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Quantification and assessment of Day-To-Day interfraction set-up errors in radiotherapy treatment delivery based on EPID detector

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Abstract

Introduction: The aim of this study was to determine whether the EPID detector can serve as an effective tool for inter-fractional dose control. Accurate radiotherapy delivery is vital for successful treatment, prompting advancements in dosimetry methods, particularly for dynamic techniques. Linear accelerators use kilovoltage and megavoltage X-rays to verify patient positioning, a standard practice essential for minimizing geometric and dosimetric errors. While integrated imaging systems typically use orthogonal radiographs, this method increases radiation exposure and fails to account for intra-fractional movements, risking undetected errors. To ensure patients receive the planned radiation dose, in-vivo dosimetry is performed by measuring the dose at various locations on the patient's body, which simultaneously verifies correct positioning. Discrepancies can reveal incorrect positioning or significant movements, thus enhancing treatment accuracy. This study investigates transit dosimetry using Electronic Portal Imaging Devices (EPID) to verify patient positioning during treatment. It establishes tolerance ranges and response criteria for the head and neck and pelvic areas, providing insights into the concordance between planned and actual dose distributions.

Material and methods: The analysis included 30 patients treated with dynamic techniques in the pelvic (Pelvis) and head and neck (Head&Neck) areas. For each fraction, a fluence map was recorded using the EPID detector. This allowed for repeated comparisons between summary fluence maps across treatment fractions, totaling 1552 comparisons for the Head&Neck area and 2339 for the Pelvis area. To evaluate the correspondence between fluence map pairs, gamma indices were calculated using specified accuracy criteria.

Results: Statistical analysis employed Chi-squared or Fisher's exact test, establishing significant correspondence within defined limits. For the Head&Neck area, repeatability was found within 3 mm and 4%; for the Pelvis area, it was within 4 mm and 4%.

Conclusions: This method of verifying treatment repeatability is practical for clinical use, requiring no additional dose and not hindering treatment delivery.

Keywords: EPID; gamma index; fluence map; interfraction set-up errors.

Introduction

The accuracy of radiotherapy delivery remains the subject of discussion, and dosimetry methods – especially in dynamic techniques – are constantly being developed.[1,2] Linear accelerators used in radiotherapy are equipped with radiation sources and detectors commonly used to verify patient positioning before or during each treatment session. These devices use both kilovoltage and megavoltage X-rays.[3,4] They are used in oncology centres to perform quality procedures such as dose verification before treatment, during treatment, and patient positioning.

The delivery of radiotherapy treatment is a complex and intricate process at every stage. Procedures related to quality control need to be continuously developed, as this is the only way to ensure that the likelihood of errors is minimized.[5,6] Errors in radiotherapy can be divided into two categories: dosimetric and geometric. Geometric errors occur when the delivered dose is deposited in the wrong place. They are influenced by many factors including: patient positioning error, finite accuracy of the linear accelerator components, etc. One step that is heavily affected by the likelihood of geometric errors is the reproduction of the patient's position on the treatment table, against the

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Authors' contribution:
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article.

reference one. The reference position is considered to be the position of the patient during the CT scan used to create the treatment plan. Ensuring a high level of reproducibility and repeatability of patient positioning during each fraction plays a key role in terms of the success of the overall therapy.

The most common tool for verifying correct patient positioning is the imaging system, using an X-ray tube and radiation detector, which is an integral part of the medical accelerator. Normally, a pair of orthogonal radiographs is used to assess the patient's correct positioning based on the alignment of the bone elements.[7] Such a solution is used, for example, in assessing the correct positioning of the head when treating the brain or directly irradiating bones. Images taken with kilovoltage Cone Beam Computed Tomography (kV CBCT) can be used to assess soft tissue elements (i.e. bladder, rectum). Such a solution is used when delivering gynecological or prostate treatment. Nowadays, however, 3D kV CBCT imaging is increasingly used in routine clinical practice regardless of the location of the irradiated area.

Although they undoubtedly have many advantages, methods of verifying patient positioning with the use of X-rays also have their drawbacks and limitations. It should be remembered that this imaging modality involves an additional dose of radiation to the patient. It is also important to note that the imaging is carried out prior to the irradiation session, and this method of verification does not return any information about the patient's positioning during the implementation of the irradiation, as it does not take into account intra-fractional movements. Consequently, any errors related to changes in the patient's position during irradiation may go undetected, leading to dosimetric inaccuracies.

To ensure and confirm that the patient receives the planned radiation dose according to the treatment plan, in-vivo dosimetry measurements are conducted at various points on the patient's body.[8] This approach also allows for verification of whether the patient is positioned as intended. Detecting dose differences can indicate incorrect patient positioning or significant, uncontrolled intra-fraction movements, thereby enhancing the accuracy of treatment delivery. In clinical practice, in-vivo dosimetry involves placing dosimeters (e.g., diode detectors, thermoluminescent dosimeters, or semiconductor detectors) on the patient's body near the treatment area. During the chosen fraction of radiotherapy, these dosimeters measure the radiation dose in real-time, enabling verification of dose compliance with the treatment plan and ensuring proper delivery to the targeted area.

The use of standard detectors in in-vivo dosimetry within the context of dynamic radiotherapy techniques presents numerous challenges related to the complexity of dose distribution, scattered radiation, and small fields.[9] As a result, there is a growing interest in alternative dosimetry methods that can better address these limitations.[10,11] One such method is transit dosimetry, which is employed in radiotherapy to assess the accuracy and repeatability of patient positioning during treatment.[12-14] It utilizes electronic imaging devices, such as the EPID (Electronic Portal Imaging Device) detector, to measure the radiation dose passing through the patient's body.[15,16]

Measurements utilizing the EPID detector, along with gamma index analysis, are routinely implemented in clinical practice for quality assurance (QA) procedures., i.e. during dosimetric plan verification before treatment.[17] It thus enables the verification of the accuracy of dose distribution calculations by comparing them with the actual distribution measured during verification assessments. The measurement made in this way also contains hidden information on the correctness of the execution of the collimator leaf movement, the speed of the arm rotation (in the VMAT technique), or the collimator rotation angle.[18-20]

This paper presents the results of a study that demonstrates how the use of an EPID detector and gamma index analysis can serve as an effective and straightforward method for verifying accurate patient positioning during radiotherapy delivery. Additionally, the study aimed to establish tolerance ranges for correct patient positioning and define response criteria for two selected anatomical locations, specifically the head and neck and the pelvis, designated as local indicators within the specific radiotherapy center. This quantitative analysis, utilizing the gamma index, also provided a means to assess the concordance between the planned and actual dose distributions in each treatment fraction.

Materials and methods

A group of 30 patients qualified for radiotherapy was selected for the study. For the 15 patients selected, the target structures were areas located in the pelvic area, i.e. prostate, bladder, uterus ("Pelvis"), and for the other 15 patients, it was the head and neck or brain area ("Head&Neck"). For the studied group of patients, no additional immobilization (such as thermoplastic masks or vacuum mattresses) was used during the delivery of radiotherapy in the Pelvis area, while for patients treated in the Head&Neck area, a 3- or 5-point thermoplastic mask was used for immobilization. Then, following the CT scan for treatment planning, a dynamic Volumetric Modulated Arc Therapy (VMAT) treatment plan was prepared for each patient.[21]

Then, the measurements during treatment delivery were carried out at two selected locations: Pelvis and Head&Neck. During each fraction, a fluence map was recorded for each radiation beam for each patient using the EPID detector. This made it possible to repeatedly compare the summary fluence maps obtained from individual fractions with the corresponding summary maps from subsequent fractions of the treatment. A total number of 1552 comparisons were analyzed for the Head&Neck location and 2339 comparisons for the Pelvis area. The measurements in this study were performed using a single Varian TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA, USA) equipped with an aS1200 EPID.

This aS1200 panel features a 43 × 43 cm² surface, with an active area of 40 × 40 cm² organized in an 1190 × 1190 pixel array for dosimetry mode, achieving a resolution of 0.34 mm at the isocenter.

The Eclipse v16 software (Varian Medical Systems, Palo Alto, CA, USA) was used to create the treatment plans. The AAA algorithm was used for the calculations. The number of arcs in the plans varied between 2 and 4. The treatment planning system was programmed to have the EPID panel record the radiation passing through the patient during the entire treatment session. Fluence maps were recorded for each field separately. In addition, each plan was dosimetrically verified and approved for clinical implementation by a medical physicist and a radiotherapist.

The generated treatment plans differed as to the number of fields implemented. Therefore, it was decided to create a sum of all images recorded during a single treatment fraction, obtaining a so-called "composite image" for further analysis. The fluence map recorded during each fraction was compared with maps from all previous and subsequent fractions using gamma analysis in dedicated Portal Dosimetry software[22] (Varian Medical Systems, Palo Alto, CA, USA).

To calculate the total number of fluence map comparisons for a single patient, the following formula was used (**Equation 1**):

$$N = \sum_{n=1}^{f-1} SMF_n \qquad \text{Eq. 1}$$

where:
N – total number of comparisons for a single patient,
f – total number of fractions,
SMF_n – summary fluence map for nth traction.

To compare the resulting dose distributions (fluence maps) from the individual fractions, the gamma index[23] was used, which simultaneously compares the measured and calculated doses at the same location and the difference between the position of the dose itself.

The gamma analysis was performed for the variable parameters ΔD_{max} and DTA. To calculate the gamma index, the following formula was used (**Equation 2**):

$$\gamma_{i,j} = \sqrt{\frac{\left|\underline{r_j} - \underline{r_i}\right|^2}{DTA^2} + \frac{|D_j - D_i|^2}{\Delta D_{max}{}^2}} \qquad \text{Eq. 2}$$

where:
- i, j – elements of the theoretical and measured matrix,
- $\left|\underline{r_j} - \underline{r_i}\right|$ – distance between points in the theoretical and measured matrix for the analyzed dose,
- $D_j - D_i$ – the difference between the planned and measured dose in the matrix element j=i,
- *DTA* – maximum distance at which recording a dose consistent with the expected dose that will result in the criterion of correct analysis being met,
- ΔD_{max} – the maximum difference between the planned and measured dose that will result in the criterion of correct analysis being met, assuming no geometrical differences.

For example, if one defines the value of DTA as 3 mm and ΔD_{max} as 3%, then the measurement is considered to be consistent with the calculations when the measuring point is contained within a volume with radii: DTA and ΔD_{max}.

In this study, in order to assess the correspondence between the respective pairs of fluence maps, gamma indices were calculated for different accuracy criteria: for the Pelvis area 1) 2%/2mm; 2) 3%/3mm; 3) 4%/4mm, and for the Head&Neck area 1) 2%/2mm; 2) 3%/3mm; 3) 4%/3mm, assuming in all three criteria correspondence for 98% of the analyzed field.

In the statistical analysis, the Chi-squared or Fisher's exact test was used to compare the repeatability of treatment in different areas for different gamma index criteria. The study assumed statistical significance at the level of $p=0.01$ for the Chi-squared or Fisher's exact test and a 98% correspondence criterion of the analyzed field.

Results and discussion

The following figures (**Figures 1-3**) present examples of measured dose comparisons from two different fractions.

Figures 1 and **2** present a comparison of doses from two fractions, in which the expected correspondence between measurements (Reference Image and Portal Image) was achieved for representative patients treated in the Head&Neck and Pelvis areas, respectively. In contrast, **Figure 3** illustrates the result obtained for a patient treated in the Head&Neck area as an example of a lack of correspondence between two fractions according to the specified gamma index criteria. Section (A) of each figure provides an analysis of the gamma evaluation between the two measurements. In the obtained maps (central area), correspondence between measurements is indicated in green, representing points for which the condition gamma index < 1 is met, while results outside the tolerance range, where the gamma index > 1, are marked in red. Detailed dose profiles (part B) along the collimator axes present the dose matching between consecutive fractions according to the axes indicated in part (A). Additionally, the gamma evaluation histogram presented in part (C) of each figure displays the number of counts that fall within or exceed the given criteria.

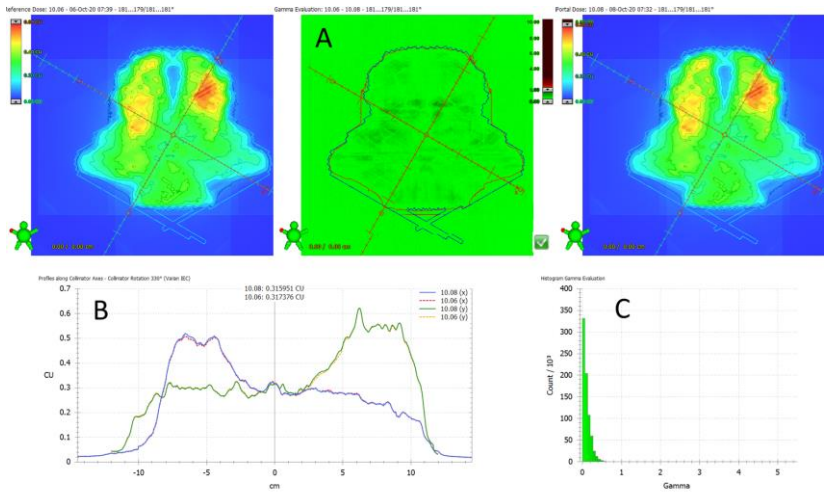


Figure 1. The results obtained from the analysis of measured doses between two fractions for a patient treated in the Head&Neck area, confirm correspondence at the expected level (criteria of 2%/2mm, 98%). In this case, the achieved correspondence was 100%. The analysis includes: A) gamma evaluation, B) dose profiles along the collimator axes, C) gamma index histogram.

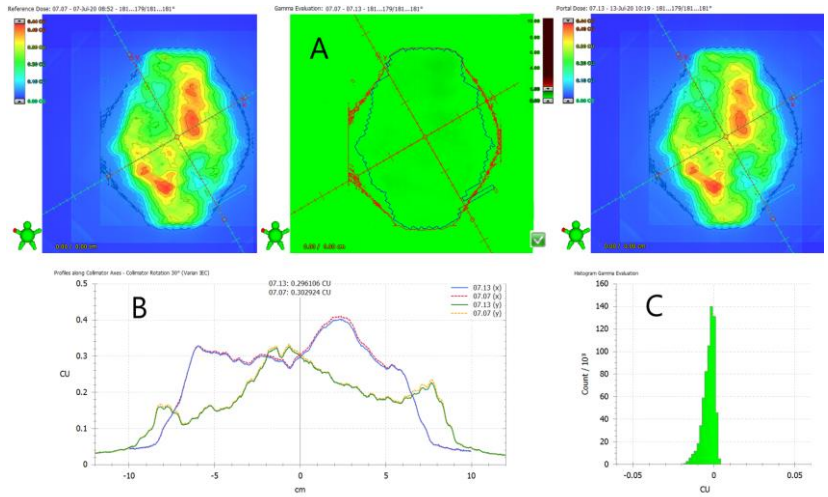


Figure 2. The results obtained from the analysis of measured doses between two fractions for a patient treated in the Pelvis area, confirm correspondence at the expected level (criteria of 3%/3mm, 98%). In this case, the achieved correspondence was 100%. The analysis includes: A) gamma evaluation, B) dose profiles along the collimator axes, C) gamma index histogram.

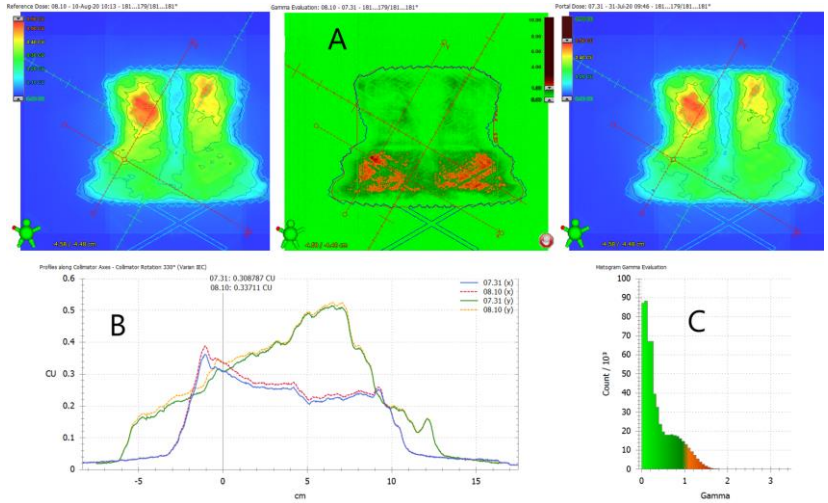


Figure 3. The results obtained from the analysis of measured doses between two fractions for a patient treated in the Head&Neck area indicate the lack of correspondence at the expected level (criteria of 2%/2mm, 98%). In this case, an unsatisfactory correspondence of only 90,5% was achieved. The analysis includes: A) gamma evaluation, B) dose profiles along the collimator axes, C) gamma index histogram.

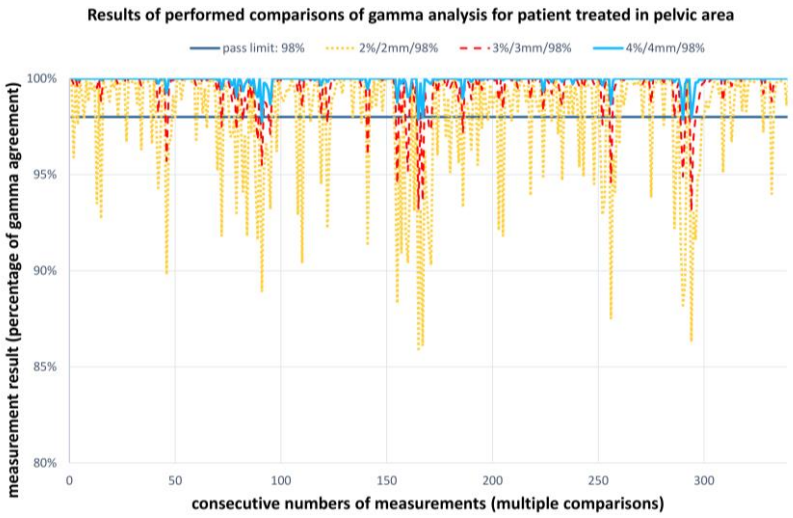


Figure 4. Results of the gamma analysis for a representative patient treated in the Pelvis group, comprising 380 comparisons from 20 consecutive treatment fractions, presented for three selected gamma index criteria: 2%/2mm, 3%/3mm, and 4%/4mm. The graph also indicates the required acceptance criterion of 98%.

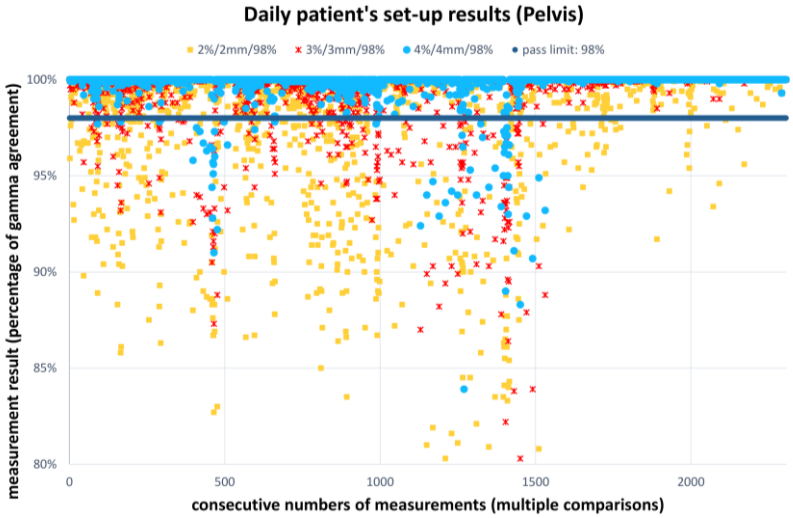


Figure 5. A scatter plot of the repeatability results for the positioning of 15 patients shows the gamma analysis outcomes for the accepted criteria obtained on consecutive days of radiotherapy delivery in the Pelvis area, along with the required acceptance level of 98%.

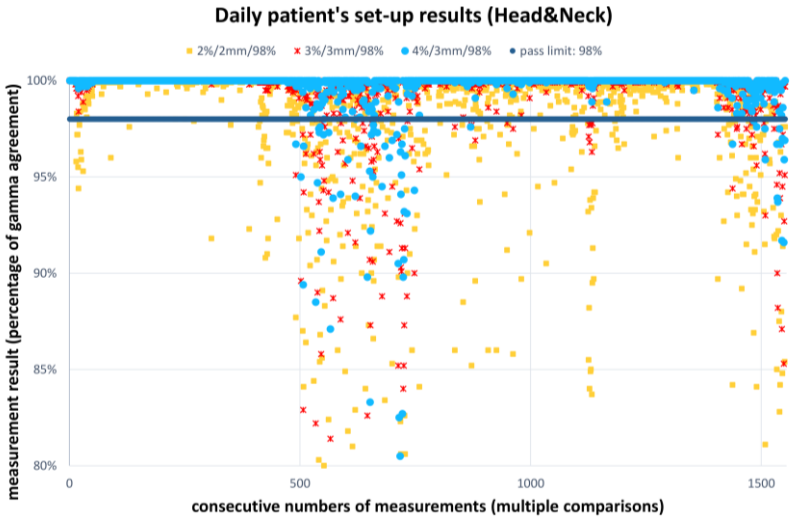


Figure 6. A scatter plot of the repeatability results for the positioning of 15 patients shows the gamma analysis outcomes for the accepted criteria obtained on consecutive days of radiotherapy delivery in the Head&Neck area, along with the required acceptance level of 98%.

Figure 4 shows the pooled results of the gamma analysis for one patient irradiated in the pelvic region across 20 treatment fractions (380 comparisons). This analysis is relative to the chosen gamma index criteria of 2%/2mm, 3%/3mm and 4%/4mm, respectively, and their impact on the acceptance or rejection of the measurement-to-measurement correspondence. It can be observed that the choice of the 2%/2mm gamma index criterion would have resulted in the rejection of the calculation-to-measurement correspondence in most fractions.

The complete scatter plots from gamma analysis results obtained for every consecutive day of radiotherapy delivery for all patients and the respective gamma index criteria for the two analyzed locations, Pelvis and Head&Neck, are presented in **Figure 5** and **Figure 6**.

Assuming statistical significance at $p = 0.01$ for the Chi-squared or Fisher's exact test and a correspondence criterion in 98% of the analyzed field, the results summarized in **Table 1** and **2** were obtained. By analyzing **Table 1** and **Table 2**, it can therefore be concluded that:

1. For the Pelvis area, the repeatability between fractions is within 4mm and 4%, and the sensitivity of the selected criterion is over 97%.
2. For the Head&Neck area, the repeatability between fractions is within 3 mm and 4%, and the sensitivity of the selected criterion is almost 96%.

The findings of this study indicate several important limitations that must be acknowledged when interpreting the results. Further research should aim to address these limitations by exploring the impact of both technical precision and anatomical variations on dose measurement.

It is essential to recognize that doses measured in this context are influenced by the technical accuracy of the accelerator's operation. In this study, the stability of the accelerator was ensured, maintaining a performance consistency of up to 1.5% for the high-energy photon beam used in the measurements. While this level of consistency was provided, it could also be beneficial to verify this performance in future studies.

On the other hand, it is also important to consider the impact of anatomical changes occurring in patients during the course of radiation therapy on the administered doses. These changes can significantly affect dose distribution and should therefore be carefully evaluated when assessing treatment outcomes.

It should be borne in mind that for different locations, it is necessary to adopt different treatment repeatability criteria. Different internal organ mobility is observed when irradiating different locations. For example, intra-fractional organ mobility in the pelvic area will be higher than in the brain or head and neck areas.[24-26]

Table 1. Results of the analysis for 15 patients undergoing radiotherapy in the Pelvis area for the three selected gamma index criteria including: (1) the quantitative breakdown of comparisons meeting the gamma criterion (> 98% gamma "pass") and not meeting the gamma criterion (< 98% gamma "not pass"), (2) the specific sensitivity level of each method (criteria sensitivity) and (3) the statistical significance score (Chi-squared or Fisher's exact test).

Comparison results (Pelvis)	**Gamma analysis criteria**		
	2%/2mm/98%	**3%/3mm/98%**	**4%/4mm/98%**
total number of results with **>98% gamma (pass)**	1830	2139	**2271**
total number of results with <98% gamma (not pass)	509	200	**68**
criteria sensitivity	78.2%	91.4%	**97.1%**
p-value	>0.01	>0.01	**<0.01**

Table 2. Results of the analysis for 15 patients undergoing radiotherapy in the Head&Neck area for the three selected gamma index criteria including: (1) the quantitative breakdown of comparisons meeting the gamma criterion (> 98% gamma "pass") and not meeting the gamma criterion (< 98% gamma "not pass"), (2) the specific sensitivity level of each method (criteria sensitivity) and (3) the statistical significance score (Chi-squared or Fisher's exact test).

Comparison results (Head&Neck)	**Gamma analysis criteria**		
	2%/2mm/98%	**3%/3mm/98%**	**4%/3mm/98%**
total number of results with **>98% gamma (pass)**	1195	1432	**1485**
total number of results with <98% gamma (not pass)	357	120	**67**
criteria sensitivity	77.0%	92.3%	**95.7%**
p-value	>0.01	>0.01	**<0.01**

In this study, the results obtained for the Pelvis area were as expected: ΔD_{max} = 4% and DTA = 4 mm along with the highest test sensitivity. Nevertheless, a better result was expected for the Head&Neck area, i.e. ΔD_{max} = 3% and DTA = 3 mm, as was indicated by an earlier pilot study on a smaller group of patients[27]. When a larger analysis was performed for 15 patients, it was found that approximately 6% of cases did not meet this criterion. This is exemplified by patient no. 6, who shows very large differences in the alignment of planned and measured values between consecutive days of treatment delivery, e.g. "6 Aug" and "10 Aug". This can be clearly seen in **Table 3**.

It should be emphasized that irradiation of the brain generally has a very high repeatability of irradiation, which is certainly influenced by the low mobility of the organs in this area and the use of immobilization, such as a thermoplastic mask. Furthermore, in the Head&Neck location, it can be assumed that the accuracy of the alignment for most cases is within 3 mm and 3%. On the other hand, in the Pelvis area, the accuracy of the alignment for most cases is within 4 mm and 4%.

Anatomical changes observed during treatment can be categorized as either progressive or random. The Head&Neck group is characterized by relatively progressive changes such as patient weight loss and tumor morphological changes, which refer to alterations that occur in a consistent direction and magnitude over time.[28] Conversely, the Pelvis group exhibits random changes, characterized by alterations that arise in an unpredictable manner. These displacements, which pertain specifically to this group of subjects, are primarily caused by the location of nearby critical organs, such as bladder filling, the position of the bowels, or the size of the rectum. Understanding these distinct characteristics is vital for accurately interpreting the study's outcomes. Analyzing the doses between all fractions enables the assessment of dose delivery accuracy for patients experiencing random changes, such as in the Pelvis group. However, since the changes are random, it is not possible to predict their direction from one fraction to the next. Nevertheless, the magnitude of these variations can still be estimated. It should be noted that this approach also helps estimate the gamma analysis criteria needed to confirm the accuracy of the administered dose to the patient.

A deeper analysis may be needed for gamma comparisons in the Head&Neck group, where progressive changes seem to be more common. These investigations could provide valuable insights for future research. For example, it would be useful to compare the first or second fraction (as a "baseline") with each subsequent fraction and monitor the differences in recorded doses. If these differences increase, it might be necessary to use more flexible gamma criteria for the analysis. This situation could raise important questions about acceptable thresholds for looser gamma criteria.

Table 3. Examples of gamma analysis results from selected treatment days of a patient that differ significantly from those of other patients undergoing radiotherapy in the Head&Neck group, illustrating either correspondence or rejection of 98% agreement across three selected gamma analysis criteria.

Day to Day comparison	2%/2mm/98%	3%/3mm/98%	4%/3mm/98%
06 Aug-05 Aug	97.5%	99.9%	100.0%
06 Aug-07 Aug	87.0%	97.2%	99.4%
06 Aug-10 Aug	70.1%	82.9%	89.4%
06 Aug-11 Aug	84.1%	94.2%	96.6%
06 Aug-12 Aug	98.9%	99.9%	100.0%
06 Aug-18 Aug	96.2%	99.1%	99.8%
06 Aug-19 Aug	86.4%	96.2%	98.6%
06 Aug-20 Aug	99.8%	100.0%	100.0%
07 Aug-06 Aug	90.4%	98.8%	99.6%
07 Aug-10 Aug	94.1%	97.2%	98.2%
07 Aug-19 Aug	100.0%	100.0%	100.0%
07 Aug-20 Aug	84.4%	96.2%	98.5%
07 Aug-21 Aug	99.9%	100.0%	100.0%
07 Aug-24 Aug	97.9%	99.8%	100.0%
07 Aug-26 Aug	70.1%	82.2%	88.5%
10 Aug-05 Aug	90.7%	98.0%	98.8%
10 Aug-06 Aug	74.3%	89.0%	94.7%

The findings of this study are based on data collected from a single institution and a relatively small patient cohort, which may limit their generalizability. Therefore, it is important to recognize that these observations should be interpreted within the context of the specific patient population studied and may not necessarily apply to the broader population. However, the methodology presented can serve as a framework for establishing similar limits in a given radiation therapy center. To confirm these observations and derive more comprehensive conclusions, further research involving a larger and more diverse group of patients is necessary.

Additionally, it should be noted that in this study, all measurements were conducted using a single EPID detector, and therefore, the obtained results cannot be generalized. To comprehensively assess the accuracy and reliability of the results, it would also be beneficial to compare the presented EPID-based dosimetry results with other established quality assurance methods[29], such as thermoluminescent or film dosimetry.

It is also important to remember that this is a comparison of relative fluence maps, which means that comparing their distributions between the selected and each subsequent day of treatment delivery gives information about the repeatability of the treatment, not about its correctness. If a given treatment plan contains a systematic error, it will not be observed during such a verification.

The proposed method therefore can give us not only information about the precision of treatment delivery. That kind of in-vivo EPID-based measurement makes it possible to assess in which treatment session the patient has been treated differently than in other fractions, and based on this, after the end of therapy, one can try to verify the final effects of the treatment. The presented method of analyzing and tracking differences gives us information about the change in either the patient's treatment position or anatomy.

The approach of conducting offline patient positioning verification proposed in this study can also be a useful tool to quantify the need for the preparation of a new treatment plan, i.e. an offline adaptive plan.

Conclusions

Performed measurements and analysis showed that the use of an EPID detector in verifying the repeatability of treatment is easy to implement in clinical practice. It does not result in the administration of an additional dose and does not hinder the delivery of treatment. The EPID device can be a useful tool for assessing the repeatability of radiotherapy.

The proposed method allows for the assessment of treatment sessions in which the patient was treated differently from other fractions, providing additional information about the precision of delivering the planned dose.

The results obtained in this manner will help promptly determine whether the patient's irradiation conditions require adjustment and whether a new treatment plan should be developed to accommodate changes in the patient's anatomy or position.

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