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Total Body Irradiation (TBI) Combining Step-And-Shoot Intensity Modulation (SS-IMRT) with Conformal 3-Dimensions (3DCRT) Radiotherapy

Hany Samy Attallah[1*], Khaled Mohamed El-Shahat[2], Radwa Mohamed Hamed[1], Emad Mostafa[3], Aliaa Mahmoud[1], Ibraheem Haggag[1], Taha Derfy[1], Haytham A. Abdelkader[4]

[1]Department of Radiation Oncology, International Medical Center, Cairo, Egypt
[2]Department of Clinical Oncology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[3]Department of Clinical Oncology, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[4]Department of Radiation Oncology, Helwan University, Cairo, Egypt
Email: *hanysamy2006@yahoo.com

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Abstract

Background: Total Body Irradiation (TBI) is integral to conditioning regimens for hematological malignancies, traditionally requiring complex and costly setups. This study introduces a simplified approach utilizing Step-And-Shoot Intensity Modulation (SS-IMRT) combined with Conformal 3-Dimensional Radiotherapy (3DCRT), aiming to maintain dosimetric rigor while enhancing practicality. **Methods:** The study retrospectively analyzed 27 patients treated with a novel TBI technique combining SS-IMRT and 3DCRT at the International Medical Center from January 2019 to July 2024. We focused on patient setup, equipment utilization, and dose distribution. SS-IMRT involves delivering radiation in segments with precise control, while 3DCRT shapes the radiation beam to conform to the shape of the target. Both methods leverage standard radiation therapy equipment without the need for specialized facilities. **Results:** The technique demonstrated precise control over the dose delivery with a mean Planning Target Volume (PTV) dose of 10.11 Gy, closely matching therapeutic targets with minimal specialized equipment. Critical organ doses were kept within safe limits, and effective management of overlapping fields at the pelvic matching volume highlighted the method's capability to mitigate over- or under-dosing risks. **Conclusion:** Combining SS-IMRT with 3DCRT simplifies the TBI process, reducing operational complexities and costs. This method offers a practical and effective alternative to traditional TBI techniques, enhancing accessibility and potentially improving patient outcomes across various clinical settings.

Keywords

TBI, SS-IMRT, Combined SS-IMRT/3DCRT

1. Introduction

Total Body Irradiation (TBI) is integral to conditioning regimens for hematological malignancies, typically used in conjunction with high-dose chemotherapy to prepare patients for Bone Marrow Transplantation (BMT). The inclusion of TBI offers distinct advantages over chemotherapy alone, particularly its ability to reach "sanctuary" sites like the central nervous system, testes, and orbits, which are less accessible to chemotherapeutic agents due to physiological barriers like blood supply, renal, and hepatic function [1] [2].

Historically, TBI required large treatment fields and often necessitated the use of custom blocks for the lungs to deliver radiation uniformly across the body. Such setups generally demanded that the patient be positioned at a significant distance from the radiation source—commonly around five meters—requiring sophisticated, costly equipment. Furthermore, the positions required for traditional TBI, such as standing or lying sideways, are particularly burdensome for immunocompromised patients, increasing the risk of discomfort and complications [3]. Innovations like the sliding floor table aimed to facilitate TBI administration but often required patients, including sedated pediatric patients, to assume prone positions, posing additional challenges and risks [4].

With the evolution of radiation therapy techniques, there has been growing interest in utilizing Step-And-Shoot Intensity Modulation (SS-IMRT), allowing for the delivery of TBI in a supine position using standard radiation therapy equipment. This approach not only enhances patient comfort but also simplifies the technical execution of TBI. Since 2019, the International Medical Center (IMC) has employed a novel technique combining SS-IMRT with Conformal 3-Dimensional Radiotherapy (3DCRT), which involves splitting the treatment volume into an upper half and a lower half around a defined pelvic mark [5]. This method allows for seamless integration of two radiation plans, delivering treatment in a more accessible, supine position without the need for specialized equipment or setups.

Despite these advancements, the generalizability of such simplified TBI techniques across different institutions could be influenced by factors such as the availability of specific technology, the expertise of the radiation therapy team, and institutional protocols, which might affect the replicability and outcomes of the method. As such, while our approach at IMC demonstrates potential benefits, similar results in other settings would depend on comparable resources and training [6]-[9].

2. Patient and Method

This study retrospectively analyzed the data of patients who underwent Total Body Irradiation (TBI) at our center from January 2019 to July 2024. Eligible participants included those who received TBI as part of their conditioning regimen for Bone Marrow Transplantation (BMT), targeting various hematological malignancies. The inclusion criteria were designed to select patients who were adult candidates for BMT, had complete medical records, and had undergone the full TBI regimen as planned without deviations.

The recruitment process involved identifying potential participants from our medical records database, followed by a detailed review of their treatment records to ensure they met the study criteria. This review was conducted by a team of clinical oncologists and radiation therapists who evaluated the suitability of each patient's data for inclusion based on the clarity of treatment documentation, completeness of dosimetric data, and adherence to the TBI protocol used in this study. A total of 27 patients' data were retrieved and included in the analysis, providing a comprehensive overview of the implementation and outcomes of the TBI technique.

2.1. Ethical Considerations

This review received approval from the International Medical Center Committee (Egypt Center of Research and Regenerative Medicine [E.C.R.R.M] under the Ministry of Defense) OHRP Reg. 1ORG0010559 - lRB000'12517. All these approvals adhered to the ethical standards established in the 1964 Declaration of Helsinki. All individuals provided informed consent before undergoing therapy.

2.2. Fixation and Scanning

Patients are simulated in supine position with head and neck custom-made mask. Both elbows were fixed to the body using a belt and both hands placed over external genitalia, as shown in **Figure 1**. For every patient, we performed two sets of CT simulation, corresponding to the two treatment plan orientations, revolving around the *pelvic mark* (the cephalic border of the acetabulum). The first CT scan includes the upper body: With a Head-first orientation, scan starts from head until at least a 5 cm caudal to the pelvic mark. The second CT scans, including the lower body: With a Feet-First orientation, scan starts from at least a 5 cm cephalic to the pelvic mark until end of the feet. Thus, a at least a 5 cm of overlap between the two scans are guaranteed for the dose calculation at the matching level of the upper body SS-IMRT plan and the lower body 3DCRT. No special equipment is needed for the processes.

2.3. PTV, OAR (Organs at Risk), Dose and Planning

The planning target volume (PTV), defined as the whole body, trimmed to 2.5 mm below the pores of the mask and skin with excluding the lungs and kidneys that are considered the organs at risk. We create two plans: 1) SS-IMRT for the upper half, with a head-first patient orientation, and 2) 3DCRT plan (AP-PA beam arrangement) to the lower half, with feet-first patient orientation. ***We create both plans in a supine position, at regular 100 cm SSD.*** Figure 2 shows the matching *pelvic volume.* The upper border of this matching volume corresponds to an imaginary horizontal line that passes just above the upper border of the alae of both ileac bone. While the lower border corresponds to an imaginary horizontal line that passes by the junction of the upper one third of both femuri with the lower two thirds. We executed the treatment planning via the Eclipse 15.6 platform (Varian Medical Systems, USA). At the IMC, we prescribe a total dose of 10 Gy in four fractions (once daily) to the PTV.

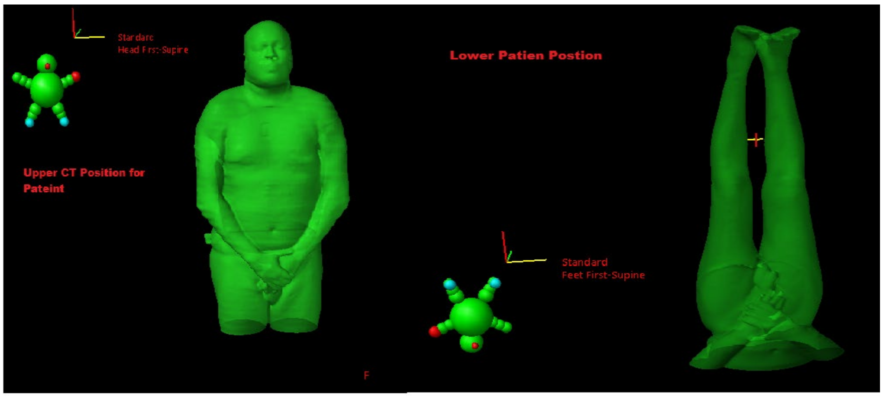

Figure 1. Simulation position.

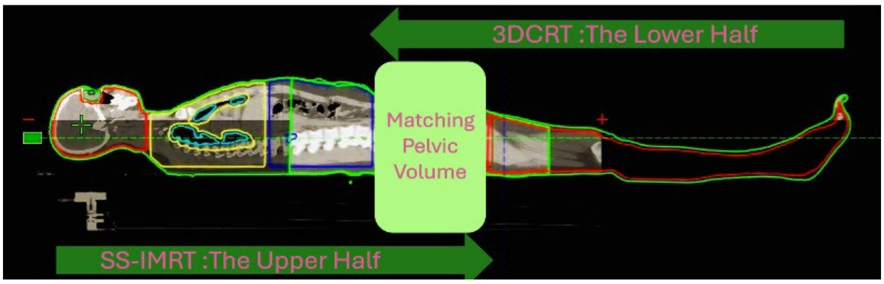

Figure 2. The matching pelvic volume.

2.4. Plan Goals

Table 1 shows the plan aims as compared to the published experience Rigshospitalet hospital and The Royal Marsden Hospital (RMH) [5]. We calculated the D2%, D98% and the mean dose to this match pelvic volume to assure avoiding the under- and over-dosing.

2.5. Treatment Planning and Optimization Details

In our study, we utilized the Eclipse 15.6 treatment planning system (Varian Medical Systems, USA) to devise and optimize two distinct plans for Total Body Irradiation (TBI): Step-And-Shoot Intensity Modulated Radiation Therapy (SS-IMRT) for the upper body and Conformal 3-Dimensional Radiotherapy (3DCRT) for the lower body.

Table 1. Plan aims.

	Rigshospitalet	The Royal Marsden	IMC Combined Technique	
			IMRT Upper Body	3DCRT Lower Body
Prescribed Dose	12 Gy (2 Gy 6 fr)	14.4 Gy (1.8 Gy 8 fr)	10 Gy (2.5 Gy 4 fr)	
PTV: D min	>90%	NA	>90%	The 95% of the prescribed dose covers 95% of the PTV.
PTV: D max	<110%	NA	<110%	
Body D min	>80%	>80%	>80%	>80%
Brain	V12 Gy < 5%	1) Dmin > 13 Gy (90%) 2)Dmean = prescription dose 3) Dmax < 15.8 Gy (110%)	Dmean = prescription dose	NA
Kidney mean dose	Between 10.2 and 12 Gy	Between 12 and 12.5 Gy, lower Preferred	Between 6-7 Gy	
Lens max	NA	NA	Less than 3 Gy	NA
Lung mean	As low as possible—it usually end up around 93% (11.3 Gy)	Between 12 and 12.5 Gy, lower preferred Usually 85% (12.24 Gy)	Less than 7.5 Gy	

2.6. IMRT Optimization Parameters

- **Objective:** Deliver a homogeneous dose distribution across the entire planning target volume (PTV) while minimizing dose to the organs at risk (OARs).
- **Constraints:**
  - **PTV:** The prescription was to ensure at least 95% of the PTV received no less than 90% of the prescribed dose (D95 ≥ 9 Gy) and the maximum dose (Dmax) did not exceed 110% (11 Gy).
  - **OARs (lungs, kidneys, brain):** Specific dose constraints were applied:
    - **Lungs:** Mean dose ≤ 8 Gy; V20 (volume receiving 20 Gy) kept under 15%.
    - **Kidneys:** Maximum dose < 12 Gy; at least 95% of each kidney received less than 10 Gy.
    - **Brain:** Maximum dose < 12 Gy to ensure protection of sensitive CNS structures.

2.7. IMRT Fields Configuration

- For the upper body, nine to eleven IMRT fields with multi-leaf collimator (MLC) adjustments were employed to modulate the dose distribution, using gantry angles from 0 - 360 degrees.
- **Energy and Dose Rate:** A fixed 6 MV photon beam was used, with a maximum dose rate of 600 MU (monitor units) per minute to maintain consistent radiation delivery.

2.8. 3DCRT Planning Parameters

- **Setup:** The lower body was treated with a straightforward AP-PA beam arrangement using a fixed jaw setting for a maximum field size of 28 × 28 cm, ensuring that the MLC leaves did not extend beyond the maximum jaw length, which aids in reducing radiation leakage.

2.9. Plan Verification

- All plans underwent a rigorous verification process using an Arc Check phantom equipped with a Sun Nuclear array. The verification focused on ensuring that the gamma pass rate met the criteria set by Low's approach (3% dose difference and 3 mm distance-to-agreement).

3. Results

In our study, we evaluated the dosimetric performance of the Total Body Irradiation (TBI) technique combining Step-And-Shoot Intensity Modulation (SS-IMRT) with Conformal 3-Dimensional Radiotherapy (3DCRT). The analysis included a total of 27 patients, and the results are presented with the mean dose, standard deviation (SD), and percentage of the prescribed dose (PD %). Table 2 shows the dosimetric analysis of the PTV, OAR and the matching pelvic volume.

Table 2. PTV, OAR and matching pelvic volume dosimetrics.

Volume	Dose Definition	Mean ± SD(Gy)	Percentage Dose
PTV	D mean	10.11 ± 0.14	101.12%
	D max	11.72 ± 0.63	117.19%
	D2% near max	10.96 ± 0.31	109.57%
	D50%	10.18 ± 0.10	101.81%
	D95%	9.16 ± 0.53	91.63%
	D98% near min	8.51 ± 0.73	85.05%
OAR	Lung Mean dose	8.41 ± 0.74	84.13%
	Lung D90	7.17 ± 0.98	71.70%
	Lung V10	10.33 ± 15.81	103.33%
	Kidney Mean dose	7.68 ± 0.56	76.85%
	Kidney Max. dose	10.62 ± 0.59	106.17%
	KidneyV10	5.67 ± 8.92	56.67%
	Kidney D5%	9.08 ± 75.19	90.8%
	Brain Mean dose	10.07 ± 0.12	100.66%
	Brain Max. dose (Gy)	10.51 ± 1.25	105.09%
	Rt Lens Max (Gy)	4.92 ± 0.85	49.17%
	Lt Lens Max (Gy)	4.89 ± 0.86	48.91%
Match Pelvic Volume	Mean Dose	10.42 ± 1.77	102.4%
	D98% near min	7.31 ± 1.73	73.1%
	D2% near max	12.23 ± 2.58	122.3%

3.1. Planning Target Volume (PTV) Doses

The mean dose delivered to the PTV was 10.11 ± 0.14 Gy, which corresponds to 101.12% of the prescribed dose, indicating effective coverage of the target volume. The maximum dose within the PTV was slightly higher, with a mean of 11.72 ± 0.63 Gy, or 117.19% of the prescribed dose, suggesting a hotspot within the target area. The doses near the maximum (D2%) and median (D50%) were 10.96 ± 0.31 Gy and 10.18 ± 0.10 Gy, respectively. The dose covering 95% of the PTV (D95%) was 9.16 ± 0.53 Gy, while the dose covering 98% (D98%) was lower, at 8.51 ± 0.73 Gy, reflecting 85.05% of the planned dose, indicating variability in dose homogeneity across the treatment volume (**Figure 3**).

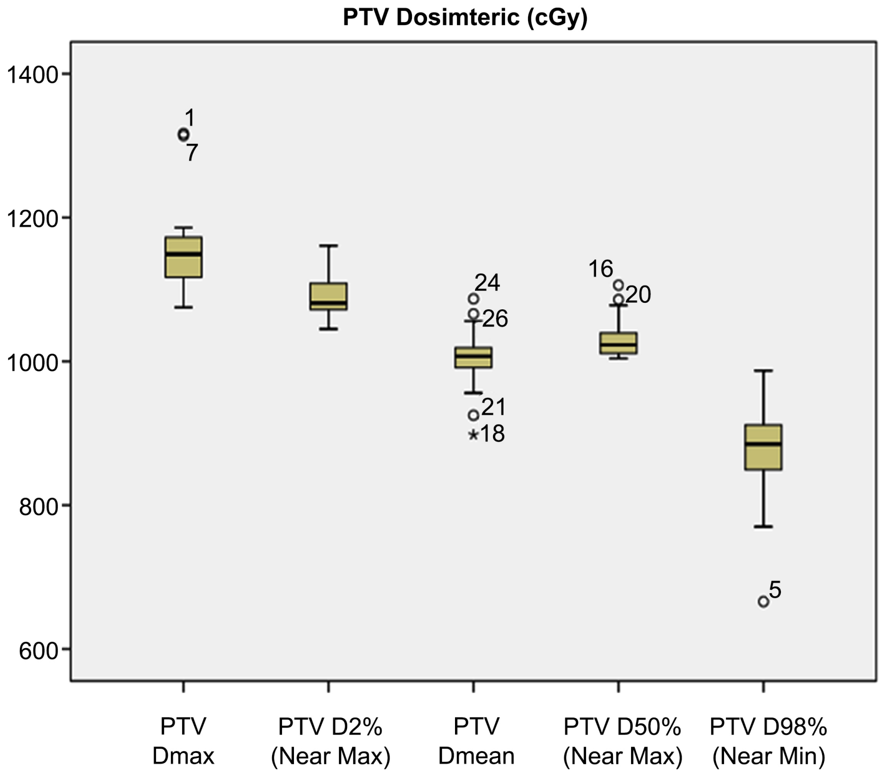

Figure 3. PTV dosimetrics.

3.2. Organ at Risk (OAR) Doses

For the critical structures, the lung received a mean dose of 8.41 ± 0.748.41 Gy (84.13%), with a D90 of 7.17 ± 0.98 Gy (71.70%). The volume of the lung receiving 100% of the prescribed dose (V10) was 10.33 ± 15.81, representing 103.33%. The kidneys' mean dose was 7.68 ± 0.56 Gy (76.85%) with the maximum dose reaching 10.62 ± 0.59 Gy (106.17%). Notably, the kidney V10 was considerably lower at 5.67 ± 8.92 (5.67%). The brain's mean dose was 10.07 ± 0.12 Gy (100.66%), with a maximum dose of 10.51 ± 1.25 Gy (105.09%). Radiation exposure to the lenses was minimized, with the right lens receiving a maximum of 4.92 ± 0.85 Gy and the left lens 4.89 ± 0.86 Gy (**Figure 4**).

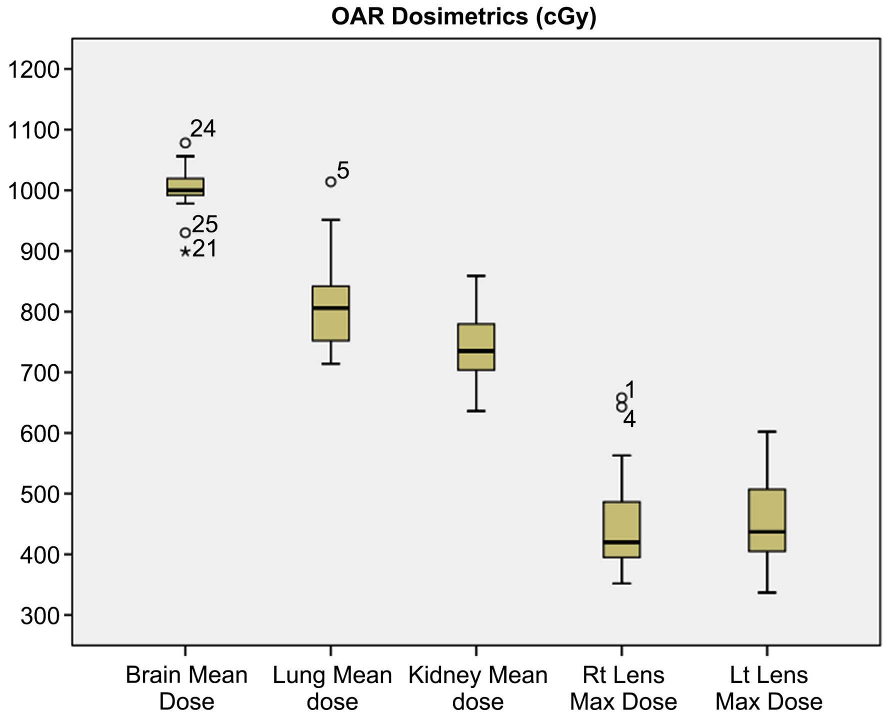

Figure 4. OAR dosimetrics.

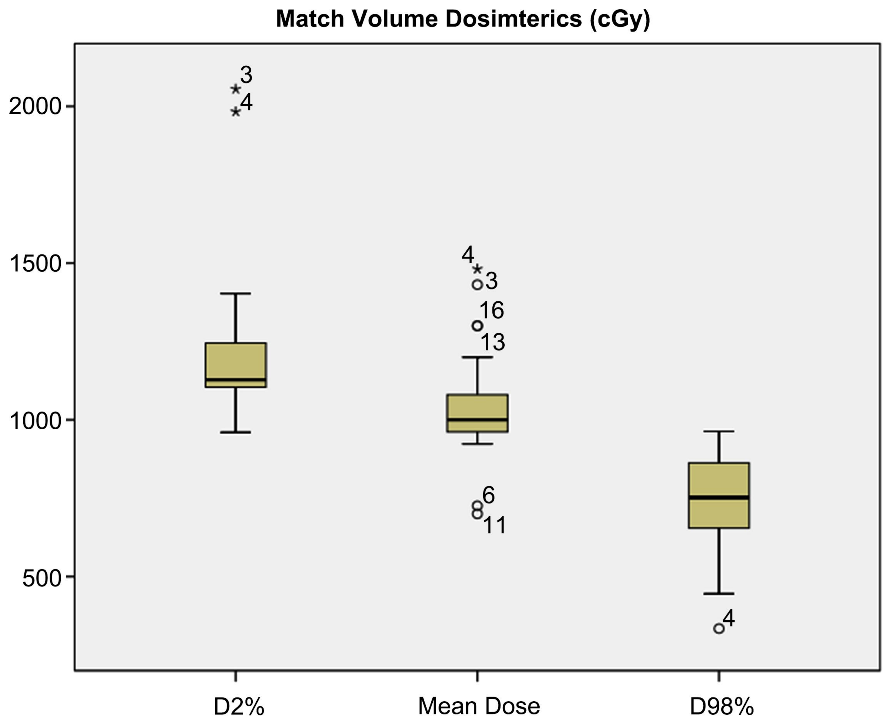

Figure 5. Matching pelvic volume dosimetrics.

3.3. Matching Pelvic Volume

The dosimetry for the match volume, where the upper and lower plans overlap, showed a mean dose of 10.42 ± 1.77 Gy (102.4%). The minimum dose covering

98% of this volume (D98%) was 7.31 ± 1.73 Gy (73.1%), while the dose near the maximum (D2%) was 12.23 ± 2.58 Gy (122.3%) (**Figure 5**).

4. Discussion

Our approach utilizes standard radiation therapy equipment for a hybrid Total Body Irradiation (TBI) technique combining Step-And-Shoot Intensity Modulation (SS-IMRT) with Conformal 3-Dimensional Radiotherapy (3DCRT). This is achieved without the need for specialized equipment or nor extended SSD setup. Patients are positioned supine. The use of a custom-made mask and straightforward body positioning aids in achieving consistent and accurate dose distribution.

Other recent studies explored new techniques for TBI. Dinç *et al.* [7] use an extended source-to-surface distance (SSD) of 400 cm, necessitating custom compensators for different body parts and lung blocks to protect critical organs. This setup requires significant modifications to the standard treatment setup, including a specialized beam spoiler to enhance skin dose and a complex arrangement of the treatment couch. This method, while potentially offering precise control over dose distribution, introduces operational complexity and could increase setup time and cost. Hansen's *et al.* [8] methods involve an intricate combination of extended SSD fields, IMRT, and VMAT techniques requiring multiple planning iterations and a sophisticated level of manual planning. The treatment planning incorporates various segments and boosts, necessitating advanced software and specialized training. This complexity could hinder rapid deployment in environments that lack the latest technology or specialized expertise. The ILROG guidelines [9] describe methods using large field sizes at extended SSDs, which could be logistically challenging. The use of large SSDs significantly reduces the dose rate, necessitating adjustments to treatment duration and potentially impacting patient throughput. Additionally, the need for compensating filters and blocks to protect organs at risk, such as lungs and kidneys, adds another layer of complexity to the treatment planning and delivery process. Compared to these techniques, our approach not only makes TBI more accessible but also reduces the likelihood of errors associated with more complex setups.

In our study, the hybrid SS-IMRT/3DCRT technique demonstrated refined dosimetric control, tailored to a total prescribed dose of 10 Gy, which contrasts with the higher prescribed doses in other studies. Specifically, our PTV mean dose was precisely managed at 10.11 Gy (101.12%), compared to Dinç *et al.*'s [7] V100% coverage at around 95%, indicating our method achieves higher dose delivery relative to the prescribed dose. Our maximum dose at 11.72 Gy (117.19%) shows more conservative escalation compared to Hansen *et al.*'s [8] approach where the mean PTV dose was notably higher at 12.7 Gy and 12.5 Gy for their respective techniques, reflecting their higher prescribed baseline of 12 Gy. Our PTV's D95%, marking the minimum dose that 95% of the PTV receives, was recorded at 9.16 Gy, closely aligning with optimal therapeutic levels, whereas Hansen *et al.* reported a more intensive treatment with D98% values consistently above 11.5 Gy.

This suggests that while our approach provides a safer margin of radiation, maintaining efficacy, Hansen's technique pushes for higher minimal coverage, increasing potential toxicity risks due to higher baseline doses. Moreover, the maximum doses within our PTV, D2%, remained well-controlled at 10.96 Gy, comparing favorably against Hansen's ranges [8] of up to 14.3 Gy for ExIMRT and 13.8 Gy for ExVMAT, emphasizing our technique's focus on minimizing peak dose regions, which is crucial for reducing the risk of dose-related complications.

In the analysis of organs at risk (OAR), our study showcases commendable dose management when compared to the parameters set by Dinç *et al.* [7], Hansen *et al.* [8], and the ILROG guidelines [9]. Our approach resulted in consistently lower mean doses across several critical structures, indicative of enhanced protective measures in our technique. For the lungs, our mean dose of 8.41 Gy starkly contrasts with the higher doses reported by Dinç *et al.*, where lung mean doses approached 9.71 Gy in VMAT-based plans. Similarly, the V10 Gy percentage in our study was significantly lower at 10.33%, compared to 40.76% in the VMAT-based plans of Dinç *et al.*, demonstrating our method's efficacy in sparing lung tissue. Kidney sparing in our study also highlighted outcomes that are more favorable; with mean doses of 7.68 Gy significantly lower than the 11.65 Gy observed in X-SSD plans by Dinç *et al.* Such comparisons underline our technique's capability to minimize radiation exposure to vital organs, thereby reducing potential toxicity. For the brain, our mean dose remained at 10.07 Gy, aligning closely with ILROG guidelines, which suggest a range of 11.1 - 11.8 Gy for similar treatments. This precision in maintaining low brain exposure underlines the tailored approach of our planning, ensuring safety without compromising treatment efficacy. Moreover, the lens doses in our study (maximum of 4.92 Gy for the right lens) are considerably lower compared to the significantly higher doses observed in X-SSD plans by Dinç *et al.*, where right lens doses could reach up to 13.08 Gy.

In our study, addressing the technical and dosimetric challenges associated with field matching in hybrid Total Body Irradiation (TBI) plans was a central focus, particularly at the critical matching volume at the pelvic region. This area often presents significant complexities in hybrid TBI approaches due to the convergence of different radiation fields, which if not carefully managed, can lead to substantial issues such as under-dosing or over-dosing. These challenges stem largely from the need to ensure seamless dose transitions between differing modalities, such as Step-and-Shoot Intensity Modulated Radiation Therapy (SS-IMRT) and 3D Conformal Radiation Therapy (3DCRT). The meticulous management of the matching volume in our study is highlighted by the dosimetric data obtained, which reflects our capability to maintain uniform dose delivery across this transitional zone. Here are the specifics from our results:

- **Mean Dose:** The average dose within the matching volume was 10.42 Gy, slightly above the prescribed level (102.4%), indicating robust dose coverage.
- **D98% (near minimum dose):** At 7.31 Gy, which represents 73.1% of the intended dose, we demonstrate control in minimizing under-dosing, crucial for

effective cancer treatment while protecting adjacent normal tissues.

- **D2% (near maximum dose):** At 12.23 Gy, corresponding to 122.3% of the target dose, our technique effectively limits the peak dose, reducing the risk of toxicity.

By effectively managing the pelvic matching volume, we ensure that the transition between the upper and lower body irradiation fields is seamless and consistent, without significant dose discrepancies that could compromise treatment efficacy or patient safety. Notably, the absence of detailed matching volume analysis in other comparative studies represents a significant gap in the existing literature and underscores the strength and uniqueness of our approach.

5. Limitations

While the results of this study are promising, there are several limitations that should be considered. The study's small sample size of only 27 patients, while sufficient to demonstrate the feasibility and initial efficacy of our novel TBI technique, may limit the generalizability of the findings. Small sample sizes can increase the risk of statistical type II errors, meaning that the ability to detect a difference when one truly exists is reduced, and may result in less precise estimates of treatment effects.

Moreover, the retrospective nature of the study design might introduce biases associated with data collection and patient selection, which could influence the outcomes. Prospective studies are needed to confirm these findings in a more controlled setting, allowing for the collection of data that could address potential confounding factors more systematically.

Additionally, the follow-up period in this study was not long enough to assess long-term outcomes and late toxicities comprehensively. Longer follow-up would provide more information on the durability of the treatment effects and the late side effects, which are critical for validating the safety and efficacy of the technique over time.

Given these factors, the findings from this study should be interpreted with caution. Further research involving larger, prospective trials is necessary to confirm the effectiveness and safety of this technique and to enhance its generalizability across different patient demographics and clinical settings.

6. Future Directions

While our study has focused primarily on the technical and dosimetric aspects of a novel Total Body Irradiation (TBI) technique combining Step-And-Shoot Intensity Modulation (SS-IMRT) with Conformal 3-Dimensional Radiotherapy (3DCRT), we acknowledge the critical importance of clinical outcomes in assessing the efficacy and safety of any radiation therapy approach. Therefore, future studies should aim to include comprehensive clinical outcome measures such as:

Treatment Response: Evaluation of immediate treatment outcomes and comparison with traditional TBI methods to assess any improvements or drawbacks in tumor control rates.

Survival Rates: Longitudinal studies to track survival rates over time, providing a more robust dataset to evaluate the long-term benefits of the SS-IMRT/3DCRT hybrid technique compared to standard practices.

Late Toxicities: Detailed monitoring and documentation of late-onset toxicities are crucial, as these can significantly impact patient quality of life and the overall success of the treatment regimen. This should include a specific focus on any late effects that may be unique to or more prevalent in the hybrid technique.

7. Conclusion

This study highlights the effectiveness of a hybrid Total Body Irradiation (TBI) technique combining Step-And-Shoot Intensity Modulation (SS-IMRT) with Conformal 3-Dimensional Radiotherapy (3DCRT) using standard radiation therapy equipment. Our results indicate precise dose management to both target areas and organs at risk, ensuring effective treatment while minimizing toxicity. The technique simplifies the TBI process, potentially reducing costs and increasing accessibility in various clinical settings. Future research should focus on multicenter trials to validate these findings and explore the integration of advanced imaging techniques for enhanced treatment accuracy.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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