Global Dose Optimization Strategy Integrating Spatially Fractionated Radiotherapy, External Beam Radiotherapy, and Brachytherapy for Cervical Cancer

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ABSTRACT

Purpose: To develop a dose optimization strategy for organs at risk (OARs) in locally advanced cervical cancer (LACC) combining spatially fractionated radiotherapy (SFRT), EBRT, and brachytherapy (BT), enabling safe dose escalation for bulky tumors.

Methods: Retrospective analysis of 31 LACC patients (Group A: PTV 45 Gy; Group B: nodal PGTVN boost 55–57.5 Gy). The "Brachytherapy Influence Zone (BI)" was defined as uterus/vagina + 1 cm expansion in EBRT planning. Phase-specific OAR constraints and a BI-guided optimization strategy were developed for SFRT+EBRT+BT and tested in five patients.

Results: In EBRT, Group B had significantly higher OAR D_2cc (bladder: 49.35 vs. 45.36 Gy; sigmoid: 47.47 vs. 44.88 Gy; $P < 0.01$). PGTVN-BI volume correlated strongly with Bladder-BI and Sigmoid-BI doses. BT showed no intergroup OAR differences. Five patients received SFRT-lattice boost + EBRT+BT. Cumulative OAR doses met constraints in three patients; two (larger PGTVN-BI) were <2 Gy above limits. Grade 2 intestinal toxicity occurred in two patients.

Conclusion: A BI-guided optimization strategy enables safe integration of SFRT-lattice boost into standard LACC radiotherapy, maintaining OAR doses near constraints and providing a practical framework for dose escalation in bulky tumors.

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INTRODUCTION

Concurrent external beam radiotherapy (EBRT) and brachytherapy (BT) is the standard radical treatment for locally advanced cervical cancer (LACC). However, for patients with bulky tumors (≥5 cm or >30 cm^3) or stage III-IVA disease, local control remains suboptimal even with radical doses. Dose escalation is often limited by nearby organs at risk (OARs), particularly during BT. Spatially fractionated radiotherapy (SFRT), such as Lattice therapy, creates heterogeneous "peak-and-valley" dose distributions that may enhance tumor control while sparing normal tissues. Adding SFRT to standard regimens could escalate target doses, but inevitably increases OAR exposure. Furthermore, when a simultaneous integrated boost (SIB) is delivered to involved lymph nodes (PGTVN up to 55–57.5 Gy), the dosimetric impact on OARs becomes more complex, especially regarding potential overlap between EBRT and BT high-dose regions. This study aims to: 1) analyze historical OAR dose data from conventional EBRT+BT; 2) introduce the novel "Brachytherapy Influence Zone (BI)" concept to proactively manage dose overlap; and 3) develop and validate a phase-specific global dose optimization strategy to safely integrate SFRT-Lattice into standard LACC radiotherapy.

METHODS AND MATERIALS

We retrospectively analyzed 31 LACC patients treated with EBRT+BT: Group A (n=12, PTV only 45 Gy) and Group B (n=19, PTV45 + SIB to PGTVN 55–57.5 Gy). Dosimetric parameters for targets and OARs (bladder, rectum, sigmoid) were collected. The Brachytherapy Influence Zone (BI) was defined as the uterus and vagina plus a 1 cm volumetric expansion on EBRT planning images, generating OAR-BI structures (Bladder-BI, Rectum-BI, Sigmoid-BI) and PGTVN-BI. Volume and dose correlations between original OARs and OAR-BI were analyzed. Based on these data, phase-specific dose constraints for EBRT, BT, and SFRT were established. A prospective cohort (Group C, n=5) received 3×8 Gy SFRT-Lattice followed by EBRT+SIB and BT, applying the BI-guided optimization strategy. Cumulative EQD_2 doses and acute toxicities were recorded.

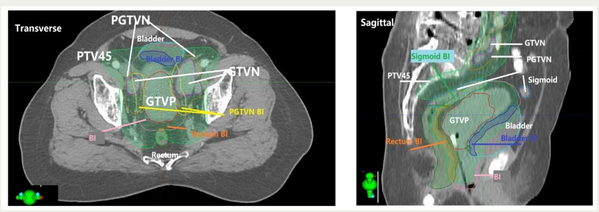


Figure 1. Contour delineation of PGTVN, OARs, and the Brachytherapy influence zone (BI) in EBRT.

RESULTS

In the EBRT phase, Group A (PTV only, 45 Gy) showed uniformly low OAR D_2cc doses (bladder: 45.36±0.48 Gy; rectum: 44.91±0.41 Gy; sigmoid: 44.88±0.34 Gy), all well below conventional tolerance limits. In contrast, Group B (with nodal SIB to 55–57.5 Gy) had significantly higher OAR D_2cc (bladder: 49.35±4.36 Gy; sigmoid: 47.47±2.35 Gy; $P < 0.01$), indicating that lymph node boost increases OAR exposure, particularly for bladder and sigmoid. PGTVN volume did not correlate with original OAR doses, but PGTVN-BI volume strongly correlated with doses to Bladder-BI and Sigmoid-BI, and marginally with Rectum-BI. In the BT phase, no significant intergroup differences in OAR EQD_2 were observed. All five prospective patients (Group C) completed SFRT-lattice boost with EBRT and BT. Cumulative OAR EQD_2 met pre-defined constraints in three patients; two patients with larger PGTVN-BI volume had OAR doses <2 Gy above constraints. Only two patients experienced grade 2 intestinal toxicity, and no grade ≥3 toxicity occurred.

Table 1. Recommended EQD_2 Dose Constraints for OARs (Gy)

Parameter	Recommended EQD_2 Dose Constraints for OARs (Gy)			
	EBRT(EQD_2)	BT (EQD_2)	SFRT Margin	Cumulative
Group：PTV45Gy				
Bladder D_{2CC}	⩽45.5	⩽38.0	BI⩽6.5	⩽90
Rectum D_{2CC}	⩽45.5	⩽27.5	BI⩽2	⩽75
Sigmoid D_{2CC}	⩽45.5	⩽22.0	BI⩽7.5	⩽75
Group：PTV45Gy+PGTVN_SIB				
Bladder D_{2CC}	BI⩽46.5	⩽38.0	BI⩽5	⩽90
Rectum D_{2CC}	BI⩽45.0	⩽27.5	BI⩽2	⩽75
Sigmoid D_{2CC}	BI⩽46.5	⩽22.5	BI⩽6	⩽75

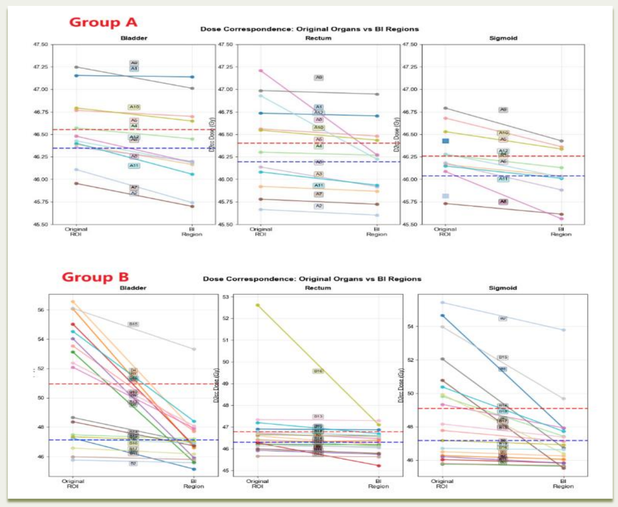


Figure2. D_{2CC} versus OARs-BI D_{2CC} by Individual Case for Groups A and B.

DISCUSSION

Conventional cumulative dose assessment often ignores spatial discordance between EBRT and BT high-dose regions. Lymph node SIB significantly increases OAR exposure (4 Gy for bladder, 3 Gy for sigmoid), making precise dose management essential. The BI concept effectively identifies potential high-dose overlap areas during EBRT planning, allowing proactive OAR sparing. Our data show that PGTVN-BI volume, not total PGTVN volume, determines OAR-BI dose, particularly for bladder and sigmoid. Rectal dose remains a challenge due to anatomical constraints and applicator limitations, leaving only a 2 Gy margin for SFRT. The 3×8 Gy Lattice plans were successfully integrated without exceeding cumulative constraints in most patients. The proposed phase-specific constraints (Table 1) provide a practical framework, though they require institution-specific calibration. Limitations include the BI's simplified geometric expansion (not full dose distribution), small prospective cohort, and need for deformable registration in future studies.

CONCLUSIONS

Using a BI-guided global dose optimization strategy, SFRT-Lattice boost can be safely integrated into standard EBRT+BT for LACC while maintaining OAR doses within acceptable limits. The BI concept helps predict and manage dose overlap between lymph node SIB and brachytherapy regions. Phase-specific dose constraints were established and prospectively validated. This approach offers a practical framework for safe dose escalation in bulky cervical tumors. Individual institutions should calibrate their own constraints based on local techniques. Future work includes refining rectal sparing in BT, larger prospective cohorts, and comparative effectiveness studies.

REFERENCES

[1] Wu X, Perez N, Zheng Y, et al. The Technical and Clinical Implementation of LATTICE Radiation Therapy (LRT)[J]. Radiat Res, 2020, 194(6): 737-746.
[2] Tanderup K, Fokdal LU, Sturdza A, et al. Effect of tumor dose, volume and overall treatment time on local control after radiochemotherapy including MRI guided brachytherapy of locally advanced cervical cancer[J]. Radiother Oncol, 2016, 120(3): 441-446.
[3] Amendola BE, Mahadevan A, Blanco Suarez JM, et al. An International Consensus on the Design of Prospective Clinical–Translational Trials in Spatially Fractionated Radiation Therapy for Advanced Gynecologic Cancer[J]. Cancers, 2022, 14(17): 4267.

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