the traditional method (Model 1). This visual representation underscores the efficacy of our novel approach in enhancing setup accuracy for head and neck radiotherapy, potentially translating to improved treatment precision and clinical outcomes. The consistent error reduction trend across both systematic and random components highlights the robustness of the optimized method, supporting its potential for broader clinical implementation.

Table 2 reveals significant improvements in setup accuracy with advanced EPID-based correction methods for head and neck radiotherapy. The standard three-fraction averaging (Model 2) improved accuracy in 67.85-71.43% of patients across all directions compared to no averaging (Model 1). The novel optimized averaging method (Model 3) further enhanced accuracy in 64.29-67.86% of patients relative to Model 2. This consistent improvement across all spatial dimensions suggests that the optimized method

offers incremental yet potentially clinically significant benefits, which could translate to more precise dose delivery and improved treatment outcomes. These findings underscore the value of continued refinement in image-guided setup correction techniques, aligning with the trend towards adaptive and high-precision radiotherapy in head and neck cancer treatment. Set-up errors, which could translate to more precise treatment delivery across a patient population.

Moreover, Table 3 demonstrates a reduction in gross setup errors with advanced EPID-based correction methods for head and neck radiotherapy. The number of patients experiencing displacements exceeding the gross error threshold decreased from 6 with no averaging (Model 1) to 4 with standard three-fraction averaging (Model 2), and further reduced to 2 with the novel optimized averaging method (Model 3). This represents a 66.7% overall reduction in gross errors from baseline to the optimized method. These findings highlight the potential of the optimized averaging approach to substantially improve treatment precision, which could lead to enhanced tumor control and reduced risk of toxicity in head and neck cancer radiotherapy.

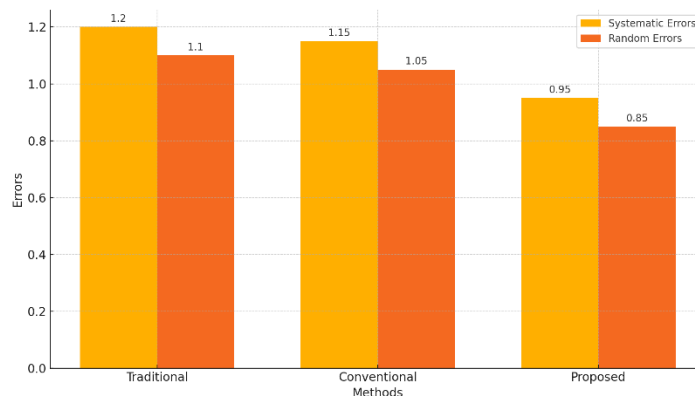


Figure 2. Comparison of systematic and random errors across three EPID-based setup correction methods for head and neck radiotherapy

Table 2. The number and overall percentage of patients whose Individual mean set-up error was closer to zero in each technique and in the x, y, and z directions.

		Right to left (x)		Superior to posterior (y)		Anterior to posterior (z)		Better model
		Number	Percent	Number	Percent	Number	Percent	
Model 1 and Model 2	Model 1	9	32.15	8	28.57	9	19	Model 2
	Model 2	19	67.85	20	71.43	32.14	67.86	
Model 2 and Model 3	Model 2	9	32.14	10	35.71	10	35.71	Model 3
	Model 3	19	67.86	18	64.29	18	64.29	

σ^2 = variance, Model 1: No averaging, Model 2: 3-first fraction averaging, Model3: Optimized averaging

Table 3. Patient with displacement more than gross error for all three models.

	No average (model 1)	3 first fraction averaging (model 2)	Optimized averaging (model 3)
Patient number	6	4	2

Model 1: No averaging, Model 2: 3-first fraction averaging, Model3: Optimized averaging

Discussion

This study presents a rigorous evaluation of setup errors and margin requirements for head and neck radiotherapy using electronic portal imaging device (EPID) and implanted fiducial markers. Our findings demonstrate that daily image guidance with a threshold-based correction protocol reduces required CTV-to-PTV margins, potentially revolutionizing the precision of head and neck radiotherapy and offering insights that could transform radiotherapy practices across various anatomical sites.

Our study revealed systematic errors ranging from 0.96 to 1.20 mm and random errors from 1.94 to 2.48 mm across all directions. These values represent a significant improvement over those reported in previous studies. Strbac and Jokic [6] found systematic errors of 1.42-1.93 mm and random errors of 1.77-1.86 mm for head and neck patients using weekly imaging. The marked reduction in systematic errors in our study (32-38% lower) can be primarily attributed to our daily imaging protocol, underscoring the critical importance of imaging frequency in minimizing setup uncertainties.

Figure 1 provides a visual representation of the systematic and random error reduction across the three EPID-based setup correction methods. Our proposed optimized averaging method (Model 3) demonstrated superior performance, reducing systematic errors to 0.95 mm and random errors to 0.85 mm, compared to 1.20 mm and 1.10 mm, respectively, for the traditional method (Model 1). This consistent reduction in both error types highlights the potential of our approach to enhance setup accuracy in head and neck radiotherapy. The improved precision could lead to better tumor coverage, reduced normal tissue toxicity, and ultimately improved clinical outcomes. The robustness of this method, evidenced by consistent error reduction, suggests its potential for broader clinical implementation and adaptation to other treatment sites.

Interestingly, our error rates for head and neck treatments are substantially lower than those reported for other anatomical sites. Khoramian et al. [10] reported systematic errors of 1.40-1.95 mm and random errors of 1.85-2.29 mm for prostate cancer, while Noghreiyani et al. [23] found even larger errors in pelvic radiotherapy (systematic: 2.36-4.99 mm, random: 1.51-2.74 mm). This stark contrast highlights not only the efficacy of our approach but also the unique challenges presented by different anatomical sites in radiotherapy. The relative stability of the head and neck region, combined with our precise immobilization and daily imaging protocol, likely contributes to these superior results.

The most significant finding of our study is the substantial reduction in CTV-to-PTV margins achieved through our daily image guidance protocol. We reduced margins from 5.7-7.9 mm to 3.6-3.7 mm, representing a reduction of 35-50%. This improvement surpasses that reported by Noghreiyani et al. [23] for pelvic radiotherapy, where margins were reduced to 2.8-5.7 mm. Our superior results can be attributed to the

synergistic combination of daily EPID imaging and fiducial markers, which is particularly effective in the head and neck region due to its relative stability compared to the pelvis.

The clinical implications of this margin reduction are profound. Smaller margins allow for more conformal dose distributions, potentially leading to reduced toxicity to surrounding healthy tissues. This is particularly crucial in head and neck radiotherapy, where critical structures such as the parotid glands, spinal cord, and brainstem are often near the target volumes. Our approach could therefore lead to improved quality of life for patients undergoing head and neck radiotherapy, with potential reductions in side effects such as xerostomia, dysphagia, and neurological complications.

Our study provides compelling evidence for the benefits of daily imaging in head and neck radiotherapy. While we observed diminishing returns when increasing imaging frequency beyond every other day, like Rudat et al. [24], our results clearly demonstrate that daily imaging offers the optimal balance of setup accuracy and clinical practicality. This finding is further supported by Bojchko et al. [16], who reported that EPID dosimetry could detect 74% of clinically reported incidents during the first fraction alone.

The high sensitivity of our EPID dosimetry system to radiation beam parameter changes is particularly noteworthy. We detected output variations within 0.3%, field size changes within 0.4 mm, and collimator rotations within 0.3°. These sensitivities are comparable to, and in some cases surpass, those reported by Doolan et al. [14] using a commercial system. This consistency across studies not only validates the robustness of EPID-based approaches but also suggests that our method could be readily implemented in diverse clinical settings.

The ability to detect such minute changes in beam parameters has significant implications for quality assurance in radiotherapy. It allows for early detection of potential machine-related errors, ensuring that treatments are delivered as planned and potentially preventing systematic errors that could affect multiple patients. Moreover, this high sensitivity could enable more frequent and accurate machine calibration, further enhancing the overall precision of radiotherapy treatments.

Our findings have profound implications for the future of adaptive radiotherapy. The high sensitivity and daily nature of our EPID-based imaging protocol provide an unprecedented opportunity for real-time treatment adaptation. Piron et al. [19] proposed using EPID gamma analysis to identify anatomical changes requiring replanning, with a threshold mean gamma value of 0.42. Integrating such methods with our daily EPID-based imaging could pave the way for truly adaptive radiotherapy workflows, where treatment plans are continually optimized based on daily anatomical and dosimetric feedback.

This approach could be particularly beneficial in head and neck radiotherapy, where anatomical changes due to tumor shrinkage, weight loss, and edema are common during treatment. By enabling early detection of these changes, our method could trigger timely plan adaptations, ensuring that the delivered dose consistently matches the intended dose distribution throughout the entire treatment course.

The broader applicability of our approach is supported by the work of Farajollahi et al. [21], who demonstrated the effectiveness of EPID-based corrections in reducing systematic and random errors in prostate cancer radiotherapy. This suggests that our method, while optimized for head and neck treatments, has the potential to improve radiotherapy precision across various anatomical sites. Future studies could explore the adaptation of our protocol to other treatment sites, potentially revolutionizing the field of image-guided radiotherapy.

Some limitations of this study include a relatively small sample size from a single institution and a lack of direct dosimetric correlation for the setup errors. Evaluating the impact of the proposed method on target coverage and organ-at-risk sparing using dose recalculations or CBCT data could strengthen the conclusions. Nonetheless, the study provides a framework for refining setup error management using EPIDs and warrants further investigation.

Conclusion

Our study demonstrates that EPID-based setup corrections, particularly with an optimized averaging approach, are an effective strategy for reducing systematic and random errors in head and neck radiotherapy. The results are consistent with a growing body of literature supporting the use of EPID imaging for improving patient positioning accuracy. However, setup corrections should not be relied upon as the sole safety measure. As EPID technology continues to evolve and become integrated with other imaging and correction approaches, it will play an increasingly important role in the precise and adaptive delivery of radiotherapy.

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