Original
ISSN 2413-0516

Optimizing Treatment Quality in Head and Neck Cancer Therapy: Impact of Adaptive Intensity-Modulated Radiotherapy on Plan Quality and Tumor Volume Changes

Muntather Habeeb Albosaabar[1], Rozilawati Binti Ahmad[1*], Haydar Hamza Alabedi[2,3,4], Faizal Mohamed[5], Noorazrul Yahya[1], Hassan Abouelenein[6], Dalia Osama Mohamed[7], Mona Mahmoud Sayed[7]

[1]Programme of Diagnostic Imaging and Radiotherapy, Faculty of Health Sciences, Universiti Kebangsaan Malaysia.
[2]Surgery Department, College of Medicine, Baghdad University, Baghdad, Iraq.
[3]College of Medicine, University of Warith Al-Anbiyaa, Karbala, Iraq.
[4]Al-Warith Cancer Institute, Karbala, Iraq.
[5]Department of Applied Physics, Faculty of Science & Technology, Universiti Kebangsaan Malaysia.
[6]Consultant of Medical Physics at Sohag Oncology Center, Egypt.
[7]South Egypt Cancer Institute (SECI), Asyut University, El- Mesak St. Asyut.
*Correspondence to: Rozilawati Binti Ahmad (E-mail: rozie.ahmad@ukm.edu.my)

(Submitted: 29 January 2024 – Revised version received: 11 February 2024 – Accepted: 02 March 2024 – Published online: 26 April 2024)

Abstract

Objective: This study examines the impact of volumetric alterations and PTV shifting on the quality of adaptive intensity-modulated radiation (IMRT) plans and their effectiveness in treating head and neck cancer.

Methods: The research was carried out at the Sohag Cancer Centre in Egypt, including a sample of 36 individuals diagnosed with head and neck squamous cell carcinoma (HNSCC). Patients were chosen based on the following criteria: locally progressed and node-positive malignancy, oropharyngeal cancer, oral cavity cancer, and unknown primary. The research used dynamic intensity-modulated radiation therapy (D-IMRT) to establish treatment plans and SIEMENS SOMATOM DEFINITION CT scanners to acquire 3D anatomical images. The median dosage per fraction was observed at 1.64 to 2.12 Gy. Using the conformance index (CI) and the homogeneity index (HI), the quality of the plan was assessed. The threshold for statistical significance was set at 0.05.

Results: The study analyzed patients with unilateral and bilateral HNSCC tumors, with most having bilateral tumors. The findings demonstrated that the tumor PTV was significantly reduced as a consequence of the suggested adaptive radiation techniques. The homogeneity and conformity indexes were used to evaluate the plan's quality (HI). The maximal homogeneity index (HI) was reached at fractions 14 and 7, respectively. The correlation between the reduction of PTV and CI was initially positive after fraction 7 but became negative after fractions 14 and 21. It was also shown that HI is positively correlated with PTV changes after fractions 7 and 14, while it was negative after 21 fractions.

Conclusion: The use of adaptive radiotherapy in intensity-modulated radiation therapy (IMRT) treatment planning improves plan quality and decreases error rates due to tumor margin movement. Following radiation fractions, PTV shifting affects the homogeneity index (HI).

Keywords: Adaptive radiotherapy, volumetric change, IMRT index of gradient, conformity, and homogeneity

Introduction

Radiation oncologists employ intensity-modulated radiation treatment (IMRT) to target cancers while minimizing damage to healthy tissues. Since the radiation beam intensity may be adjusted all across the treatment region using IMRT, tumors can be targeted more precisely.[1] As the patient undergoes treatment, adaptive IMRT makes real-time adjustments to the imaging and treatment protocols. To evaluate the tumor's size, form, and position, in addition to the patient's anatomy, regular CT or MRI scans are required. Because of these advancements, the treatment plan may be adjusted to maximize radiation delivery to the tumor and minimize radiation exposure to nearby healthy tissues.[2,3]

A promising new approach to improving radiation treatment accuracy and accommodating internal anatomical changes is adaptive intensity-modulated radiation therapy, more commonly known as adaptive IMRT.[4,5] Advanced radiation therapy techniques like adaptive radiation therapy (ART) allow for real-time adjustments to radiation dose in response to tumor characteristics and other anatomical changes. Incorporating real-time dynamic adjustment allows for better-targeted radiation treatment, which improves the therapeutic ratio by reducing radiation damage to nearby healthy tissues and guaranteeing efficient tumor localization.[6] This method ensures the tumor is targeted as effectively as possible while causing the least amount of harm to nearby healthy tissues.[7] Radiation treatment for head and neck cancer patients often causes changes in tumor size, abnormalities in anatomy, and relative body mass.

The optimization of tumor therapy while avoiding radiation exposure to adjacent healthy tissues is a complex balancing act, and these changes pose serious hurdles to the efficacy of originally optimized treatment techniques. Researching the complex interplay between volume changes, weight loss, and plan quality indicator assessment is crucial in the context of adaptive IMRT.[8,9] Volume variations can impact the achievement of therapeutic objectives, as the initial radiation dose may not be sufficient after malignancies shrink or grow, potentially affecting the desired outcome. Weight loss during cancer treatment can worsen the situation by altering the patient's body and affecting radiation distribution throughout the body.[10] Adaptive IMRT offers potential benefits, but understanding how physiological variables, like weight loss and volume changes, influence plan quality criteria is crucial, as highlighted in a recent study. David et al.[11] examined the impact of weight loss and anatomical factors on spinal cord dosimetry during head and neck (H&N) radiation to throw light on a poorly understood subject.

This sector's lack of complete knowledge has hindered the development of evidence-based adaptive management techniques.

The research included one hundred thirty-three head and neck patients using TomoTherapy for daily mega-voltage CT image guidance (MVCT-IG). From planning scans to MVCT-IG images, the researchers used Elastix software to distort the spinal cord outlines and collect the dose. The two spinal cord diameters, D P and D A were compared (SCD 2%). Alves et al.'s[12] research mainly aimed to determine if Adaptive IMRT was necessary for patients with head and neck (H&N) cancer using a retrospective planning study and an automated planning tool. The research included data from 30 H&N patients with adaptive radiation. The patients followed the clinic's procedure and had a CT scan before therapy began and again throughout treatment for verification purposes.

Using these imaging datasets, three separate plans were generated retroactively using the iCycle tool to simulate both adaptation- and non-adaptation-related scenarios: 1) the optimised plan derived from the planning CT; 2) the optimised plan derived from the verification CT (called the ART-plan); and 3) the plan that was obtained by recalculating the treatment plan (called the non-ART plan) from scenario one on the verification CT. Between scenarios 2 and 3, the SPIDER plan was used to compare dosimetric endpoints for target volumes and organs at risk (OAR). The goal was to evaluate the quality of the plans. The results of their study highlight the positive effects of adaptive radiation on H&N patients, especially when it comes to covering target volumes efficiently. Incorporating an automated planning tool helps reduce planner-induced biases, confirming that the improvements seen are due to adaptive radiotherapy. As a proof of concept, the method's usefulness was shown by looking back at weekly CBCT scans from fifteen patients with head and neck conditions.

The study examined external alterations in a 2D radial difference map after 23 fractions, which were linked to changes in gross tumor sizes and organs at risk. The dosimetric effects were examined, and an interactive software program was developed to create and understand the 2D intensity map. The margin for planning target volume (PTV) is a geometric expansion that ensures the projected radiation dosage adequately covers the clinical target volume (CTV) despite treatment delivery uncertainties, accounting for potential errors in radiation therapy administration and other factors such as patient positioning and internal organ motions.[13] The PTV margins are determined by considering various uncertainties, with the set-up or shifting error being a significant component. Shifting errors occur when the patient's position deviates from the expected position during each treatment session, requiring additional margins to produce the PTV.[14] Alabedi's 2023[13] study explores the impact of EPIDs on PTV margins in the 3DCRT-treated head, neck, and breast cancers, demonstrating their role in establishing verification methods. This study examines the effects of volumetric changes and shifting of PTV on plan quality of the adaptive treatment of Intensity-Modulated Radiation Therapy (IMRT) and its use in treating head and neck cancer throughout treatment.

Materials and Methods

This is a prospective cohort study with a purposive sampling technique involving 36 patients diagnosed with head and neck squamous cell carcinoma (HNSCC) and forwarded by an oncologist for intensity-modulated radiotherapy (IMRT) and fit the criteria of adaptive radiotherapy (ART). Ethical approval for this study was secured through a letter from the general secretariat of the specialised medical centres, at the Ministry of Health in Egypt. Ethical consent was obtained for this study. The study was conducted at the Sohag Cancer Centre in Egypt, and written informed consent was obtained from each patient before the initiation of the treatment.

The inclusion criteria are patients with nasopharyngeal cancer (hypopharynx, oropharynx, and larynx) that is locally advanced and node-positive; locally advanced larynx and node-positive supraglottic, subglottic, and transglottic; patients with oropharyngeal cancer (tongue, soft palate, tonsillar, paranasal sinuses), locally advanced and node-positive disease; oral cavity; and unknown primary, they will receive definitive radiation therapy with or without chemotherapy and any other locally advanced head and neck cancer that is node-positive. The positive node means (N2, N3), and the locally advanced tumor means (T3, T4). While female participants who are pregnant or breast-feeding, participants who are not able to comply with study and/or follow-up procedures, or had prior head and neck radiation therapy, patients with metastatic disease, stage I nasopharyngeal cancer and node-negative, stage I and II larynx cancer and glottic larynx, other head and neck cancer like parotid cancer, lip cancer, thyroid cancer, or had node-negative disease in general, were excluded from the study.

The 3D anatomical images of the patients were acquired using Siemens' SOMATOM DEFINITION CT scanners, named Initial Treatment Planning (ICT). The CT slices that were produced were 2 millimeters thick. The treatment planning for all patients was generated using dynamic intensity-modulated radiation therapy (D-IMRT) utilizing Monaco version 5.11.02 manufactured by Elekta, Sweden. The treatment planning follows the guidelines provided by RTOG 1016 for the defined tumour volumes (GTV, CTV, and PTV) and organs at risk (OAR). A linear accelerator was used to provide radiation to the subjects, while they were secured in place utilizing a head-step shoulder system and five-point thermoplastic masks.

Radiation oncologists use the delineation technique to identify affected organs and treatment regions, with a median dosage per portion of 2 Gy. The recommended total dose for gastrointestinal tracts (GTVs) ranges between 1.64 and 2.12 Gy. The decision-making process involves evaluating tumor characteristics, risk classification, treatment goals, healthy tissue constraints, radiation methodologies, patient characteristics, evidence-based suggestions, and interdisciplinary collaboration. Tumors are classified as high-risk, intermediate-risk, or low-risk based on histology, histological characteristics, stage, and poor prognostic indicators, determining appropriate therapeutic doses.

Doses were recommended for low-risk 54Gy, intermediate-risk 60Gy, high-risk CTV, and GTV 70Gy.

According to the IGRT standard, expanding the CTV by 3 mm will result in the plan target volume (PTV). These doses were split into 33 fractions. Rescanning, re-delineation, and replanning were repeated once every 7 fractions for each patient, which means that after 7, 14, and 21 fractions, IMRT plans generated using seven beams were evenly spaced to compose the treatment plans with Monte Carlo algorithmic calculations. The plan isocenter was positioned in the center of the PTV. For OARs, physical cost functions were employed for target volume optimization. In contrast, biological dose-volume histogram (DVH) parallel cost functions were used for dose constraint optimisation, the optimisation aimed to achieve target coverage while controlling dose gradients inside essential structures. A head mask made from plastic was applied to the patient's head for fixation purposes. The evaluation of the plan quality was performed mainly by the conformity index (CI) and homogeneity index (HI), as shown in Equations (1) and (2), respectively:[15]

$$CI = \frac{V_{PTV} \times V_{TV}}{TV_{PV}^{2}} \tag{1}$$

V_{PTV} stands for volume of PTV, V_{TV} means volume of the actual prescribed dose, and TV_{PV} is for volume of V_{PTV} inside V_{TV}. According to the literature, CI = 1 is the sweet spot for treatment compliance.[16]

$$HI = \frac{D2\% - D98\%}{D50\%} \tag{2}$$

When the homogeneity index (HI) is zero, the absorbed doses in different fractions of the isodose lines are D2%, D98%, and D50 %, respectively. This points to a very uniform distribution of the absorbed dose.[16] The statistical analysis was performed using SPSS 28. A one-way ANOVA test is used to compare three or more groups of variables. Student-paired T-test was used to compare two dependent variables. Pearson correlation and regression curves test the correlation between the two variables. The results are considered significant if the *P*–value is ≤ 0.05.

Results

The characteristics of the patients were laterality and TN staging. Six patients (8%) showed unilateral tumours, while 30 (92%) patients had bilateral HNSCC tumours. The patients distributed to the clinical T stage are 1 (3%) for T1, 6 (17%) for T2, 19 (53%) for T3, and 10 (28%) for T4. N staging shows that 16 (44%) of the patients were N0, while both N1 and N2 were 10 (28%) equally, as shown in Table 1.

The Volume Change in the PTV

The results of volumetric changes of the planning target volume (PTV) from initial CT planning and after 7, 14, and 21 fractions of the IMRT treatment were illustrated in Table 2. The statistical analysis shows a highly significant decrease in tumour PTV as a response to the adaptive radiotherapy technique during the treatment fractions.

The mean volumetric differences of the planning target volume (PTV) before the treatment (ICT) were compared with the volumes after 7, 14, and 21 fractions and tabulated in Table 2. The proposed strategy of replanning indicated that after 21 fractions, there was the highest difference in volumetric shifting of PTV, followed by a decrease at fractions 14 and 7, respectively. This decrease was clear during the treatment, as shown in Figure 1.

An evaluation of the volumetric changes in the figure shows that all stages of replanning have significant changes, as the *P*-value is less than 0.05. Statistically, the standard deviation was high because the data was more spread out around the mean (the patients' PTV volumes varied widely).

When adaptive techniques are used in radiation therapy, changes in the patient's response or changes in their anatomy mean that the planning target volume (PTV) changes over time. This makes the shifting difference in the PTV very important. The results in Table 3 show a gradual increase in shifting differences in the PTV during the three times of replanning; the highest shifting was after 21 fractions, and then after fractions 14, and 7, respectively. The evaluation of the shifting differences in the PTV leads to the precise delivery of the planned dose while reducing the possibility of underdosing the target or overdosing normal tissues.

Table 1. **The percentage of patient distribution of T-stage, and the percentage of patient distribution of N-stage**

T - Staging	Patient no. (%)	N- Staging	Patient no. (%)
T1	1 (3%)	N0	16 (44%)
T2	6 (17%)	N1	10 (28%)
T3	19 (53%)	N2	10 (28%)
T4	10 (28%)		

T1, T2, T3, T4: refer to the volume of the primary tumour. A higher numerical value after the T indicates a larger tumour size or a greater extent of infiltration into adjacent tissues. N0: There is an absence of malignancy in the lymph nodes located nearby. N1, N2, N3: refer to the location and number of cancer-involved lymph nodes. The greater the numerical value after the N, the bigger the number of lymph nodes affected by malignancy.

Table 2. **The planning target volume (PTV) at initial CT planning and at replanning after 7, 14, and 21 fractions**

PTV	Mean ± Std	95% confidence interval for mean		Minimum	Maximum	*P*-value
		Lower bound	Upper bound			
Initial planning PTV (cm^3)	202.74 ± 188.44	138.98	266.50	21.39	1056.38	0.0367^*
PTV after 7 fractions (cm^3)	171.68 ± 182.26	110.01	233.34	19.79	1023.81	
PTV after 14 fractions (cm^3)	149.33 ± 174.62	90.25	208.42	12.93	980.17	
PTV after 21 fractions (cm^3)	133.39 ± 152.44	81.81	184.97	12.76	801.62	

*One-way ANOVA test is significant at *P* – *P*-value level ≤ 0.05. Std, Standard deviation.

Conformity Index (CI) and Homogeneity Index (HI)

The quality of the plan evaluated in this study is conformity index (CI) and homogeneity index (HI). The value of the conformity index (CI) of initial CT planning before fractions was compared with Adaptive IMRT therapy after 7, 14, and 21 fractions, as shown in Table 4. The analysis indicates high conformity index changes before and after the adaptive replanning. The better replanning achieves a good CI after 14 fractions, even better than the initial CT planning, followed by CI after 7 and 21, respectively. No significant difference was observed for the conformity index (CI).

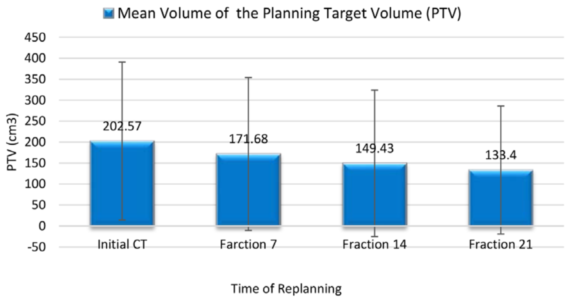


Fig. 1 **The comparison between the planning target volume (PTV) at initial CT planning and the replanning after 7, 14, and 21 fractions.**

The homogeneous dose distribution to the PTV was calculated in initial CT planning and after every planning and presented in Table 5. There was a highly significant difference in HI values between the initial planning and fractions after adaptive replanning. The analysis shows that the best HI of the planning was acquired after 21 fractions, followed by planning after 7 fractions.

A comparative analysis of CI and HI was performed between the initial CT planning and each replanning after 7, 14, and 21 treatment fractions, as presented in Table 6. The results show an important homogeneity index (HI) difference between the initial CT planning and after 7 and 21 fractions. The difference after 21 fractions is higher than after 7 fractions.

The Correlation Between the Volumetric Changes of PTV and the Parameters of Plan Quality (HI and CI)

A regression curve was estimated to test the correlation between the effect of volumetric changes of planning target volume of the tumour and the results parameters of plan quality (HI and CI). For CI, the analysis shows a positive correlation after 7 fractions with the mean difference of PTV, while a negative correlation was observed after 14 and 21 fractions, as shown in Figure 2. The positive relationship represents that when the reduction in PTV increases, a more conformal plan will be achieved. In contrast, the negative relationship means that when the difference of volumetric changes increases, the

Table 3. **Mean shifting difference of planning target volume (PTV) at initial CT planning and replanning after 7, 14, and 21 fractions**

PTV difference	**Mean ± Std**	**95% confidence interval for mean**		**Minimum**	**Maximum**	***P*-value**
		Lower bound	**Upper bound**			
PTV after 7 fractions (cm^3)	31.06 ± 28.84	21.30	40.82	–.96	113.66	<0.001*
PTV after 14 fractions (cm^3)	53.40 ± 35.15	41.51	65.29	6.70	147.53	
PTV after 21 fractions (cm^3)	68.69 ± 52.60	50.41	86.98	2.97	254.76	

*One-way ANOVA test is significant at *P* – *P*-value level ≤ 0.05. Std, Standard deviation.

Table 4. **Conformity Index (CI) values at initial CT planning and replanning after 7, 14, and 21 fractions**

CT planning	**Mean ± Std**	**95% confidence interval for mean**		**Minimum**	**Maximum**	***P*-value**
		Lower bound	**Upper bound**			
Initial planning	1.07 ± 0.02	1.07	1.08	1.04	1.13	0.524*
After 7 fractions	1.08 ± 0.04	1.06	1.10	1.01	1.28	
After 14 fractions	1.07 ± 0.07	1.04	1.10	1.01	1.49	
After 21 fractions	1.10 ± 0.16	1.05	1.16	1.02	2.01	

*One-way ANOVA test is significant at *P* – *P*-value level ≤ 0.05. Std, Standard deviation.

Table 5. **Homogeneity Index (HI) values at initial CT planning and replanning after 7, 14, and 21 fractions**

CT planning	**Mean ± Std**	**95% confidence interval for mean**		**Minimum**	**Maximum**	***P*-value**
		Lower bound	**Upper bound**			
Initial planning	0.75 ± 0.15	0.69	0.80	0.17	0.90	<0.001*
After 7 fractions	0.69 ± 0.17	0.64	0.75	0.24	0.92	
After 14 fractions	0.71 ± 0.15	0.66	0.76	0.30	0.89	
After 21 fractions	0.68 ± 0.16	1.05	1.16	1.02	2.01	

*One-way ANOVA test is significant at *P* – *P*-value level ≤ 0.05. Std, Standard deviation.

CI value decreases. No significant effect was demonstrated in CI with PTV difference.

In Figure 3, we plotted regression curves of the Homogeneity Index (HI) against the variations in volumetric changes of the Planning Target Volume (PTV). Our analysis revealed distinct patterns: a positive correlation between HI and PTV volumetric changes was observed after 7 and 14 fractions, indicating that an increase in volumetric changes corresponded to improved homogeneity. However, after 21 fractions, a negative correlation emerged, suggesting that further volumetric changes led to a decline in homogeneity. These findings underscore the dynamic relationship between PTV changes and homogeneity throughout the course of treatment.

Table 6. **Comparison of homogeneity and conformity indexes between the initial CT planning and replanning after 7, 14, and 21 fractions of treatment**

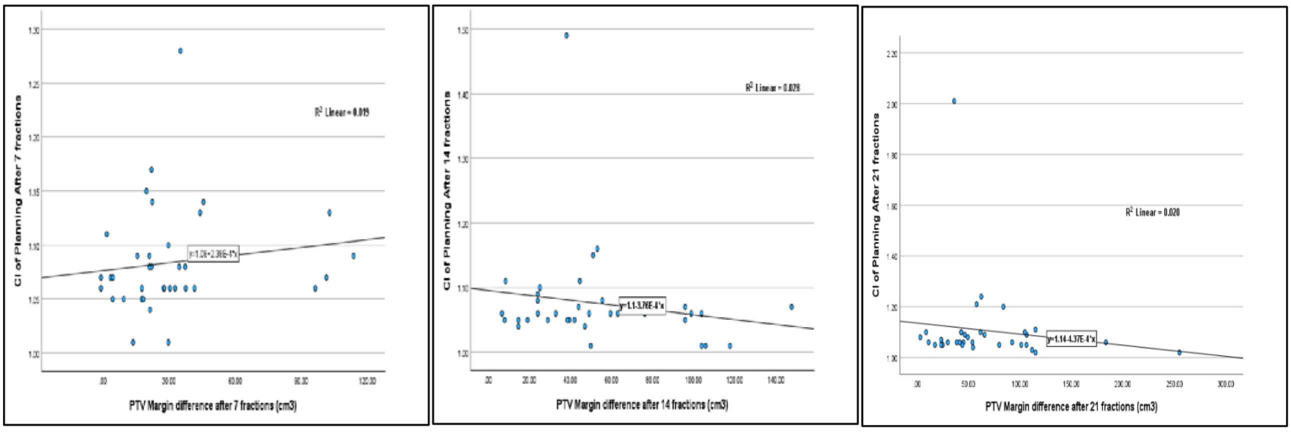
	Conformity Index (CI)	Homogeneity Index (HI)
After 7 fractions	0.249	0.048*
After 14 fractions	0.418	0.063
After 21 fractions	0.166	0.006*

*Paired T-Test is significant at *P* – *P*-value level ≤ 0.05.

Discussion

Demography

This study examines the plan's quality by evaluating the relationship between the conformity index (CI) and the homogeneity index (HI) in adaptive radiotherapy. It uses patient characteristics like TN staging and laterality to understand treatment response. Results show bilateral HNSCC tumors are more common, consistent with real-life cases. The TN staging shows a wide range of stages, with a significant portion falling into the T3 group. This study sheds light on the nuances of treatment response. There was a wide range of clinical outcomes among the patients in the research group, as shown by the fact that a significant proportion of patients were classified as N0 according to the distribution of nodal staging (N staging). Gugić et al. (2013)[17] and Huang et al. (2010)[18] performed investigations that revealed that the

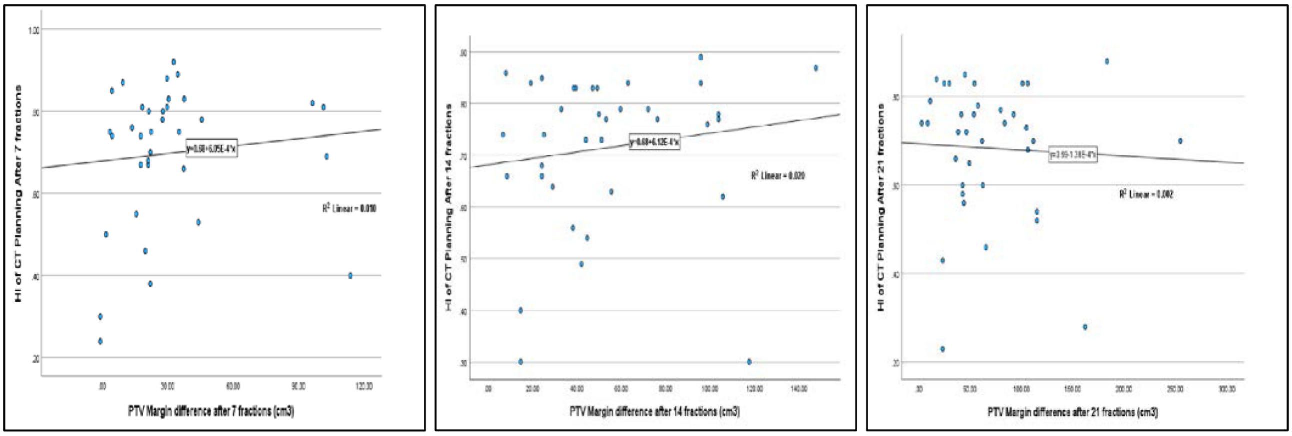


a. r **= 0.456,** ***p*****-value =0.005**

b. r **= 0.165,** ***p*****-value =0.335**

c. r **= -0.059,** ***p*****-value =0.732**

Fig. 2 **Regression curve between conformity index (CI) and PTV margin differences after (a) 7 fractions, (b) 14 fractions, and (c) 21 fractions.**



a. r **= 0.169,** ***p*****-value =0.323**

b. r **= -0.119,** ***p*****-value =0.489**

c. r **= -0.101,** ***p*****-value =0.557**

Fig. 3 **Regression curve between Homogeneity index (HI) and PTV margin differences after (a) 7 fractions, (b) 14 fractions, and (c) 21 fractions.**

typical head and neck cancers are characterized by a preponderance of bilateral head and neck squamous cell carcinomas (HNSCC) (92%). On top of that, to obtain optimum coverage, cancers that have migrated to other areas of the body often need a treatment strategy that is more complex and flexible. In addition, there is a discernible presence in the T3 and T4 stages, which is indicative of the presence of advanced medical disorders. Furthermore, the distribution of the tumor throughout clinical T stages is correlated to the extent to which the tumor has developed. Given the complexity of these circumstances, volumetric change patterns and plan quality may be affected.

Volume Reduction of (PTV)

Adaptive radiotherapy significantly decreased the tumor's planned target volume (PTV) during treatment fractions, demonstrating its ability to adapt to changing anatomical conditions. This dynamic response across all treatment fractions demonstrates the radiation technique's adaptability. Factors such as treatment-induced side effects, tumor regression, and architectural modifications could affect this response. The cumulative impact, as seen in volumetric displacement after 21 fractions, may be due to increasing changes in the tumor and surrounding tissues.

De Lamarliere et al.'s[19] research on Adaptive IMRT for extremity soft tissue sarcoma (ESTS) tomotherapy before tumor removal surgery found significant changes in tumor volume in all 17 patients. The study used patents to record volume and dosimetric data, with adaptive IMRT running once a week. Due to departmental practice constraints, seven patients' plans had to be altered, as 18% of the patients had substantial reductions in tumor dosage coverage. The researchers concluded that volume change monitoring is crucial, and adaptive IMRT was used to estimate gross tumor volume and identify patients requiring treatment rescheduling, especially during the first two weeks of treatment.

Homogeneity Index (HI) and Conformity Index (CI)

The plan's quality was assessed using CI and HI indices, showing a significant improvement in conformance index (CI) after 14 treatment fractions compared to the original CT planning. This finding suggests that subsequent to replanning, the adaptive IMRT approach effectively improved conformity to the destination volumes. Conversely, distinct patterns were seen in the HI values; seven fractions of replanning produced the most favourable uniformity, highlighting the dynamic nature of the treatment response. The reduction shown after 21 fractions of replanning may have been influenced by accumulating anatomical changes. However, the optimal HI indicated after 21 fractions may have been the result of an early adjustment phase.

Our results on the significance of CI and HI indices for assessing plan quality are consistent with those of Patel et al.[20] and Huang et al. 2015.[21] Patel et al[20] conducted a study in Adaptive IMRT that highlights the dynamic nature of plan evaluation indicators, including the gradient index (GI), conformity index (CI), and homogeneity index (HI). The researchers observed a significant enhancement in the CI after 14 fractions, while in our investigation, the homogeneity index (HI) significantly varied between seven and twenty-one fractions in this study's comparison of the initial CT planning to each successive replanning. This observation demonstrated the variation in dosage homogeneity across the treatment programme. Plan conformance is enhanced by a reduction in PTV, as shown by the detected positive connection between CI and the mean difference in PTV after seven fractions. However, when the differences in volumetric changes rise, CI decreases, as seen by the negative connection between 14 and 21 fractions. Consequently, adaptive approaches are essential.

By displaying the association between HI and volumetric changes in PTV using regression graphs, the effect of adaptive approaches on dose homogeneity may be better comprehended. According to the link between fractions 7 and 14, an increase in volumetric changes results in a corresponding enhancement in the homogeneity. Still, the inverse correlation found after 21 fractions suggests a possible break from this pattern, calling for more research into the basic processes that cause the changes that have been seen. An approximate finding was shown by Hang et al.[21] who conducted a study to determine the optimal time for replanning adaptive IMRT for nasopharyngeal carcinoma (NPC). They studied changes in target volumes and organs at risk (OARs) during intensity-modulated radiation therapy (IMRT) using CT scans. They found that parotids, implicated lymph nodes, and gross target volume decreased during therapy. The study also found significant advances in dosimetric parameters, such as mean dose, dosage to 95% of volume, percentage of volume getting 95% of the prescribed dose, and conformity index, starting with the 10th fraction.

However, PTV2's dosimetric characteristics remained mostly constant, with some improvements at specific time intervals. The study also highlighted the importance of vigilantness to avoid overdose in vital structures, even if hybrid plans did not compromise goal dosage coverage. They concluded that replanning at the 5th and 15th fractions to successfully handles substantial dosimetric changes.

Significance and the Importance of this Study

The significance of this study shows that Adaptive IMRT is effective in improving treatment conformance and homogeneity by dynamically adjusting treatment plans to tumor size and shape changes during therapy. This is the first study to offer an understanding of the complex relationship between adaptive radiotherapy, volumetric changes in the planning target volume (PTV), and indices that measure the quality of treatment plans. The findings emphasise the need for continuous adjustment to get the best possible coverage of the target area. They also draw attention to the potential complications in the connection between changes in volume and the quality of the treatment plan during the treatment process. According to our knowledge, no previous publication involves the quality of the plan or compares it with the change in PTV for adaptive IMRT. Additional studies and future studies are necessary to confirm and enhance these findings, eventually progressing the area of adaptive radiation for enhanced patient results.

Conclusion

In conclusion, our study contributes a unique perspective on the interplay between adaptive radiotherapy, volumetric changes in PTV, and plan quality metrics. The study shows that the homogeneity index (HI) is mainly affected by the PTV shifting during the radiotherapy fractions, especially after the 7th and 21st fractions. These findings underscore the need for ongoing adjustments to optimize target coverage, emphasizing the potential complexities in the relationship between volume changes and treatment plan quality. While acknowledging the study's limitations, this research lays the groundwork for future investigations to refine adaptive radiation strategies and enhance patient outcomes.

Acknowledgement

The authors express their gratitude to the Department of Oncology staff for their unwavering assistance and attentiveness, as well as to all the patients who participated in the study.

Conflicts of Interest Disclosure

All authors declare that there are no conflicts of interest.

References

1. Jubbier ON, Abdullah SS, Alabedi HH, Alazawy NM, Al-Musawi MJ. The Effect of Modulation Complexity Score (MCS) on the IMRT Treatment Planning Delivery Accuracy. J Phys Conf Ser. 2021 Apr 7;1829(1):12017.
2. Hameed DD, Abdulhakeem VH, Madlool SA, Ali NM, Salih DA, Mohammed FJ. The efficiency of Intensity Modulated Radiation Therapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) in bone marrow of lumber spinal cord tumor radiotherapy. Onkologia i Radioterapia. 2023;17(9):290–7.
3. Chen AM, Farwell DG, Luu Q, Donald PJ, Perks J, Purdy JA. Evaluation of the planning target volume in the treatment of head and neck cancer with intensity-modulated radiotherapy: What is the appropriate expansion margin in the setting of daily image guidance? Int J Radiat Oncol Biol Phys. 2011;81(4):943–9.
4. Hong TS, Ritter MA, Tomé WA, Harari PM. Intensity-modulated radiation therapy: Emerging cancer treatment technology. British Journal of Cancer. 2005;92(10):1819–1824.
5. Jubbier ON, Abdullah SS, Alabedi HH, Alazawy NM, Al-Musawi MJ. The Effect of Modulation Complexity Score (MCS) on the IMRT Treatment Planning Delivery Accuracy. J Phys Conf Ser [Internet]. 2021;1829(1):12017. Available from: https://dx.doi.org/10.1088/1742-6596/1829/1/012017.
6. Grégoire V, Guckenberger M, Haustermans K, Lagendijk JJW, Ménard C, Pötter R, et al. Image guidance in radiation therapy for better cure of cancer. Molecular Oncology. 2020;14(7):1470–1491.
7. Rehman J ur, Zahra, Ahmad N, Khalid M, Noor ul Huda Khan Asghar HM, Gilani ZA, et al. Intensity modulated radiation therapy: A review of current practice and future outlooks. J Radiat Res Appl Sci. 2018;11(4):361–7.
8. van Timmeren JE, Chamberlain M, Bogowicz M, Ehrbar S, Dal Bello R, Schüler HG, et al. MR-guided adaptive radiotherapy for head and neck cancer: Prospective evaluation of migration and anatomical changes of the major salivary glands. Cancers (Basel). 2021;13(21):5404.
9. Figen M, Çolpan Öksüz D, Duman E, Prestwich R, Dyker K, Cardale K, et al. Radiotherapy for Head and Neck Cancer: Evaluation of Triggered Adaptive Replanning in Routine Practice. Front Oncol. 2020;10:579917.
10. Burnet NG, Thomas SJ, Burton KE, Jefferies SJ. Defining the tumour and target volumes for radiotherapy. Cancer Imaging. 2004;4(2):153–61.
11. Noble DJ, Yeap PL, Seah SYK, Harrison K, Shelley LEA, Romanchikova M, et al. Anatomical change during radiotherapy for head and neck cancer, and its effect on delivered dose to the spinal cord. Radiotherapy and Oncology. 2019;130:32–38.
12. Alves N, Dias JM, Rocha H, Ventura T, Mateus J, Capela M, et al. Assessing the need for adaptive radiotherapy in head and neck ancer patients using an automatic planning tool. Reports of Practical Oncology and Radiotherapy. 2021;26(3):423–432.
13. Alabedi H. Assessing setup errors and shifting margins for planning target volume in head , neck , and breast cancer. J Med Life. 2023;16(3):394–8.
14. Kanakavelu N, Samuel JJ. Determination of patient set-up error and optimal treatment margin for intensity modulated radiotherapy using image guidance system. Journal of BUON. 2016;21(2):505–11.
15. Madlool SA, Abdullah SS, Alabedi HH, Alazawy N, Al-Musawi MJ, Saad D, et al. Optimum Treatment Planning Technique Evaluation For Synchronous Bilateral Breast Cancer With Left Side Supraclavicular Lymph Nodes. Iranian Journal of Medical Physics [Internet]. 2021;18(6):414–420. Available from: https://ijmp.mums.ac.ir/article_16970.html
16. Prescribing, Recording, and Reporting Photon-Beam Intensity-Modulated Radiation Therapy (IMRT): J ICRU. 2010;10(1):NP-NP.
17. Gugić J, Strojan P. Squamous cell carcinoma of the head and neck in the elderly. Reports of Practical Oncology and Radiotherapy. 2013;18(1):16–25.
18. Huang S, Goldstein D, Weinreb I, Perez-Ordonez B, Fung S, Irish J, et al. Positive Postradiotherapy Planned Neck Dissection is Strongly Associated with Increased Distant Metastasis Rather Than Regional Relapse. International Journal of Radiation Oncology Biology Physics. 2010;78(3):S454.
19. De Lamarliere MG, Lusque A, Khalifa JA, Esteyrie V, Chevreau C, Valentin T, et al. Management of tumor volume changes during preoperative radiotherapy for extremity soft tissue sarcoma: a new strategy of adaptive radiotherapy. Radiol Oncol. 2023 Dec;57(4):507–15.
20. Patel G, Mandal A, Choudhary S, Mishra R, Shende R. Plan evaluation indices: A journey of evolution. Vol. 25, Reports of Practical Oncology and Radiotherapy. Urban and Partner; 2020. p. 336–44.
21. Huang H, Lu H, Feng G, Jiang H, Chen J, Cheng J, et al. Determining appropriate timing of adaptive radiation therapy for nasopharyngeal carcinoma during intensity-modulated radiation therapy. Radiation Oncology. 2015;10(1):192.