Research Square

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Exploring the Limits of Radiation Dose Gradient Compression in Bulky Solid Tumors Invading the Spinal Cord: An Exploratory Study of Conventional Volumetric Modulated Arc Therapy versus LATTICE Radiotherapy on a 10-mm Multi-Leaf Collimator Platform

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Abstract

Background

Radiotherapy for bulky tumors involving the spinal cord is limited by the conflict between adequate target coverage and spinal cord protection, particularly in resource-limited centers with lower-resolution multileaf collimators. LATTICE radiation therapy may address this limitation by delivering high-dose vertices within the tumor while maintaining a low peripheral dose. This study compared LATTICE radiation therapy with conventional volumetric modulated arc therapy for bulky spinal cord-involving tumors using a 10-mm multileaf collimator platform.

Methods

This study combined retrospective clinical analysis and dosimetric simulation. Nine patients with bulky tumors treated with LRT (12 Gy/fraction at peaks and 4 Gy/fraction at valleys, 5 fractions) were evaluated for symptom relief and safety. Virtual spinal cord-involved models were generated to compare target-prioritized and spinal cord-prioritized VMAT plans under 10-mm MLC constraints, and the minimum geometric margin required to achieve spinal cord safety (Dmax ≤ 45 Gy) with adequate target coverage (D95% = 100% prescription dose) was determined.

Results

LRT significantly reduced median NRS pain scores from 6 to 2 ($P < 0.001$), achieving an 88.9% symptom relief rate without radiation-induced neurological toxicity. Dosimetric simulations demonstrated that conventional VMAT was physically constrained in the extreme scenario of a 0-mm tumor-spinal cord gap, where prioritizing spinal cord protection reduced target V50Gy coverage from 99.26% to 94.12% ($P < 0.001$). The minimum safe margins for conventional VMAT under a 10-mm MLC configuration were 0.45 cm and 0.40 cm for full-length and partial spinal cord involvement, respectively. LRT achieved a stable peak-to-valley ratio (2.49 ± 0.11) with low peripheral dose exposure, indicating favorable dosimetric safety.

Conclusion

A physical limitation exists for conventional VMAT under a 10-mm MLC configuration when treating bulky tumors involving the spinal cord, with a critical tumor–cord margin of approximately 0.45 cm required to balance target coverage and spinal cord safety. LRT overcomes this limitation through spatially heterogeneous dose distribution, providing a potential strategy for achieving local tumor control while preserving neurological function in extreme cases with minimal tumor–cord separation.

Introduction

Advanced malignant tumors frequently present as bulky masses, intractable pain, and extensive distant metastases[1–3]. In resource-scarce regions, limited healthcare access, low health literacy, and economic burdens frequently delay diagnosis until the disease reaches an advanced stage[4]. Such lesions frequently cause obstinate functional impairments and pose clinical emergency risks, such as spinal cord compression, where delayed intervention can induce irreversible neurological damage[5, 6].

Although palliative external beam radiation therapy (EBRT) is the standard treatment for metastatic tumors [7, 8], its therapeutic ratio is significantly limited when managing large-volume lesions or those adjacent to organs at risk (OARs). Conventional radiotherapy struggles to deliver an ideal biologically equivalent dose to the target volume while strictly constraining the dose to OARs[9]. Furthermore, the hypoxic microenvironment within bulky tumors mediates radioresistance, further increasing the risk of local recurrence[10]. While Stereotactic Body Radiation Therapy (SBRT) has demonstrated excellent local control rates in oligometastases[11, 12], its application in bulky tumors involves larger planning target volumes (PTVs), which significantly expands the low-to-intermediate dose spillage into surrounding normal tissues, thereby increasing the risk of radiation toxicity[13]. When tumors invade or lie in close proximity to critical structures such as the spinal cord, clinical practice often necessitates sacrificing target coverage to ensure spinal cord safety, generating dose cold spots that compromise local control (Fig. 1). Research indicates that for massive metastatic lesions, long-course radiotherapy may be superior to conventional SBRT[14]; however, balancing the maximum spinal cord dose with adequate target coverage remains a clinical dilemma in cases involving the spinal cord.

In this context, LATTICE radiation therapy, an innovative modality of spatially fractionated radiation therapy (SFRT), has demonstrated unique clinical potential[15]. LRT constructs a 3D high-dose vertex array within the gross tumor volume, achieving a highly heterogeneous spatial dose distribution: it delivers ablative doses to focal areas while maintaining a low overall average dose[16, 17]. By spatially redistributing radiation energy in three dimensions, this technique subverts the uniform dose deposition paradigm of traditional radiotherapy, providing an immunobiological and physical theoretical foundation for improving the treatment efficiency of bulky tumors while protecting surrounding normal tissues.

To address the challenging clinical scenario of spinal cord-invading bulky tumors, this study explores LRT optimization strategies, characterized by low peripheral and high internal vertex doses. Given the hardware constraints of primary healthcare institutions (e.g., lower resolution multi-leaf collimators), this study conducted a "physical stress test" on conventional VMAT plans using a 10-mm MLC hardware platform. The objective is to define the "physical failure boundary" of conventional radiotherapy in protecting neurological function, while evaluating the potential advantages of LRT in breaking through this physical bottleneck to balance safety and local efficacy. Ultimately, this study seeks to explore an efficient, precise, and cost-effective clinical intervention pathway for resource-limited centers managing such complex advanced cases.

Materials and Methods

Study Design and Patient Selection

This retrospective observational study, conducted at The Third People's Hospital of Chengdu, utilized a dual pathway approach—combining clinical efficacy evaluation with virtual spinal cord involvement modeling—to investigate the clinical benefits and physical dosimetric limitations of LRT for bulky tumors invading the spinal cord. A total of nine patients with advanced solid tumors who received radiotherapy at our institution between November 2024 and November 2025 were retrospectively enrolled in this study. Eligible patients were required to meet the following inclusion criteria: (1) pathologically confirmed malignancy, (2) a bulky lesion with a maximum tumor diameter exceeding 7 cm, and (3) management with an LRT regimen without prior surgical decompression of the target volume. Patients were excluded if they presented with incomplete medical records, concurrent primary malignancies, or were under 18 years of age. To eliminate confounding factors from individual anatomical variations and to precisely define the physical limits of the hardware platform, dose models based on virtual spinal cord involvement were simultaneously constructed.

Radiotherapy Planning and Delivery

All plans were optimized in the Monaco treatment planning system (v5.11) and delivered using an Elekta Synergy linear accelerator equipped with a 10-mm leaf-width MLC (6 MV, 600 MU/min). The LRT plans were designed utilizing a simultaneous integrated boost (SIB) technique to delineate the high-dose peak and low-dose valley regions. The prescribed doses for the peak and valley regions were 12 Gy/fraction and 4 Gy/fraction, respectively, delivered over a total of 5 fractions. Radiation delivery was modeled using a dual-arc VMAT technique with an isotropic 3-mm dose calculation grid. For the conventional VMAT control plans, a hypofractionated regimen was employed with a total prescription dose of 50 Gy, delivered over 17 fractions (3 Gy for 16 fractions followed by a single 2 Gy fraction). To ensure a rigorous comparative analysis, the dose calculation grid and all physical optimization parameters were kept completely identical to those utilized in the LRT plans.

Digital Simulation of Spinal Cord Involvement Models and Testing

To quantitatively define the dosimetric limitations of the 10-mm MLC hardware platform under extreme spatial constraints, a series of virtual dose simulation tests were executed based entirely on conventional VMAT geometries.In the first phase of simulation, we modeled an extreme scenario featuring full-length virtual spinal cord involvement, wherein a massive tumor maintained continuous longitudinal contact with the spinal cord, establishing a 0-mm anatomical gap. Within this framework, dosimetric conflicts were systematically quantified using two competing optimization strategies. Under the target-priority strategy, planning constraints strictly enforced a target V50Gy > 99%, and the resulting dose spillover—defined as the volume where the spinal cord maximum dose Dmax exceeded the 45 Gy safety limit—was recorded. Conversely, the spinal cord-priority strategy prioritized critical organ safety by strictly constraining the spinal cord Dmax to 45 Gy, allowing us to quantify the subsequent volumetric and dosimetric compromise (specifically in D95%, D99%, and V 50Gy) within the tumor target.

To establish a definitive spatial boundary for safe treatment planning, a gradient spatial translation method was subsequently introduced within the conventional VMAT optimization framework to define and validate the safety distance threshold. The anatomical gap between the tumor boundary and the spinal cord was incrementally expanded in steps of 0.05 cm. Optimization success was defined as the complete restoration of target D95% to 100% of the prescription dose while simultaneously maintaining a spinal cord Dmax 45Gy. Upon aggregating the dosimetric data across all simulated models, the 95th percentile of the minimum gap distribution was designated as the system's "GTV-to-spinal cord safety distance threshold." To verify the robustness of this optimization threshold, the defined distance was subsequently fed back into all initial models as a fixed geometric constraint for re-optimization. In the second phase, a partial virtual spinal cord involvement model was constructed to simulate a localized extreme scenario. Here, the direct 0-mm contact was restricted to a core segment of the bulky tumor, spanning a longitudinal length of 3.3 cm across 11 contiguous CT slices. The dosimetric conflicts under the two competing optimization strategies, as well as the iterative determination and validation of the safety distance threshold, were evaluated using methodology identical to that described in the first phase (Fig. 2).

Statistical Analysis

Data were analyzed using SPSS 26.0 software. Normally distributed data were expressed as mean ± standard deviation. Inter-group comparisons were performed using paired-sample t-tests or Wilcoxon signed-rank tests. A P-value < 0.05 was considered statistically significant.

Results

Patient Baseline Characteristics and Clinical Efficacy

The median age of the 9 patients was 64 years, with a median maximum tumor diameter of 14.71 cm (range: 7.74–24.72 cm) and a median GTV volume of 501.96 cm^3. Following LRT, all patients achieved significant symptom palliation, with the median NRS pain score decreasing from 6 pre-treatment to 2 post-treatment ($P < 0.001$). A total of 88.9% (8/9) of the patients reported pain relief by the third fraction. Four patients presenting with spinal cord compression symptoms maintained stable neurological status post-treatment, and no radiation-induced progressive neurological damage was observed during follow-up (Table 1).

Table 1
Baseline Patient Characteristics and Clinical Outcomes

Case No.	Gender	Age (y)	Diagnosis	Stage (TNM)	Treated Site	Tumor Origin	Tumor Size (cm)	Target Volume (cm^3)	Pain Score (Pre-RT)	Pain Score (Post-RT)	Status at follow-up
1	M	74	Lung Cancer (LUL)	T4N2M1c IVB	Ilium	Metastatic	17.48	758.04	3	1	NED
2	F	56	Soft Tissue Sarcoma	T3N1M1 G2 IVB	Adrenal Gland	Metastatic	7.74	141.99	6	0	NED
3	F	73	Gallbladder Ca.	T4NxM1 IV	Gallbladder	Primary	14.16	385.44	4	2	DOD
4	F	60	Gallbladder Ca.	T3N1M1 IVB	Liver	Metastatic	11.55	501.96	4	4	NED
5	M	68	Lung SCC	T4N3M1c IVB	Chest Wall (R)	Metastatic	14.71	1069.49	7	2	NED
6	M	64	Colon Adenoca.	T3N1bM1c IVC	Liver	Metastatic	9.92	249.63	6	0	NED
7	F	79	Lung Cancer (LUL)	T4N2M1c IVB	Chest Wall (L)	Metastatic	14.97	260.08	6	2	AWD
8	F	46	Sigmoid Colon Ca.	T3N2aM1b IVB	Liver	Metastatic	18.15	1469.54	8	3	AWD
9	M	54	Thymic Malignancy	T4N2M1b IVb	Thymus	Primary	24.72	3586.8	7	4	DWD

Abbreviations: AWD: Alive with disease; DOD: In hospice or dead of disease; DWD: Dead with disease; NED: No evidence of disease.

Dosimetric Changes under Different Treatment Strategies in Extreme Spatial Constraints

In the full-length compression model with a 0 mm gap, conventional VMAT exhibited irreconcilable strategic trade-off conflicts. Under the "spinal cord-priority" strategy, target coverage significantly decreased: D95% dropped from 5197.33 ± 11.02 cGy to 4946.17 ± 78.02 cGy ($t = 10.704$, $P < 0.001$); V50Gy declined from 99.26 ± 0.11% to 94.12 ± 2.74% ($P < 0.001$). Conversely, when forcing full target coverage ("target-priority"), the average spinal cord Dmax reached 51.84 ± 2.15 Gy, severely exceeding the safety threshold (Fig. 3).

Definition and Validation of Safety Distance Thresholds

Physical dose gradient measurements indicated that in the virtual full-length spinal cord involvement scenario, 95% of the dose spillover distances for the 10-mm MLC platform fell within 0.45 cm. When the anatomical gap was maintained at 0.45 cm, the median spinal cord Dmax was 44.78 Gy, and the target V50Gy recovered to 98.23 ± 0.61%, establishing 0.45 cm as the universal absolute safety distance for this model. In the virtual partial spinal cord involvement model, this absolute safety distance was 0.40 cm (mean spinal cord Dmax = 38.77 Gy, with stable target coverage) (Table 3).

Table 3
Descriptive Statistics of the Measured Tumor-Spinal Cord Safety Distances

Parameter	
Slices	n = 351
Distance	
Median (IQR)	0.32 (0.08)
Range (Min - Max)	0.20–0.49
Q1 - Q3	0.28–0.36
95th Percentile (D95)	0.45
Abbreviations: IQR, interquartile range; Q1, first quartile; Q3, third quartile.	

Dosimetric Advantages and Parameter Correlations of LRT Plans

LRT plans successfully circumvented the dose fall-off bottleneck through spatial fractionation. The average peak-to-valley ratio for the cohort was 2.49 ± 0.11. The mean maximum peripheral dose to the target volume in LRT plans remained remarkably low (2771.3 ± 175.6 cGy), demonstrating high inherent physical safety. Pearson correlation analysis revealed a significant positive correlation between Monitor Units (MUs) and target volume ($r = 0.91$, $P < 0.001$) (Table 2).

Table 2
Dosimetric Parameters and Treatment Characteristics of the LATTICE Radiotherapy Plans

Case	Max Dose (cGY)	Target Vol	V6000	V2000	Tx MU
1	2754.1	758.04	29.05	639.95	7879.6
2	2419.6	141.99	6.83	127.79	6585.37
3	2998.6	385.44	16.73	346.98	9338.81
4	2679.8	501.96	20.94	451.73	7008.8
5	2714.3	1069.49	47.6	962.51	11405.92
6	2998.2	249.63	11.42	224.66	6905.8
7	2739.5	260.08	29.27	604.06	8763.61
8	2854.2	1469.54	34.11	1351.97	10741.3
9	2783.2	3586.8	27.6	3585.77	14870.84
Abbreviations: Max Dose, maximum dose; cGy, centiGray; Target Vol, target volume; V6000, volume receiving ≥ 6000 cGy; V2000, volume receiving ≥ 2000 cGy; Tx MU, treatment monitor units.					

Discussion

Through simulation, this study evaluated the dosimetric boundaries of conventional radiotherapy and the potential benefits of LRT when managing bulky solid tumors invading the spinal cord on a 10-mm MLC hardware platform.

The core contribution of this study is the quantitative definition of the "physical failure boundary" of conventional VMAT in protecting the spinal cord, established via stress modeling. Simulation data demonstrate that 0.45 cm is the universal red-line distance for this hardware platform within the conventional radiotherapy optimization framework to ensure the spinal cord Dmax remains at the 45 Gy safety threshold without sacrificing ablative target coverage. Constrained by the physical dimensions of the 10-mm MLC, the dose penumbra width frequently exceeds the ultra-narrow gap between the tumor and the spinal cord. Consequently, during conventional optimization, this physical bottleneck forces a clinical compromise between spinal cord safety and target coverage.

From the perspective of radiological physics, LRT provides a potential paradigm shift from "uniform coverage" to "heterogeneous distribution" compared to conventional radiotherapy[18]. In this simulation study, LRT plans did not seek uniform peripheral ablation;

rather, they generated damage via internal high-dose "peak regions" and compensated for relative peripheral under-dosing through mechanisms such as the bystander effect[19–21]. This heterogeneous distribution naturally places the spinal cord in a dose "valley," strategically circumventing the "forced avoidance" that conventional VMAT fails to achieve due to penumbra control limitations[20]. When the anatomical gap is compressed to less than 0.40 cm, the dose distribution profile exhibited by LRT serves as a viable alternative optimization direction—accepting non-uniform peripheral dosing in exchange for a higher tier of neurological safety.

Although these digital simulations highlight LRT's potential to overcome physical gradient bottlenecks[22–24], successful clinical translation must account for respiratory motion, setup errors, and biological uncertainties. LRT and conventional radiotherapy may harbor synergistic potential, for instance, by utilizing LRT as a "spatial dose boost" in sequential or concurrent combination with conventionally fractionated radiotherapy.

Based on these quantitative findings, this study provides a tiered reference for clinical decision-making: When the tumor-spinal cord gap is > 0.45 cm, conventional VMAT remains a robust choice to secure therapeutic gain. If the gap narrows to between 0.40 and 0.45 cm, LRT should be considered as a potential alternative to circumvent hardware bottlenecks. For extreme scenarios where the gap is < 0.40 cm, clinicians should anticipate the risk of compromised coverage and consider multi-modal combined interventions.

Conclusion

This study defined the "physical failure boundaries" of conventional VMAT at a tumor-spinal cord gap of 0.45 cm for full-length involvement and 0.40 cm for partial involvement. Conversely, LATTICE radiation therapy overcomes these low-resolution hardware limitations by nesting critical neurological structures within a natural low-dose valley, establishing a superior equilibrium of safety and local control within ultra-narrow anatomical gaps.

Abbreviations

3D
Three-dimensional
CT
Computed tomography
Dmax
Maximum dose
D95%
Dose received by 95% of the target volume
D99%
Dose received by 99% of the target volume
EBRT
External beam radiation therapy
GTV
Gross tumor volume
LRT
LATTICE radiation therapy
MLC
Multileaf collimator
MU
Monitor unit
NRS
Numerical Rating Scale
OAR
Organ at risk
PTV
Planning target volume
SBRT
Stereotactic body radiation therapy

SFRT
Spatially fractionated radiation therapy
SIB
Simultaneous integrated boost
SPSS
Statistical Package for the Social Sciences
V50Gy
Percentage of the volume receiving at least 50 Gy
VMAT
Volumetric modulated arc therapy.

Declarations

Ethics approval and consent to participate

This retrospective substudy was approved by the Ethics Committee of Chengdu Third People's Hospital (approval No. 2025-S-385). The requirement for informed consent was waived by the Ethics Committee owing to the retrospective nature of the study and the use of de-identified data. The study was conducted in accordance with the Declaration of Helsinki and relevant institutional and national guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The clinical data and dosimetric datasets generated and/or analyzed during this study are not publicly available because they contain potentially identifiable patient information. However, de-identified data may be available from the corresponding author upon reasonable request and approval by the institutional ethics committee.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LH, YH, and XP contributed equally to this work. LH and YH collected the clinical data and performed the statistical analyses. XP developed the radiotherapy plans and performed the dosimetric analyses and computational simulations. LH, YH, and XP drafted the manuscript. BY and YC contributed equally as senior authors and were responsible for the conception and design of the study, methodological guidance, supervision, interpretation of the results, and critical revision of the manuscript. All authors read and approved the final manuscript.

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Figures

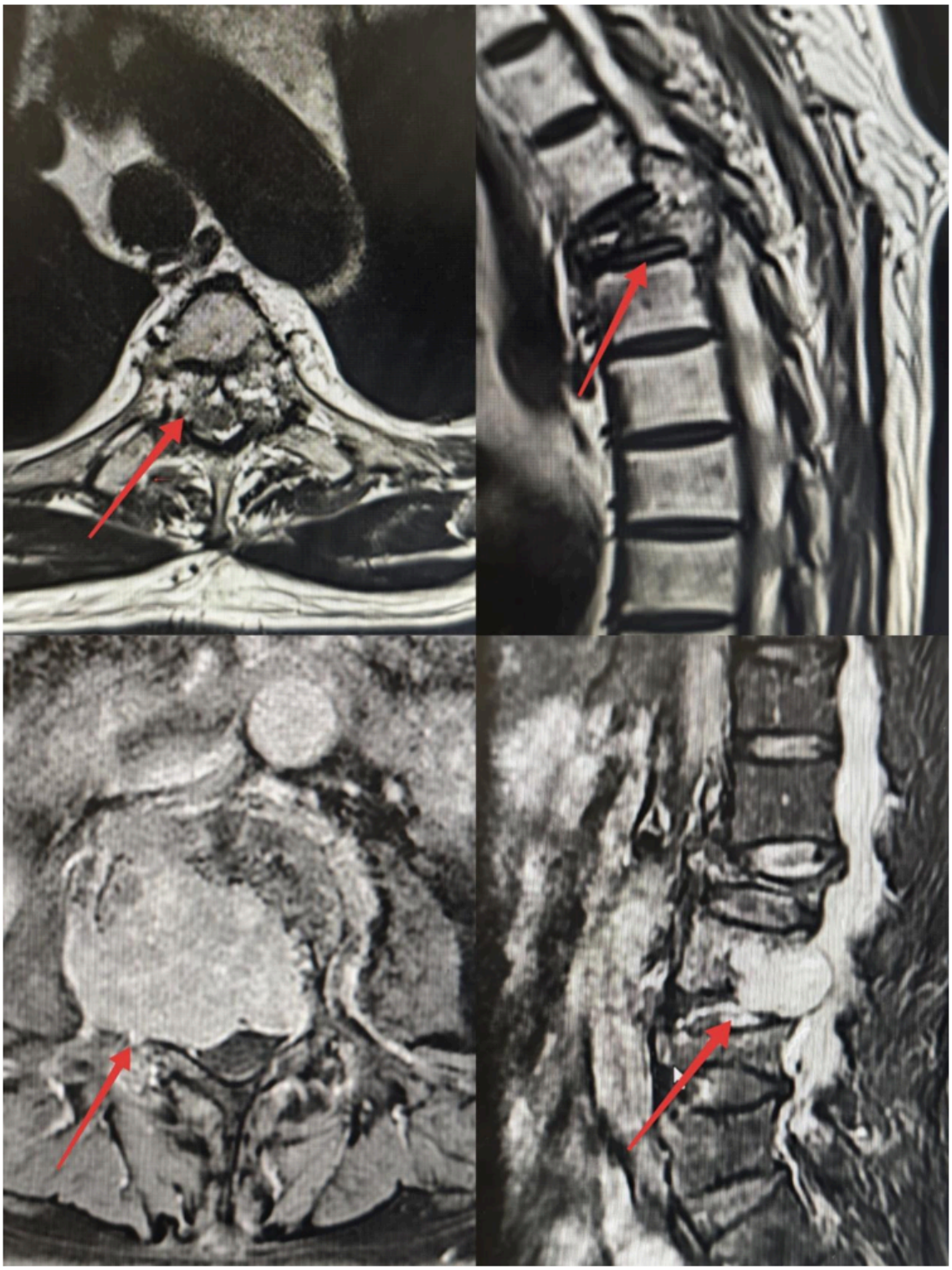


Figure 1

Anatomical reference illustrating the extreme clinical scenario for the virtual simulation model. The composite MRI shows axial (left) and sagittal (right) views of a tumor invading the spinal canal. Red arrows indicate the mass directly abutting and compressing the

spinal cord. This anatomical relationship represents a 0-mm geometric gap between the target volume and the critical organ at risk.

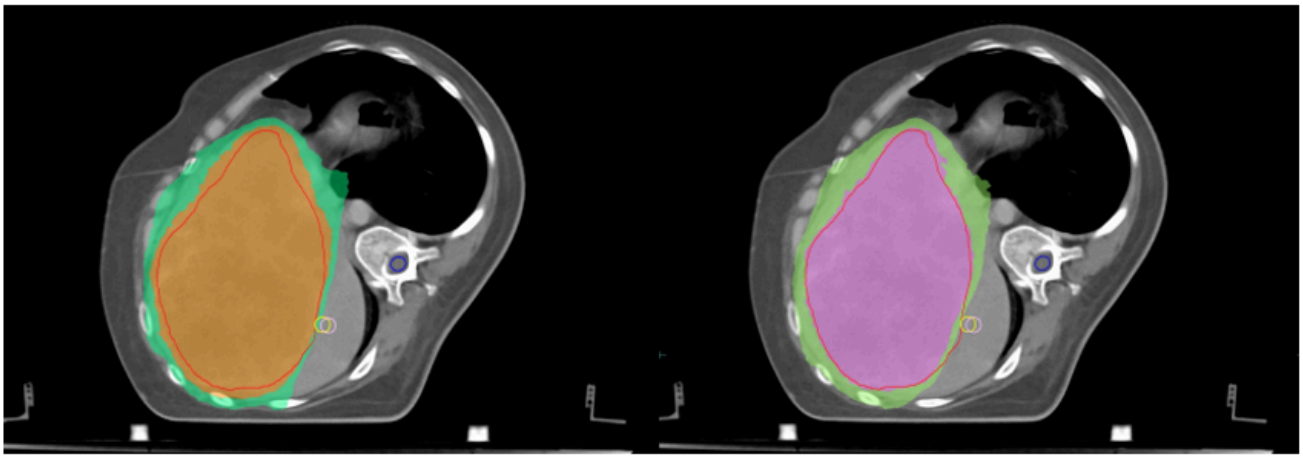


Figure 2

Setup of the digital simulation model for evaluating dose gradient compression limits within a treatment planning system. Axial CT slices show the spatial relationship between the target volume (red shaded region) and artificial "virtual spinal cords" placed at various geometric margins. The anatomical spinal cord is indicated by the blue circle. To quantitatively assess the dose fall-off capability of the 10-mm multileaf collimator (MLC), two virtual spinal cords were contoured: a yellow circle representing an extreme scenario with a 0-mm gap (directly abutting the target), and a pink circle representing a virtual spinal cord placed 0.4 cm from the target boundary. Using a target-priority optimization strategy (designed to maintain target V50Gy coverage), this model determines the physical distance required for the dose to drop from the prescription level (50 Gy) to the spinal cord tolerance limit (45 Gy).

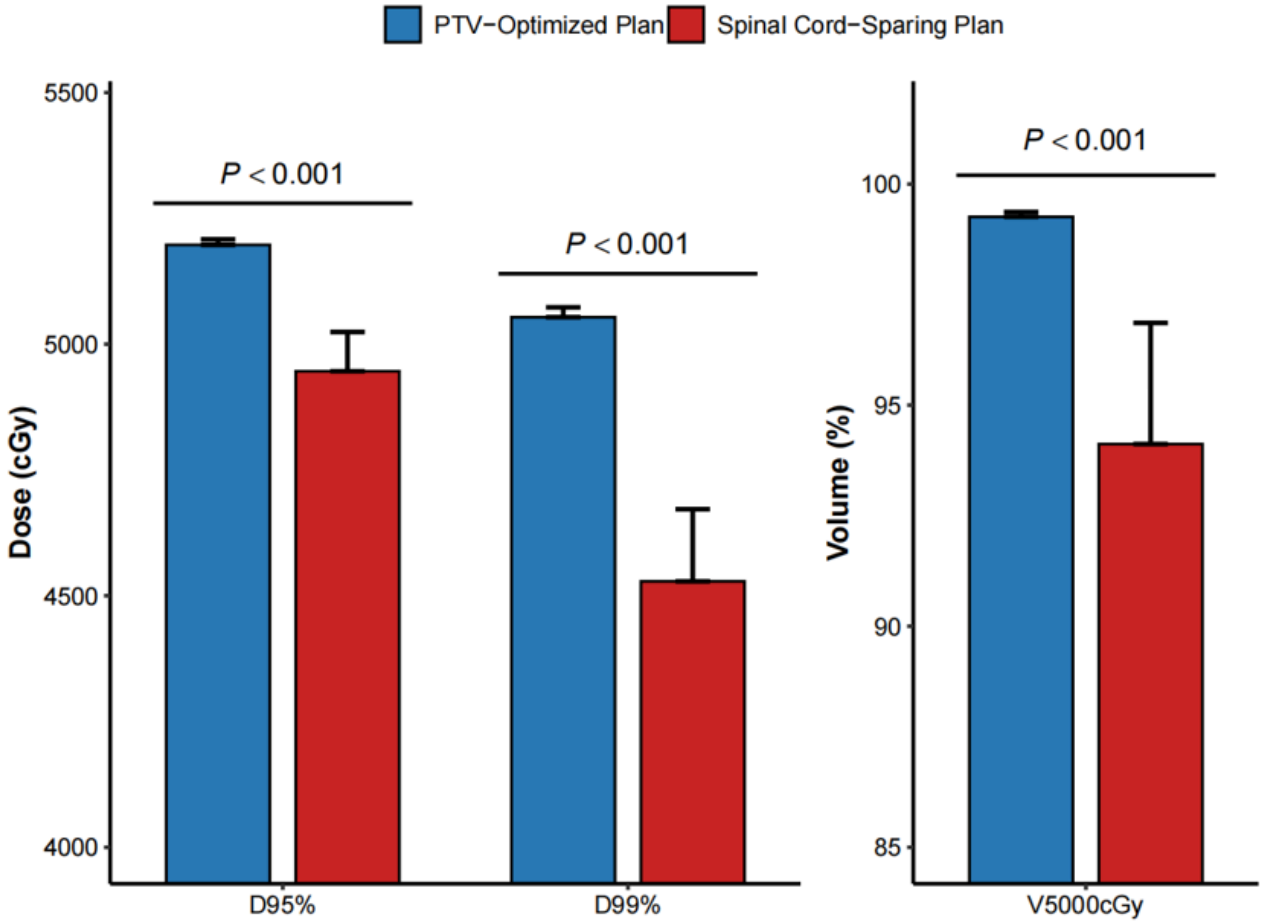


Figure 3

Dosimetric compromise in target coverage under strict spinal cord constraints in the 0-mm gap simulation. Bar charts compare target dose-volume metrics between the PTV-Optimized Plan (target-priority, blue bars) and the Spinal Cord-Sparing Plan (spinal cord-priority, red bars) using a 10-mm MLC. The left panel shows significant reductions in the D95% and D99% absolute doses (cGy) to the target volume when spinal cord constraints (Dmax ≤ 45 Gy) are strictly enforced. The right panel illustrates a critical drop in the target V5000cGy (the percentage of the volume receiving the 50 Gy prescription dose), decreasing from 99.26% to 94.12% (P < 0.001). Error bars represent standard deviations.