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Clinical Investigation

Consensus Contouring Guidelines for Postoperative Stereotactic Body Radiation Therapy for Metastatic Solid Tumor Malignancies to the Spine

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Summary

We sought to develop consensus contouring

Purpose: To develop consensus contouring guidelines for postoperative stereotactic body radiation therapy (SBRT) for spinal metastases.

Methods and Materials: Ten spine SBRT specialists representing 10 international centers independently contoured the clinical target volume (CTV), planning target volume (PTV),

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guidelines to promote safe and effective practice of SBRT for spinal metastases in the postoperative setting. Ten spine specialists from 10 international centers independently contoured target volumes for 10 common clinical scenarios. Agreement between physicians was calculated quantitatively with an expectation minimization algorithm using simultaneous truth and performance level estimation with κ statistics. This article summarizes and presents the consensus contours.

spinal cord, and spinal cord planning organ at risk volume (PRV) for 10 representative clinical scenarios in postoperative spine SBRT for metastatic solid tumor malignancies. Contours were imported into the Computational Environment for Radiotherapy Research. Agreement between physicians was calculated with an expectation minimization algorithm using simultaneous truth and performance level estimation with κ statistics. Target volume definition guidelines were established by finding optimized confidence level consensus contours using histogram agreement analyses.

Results: Nine expert radiation oncologists and 1 neurosurgeon completed contours for all 10 cases. The mean sensitivity and specificity were 0.79 (range, 0.71-0.89) and 0.94 (range, 0.90-0.99) for the CTV and 0.79 (range, 0.70-0.95) and 0.92 (range, 0.87-0.99) for the PTV), respectively. Mean κ agreement, which demonstrates the probability that contours agree by chance alone, was 0.58 (range, 0.43-0.70) for CTV and 0.58 (range, 0.37-0.76) for PTV ($P<.001$ for all cases). Optimized consensus contours were established for all patients with 80% confidence interval. Recommendations for CTV include treatment of the entire preoperative extent of bony and epidural disease, plus immediately adjacent bony anatomic compartments at risk of microscopic disease extension. In particular, a "donut-shaped" CTV was consistently applied in cases of preoperative circumferential epidural extension, regardless of extent of residual epidural extension. Otherwise more conformal anatomic-based CTVs were determined and described. Spinal instrumentation was consistently excluded from the CTV.

Conclusions: We provide consensus contouring guidelines for common scenarios in postoperative SBRT for spinal metastases. These consensus guidelines are subject to clinical validation.

Introduction

Surgery is a critical therapeutic modality in the management of complex spinal metastases. For patients with symptomatic single spinal level malignant epidural spinal cord compression (MESCC), surgical decompression followed by conventional radiation therapy (RT) has been proven to be superior with respect to ambulatory function as compared with RT alone (1). A more modern, although not randomized, prospective study also suggests a significant benefit in quality of life in those patients with MESCC treated with surgery plus RT (2). The surgical intent is circumferential decompression with stabilization of the vertebral column. Frank mechanical instability, impending instability, or MESCC are other typical surgical indications. Regardless of the type of surgery, adjuvant conventional external beam RT is delivered with the intent of tumor control, and most typically a regimen of 30 Gy in 10 fractions is used. As patients with metastatic disease live longer owing to more effective systemic therapy, the complexity of spinal metastases management will only continue to evolve in both surgical and RT domains. One such development in spine RT has been the transition from conventional RT to the use of stereotactic body radiation therapy (SBRT).

Spine SBRT was developed with the intent to deliver a higher biologically equivalent dose in a hypofractionated treatment schedule as compared with conventional RT. The goal was to maximize both local and pain control because conventional RT is associated with suboptimal results. Although no randomized, controlled trials have been published to confirm the benefit of SBRT over conventional RT, an increasing body of literature demonstrates excellent local control after SBRT for both radio-sensitive and radio-resistant primary tumors, with rates of in-field failure <20% with median follow-up ranging from 6 to 21 months (3-8). As the technique has matured, its application to the postoperative patient is emerging (7, 9-14). Historically, postoperative RT has been associated with local control rates ranging from 4% to 79% (15-18), and the current, albeit few, postoperative spine SBRT series suggest rates of approximately 70% to 100% (7, 9-13, 17-21).

The practice of postoperative spine SBRT is unique compared with intact metastases because considerations must be made specific to the preoperative tumor location, residual disease, spinal hardware, and more specifically the epidural space. It has been shown that the most common pattern of failure after SBRT in both intact and postoperative patients is within the epidural space (9, 11, 13), and as such in both the surgical and RT domains there is increasing attention to the management of epidural disease. This is highlighted by the increasing adoption of separation surgery, in which the intent is to decompress, downgrade the epidural disease, and minimize tumor debulking as this surgical approach is coupled to postoperative spine SBRT as the modality to render tumor control (11-13). The consequences of epidural failure cannot be underscored because there is potential for neurologic compromise, reoperation, and deterioration in quality of life. Therefore, the potential for geographic miss due to the conformality of spine SBRT should be minimized. The success of prior contouring guidelines for spine SBRT

(22) for intact spinal metastases prompted this present effort aiming to develop consensus contouring guidelines for representative postoperative cases, based on the preoperative and postoperative imaging among experts in the field. We propose uniform reproducible guidelines, but future prospective evaluation is required to evaluate the impact on clinical outcomes.

Methods and Materials

Nine spine radiation oncologists and 1 neurosurgeon with a collective experience of more than 1400 postoperative spine SBRT cases participated in the project, which was institutional review board–approved by the coordinating center. Providers were selected from programs with large clinical and academic experience in spine SBRT techniques. Ten cases from real patients treated at a single institution were identified and reviewed by the participants. Clinical scenarios were designed to represent a diverse spectrum of preoperative tumor locations with varying degrees and anatomic locations of epidural involvement and paraspinal extension.

For each of the 10 cases, physicians were given a synopsis of clinical scenario, including the patient's age, oncologic history, neurologic examination results, and details regarding the surgical approach, technique, and findings, as well as applicable pre- and postoperative radiographic results, such as the extent of bony and epidural involvement. Patients were simulated in site-specific custom immobilization. A complete set of anonymized coregistered datasets, including preoperative MRI, postoperative MRI, CT simulation, and CT myelogram when necessary for spinal cord delineation, were provided in Digital Imaging and Communications in Medicine format. Physicians were told that all patients would be treated with SBRT and were asked to independently delineate the clinical target volume (CTV), planning target volume (PTV), and the spinal cord avoidance structure on the axial treatment planning simulation CT scan with 1-mm slices.

Finalized structures were returned to the coordinating center in Digital Imaging and Communications in Medicine format and imported into a commercial treatment planning system for initial review. All contours for each patient were then exported to the Computational Environment for Radiotherapy Research (23) for analysis. Agreement between physician contours was calculated quantitatively using κ statistics, which correct for the probability that contours agree by chance alone. Interpretation of κ results are as follows (23): <0, poor agreement; 0.01 to 0.20, slight agreement; 0.21 to 0.40, fair agreement; 0.41 to 0.60, moderate agreement; 0.61 to 0.80, substantial agreement; 0.81 to 1.00, almost perfect agreement (24). Statistical significance was assessed according to the standard error of the κ statistic, with P values <.01 reflecting a significant difference between observed agreement and chance agreement. Final consensus contours were generated with an expectation minimization algorithm using simultaneous truth and performance level estimation (STAPLE) (25, 26).

In this algorithm the consensus contour is estimated by iteratively optimizing measures of sensitivity and specificity. Sensitivity reflects the probability that a voxel in the consensus contour is also in each of the expert contours, whereas specificity reflects the probability that a voxel outside the consensus contour is also outside 1 or more expert contours. Final consensus contours were generated based on an 80% confidence level, consistent with similar work by Cox et al (22).

Anatomic descriptions of consensus contours were developed using the International Spine Radiosurgery Consortium (ISRC) anatomic classification system previously utilized in the development of consensus contouring guidelines for intact vertebrae (22). Figure 1 outlines this system in which each vertebral level is divided into 6 sectors, including the body (sector 1), left pedicle (sector 2), left transverse process and lamina (sector 3), spinous process (sector 4), right transverse process and lamina (sector 5), and right pedicle (sector 6).

Results

Radiographic characteristics of each case are shown in Table 1, with anatomic descriptions and representative preoperative axial MRI, preoperative sagittal MRI, postoperative

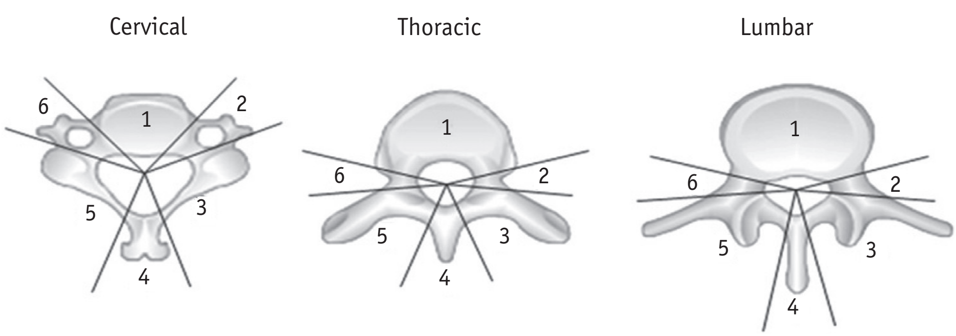
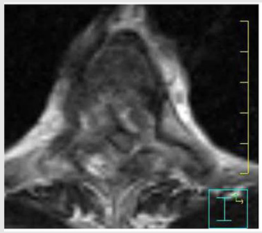
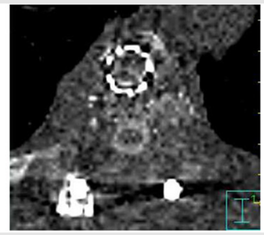
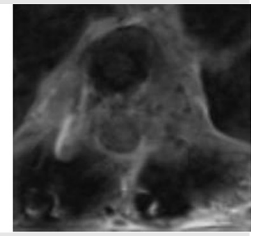
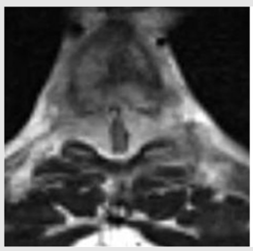
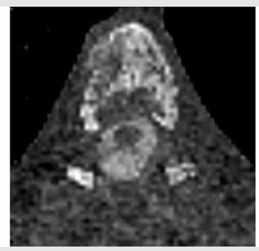
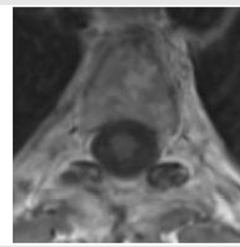
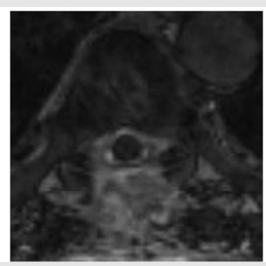
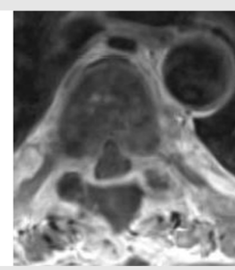
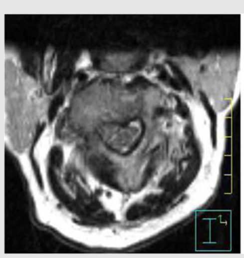
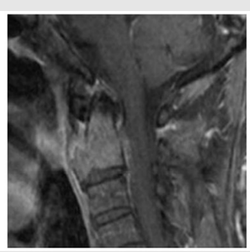
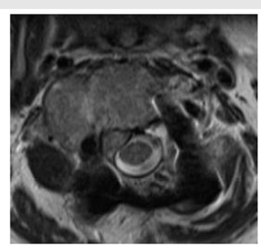
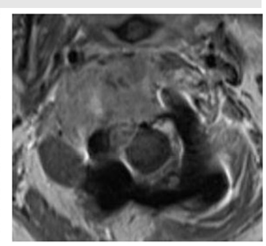
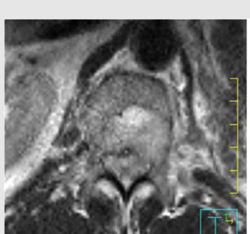
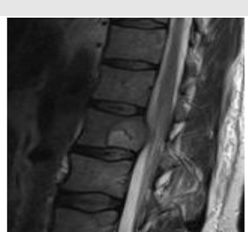
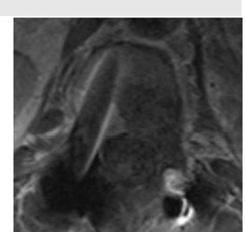


Fig. 1. International Spine Radiosurgery Consortium anatomic classification system for consensus target volumes for spine radiosurgery (28). Reprinted with permission from Elsevier.

Table 1 Summary of cases for postoperative stereotactic body radiation therapy consensus contours for spine metastases

Anatomic description	Preoperative axial MRI	Preoperative sagittal MRI	Postoperative axial CT myelogram or T2 MRI	Postoperative axial T1 post-MRI
Case 1: T5 level. Preoperative circumferential epidural disease with no residual epidural disease postoperatively. Preoperative bony involvement includes the body, bilateral pedicles, bilateral transverse processes, bilateral laminae, and spinous process.				
Case 2: T4 level. Preoperative circumferential epidural disease with focal residual anterior epidural disease postoperatively. Preoperative bony involvement includes the body, bilateral pedicles, bilateral transverse processes, bilateral laminae, and spinous process.				
Case 3: T6 level. Preoperative circumferential epidural disease with residual near circumferential epidural disease postoperatively. Preoperative bony involvement includes the body, bilateral pedicles, bilateral transverse processes, and bilateral laminae.				
Case 4: C2 level. Preoperative anterior and right lateral epidural disease status post stabilization and biopsy. Postoperative residual antero-lateral epidural disease. Preoperative bony involvement includes the body, odontoid, right pedicle, and right transverse process.				
Case 5: L1 level. Preoperative anterior epidural disease. No residual epidural disease postoperatively. Preoperative bony involvement includes the body and bilateral pedicles.				

(*continued on next page*)

Table 1 (*continued*)

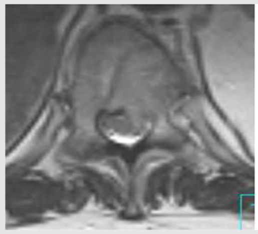
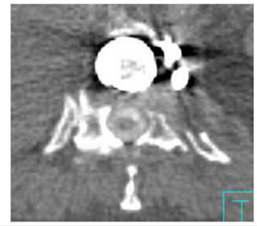
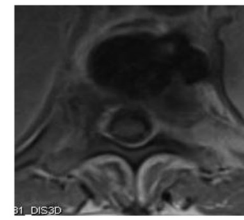
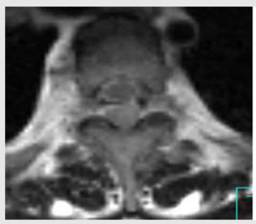
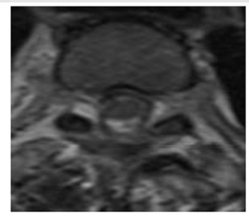
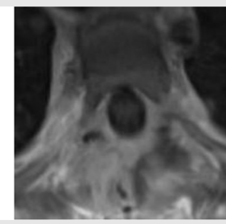
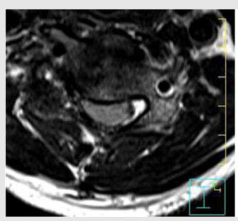
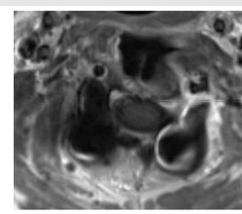
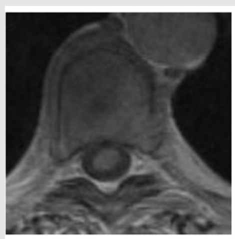
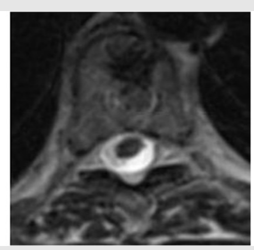
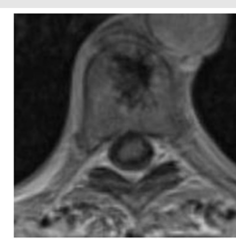
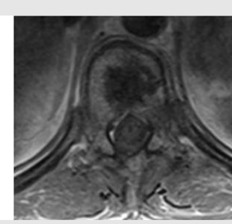
Anatomic description	Preoperative axial MRI	Preoperative sagittal MRI	Postoperative axial CT myelogram or T2 MRI	Postoperative axial T1 post-MRI
Case 6: T11 level. Preoperative anterior and left lateral epidural disease. Postoperative residual antero-lateral epidural disease. Preoperative bony involvement includes the body and left pedicle.				
Case 7: T3 level. Preoperative posterior epidural disease. No residual epidural disease postoperatively. Preoperative bony involvement includes the spinous process, bilateral laminae, and bilateral transverse processes.				
Case 8: C4 level. Preoperative anterior, right lateral, and posterior epidural disease. No residual epidural disease postoperatively. Preoperative bony involvement includes the body, right pedicle, right transverse process, right lamina, and spinous process.				
Case 9: T9 level. Preoperative vertebral body fracture without epidural disease status post vertebroplasty. No residual epidural disease postoperatively. Preoperative bony involvement in the body.				
Case 10: T11 level. Preoperatively anterior and left lateral epidural disease with extensive paraspinal extension. Postoperative residual antero-lateral epidural disease. Preoperative bony involvement includes the body, left pedicle, left transverse process, and left lamina.				

Table 2 Absolute κ agreement, sensitivity, and specificity for CTV target delineation between participating spinal oncology specialists, based on the STAPLE analysis

	CTV				PTV			
Case	Mean sensitivity, average ± SD	Mean specificity, average ± SD	κ measure	P	Mean sensitivity, average ± SD	Mean specificity, average ± SD	κ measure	P
1	0.74 ± 0.22	0.95 ± 0.07	0.57	<.001	0.74 ± 0.20	0.96 ± 0.06	0.59	<.001
2	0.76 ± 0.23	0.93 ± 0.09	0.52	<.001	0.75 ± 0.24	0.92 ± 0.12	0.53	<.001
3	0.77 ± 0.26	0.99 ± 0.02	0.70	<.001	0.70 ± 0.24	0.99 ± 0.02	0.66	<.001
4	0.86 ± 0.16	0.91 ± 0.12	0.63	<.001	0.87 ± 0.12	0.88 ± 0.19	0.60	<.001
5	0.86 ± 0.16	0.94 ± 0.07	0.67	<.001	0.86 ± 0.12	0.93 ± 0.10	0.67	<.001
6	0.78 ± 0.28	0.95 ± 0.05	0.60	<.001	0.77 ± 0.22	0.94 ± 0.10	0.59	<.001
7	0.71 ± 0.29	0.93 ± 0.12	0.43	<.001	0.71 ± 0.29	0.90 ± 0.15	0.37	<.001
8	0.75 ± 0.16	0.93 ± 0.09	0.52	<.001	0.78 ± 0.16	0.91 ± 0.14	0.51	<.001
9	0.89 ± 0.20	0.93 ± 0.07	0.70	<.001	0.95 ± 0.04	0.90 ± 0.11	0.76	<.001
10	0.77 ± 0.30	0.90 ± 0.15	0.46	<.001	0.80 ± 0.20	0.87 ± 0.18	0.47	<.001

Abbreviations: CTV = clinical target volume; PTV = planning target volume; STAPLE = simultaneous truth and performance level estimation.

axial CT myelogram or T2-weighted MRI, and axial T1 post-gadolinium MRI images presented for each case. Two cases involved the cervical spine, 7 involved the thoracic spine, and 1 involved the lumbar spine. Nine of the patients had MESCC preoperatively, and 1 patient had a vertebral body fracture without epidural extension of tumor, which had undergone vertebroplasty. Ten physicians submitted contours for all 10 cases of the CTV, PTV, spinal cord, and spinal cord planning risk volume.

CTV and PTV delineation

Table 2 shows the CTV and PTV contour agreement according to the STAPLE analysis. For the CTV, there was a high level of agreement between contouring physicians, with a mean sensitivity of 0.79 (range, 0.71-0.89) and mean specificity of 0.94 (range, 0.90-0.99) for the CTV. The mean κ agreement for the CTV was 0.58 (range, 0.43-0.70) and was statistically significant, with $P<.001$ for all cases. Similarly, for the PTV the mean sensitivity was 0.94 (range, 0.90-0.99), and the mean specificity was 0.92 (range, 0.87-0.99). The mean κ agreement for the PTV was 0.58 (range, 0.37-0.76), and the agreement was again statistically significant, with $P<.001$ for all cases. The lowest κ scores, representing the most variability between contours, were for cases 7 and 10. Table 3 shows the simulation MRI, with individual contours represented by thin lines and the 80% consensus contours represented by thick red lines, as well as a schematic diagram of these consensus contours as they apply to the ISRC anatomic classification system. Axial preoperative MR images and axial postoperative images are also shown for each patient.

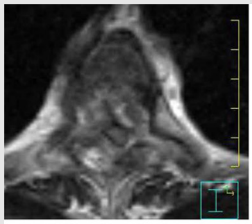
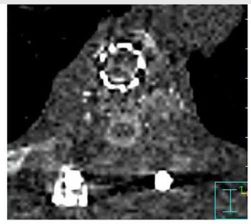
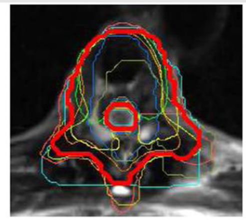
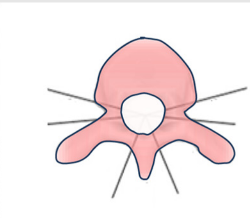
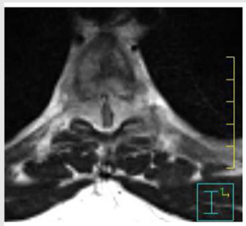
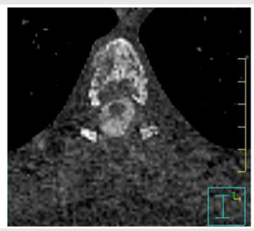
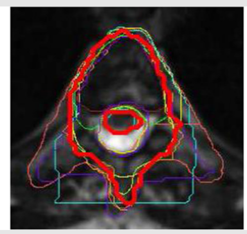
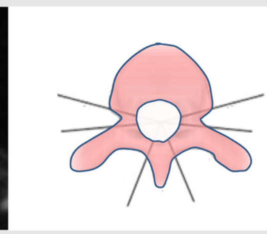
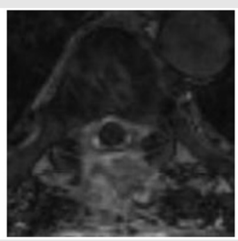
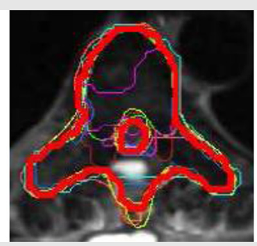
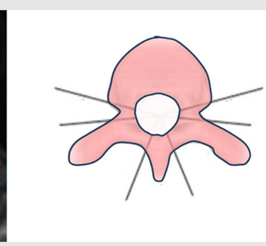
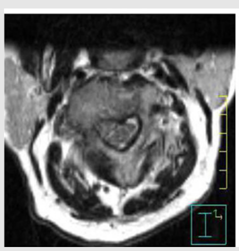
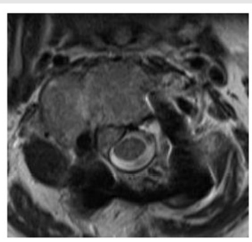
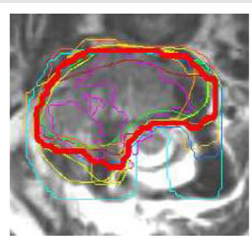
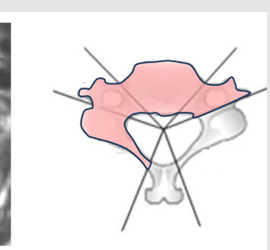
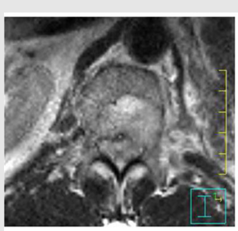
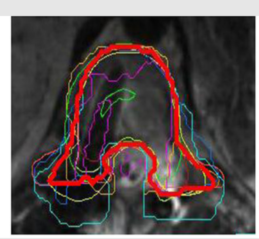
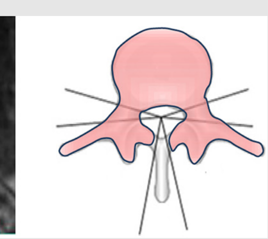
Evaluation of the CTV 80% consensus contours suggests coverage is driven by the preoperative sites of osseous and epidural disease, irrespective of the extent of surgical resection. The CTV generally includes not only the sites of gross residual disease on postoperative CT and MRI, but also the regions that were involved preoperatively according to CT and MRI. There is consistent inclusion of adjacent anatomic compartments at risk of microscopic disease extension. Table 4 describes the postoperative CTV based on preoperative bony and epidural involvement using the ISRC anatomic classification as a framework. The PTV expansions varied between institutions, ranging from no expansion to an approximately 2.5-mm expansion. The cord avoidance structure was consistently subtracted out from the final PTV for treatment planning. Surgical instrumentation and incision do not need to be included unless believed to be specifically at risk of tumor involvement. Table 5 summarizes the overall consensus contouring guidelines for gross tumor volume, CTV, and PTV.

Discussion

Stereotactic body radiation therapy for spinal metastases in the post-operative setting is being increasingly practiced in both community and academic centers, with more recent applications to the postoperative setting (7, 9-14). The historical standard of care has been large, aggressive surgery (often corpectomy) followed by palliative doses of radiation therapy. However, the development of SBRT now allows dose escalation and delivery of ablative radiation doses with excellent local control when SBRT is used as the sole modality of treatment (3-8). Furthermore, innovations in surgical techniques include minimally invasive surgical interventions designed to decompress the spinal cord and stabilize the vertebral column, with substantially shorter recovery periods and more rapid return to systemic therapy than traditional aggressive surgical interventions (11, 13, 19, 27). Therefore, the emerging treatment paradigm of limited surgical intervention followed by aggressive SBRT allows the benefit of surgical intervention and preservation of neurologic function to a broader group of metastatic patients.

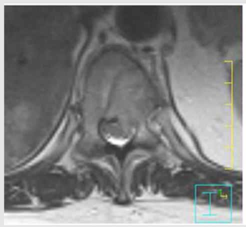
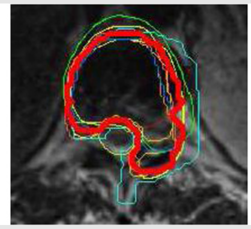
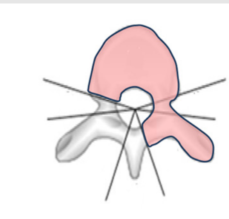
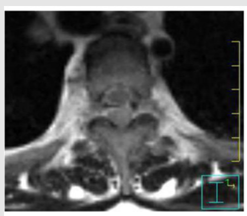
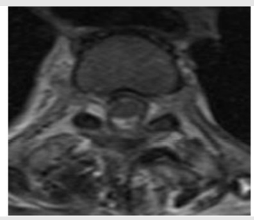
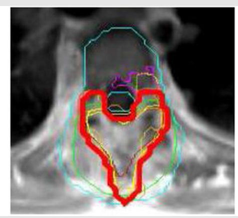
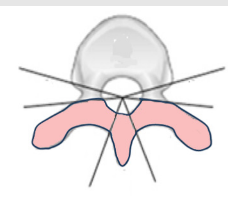
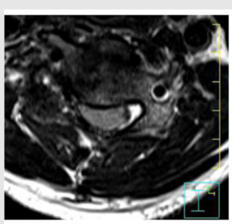
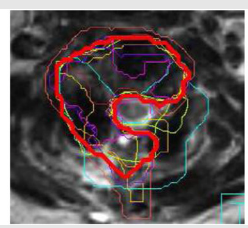
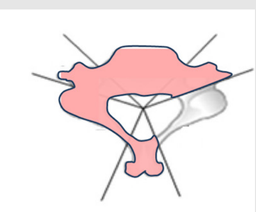
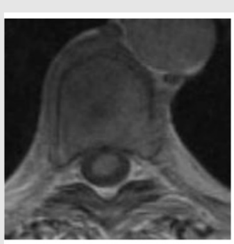
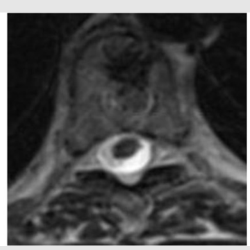
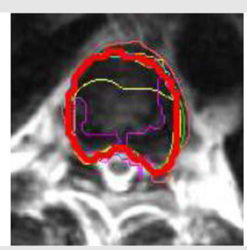
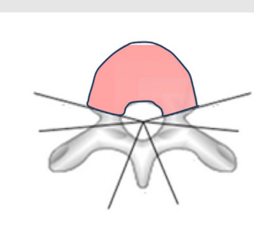
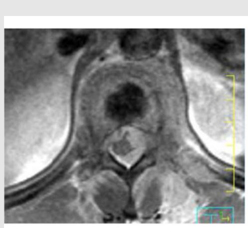
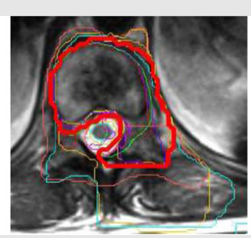
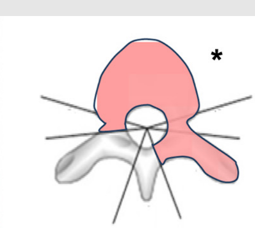
Although consensus guidelines have been established for contouring intact vertebral bodies (22), there are presently no recommendations specific to the postoperative patient. The

Table 3 Consensus clinical target volume contours for postoperative stereotactic body radiation therapy for spine metastases

Patient no.	Preoperative axial MRI	Postoperative axial CT myelogram or T2 MRI	Simulation MRI with individual and consensus CTV contour	Schematic diagram
1				
2				
3				
4				
5				

(*continued on next page*)

Table 3 (*continued*)

Patient no.	Preoperative axial MRI	Postoperative axial CT myelogram or T2 MRI	Simulation MRI with individual and consensus CTV contour	Schematic diagram
6				
7				
8				
9				
10				

Consensus contours are shown in bold red and individual contours are shown in unique colors. *As indicated in the recommendations, the entire preoperative extent of paraspinal disease should at minimum be encompassed in the CTV. (A color version of this table is available at www.redjournal.org.)

need for such guidelines is of paramount importance given developments in spinal surgery that depend on the SBRT to locally control the disease so that surgical morbidity can be reduced by focusing on epidural decompression and stabilization without performing a vertebrectomy. Our study has successfully established consensus in contouring common postoperative spinal metastases cases on the basis of both the pre- and postoperative disease locations according to

Table 4 Guidelines for CTV contouring for postoperative SBRT for spine metastases based on preoperative epidural involvement, and both preoperative and postoperative bony involvement

Preoperative epidural involvement	Preoperative ISRC bony anatomic involvement	Postoperative ISRC bony CTV recommendation	Postoperative CTV description
Circumferential epidural disease	1-3, 5, 6, ±4	1-6	Circumferential treatment including the preoperative body, bilateral pedicles, bilateral transverse processes, bilateral laminae, and spinous process
Anterior epidural involvement in region of central body	1	1	Preoperative body
Anterior epidural involvement in lateral region of body	1	1, 2	Preoperative body plus ipsilateral pedicle ± lamina
Epidural involvement anteriorly in the region of the body and unilaterally in the region of pedicle	1, 2	1-3	Preoperative body plus ipsilateral pedicle, ipsilateral transverse process and ipsilateral lamina
Epidural involvement anteriorly in the region of the body, unilaterally in the region of pedicle, and posteriorly in the region of the spinous process	1, 4-6	1, 3-6, ±2	Preoperative body plus ipsilateral pedicle, bilateral transverse process, bilateral laminae, and spinous process
Posterior epidural involvement in region of spinous process	4	3-5	Preoperative spinous process, bilateral laminae and bilateral transverse processes
Any of the above plus extensive paraspinal extension	As above	As above	As above plus coverage of the entire preoperative extent of paraspinal extension

Abbreviations: CTV = clinical target volume; ISRC = International Spine Radiosurgery Consortium; SBRT = stereotactic body radiation therapy.

the ISRC template, with high sensitivity and specificity (Tables 2 and 3). The significance in the κ statistics confirms nonrandom agreement among the contouring physicians. The automated STAPLE segmentation evaluation limits human-associated inter- and intraobserver errors. The similarity between the contouring guidelines for both intact and postoperative spine SBRT should be noted. Specifically, these guidelines are consistent with the previously published definitive guidelines to include the involved and adjacent ISRC sites but use the extent of preoperative tumor involvement and take into account anatomic changes from surgery. The most variability between physician contours was found in cases 7 and 10. This seems to be due to variability in the subclinical bony coverage in case 7 and paraspinal extension margin in case 10. The recommendations presented in this article are supported by a recent pattern-of-failure analysis (28) specific to postoperative spine SBRT failures and epidural disease. The methodology consisted of examining the location of epidural disease on the preoperative and postoperative MRI, and the relationship to where epidural disease progression was observed according to the 6 sectors previously described by the ISRC. The investigators confirmed that the site at the highest risk of local failure after postoperative spine SBRT is within the epidural space (9, 28).

Table 5 Summary of GTV, CTV, and PTV contouring guidelines for postoperative spine SBRT for spinal metastases

Target volume	Guidelines
GTV	• Gross tumor based on postoperative CT and MRI with attention to residual epidural or paraspinal disease • Include postoperative residual epidural and paraspinal components of tumor
CTV	• Include the postoperative region and entire anatomic compartment corresponding to all preoperative MRI abnormalities suspicious for tumor involvement • Include entire GTV • Surgical instrumentation and incision not included unless involved • Judicious use of circumferential CTVs limited to cases of preoperative circumferential osseous and/or epidural involvement; however, can be considered for near-circumferential epidural disease involvement • Modified at reconstructed dural space and to account for changes in anatomy after surgery at discretion of treating physician • Consider additional anatomic expansions of up to 5 mm beyond paraspinal extension and cranio-caudally for epidural disease
PTV	• Uniform CTV to PTV expansion of up to 2.5 mm • Treating physician may modify expansion at the interface with critical organs at risk • May subtract cord avoidance structure from PTV as a modified PTV for planning and dose reporting purposes • Include entire GTV and CTV

Abbreviations: CTV = clinical target volume; GTV = gross tumor volume; PTV = planning target volume; SBRT = stereotactic body radiation therapy.

The preoperative epidural disease location was observed to be a significant predictor of location of progression, as opposed to the postoperative location of residual epidural disease. This led the investigators to conclude that the CTV must include the anatomy involved according to the preoperative MRI and postoperative MRI. This finding is in agreement with the contouring guidelines proposed in this study. The study by Chan et al (28) also observed that patients with preoperative anterior epidural disease (sectors 1, 6, and 2) alone rarely recurred in the region of the posterior elements (sector 4). However, they did occasionally develop recurrences in the postero-lateral epidural space (sectors 3 and 5), suggesting that if the epidural disease is discrete and centralized, a donut distribution is not required. By contrast, patients with preoperative circumferential epidural disease involvement were at risk of failure in any sector despite surgical clearance, suggesting that a circumferential donut CTV is necessary in these patients. The consensus contours in this study are in agreement with these findings.

It is important to note that there are several limitations of this study. First, although the selected cases were chosen to encompass a wide range of clinical scenarios, they may not be directly applicable to all situations and cannot replace clinical expertise and unique patient-specific decision making. Second, although these consensus guidelines are consistent with the aforementioned patterns-of-failure analysis (28), they are ultimately based on clinical practice patterns of experienced providers and have not been validated. Finally, the cases selected for this contouring exercise were all radiation naïve, and management in the setting of reirradiation has not yet been addressed. It should be noted that this article is not intended as a comprehensive summary of the literature, but reference is provided for a recently published critical review (29).

Conclusions

Our study represents a novel and important contribution to assist in the safe and effective delineation of the CTV in the postoperative spine SBRT patient. Our future research will focus on clinical validation.

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