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Dose Evaluation of Fractionated Schema and Distance From Tumor to Spinal Cord for Spinal SBRT with Simultaneous Integrated Boost: A Preliminary Study

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Background: This study investigated and quantified the dosimetric impact of the distance from the tumor to the spinal cord and fractionation schemes for patients who received stereotactic body radiation therapy (SBRT) and hypofractionated simultaneous integrated boost (HF-SIB).

Material/Methods: Six modified planning target volumes (PTVs) for 5 patients with spinal metastases were created by artificial uniform extension in the region of PTV adjacent spinal cord with a specified minimum tumor to cord distance (0–5 mm). The prescription dose (biologic equivalent dose, BED) was 70 Gy in different fractionation schemes (1, 3, 5, and 10 fractions). For PTV V_{100}, D_{min}, D_{98}, D_{95}, and D_1, spinal cord dose, conformity index (CI), V_{30} were measured and compared.

Results: PTV-to-cord distance influenced PTV V_{100}, D_{min}, D_{98}, and D_{95}, and fractionation schemes influenced D_{min} and D_{98}, with a significant difference. Distances of ≥2 mm, ≥1 mm, ≥1 mm, and ≥0 mm from PTV to spinal cord meet dose requirements in 1, 3, 5, and 10 fractionations, respectively. Spinal cord dose, CI, and V_{30} were not impacted by PTV-to-cord distance and fractionation schemes.

Conclusions: Target volume coverage, Dmin, D_{98}, and D_{95} were directly correlated with distance from the spinal cord for spine SBRT and HF-SIB. Based on our study, ≥2 mm, ≥1 mm, ≥1 mm, and ≥0 mm distance from PTV to spinal cord meets dose requirements in 1, 3, 5 and 10 fractionations, respectively.

MeSH Keywords: Distance Perception • Dose Fractionation • Neoplasm Metastasis • Radiosurgery • Spine

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Background

Although no high-quality prospective randomized study data are available so far, some studies have demonstrated stereotactic body radiation therapy (SBRT) with simultaneous integrated boost (SIB) for metastatic tumors of the spine is safe and clinically effective [1,2]. This technique markedly improved local control with an excellent symptomatic response compared with conventional external beam radiation therapy techniques, and is beginning to change the treatment paradigms for metastatic spine disease, both as post-operative adjuvant therapy and primary definitive local treatment [3].

Spine metastasis SBRT delivers conformal high radiation dose to the tumor target, and steep falloff dose gradients protect adjacent normal structures, especial the spinal cord. The dose falloff and the dose constraints for spinal cord require a certain target-to-cord distance, and a too-narrow distance results in an under-dose in the epidural space, where metastatic progression is the most common [4–9]. The indication of SBRT as the primary treatment for metastatic epidural spinal cord compression (MESCC) and tumors abutting the spinal cord is controversial [1,3]. Some research institutions and clinical trials, including the RTOG 0631 trial, suggest a minimum distance of at least 2–5 mm from tumor to spinal cord to ensure a good dose distribution [7,10–13]. However, the optimal target-to-cord distance is unknown.

Based on radiobiology rationale, multisession or hypofractionated (>5 fractions) therapy can deliver higher biologically effective doses (BED) to tumor targets, especially when it is close to the spinal cord, compared with a single-fractioned radiosurgery regimen [5,14]. In addition, some studies showed that multisession or hypofractionated treatment reduced under-dose at the epidural space and local failure in this region [5,15,16]. Although multiple studies have demonstrated success in treating spine metastases with SBRT, the ideal dose and fractionation regimens have yet to be determined. Thus, in the study we evaluated the impact of target-to-cord distance (0–5 mm) and fractionation regimen (1, 3, 5, and 10 fractions) on SIB-SBRT dosimetry.

Material and Methods

Patients

This study involved 5 patients with isolated spine metastases (single solitary spine metastasis involving 1 spine level, without epidural compression) and treated with image-guided linear accelerator based SIB-SBRT, and selected to represent various spinal lesion locations at 3 spinal levels (1 cervical, 3 thoracic, and 1 lumbar).

Patients were positioned in a stable supine position immobilized by a thermoplastic mask. Before treatment planning, contrast-enhanced planning CT scanning (Brilliance TM CT BigBore, Philips) with 1.5-mm slice thickness and contrast-enhanced 3D planning MR imaging (GE) with FSPGR sequence and 1.2-mm slice thickness were performed for each patient.

Targets and organs-at-risk (OARs) delineation

Planning CT and MR images were fused for gross tumor volume (GTV) and cord contouring. Clinical target volume (CTV) contours were consistent with International Spine Radiosurgery Consortium consensus guidelines [17], and included the entire vertebral body for lesions involving the vertebral body, or adjacent bony structures for lesions involving the lamina, pedicles, and transverse or spinous process, depending on lesion location and extent. The elective CTV (CTV-elective) was the entire vertebra at the metastasis-involved level for the 10-fraction regimen [17]. For each patient, 6 planning target volumes (PTVs) were created by artificial uniform extension from CTV to ensure the minimum PTV-to-cord distance was 0, 1, 2, 3, 4, and 5 mm, respectively.

Two spinal cord contour sets were required in this study: the partial and the conventional spinal cord volumes. The partial spinal cord was contoured by extending 6 mm above and below the PTV for SIB-SBRT with 1–5 fractions, and the conventional spinal cord was contoured by extending 10 cm above and below the PTV for SIB-SBRT with 10 fractions [10,12]. The spinal cord defined above was not enlarged to ensure consistency in all plans, even for the 10-fraction regimen. Additional OARs included pharynx, esophagus, lungs, kidneys, and liver, and the esophagus was extended 6 mm above and below the PTV in the cranio-caudal direction.

SIB-SBRT planning

Inversely optimized intensity-modulated radiation therapy (IMRT), with single-isocenter and coplanar 11 fields, was mandatory with the Pinnacle system (Pinnacle^3 version 9.6, Phillips Medical Systems, Andover, MA). Patients were treated with Elekta Synergy S system consisting of a step-and-shoot IMRT function and a high-resolution multi-leaf collimator (MLC) with 40 leaf pairs, with a leaf width of 4 mm (Beam modulator, Elekta, Crawley, UK). Volumetric image-guidance was performed with kV cone-beam CT CBCT technique (Elekta XVI, Crawley, UK). Informed consent was obtained from all patients before receiving treatment.

For all plans, planning parameters were set as follows: 1 mm for dose grid, 2 cm^2 for minimum segment area, 5 MU for minimum MU, and 50 for the maximum number of optimization iterations. The parameters were isocenter location, the number

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Table 1. Dose constraints* for target and OARs.

Target/OAR	D_{max}	Prescription dose			
		1 Fraction	3 Fractions	5 Fractions	10 Fractions
Dose (Gy)/fractions	–	22/1	33/3	39/5	47.5/10
PTV/BED10 (Gy)	–	22/70	33/70	39/70	47.5/70
PTV-elective/BED10 (Gy)	–	–	–	–	30/39
Spinal cord (Gy)	Point D_{max}	14	22	30	36
	<1.2 mL	7	11.1	13.5	–
	<0.25 mL	10	18	22.5	–
Cauda equina (Gy)	Point D_{max}	16	24	34	37.5
	<5 mL	14	21.9	30	–
Esophagus (Gy)	Point D_{max}	19	27	35	47.5
	<5 mL	14.5	21	27.5	<1 mL <40
Bowel (Gy)	Point D_{max}	22	30	38	–
	< 20 mL	11	20.4	25	<1 mL <37
Kidney (Gy)	< 200 mL	8.4	14.4	17.5	D_{mean} <12
Liver (Gy)	< 700 mL	9.1	17.1	21	D_{mean} <17.5

* Dose constraints for OARs refer to [10,17,39].

of fields, the MLC margin, the gantry, collimator, and couch angles for each beam. The planning objective for the PTV prescription dose was 70 Gy as a biologically effective dose with an α/β of 10 Gy (BED_{10}). An increasing number of clinical studies have demonstrated that high doses (BED_{10}=70 Gy) are required for lasting control of spine metastatic disease [17–20]. The planning objectives for PTV prescription dose and dose constraints for OARs are summarized in Table 1.

In this study, the 5 patients were initially planned with constraint of low-dose spillage (restriction group); and subsequently replanned without constraint of low-dose spillage. The planners tried their best to meet the cord constraints and get the best coverage that they deemed possible (no-restriction group).

Planning evaluation

Dose distributions and dose volume histograms (DVHs) for all plans were evaluated with the following indices:

PTV coverage

V_x means the volume within the target receiving ≥x% of the prescribed dose [21]. For example, the V_{100} of the PTV was used to prescribe the PTV coverage. In this study, PTV coverage required at least 90% of the target volume be covered by the prescription dose. Coverage of 80–90% was acceptable.

Dose parameters of PTV

D_x is defined as the dose covering x% of the target volume [22]. Hence, maximum dose (D_{max}) delivered to the PTV was evaluated by using dose-volume D_1 and point D_{max}, minimum dose (D_{min}) delivered to the PTV, evaluated by using dose-volume D_{99} and point D_{min}. In addition, we also analyzed BED D_{98} and BED D_{95}, which are associated with local control [23].

Conformity index (CI)

CI is the ratio of the prescription isodose volume (PIV) to the PTV volume. In this study, the CI constraint was no more than 1.2 (acceptable deviation: CI <1.5).

V_{30}

V_{30} represents low dose distribution in the normal tissues near the PTV.

Statistics

All statistical analyses were performed using SPSS software (version 13.0, SPSS, Inc., Chicago, IL). The paired t-test was used to compare the dosimetric differences between the restriction and non-restriction groups. The Wilcoxon signed rank test was used to determine the statistically significant differences for

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Table 2. Planning parameters based on different distance of tumor to spinal cord and different fractionation schemes.

Parameters	Distance	Fractionation schemes				*p*
		1F	3F	5F	10F	
V_{100} (%)	0 mm	90.8	92.3	93.6	91.8	0.642
	1 mm	93.6	94.3	94.4	92.8	0.648
	2 mm	95.1	95.1	97.0	94.3	0.179
	3 mm	96.0	96.6	97.9	95.9	0.386
	4 mm	98.0	97.5	98.8	97.0	0.468
	5 mm	99.1	98.6	99.2	98.2	0.651
	p	<0.001	0.002	<0.001	0.002	
BED D_{min} (D_{min}) (Gy)	0 mm	21.4 (10.4)	26.4 (16.8)	29.6 (20.8)	42.8 (32.4)	< 0.001
	1 mm	28.5 (12.6)	33.8 (20.2)	35.8 (24.1)	47.6 (35.2)	< 0.001
	2 mm	35.2 (14.4)	40.0 (22.7)	43.8 (28.0)	53.2 (38.4)	< 0.001
	3 mm	42.3 (16.1)	49.4 (26.3)	51.6 (31.6)	57.5 (40.8)	< 0.001
	4 mm	49.2 (17.7)	56.3 (28.7)	57.8 (34.3)	61.7 (43.1)	0.002
	5 mm	56.3 (19.2)	60.1 (30.0)	59.8 (35.1)	65.7 (45.2)	0.019
	p	<0.001	<0.001	<0.001	<0.001	
BED D_{98} (D_{98}) (Gy)	0 mm	42.8 (16.2)	50.8 (26.8)	55.1 (33.1)	58.3 (41.3)	0.002
	1 mm	52.6 (18.4)	58.4 (29.4)	61.1 (35.6)	62.6 (43.6)	0.032
	2 mm	60.1 (20.0)	63.7 (31.2)	66.4 (37.8)	66.2 (45.5)	0.005
	3 mm	64.7 (20.9)	67.5 (32.4)	69.1 (38.9)	68.6 (46.7)	0.007
	4 mm	69.8 (21.9)	68.7 (32.8)	70.3 (39.3)	69.1 (47.0)	0.009
	5 mm	72.2 (22.3)	69.6 (33.1)	70.8 (39.5)	70.1 (47.5)	0.029
	p	<0.001	<0.001	<0.001	<0.001	
BED D_{95} (D_{95}) (Gy)	0 mm	60.7 (20.1)	63.8 (31.3)	65.8 (37.6)	66.6 (45.7)	0.177
	1 mm	66.4 (21.3)	67.6 (32.5)	68.0 (38.4)	68.1 (46.5)	0.721
	2 mm	69.4 (21.8)	69.3 (33.0)	70.3 (39.4)	69.4 (47.2)	0.625
	3 mm	70.5 (22.0)	70.1 (33.3)	71.0 (39.6)	70.4 (47.7)	0.830
	4 mm	71.5 (22.2)	70.5 (33.4)	71.3 (39.7)	70.9 (47.9)	0.502
	5 mm	72.9 (22.5)	71.2 (33.6)	71.6 (39.9)	71.7 (48.3)	0.082
	p	<0.001	0.013	0.001	0.020	
BED D_1 (D_1) (Gy)	0 mm	105.0 (27.8)	102.5 (42.4)	97.8 (49.3)	85.2 (55.0)	0.001
	1 mm	104.9 (27.7)	102.2 (42.4)	97.3 (49.1)	85.3 (55.0)	0.012
	2 mm	104.4 (27.7)	99.2 (41.6)	95.3 (48.4)	84.8 (54.8)	0.010
	3 mm	101.0 (27.1)	94.0 (40.2)	90.7 (46.9)	84.6 (54.7)	0.027
	4 mm	93.1 (25.9)	88.8 (38.8)	86.0 (45.2)	82.1 (53.5)	0.042
	5 mm	94.4 (26.1)	83.4 (37.3)	82.7 (44.0)	82.7 (53.8)	0.076
	p	0.381	< 0.001	< 0.001	0.507	
CI	0 mm	1.12	1.14	1.16	1.16	0.552
	1 mm	1.14	1.15	1.14	1.17	0.816
	2 mm	1.15	1.15	1.13	1.16	0.793
	3 mm	1.16	1.11	1.15	1.17	0.425
	4 mm	1.15	1.13	1.11	1.19	0.105
	5 mm	1.16	1.16	1.18	1.16	0.867
	p	0.932	0.549	0.211	0.729	

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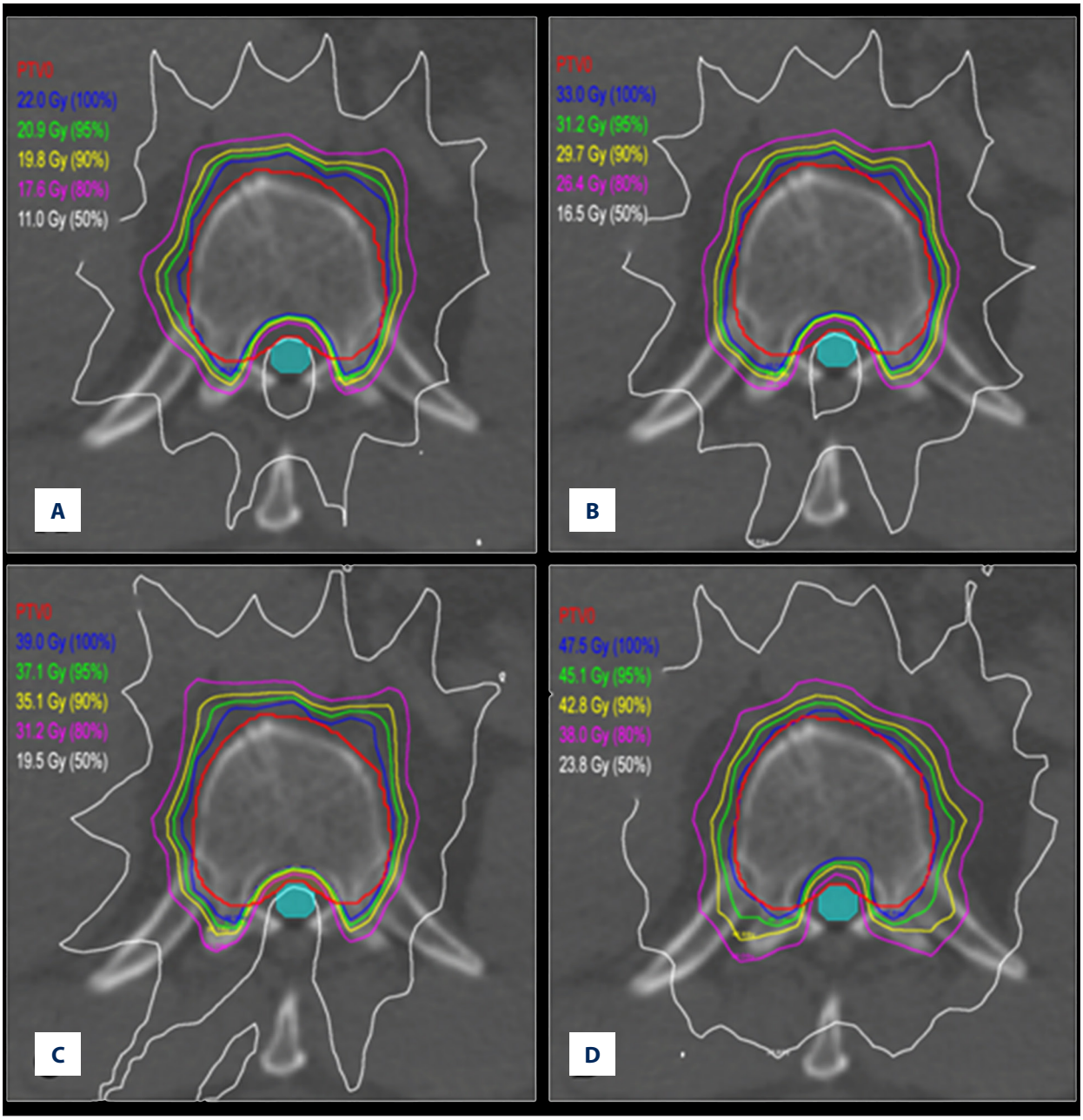

Figure 1. Dose distributions of PTV0 in different fractionated schemes (numbers indicate distance of the PTV to the spinal cord). (**A**) 1 fraction; (**B**) 3 fractions; (**C**) 5 fractions; (**D**) 10 fractions.

all the parameters in different PTV-to-cord distances if the sample sizes were the unequal variances or abnormal distribution. A 2-tailed value of $p<0.05$ was defined as having statistical significance.

Results

A total of 120 SBRT plans were analyzed. Table 2 summarizes the planning parameters based on different distances of tumor to spinal cord (0–5 mm) and different fractionation schemes (1, 3, 5, and 10 fractions).

PTV and PTV-elective coverage

The average PTV V_{100} increased with the increasing distance from the PTV to the spinal cord in different fractionation schemes, with a statistically significant difference. The minimum PTV V_{100} is 87.3% when the distance from the PTV to the spinal cord is 0 mm in 1 fractionation. The average PTV

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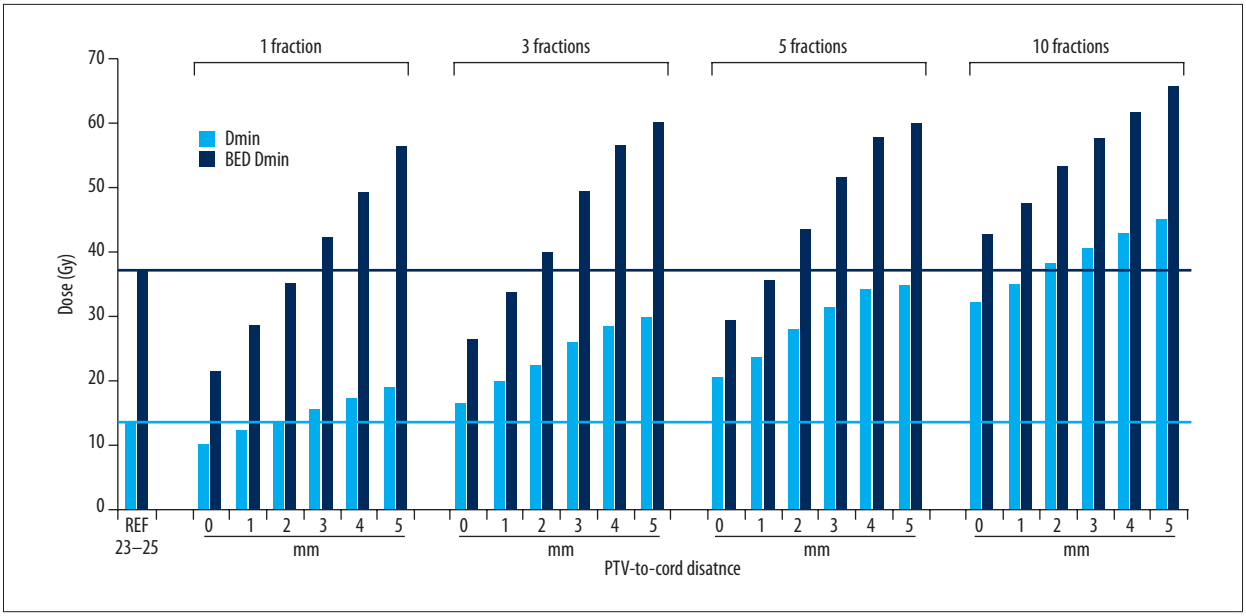

Figure 2. The mean PTV D_{min} and BED D_{min} at different distances (33.6 Gy was at least BED-reduced local recurrence based on references).

V_{100} was not statistically different among different fractionation schemes in the same distance from the PTV to the spinal cord (Table 2).

The average PTV-elective V_{100} was not statistically different among different distances between the PTV and spinal cord in 10-fraction regimen of HF-SIB, with 97.6, 97.8, 97.7, 97.8, 97.7, and 97.8% for the 0, 1, 2, 3, 4, and 5 mm, respectively, (p=0.998).

Dose distributions of PTV in different fractionated schemes are illustrated in Figure 1.

Dosimetry of PTV

Mean PTV minimum dose (D_{min}) and BED D_{min} were enhanced markedly with the increasing PTV-to-spinal cord distance, with a significant difference in the different fractionation schemes (for 4 fractionation schemes: $P<0.001$). Mean PTV D_{min} and BED D_{min} increased with increasing fractionations in the same distance from PTV to spinal cord, with a significant difference.

Mean PTV BED D_{98} were dramatically increased with increasing PTV-to-spinal cord distance and the fractionations in the same distance from PTV to spinal cord, with a significant difference in the different fractionation schemes.

Mean PTV BED D_{95} had the same tendency as PTV BED D_{98}, with increasing PTV-to-spinal cord distance. However, there were no significant differences for BED $D_{95\%}$ in the different fractionation schemes.

Several study results indicated that D_{min} might be an important risk factor for local failure, and recommend maintaining a PTV D_{min} above 14 Gy in 1 fraction (BED_{10}=33.6 Gy) [23–25], 15 Gy in 1 fraction (BED_{10}=37.5 Gy) [26], or 21 Gy in 3 fractions (BED_{10}=35.7 Gy) [23]. Figure 2 displays the mean PTV D_{min} and BED D_{min} in the different distances of the PTV to the spinal cord, as compared with at least BED of reducing local recurrence. Additionally, BED D_{98} and BED D_{95} were not less than 47.1 and 50.4 Gy might reduce local failure according to Bishop et al. [23]. Figure 3 displays the mean PTV BED D_{min}, BED D_{95}, and BED D_{98} in the different distances of the PTV to the spinal cord, as compared with at least BED of reducing local recurrence.

PTV Conformality

The median of CI for different distances from PTV to the spinal cord and the different fractionation schemes were not statistically significant (Table 2).

PTV $V_{30\%}$

The mean V_{30}, representing low-dose distribution of the SBRT plans, was not statistically significant in different distances from PTV to the spinal cord and the different fractionation schemes (Table 3).

Spinal cord dose

For the spinal cord D_{max}, 0.25, and 1.2 cm^3, spinal cord doses meet the requirements of plan, were not statistically significant

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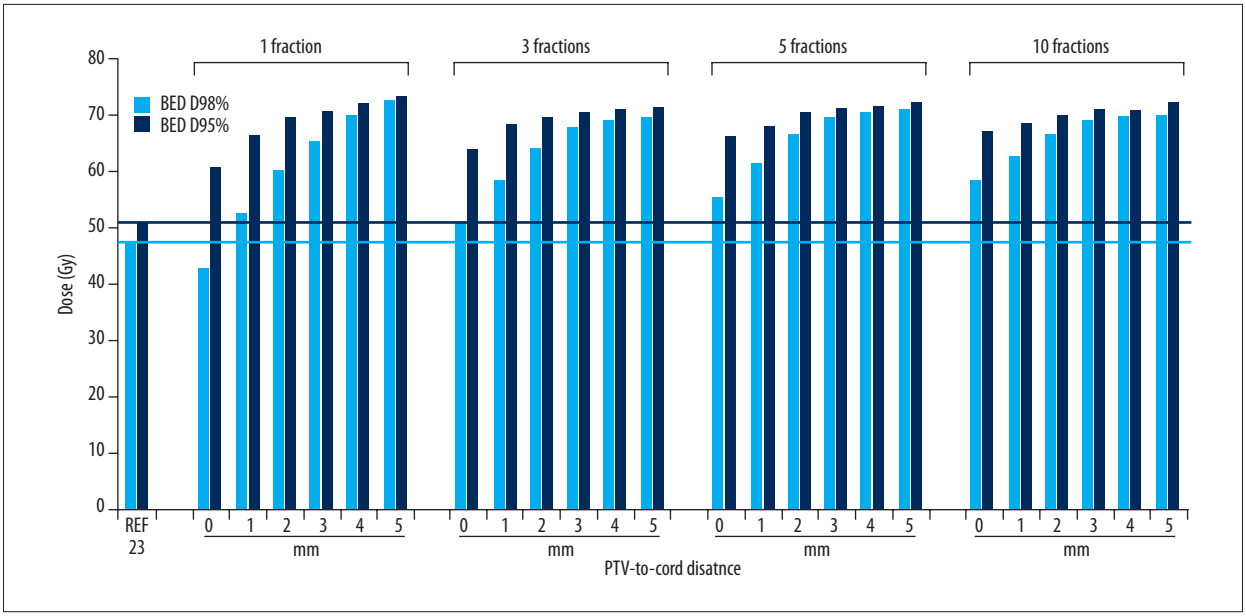

Figure 3. The mean PTV D_{98} and D_{95} (48.1 Gy and 50.5 Gy were at least BED of reducing local recurrence based on reference.

in different distances from the PTV to the spinal cord in the different fractionation schemes. For the spinal cord D_{max}, 0.25, and 1.2 cm^3, spinal cord doses had a reducing trend with the increasing numbers of fractionations in the same distance from the PTV to the spinal cord. Because of spinal cord dose constraints of BED, D_{max} was in conformity in different fractionation schemes, and there are no comparisons to show.

Discussion

The use of SBRT and HF-SIB has been increasing in the treatment of metastatic spinal tumors. A survey of clinical practice in the United States reported that with the adoption of SBRT, the spine is the second most common disease site treated with SBRT (67.5% of the SBRT users) [27]. SBRT and HF-SIB, whether definitive local treatment or postsurgical decompressing and stabilizing the spine adjuvant treatment, has an advantage of allowing the delivery of a high ablative dose to the tumor while sparing the surrounding normal tissues. Thus, SBRT and HF-SIB plans require not only optimal dose conformity in the high dose region, but more importantly, must have a sharp dose fall-off outside the target.

However, the distance between tumor and spinal cord is the major factor influencing dose fall-off, and distances that were too short caused under-dosed in the epidural space. On the one hand, in treatment plans, because the spine and target volume shape are irregular, the dose fall-off distance from the point of high radiation dose to another point of lower radiation dose (usually the prescription isodose line from 90 to 50% isodose lines) is 2–5 mm between these 2 isodose lines. On the other hand, several clinical studies suggest a minimum distance of at least 2–5 mm from tumor to spinal cord to reduce failure to enter the epidural space [7,10–13]. This precludes exactly those patients at highest risk of spinal cord compression.

Our study determined the minimum distance between the tumor and the spinal cord, with no impact on inferior dosimetry causing local recurrences, for patients undergoing IMRT-based image-guided spine SBRT and HF-SIB in different fractionated schemes. Bishop et al. [23] reported 332 spinal metastases consecutively treated with SBRT, and 44 patients (13%) with local recurrences. Notably, the only factors associated with local relapse on univariate analysis were the PTV dosimetric parameters, including D_{min}, D_{98}, and D_{95}. The results indicated that D_{min} might be important risk factors for local failure and recommended maintaining a PTV D_{min} above 14 Gy in 1 fraction (BED_{10}=33.6 Gy) and 21 Gy in 3 fractions (BED_{10}=35.7 Gy). Additionally, BED D_{98} and BED D_{95} were not less than 47.1, and 50.4 Gy might reduce local failure. Similar findings were reported by Lovelock et al. [26], who observed a correlation of D_{min}, D_{98}, and D_{95} among 7 patients with local failure for 91 consecutively treated lesions observed in 79 patients. Specifically, they reported no local failures in patients with a D_{min} above 15 Gy (BED_{10}=37.5 Gy), which is very close to results in several other studies. Ryu et al. [25,28] analyzed the pain relief effect in various factors, showing a strong trend of increased pain control with higher radiation dose ≥14 Gy, although without reaching statistical significance. Based on our study, the distance from PTV to spinal cord ≥2 mm, ≥1 mm, ≥1 mm, and ≥0 mm in 1, 3, 5, and 10 fractions meet PTV BED D_{min}, D_{98} and D_{95}, respectively. Recommend fractionated schemes based on dosimetric parameters and different distances are shown in Table 4.

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Table 3. Spinal cord dose and V_{30} based on different distances and different fractionation schemes.

Parameters	Distance	Fractionation schemes				*p*
		1F	3F	5F	10F	
Spinal cord BED D_{max} (Gy)	0 mm	109.1 (13.8)	98.7 (21.5)	111.2 (28.7)	99.0 (35.6)	0.014
	1 mm	109.3 (13.8)	100.8 (21.8)	104.7 (27.7)	99.1 (35.6)	0.070
	2 mm	104.5 (13.5)	99.5 (21.6)	108.3 (28.3)	98.5 (35.5)	0.154
	3 mm	107.3 (13.7)	97.6 (21.4)	102.1 (27.3)	97.7 (35.3)	0.018
	4 mm	108.6 (13.8)	98.4 (21.5)	101.7 (27.3)	99.4 (35.7)	0.058
	5 mm	107.3 (13.7)	97.2 (21.3)	101.5 (27.2)	98.8 (35.6)	0.063
	p	0.149	0.208	0.621	0.786	
Spinal cord 0.25 mL (Gy)	0 mm	57.6 (9.8)	60.3 (16.3)	61.9 (20.3)	79.7 (31.2)	0.005
	1 mm	58.8 (9.9)	61.6 (16.5)	61.5 (20.2)	80.0 (31.2)	0.011
	2 mm	57.0 (9.7)	59.8 (16.2)	63.3 (20.6)	79.5 (31.1)	0.008
	3 mm	58.5 (9.9)	61.1 (16.4)	62.3 (20.4)	79.5 (31.1)	0.006
	4 mm	58.9 (9.9)	60.4 (16.3)	62.9 (20.5)	80.0 (31.2)	0.004
	5 mm	58.3 (9.9)	61.0 (16.4)	61.9 (20.3)	81.3 (31.5)	0.007
	p	0.701	0.937	0.998	0.990	
Spinal cord 1.2 mL (Gy)	0 mm	29.3 (6.7)	31.0 (11.0)	29.5 (12.9)	62.2 (26.6)	0.011
	1 mm	28.5 (6.6)	30.9 (10.9)	30.3 (13.1)	63.7 (27.0)	0.006
	2 mm	28.8 (6.6)	31.0 (11.0)	29.1 (12.8)	63.9 (27.1)	0.009
	3 mm	29.2 (6.7)	30.7 (10.9)	30.0 (13.0)	64.2 (27.2)	0.006
	4 mm	28.7 (6.6)	30.2 (10.8)	29.4 (12.9)	64.1 (27.2)	0.012
	5 mm	29.0 (6.7)	30.8 (10.9)	26.3 (12.0)	66.5 (27.8)	0.004
	p	0.999	0.442	0.399	0.960	
V_{30}	0 mm	749.8	769.8	816.8	698.4	0.673
	1 mm	778.8	801.9	841.1	710.7	0.416
	2 mm	750.8	809.8	830.0	705.2	0.535
	3 mm	774.0	784.8	807.5	700.4	0.427
	4 mm	743.1	776.4	768.1	716.4	0.748
	5 mm	741.5	772.2	746.8	707.3	0.504
		0.985	0.981	0.889	0.997	

Ma et al. [29] reported results of intracranial radiosurgery, suggesting that hypofractionated treatments with the sharp dose fall-off for fast-growing tumors with α/β ranging from 10 to 20 may be as effective in sparing the normal brain tissue. In spinal metastases, for tumor response, some studies had reported BED with α/β=10 Gy, and for central nervous system late tissue effects (e.g., spinal cord) α/β=2 or 3 Gy [30]. HF-SIB delivers a high dose to a localized tumor by a stereotactic approach and spares the adjacent spinal cord, while meeting PTV BED D_{min}, D_{98}, and D_{95} dosimetric parameters and achieves a considerably higher 2-Gy equivalent dose in the region adjacent to the spinal cord. Thus, HF-SIB could be used as the primary treatment for tumors abutting the spinal cord or metastatic epidural spinal cord compression (MESCC), and the

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Table 4. Recommend fractionated scheme based on dosimetric parameters and different distances.

Distances	PTV coverage				BED Dmin				BED D_{98}				BED D_{95}			
	≥86%				≥33.6 Gy				≥47.1 Gy				≥50.4 Gy			
	1F	3F	5F	10F	1F	3F	5F	10F	1F	3F	5F	10F	1F	3F	5F	10F
0 mm	√	√	√	√	×	×	×	√	×	√	√	√	√	√	√	√
1 mm	√	√	√	√	×	√	√	√	√	√	√	√				√
2 mm	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
3 mm	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
4 mm	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
5 mm	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

conclusion on the basis of treatment techniques is supported by several clinical studies [2,17,31].

To the best of our knowledge, few studies have reported target coverage as a predictor of local failure following SBRT for spinal tumors. Jawad et al. [32] reported 67 spinal tumors treated with SBRT, and the median prescription dose was 18 Gy delivered in 1–5 fractions. The absolute volume of PTV receiving <80% of the prescription dose was significantly higher for tumors with local failure (p=0.003). Bishop et al. [23] found that in 44 patients with local recurrences, approximately half of the recurrences occurred at the margin of the prescription isodose line. Furthermore, patients with marginal recurrences had significantly worse PTV prescription coverage than those without relapse (86% *vs.* 91%, p=0.002). In our study, average target coverage reached 90.8%, and minimum target coverage reached 87.3%, even if the minimum distance from PTV to spinal cord is 0 mm. Our study results of target coverage met dosimetric parameters of the PTV and were superior to the 2 studies mentioned above; this might be relevant to large mean PTV volumes (minimum volume is 37.9 *vs.* 17.2 cm^3 in our study and Bishop et al. [23], respectively).

CI is an objective and valuable tool to achieve dose distribution conforming to the shape of the target volumes, and an objective comparison of different treatment plans in spine SBRT and HF-SIB. The study based on Hong et al. [33] and RTOG 0915 [34] protocol criteria defined and evaluated CI achieving improved treatment plan quality. For the CI in our study, the statistical analysis shows that there is no correlation with distance from PTV to spinal cord and fractionation schemes at the same BED. Some studies have reported that CIs are affected by different treatment techniques (e.g., IMRT and VMAT) and multileaf collimator leaf width [35–37].

Spine SBRT is associated with a significant skin dose and potential toxicity that is rarely observed in conventionally fractionated radiotherapy [38]. Therefore, it is essential to limit low-dose spillage of normal tissue outside target volumes. RTOG 0613 has established detailed requirements for treatment planning of spine SBRT about low-dose spillage, and demands that the falloff gradient beyond the target volume extending into normal tissue structures must be rapid in all directions. However, there is no quantitative guidance regarding the low-dose spillage. In our study, the mean V_{30}, representing low-dose distribution of the SBRT and HF-SIB plans, was not affected by distance from PTV to spinal cord or the fractionation schemes. Using the steep falloff gradient of the target dose with negligible skin and muscle tissue dose and limiting low dose spillage, SBRT and HF-SIB can protect the surrounding normal tissue and can be given early in the postoperative period without adding to risk of wound breakdown [4] or being affected by distance from PTV to cord and the fractionation schemes.

In the present study, all the treatment plans were designed to obtain the maximal target volume coverage, D_{min}, D_{98}, and D_{95} and minimum low-dose spillage, and were required to meet dose constraints of the OARs (e.g., spinal cord). Our study was designed mainly to compare dosimetry indices and was not an intentional strict constraint of the OARs in order to induce influence factor of dosimetry; therefore, there were no differences in the comparison of the indices for the spinal cord, although it is the most important organ at risk in spine SBRT and HF-SIB.

Conclusions

Target volume coverage, D_{min}, D_{98}, and D_{95} were directly correlated with distance from the spinal cord for spine SBRT and HF-SIB. Based on our study, ≥2 mm, ≥1 mm, ≥1 mm, and ≥0 mm distance from PTV to spinal cord meet dose requirements in 1, 3, 5 and 10 fractionations, respectively.

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In our study, low-dose distribution and the indices for the spinal cord of the SBRT and HF-SIB plans were not affected by distance from PTV to spinal cord or the fractionation schemes. However, the conclusions may apply to no more than 70 Gy (BED_{10}) due to our prescribed dose BED_{10} equalling 70 Gy.

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Conflict of interests

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