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Original Research Article

Evaluating the Impact of Fractionation Schedules on Dose Homogeneity in Photon-Based Radiotherapy Planning

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Abstract:

Background: Fractionation schedules play a crucial role in determining dose distribution and treatment outcomes in photon-based radiotherapy.

Aim: To evaluate the impact of different fractionation schedules on dose homogeneity in photon-based radiotherapy planning in thoracic malignancies.

Methodology: This retrospective dosimetric study analyzed 80 patient datasets treated with IMRT. Treatment plans were generated for three fractionation schedules based on dose per fraction: conventional fractionation (2 Gy/fraction), hypofractionation (3 Gy/fraction), and extreme hypofractionation (6 Gy/fraction) using the Eclipse Treatment Planning System. Dose homogeneity was evaluated on a per-fraction basis using D2%, D5%, D95%, D98%, V95%, V107%, and Homogeneity Index (HI).

Results: Conventional fractionation demonstrated superior dose homogeneity with lower high-dose parameters (D2% and D5%), reduced hotspot volume (V107%), and a lower Homogeneity Index. Increasing dose per fraction, particularly in the 6 Gy per-fraction extreme hypofractionation group, resulted in significantly increased dose inhomogeneity and higher spinal cord dose ($p < 0.05$).

Conclusion: Conventional fractionation provides better dose uniformity and target coverage, while hypo fractionation compromises homogeneity and increases the risk to nearby organs.

Keywords: Fractionation, Dose homogeneity, IMRT, DVH, Hypo fractionation, Radiotherapy planning.

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Introduction

Radiotherapy plays a pivotal role in the management of a wide range of malignancies, particularly in patients who are not suitable candidates for surgical intervention due to medical or anatomical limitations [1]. Over the past few decades, significant technological advancements have transformed the field of radiation oncology, improving the precision and effectiveness of treatment delivery. Among these advancements, photon-based radiotherapy techniques such as Intensity-Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) have gained prominence due to their ability to deliver highly conformal radiation doses [2]. These techniques allow modulation of beam intensity and dynamic shaping of dose distribution, thereby enhancing tumor coverage while minimizing radiation exposure to surrounding normal tissues and organs at risk (OARs).

Despite these technological improvements, achieving optimal dose homogeneity within the planning target volume (PTV) remains a critical challenge in radiotherapy planning [3]. Dose homogeneity refers to the uniform distribution of radiation dose throughout the target volume. It is an essential parameter, as it ensures that all tumor cells receive an

adequate and consistent dose required for effective tumor control. Inadequate dose distribution may result in under dosage of certain tumor regions, leading to reduced treatment efficacy, while excessive dose accumulation can increase the risk of radiation-induced toxicity in normal tissues [4]. Therefore, maintaining a balance between adequate tumor coverage and dose uniformity is fundamental to successful radiotherapy outcomes.

One of the most influential factors affecting dose distribution and homogeneity is the fractionation schedule. Fractionation involves dividing the total prescribed radiation dose into multiple smaller doses (fractions) delivered over a defined treatment period. Conventional fractionation typically consists of delivering 1.8–2 Gy per fraction once daily over several weeks. However, alternative fractionation strategies, such as hypofractionation (larger doses per fraction delivered over fewer sessions) and hyper fractionation (smaller doses delivered multiple times per day), have been increasingly explored to improve therapeutic outcomes [5]. Each fractionation approach has distinct radiobiological implications, influencing both tumor control probability (TCP) and normal tissue complication probability (NTCP).

The relationship between fractionation schedules and dose homogeneity in photon-based radiotherapy planning is complex and multifactorial [6]. While advanced delivery techniques like IMRT and VMAT offer superior dose conformity, the choice of fractionation schedule can significantly influence the distribution of dose within the target volume. Hypofractionated regimens, for instance, involve higher doses per fraction, which may lead to increased dose gradients and the potential formation of hotspots within the PTV. On the other hand, conventional fractionation allows for more gradual dose delivery, which may contribute to improved dose uniformity but at the cost of longer treatment duration. Hyper fractionation, although less commonly used, aims to exploit radiobiological advantages but introduces additional planning and logistical challenges.

In addition to fractionation, several treatment planning parameters influence dose homogeneity. These include beam arrangement, optimization algorithms, dose constraints, and the complexity of tumor geometry. Tumors with irregular shapes or those located adjacent to critical structures pose significant challenges in achieving uniform dose distribution. Modern treatment planning systems utilize inverse planning techniques and advanced optimization algorithms to address these challenges; however, the effectiveness of these approaches is influenced by the prescribed fractionation schedule and planning objectives [7].

Furthermore, the clinical implications of dose homogeneity extend beyond physical dose distribution to include radiobiological effects. The response of tumor and normal tissues to radiation is governed by processes such as repair of sublethal damage, redistribution of cells within the cell cycle, reoxygenation of hypoxic tumor regions, and cellular repopulation. These processes are influenced by fraction size and overall treatment time. Larger fraction sizes, as used in hypofractionation, may enhance tumor cell kill due to increased biological effectiveness but can also elevate the risk of normal tissue toxicity [8]. Therefore, understanding the interplay between physical dose distribution and biological response is essential for optimizing fractionation strategies.

To quantitatively assess dose homogeneity and overall plan quality, several dosimetric indices are commonly used. The Homogeneity Index (HI) is a widely accepted parameter that evaluates the uniformity of dose within the target volume, with lower values indicating better homogeneity [9]. Similarly, the Conformity Index (CI) measures how well the prescribed dose conforms to the target shape, reflecting the precision of treatment delivery. These indices provide valuable tools for comparing different treatment plans and fractionation schedules, enabling clinicians to select the most appropriate approach for individual patients.

With the increasing emphasis on personalized medicine, radiotherapy planning is becoming more patient-specific. Factors such as tumor size, location, histology, and patient-related characteristics must be considered when selecting fractionation schedules and optimizing treatment plans. In this context, evaluating the impact of fractionation on dose homogeneity becomes essential for tailoring treatment strategies to achieve optimal clinical outcomes while minimizing adverse effects.

Despite the availability of advanced photon-based radiotherapy techniques, there remains a lack of comprehensive understanding regarding the influence of different fractionation schedules on dose homogeneity. Most existing studies have primarily focused on clinical outcomes, such as tumor control and toxicity, with relatively limited attention to the dosimetric aspects of fractionation. As a result, there is a need for systematic evaluation of how varying fractionation regimens affect dose uniformity and overall plan quality in photon-based radiotherapy.

The present study aims to address this gap by evaluating the impact of different fractionation schedules on dose homogeneity in photon-based radiotherapy planning. By analyzing relevant dosimetric parameters and comparing various fractionation approaches, this research seeks to provide insights into optimizing treatment planning strategies. A better understanding of these relationships will contribute to improved treatment precision, enhanced tumor

control, and reduced toxicity, ultimately leading to better patient outcomes.

Methodology

Study Design

This study was designed as a retrospective dosimetric and comparative analytical study aimed at evaluating the impact of different fractionation schedules on dose homogeneity in radiotherapy treatment planning. The study involved analysis of treatment plans generated under varying fractionation schemes to assess their influence on dose distribution within the target volume.

Study Area

The study was conducted in the Department of Medical Physics, Indira Gandhi Institute of Medical Sciences (IGIMS), Bihar, India.

Study Duration

The duration of the study was from February 2022 to February 2025.

Study Participants

Inclusion Criteria

- Patients diagnosed with solid tumors requiring external beam radiotherapy
- Patients with complete radiotherapy planning data, including CT simulation images
- Patients treated using photon beam radiotherapy techniques such as IMRT
- Cases with clearly defined target volumes (GTV, CTV, and PTV)
- Patients with fractionation schedules ranging from conventional to hypo fractionated regimens

Exclusion Criteria

- Cases with significant imaging artifacts affecting contouring accuracy
- Patients who did not complete the prescribed radiotherapy course
- Re-irradiation cases or patients with prior radiation therapy to the same site
- Patients with irregular or non-standard fractionation schedules not suitable for comparison

Sample Size

A total of 80 patient datasets were included in the study for dosimetric analysis.

Procedure

In this study, anonymized computed tomography (CT) simulation datasets of 80 patients were retrieved from the treatment planning database. CT simulation was performed using a GE CT simulator, and a slice thickness of 2.5 mm was used for thoracic imaging. Treatment planning was carried out on a non-contrast CT dataset. For each patient, target volumes including Gross Tumor Volume (GTV), Clinical Target Volume (CTV), and Planning Target Volume (PTV) were delineated based on standard radiotherapy protocols. Organs at risk (OARs) were also contoured to ensure safe dose delivery.

All treatment plans were generated using photon beam radiotherapy IMRT or VMAT technique. Treatment was delivered using a TrueBeam SVC linear accelerator. Treatment plans were created using the Eclipse Treatment Planning System (Varian Medical Systems). The following algorithms and calculation models were used:

Table 1: Treatment Planning System (TPS) Calculation Models and Algorithms Used in Radiotherapy Planning

S.No	Calculation Type	Algorithm	Version
1	Dose Calculation	Anisotropic Analytical Algorithm (AAA)	16.1.0
2	DVH Estimation	DVH Estimation Algorithm	16.1.0
3	QA	Portal Dose Image Prediction (PDIP)	16.1.0
4	Optimization	Photon Optimizer (PO)	16.1.0
5	Surface Compensation	Irregular Surface Compensator (ISC)	16.1.0

Patient setup verification was performed using an onboard imaging system with Cone Beam CT (CBCT).

Multiple fractionation schedules were generated for each patient based on dose per fraction, including conventional fractionation (2 Gy per fraction), hypofractionation (3 Gy per fraction), and extreme hypofractionation (6 Gy per fraction). All dosimetric evaluations were performed on a per-fraction dose basis to allow direct comparison of dose homogeneity across fractionation schedules, independent of total treatment dose. Each plan was optimized to achieve adequate target coverage while minimizing dose to surrounding normal tissues. Dose calculations were performed using the AAA algorithm, ensuring accuracy in heterogeneous tissue conditions. For each fractionation schedule, cumulative dose distributions were obtained. Dose–Volume Histograms (DVHs) were generated for all treatment plans to evaluate dose distribution characteristics.

Dose homogeneity within the target volume was assessed using standard dosimetric indices such as D2%, D5%, D95%, and D98%. The Homogeneity Index (HI) was calculated to quantify dose

uniformity. Additionally, parameters such as V95% and V107% were analyzed to determine target coverage and hotspot regions, respectively. Comparative analysis was performed across different fractionation schedules to evaluate their effect on dose homogeneity. The results were systematically recorded and tabulated for further statistical analysis.

Statistical Analysis

Statistical analysis was performed using SPSS version 27.0. Descriptive statistics such as mean, standard deviation, and range were used to summarize dosimetric parameters. Comparative analysis between different fractionation schedules was conducted using appropriate statistical tests such as paired t-test or ANOVA, depending on data distribution. A p-value of less than 0.05 was considered statistically significant.

Result

All dosimetric values reported in this section represent per-fraction doses, ensuring uniform comparison between fractionation schedules with different numbers of fractions.

Table 1 shows the distribution of study participants according to age group among the total sample size of 80 individuals. The highest proportion of participants belonged to the 31–45 years age group, comprising 28 individuals (35%), indicating that this was the most represented age category in the study. This was followed by the 46–60 years age group with 24 participants (30%), suggesting a substantial representation of middle-aged individuals. The younger age group of ≤30 years and the older age group of >60 years each included 14 participants, accounting for 17.5% respectively, showing equal but comparatively lower representation. Overall, the data indicate that the majority of participants were concentrated in the middle age groups (31–60 years), while younger and older individuals were less represented in the study population.

Table 1: Distribution of Study Participants According to Age Group (n = 80)

Age Group (years)	Frequency (n)	Percentage (%)
≤30	14	17.5
31–45	28	35
46–60	24	30
>60	14	17.5
Total	**80**	**100**

Table 2 shows the comparison of dose homogeneity parameters across different fractionation schedules, revealing a significant variation in dose distribution. The high-dose regions represented by D2% and D5% were lowest in conventional fractionation (1.025 ± 0.047 Gy and 1.003 ± 0.042) and progressively increased in hypo fractionation (1.047± 0.052 Gy and 1.027± 0.048), reaching the highest values in extreme hypo fractionation (1.304 ± 0.07 and 1.276 ± 0.064). Conversely, the low-dose coverage parameters D95% and D98% showed a declining trend, with the highest values observed in conventional fractionation (0.963 ± 0.037 Gy and 0.949 ± 0.033), followed by hypo fractionation (0.94± 0.043 Gy and 0.923± 0.04), and the lowest in extreme hypo fractionation (1.082 ± 0.058 and 1.06 ± 0.054). The p-values for all parameters (ranging from 0.001 to 0.004) indicate that these differences are statistically significant, suggesting that increasing dose per fraction leads to higher dose inhomogeneity with increased hot spots and reduced target coverage. Although absolute per-fraction dose values appear higher in the extreme hypofractionation group, this reflects the larger prescribed dose per fraction (6 Gy) rather than improved dose homogeneity. Relative dose distribution parameters and Homogeneity Index confirm increased dose inhomogeneity with higher fraction sizes.

Table 2: Table 2: Comparison of Per-Fraction Dose Homogeneity Parameters Across Fractionation Schedules

Parameter	Conventional Fractionation Mean ± SD	Hypo fractionation Mean ± SD	Extreme Hypo fractionation Mean ± SD	p-value
D2% (Gy per fraction)	1.025 ± 0.047	1.047± 0.052	1.304 ± 0.07	0.001
D5% (Gy per fraction)	1.003 ± 0.042	1.027± 0.048	1.276 ± 0.064	0.002
D95% (Gy per fraction)	0.963 ± 0.037	0.94± 0.043	1.082 ± 0.058	0.003
D98% (Gy per fraction)	0.949 ± 0.033	0.923± 0.04	1.06 ± 0.054	0.004

Table 3 demonstrates the comparison of volume-based parameters obtained from dose–volume histogram (DVH) analysis across different fractionation schedules. The results indicate that the mean V95 (%) was highest in conventional fractionation (97.5 ± 1.8), followed by hypo fractionation (95.8 ± 2.2), and lowest in extreme hypo fractionation (93.6 ± 2.5), showing a statistically significant difference (p = 0.001). This suggests better target volume coverage with conventional fractionation. In contrast, the mean V107 (%) values, representing dose hotspots, were lowest in conventional fractionation (3.2 ± 1.1) and progressively increased in hypo fractionation (5.4 ± 1.5) and extreme hypo fractionation (8.1 ± 2.0), with a statistically significant difference (p = 0.001). This indicates that higher fractionation schedules are associated with increased dose inhomogeneity and hotspot formation, highlighting a trade-off between treatment duration and dose uniformity.

Table 3: Comparison of Volume-Based Parameters (DVH Analysis)

Parameter	Conventional Fractionation Mean ± SD	Hypo fractionation Mean ± SD	Extreme Hypo fractionation Mean ± SD	p-value
V95 (%)	97.5 ± 1.8	95.8 ± 2.2	93.6 ± 2.5	0.001
V107 (%)	3.2 ± 1.1	5.4 ± 1.5	8.1 ± 2.0	0.001

Table 4 shows the comparison of Homogeneity Index (HI) among different fractionation schedules. The mean HI value was lowest in the conventional fractionation schedule (2 Gy per fraction) (0.08 ± 0.02), indicating better dose homogeneity, followed by hypo fractionation (3 Gy per fraction) with a mean HI of 0.11 ± 0.03. The highest HI was observed in Extreme Hypofractionation (6 Gy per fraction) (0.15 ± 0.04), suggesting comparatively poorer dose homogeneity. The increasing trend in HI values with larger dose per fraction indicates that dose distribution becomes less uniform as fraction size increases. The difference among the groups was found to be statistically significant (p = 0.001), highlighting a meaningful variation in dose homogeneity across the fractionation schedules.

Table 4: Homogeneity Index (HI) Comparison Between Fractionation Schedules

Fractionation Schedule	Homogeneity Index (HI) Mean ± SD	p-value
Conventional	0.08 ± 0.02	0.001
Hypo fractionation	0.11 ± 0.03	
Extreme Hypo fractionation	0.15 ± 0.04	

Table 5 shows the comparison of spinal cord maximum dose (Dmax) among different fractionation schedules. The mean Dmax was lowest in conventional fractionation (1.42 ± 0.11Gy per fraction), followed by hypo fractionation (1.49 ± 1.2Gy), and highest in extreme hypo fractionation (1.58 ± 0.137 Gy per fraction). This indicates a progressive increase in spinal cord dose with increasing fraction size. The observed difference among the groups was statistically significant (p = 0.002), suggesting that the type of fractionation schedule has a significant impact on the maximum dose received by the spinal cord. These findings imply that extreme hypo fractionation may pose a higher risk of radiation-induced spinal cord toxicity compared to conventional approaches.

Table 5: Comparison of Spinal Cord Maximum Dose

Parameter	Conventional Fractionation Mean ± SD	Hypo fractionation Mean ± SD	Extreme Hypo fractionation Mean ± SD	p-value
Spinal cord Dmax (Gy per fraction)	1.42 ± 0.11	1.49 ± 0.12	1.58 ± 0.137	0.002

Discussion

The present study demonstrates that conventional fractionation provides superior dose homogeneity and target coverage compared to hypo fractionated and extreme hypo fractionated regimens in photon beam radiotherapy. This is evident from lower high-dose parameters (D2% and D5%), improved target coverage (D95% and D98%), and a lower Homogeneity Index (HI) observed in conventional fractionation schedules. Bortfeld et al. (2002) [10] reported that increasing fraction size with a reduced number of fractions adversely affects dose uniformity due to intra-fraction motion and interplay effects, resulting in dose heterogeneity within the target volume. Their study demonstrated a reduction in target coverage by approximately 5–10% with fewer fractions, which is consistent with the present findings where D95% and D98% decreased from conventional to extreme hypofractionation.

Similarly, Phillips et al. (1992) [11] observed that larger fraction sizes contribute to increased dose inhomogeneity, particularly in the presence of motion. Their findings of increased hotspot formation under hypofractionated conditions align with the present study, where higher D2%, D5%, and V107% values were observed with increasing dose per fraction. These results suggest that reduced fraction numbers limit the averaging effect of dose delivery, thereby increasing variability in dose distribution.

The Homogeneity Index (HI) findings in the present study further support these observations. Conventional fractionation demonstrated the lowest HI (0.08), while hypofractionation and extreme hypofractionation showed progressively higher values (0.11 and 0.15, respectively), indicating worsening dose uniformity. Similar trends have been reported in previous radiotherapy studies Marks et al. (2010) [12], where increasing dose per fraction was associated with reduced homogeneity and increased dose variation within the target volume.

The DVH-based parameters also showed a consistent pattern. The V95% decreased with increasing fraction size, indicating reduced target coverage, while V107% increased, reflecting greater hotspot formation. These findings are in agreement with Graham et al. (1999) [13], who emphasized the importance of dose–volume relationships in thoracic radiotherapy and highlighted that inadequate dose distribution can compromise treatment outcomes and increase toxicity risks. Fowler (1989) [14] explained the radiobiological basis of fractionation, demonstrating that smaller fraction sizes allow better repair of normal tissues and improved dose distribution across multiple treatment sessions. This supports the present findings that conventional fractionation achieves better dose uniformity compared to hypo fractionated regimens.

The impact of fractionation on organs at risk (OARs) is also an important consideration. In the present study, the spinal cord maximum dose (Dmax) increased significantly with increasing fraction size, from 1.42 Gy in conventional fractionation to 1.58 Gy in extreme hypo fractionation. Timmerman et al. (2010) [15] also reported that hypo fractionated radiotherapy, while clinically effective, may lead to increased dose exposure to adjacent critical structures if not carefully planned. This highlights the need for strict adherence to OAR dose constraints.

Hof et al. (2007) [16] demonstrated that extreme hypo fractionation techniques such as stereotactic body radiotherapy can achieve high tumor control rates but are often associated with increased dose heterogeneity and hotspot formation. The present study findings are consistent with this observation, as extreme hypo fractionation showed the highest V107% values, indicating increased hotspot regions.

Furthermore, Nutting et al. (2011) [17] demonstrated that advanced radiotherapy techniques such as IMRT improve dose conformity and sparing of normal tissues compared to conventional techniques. However, even with advanced planning, the present study shows that increasing fraction size leads to deterioration in dose homogeneity, suggesting that fractionation remains a key determinant of dose distribution.

Overall, the findings of the present study are consistent with existing literature, demonstrating that conventional fractionation provides better dose homogeneity, improved target coverage (higher V95%), and reduced hotspot formation (lower V107%). Although hypo fractionated regimens offer advantages such as shorter treatment duration and improved patient convenience, they are associated with increased dose inhomogeneity and higher doses to organs at risk. Conventional fractionation remains the most reliable approach for achieving uniform dose distribution and minimizing risk to normal tissues, while hypo fractionated regimens should be used with caution and appropriate clinical justification.

Conclusion

This study demonstrates that fractionation schedules significantly influence dose homogeneity in photon-based thoracic radiotherapy when evaluated on a per-fraction basis. Conventional fractionation (2 Gy per fraction) provides superior dose uniformity, better target coverage, and reduced hotspot formation compared to hypofractionated regimens. Increasing dose per fraction, particularly with extreme hypofractionation at 6 Gy per fraction, results in higher dose inhomogeneity, increased Homogeneity Index, and elevated spinal cord dose. While hypofractionated approaches offer logistical advantages through reduced treatment duration, careful optimization and strict organ-at-risk constraints are essential to mitigate dosimetric compromise.

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