JJCO Japanese Journal of Clinical Oncology

Japanese Journal of Clinical Oncology, 2022, 52(8)911–916
https://doi.org/10.1093/jjco/hyac070
Advance Access Publication Date: 23 April 2022
Original Article

OXFORD

Original Article

Risk of radiculopathy caused by second course of spine stereotactic body radiotherapy

Kei Ito[1,*], Yujiro Nakajima[1,2], Hiroaki Ogawa[1], Kentaro Taguchi[1] and Shurei Sugita[3]

[1]Division of Radiation Oncology, Department of Radiology, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Bunkyo-ku, Tokyo, Japan, [2]Department of Radiological Sciences, Komazawa University, Setagaya-ku, Tokyo, Japan and [3]Department of Orthopedic surgery, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Bunkyo-ku, Tokyo, Japan

*For reprints and all correspondence: Kei Ito, Division of Radiation Oncology, Department of Radiology, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo 113-8677, Japan. E-mail: keiito600601@gmail.com

Received 29 January 2022; Editorial Decision 4 April 2022; Accepted 8 April 2022

Abstract

Objective: Stereotactic body radiotherapy is used to treat spinal metastases; however, 10% of patients experience local failure. We aimed to clarify the outcomes of the second course of stereotactic body radiotherapy for spinal metastases with a uniform fractionation schedule at our institution.

Methods: Data of patients treated with a second salvage stereotactic body radiotherapy course at the same spinal level or adjacent level from July 2018 to December 2020 were retrospectively reviewed. The initial prescribed dose was 24 Gy in two fractions, and the second dose 30 or 35 Gy in five fractions. The spinal cord dose constraint at the second course was 15.5 Gy at the maximum point dose. The endpoints were local failure and adverse effects. Local failure was defined as tumor progression using imaging.

Results: We assessed 19 lesions in 17 patients, with radioresistant lesions in 14 (74%) cases, the second stereotactic body radiotherapy to the same/adjacent spinal level in 13/6 cases, the median interval between stereotactic body radiotherapy of 23 (range, 6–52) months, and lesions compressing the cord in 5 (26%) cases. The median follow-up period was 19 months. The 12- and 18-month local failure rates were 0% and 8%, respectively. Radiation-induced myelopathy, radiculopathy and vertebral compression fractures were observed in 0 (0%), 4 (21%) and 2 (11%) lesions, respectively. Three patients with radiculopathy experienced almost complete upper or lower limb paralysis.

Conclusions: The second course of salvage stereotactic body radiotherapy for spinal metastases achieved good local control with a reduced risk of myelopathy. However, a high occurrence rate of radiation-induced radiculopathy has been confirmed.

Key words: re-irradiation, second course, stereotactic body radiotherapy, spinal metastases, radiculopathy, toxicity

Introduction

Stereotactic body radiotherapy (SBRT) is a treatment option for spinal metastases (1). SBRT can deliver high-dose radiation to the target volume while sparing adjacent at-risk organs; therefore, it is associated with several clinical advantages, such as high pain control and local control rates (2), high response rates in bone metastases from radioresistant tumors (3) and safe re-irradiation treatments (4). In spine SBRT for pain palliation, the SC.24 trial proved the superiority of SBRT over the conventional external beam radiotherapy (EBRT) (5). Consequently, SBRT is performed more often as the first treatment choice for spinal metastases.

Spine SBRT has shown an excellent local control rate of 80%–90% (2); however, more than 10% of patients experience local failure (LF). Although a second SBRT course may be a treatment option for such patients, data on its effectiveness and safety are lacking. Since innovations in systemic therapy have extended the life expectancy in patients with metastatic disease, the need for a safe re-irradiation protocol for spinal metastases is growing. Therefore, the aim of this study was to clarify the clinical outcomes in patients with spinal metastases treated with a second salvage SBRT course at the same or adjacent spinal level.

Methods

Patients and data acquisition

The database of our institution was retrospectively reviewed to identify patients treated with a second course of spine SBRT between July 2018 and December 2020. We administered a second SBRT course to patients who (i) experienced LF in the same spinal segments treated with SBRT previously or had new lesions in the adjacent spinal level diagnosed by magnetic resonance imaging (MRI), (ii) had a predicted overall survival (OS) of >6 months and (iii) understood the risk of re-treatment after the explanation by radiation oncologists and chose to receive it. Spine SBRT was conducted with a curative intent for oligometastasis, with a palliative intent of painful lesions, or for improvement of neurologic function for epidural spinal cord compression. Patients were included in this study if they met the following criteria: (i) spinal lesion treated with SBRT twice at the same level or using two overlapping SBRT fields due to adjacent spinal lesions, and (ii) evaluation of the lesion images of the irradiated region at least once after the second SBRT.

This study was approved by our institutional ethical review board (approval number 2312), and informed consent was obtained in the form of an opt-out option displayed on the website.

Stereotactic body radiotherapy

The SBRT technique is discussed in detail in a previous publication (6) and briefly summarized here (the methodology used was common in the first and second courses). The clinical target volume (CTV) included the gross tumor volume and immediately adjacent bony anatomic compartments at risk of microscopic disease extension, as described by the contouring guidelines for spine SBRT (7,8). The CTV of the second SBRT did not necessarily include the entire extent of the tumor covered at the initial SBRT. A 2-mm margin was added to the CTV to create the planning target volume (PTV). A 1.5-mm margin was added to the spinal cord and defined as the planning organ-at-risk volume of the cord (PRV_{cord}). The thecal sac was contoured without margins for the cauda equina. The nerve roots and peripheral nerves outside the dura were not set as risk organs.

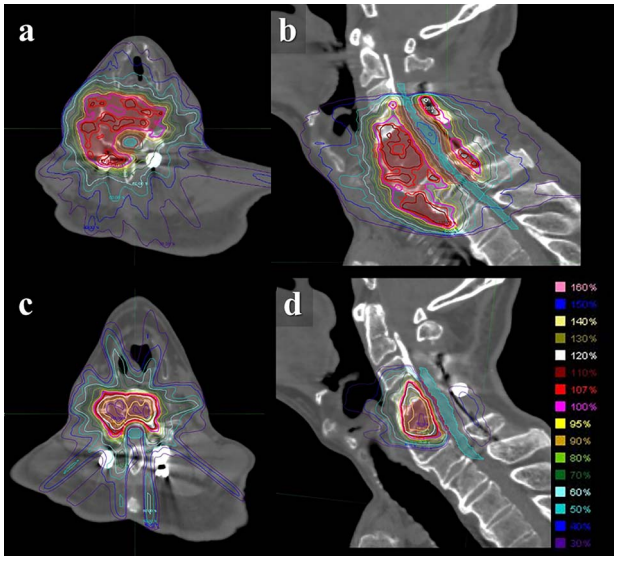

Figure 1. Imaging findings for a 79-year-old man with cervical spinal metastases from thyroid cancer. (a) Axial and (b) sagittal computed tomography images with contouring (red = clinical target volume) and dose distribution of initial stereotactic body radiotherapy (SBRT) with a dose of 24 Gy administered in two fractions at the C5–C6 level. (c) Axial and (d) sagittal computed tomography images obtained during the second SBRT course, which involved administration of 35 Gy in five fractions at the C5 level. He experienced almost complete both upper limb paralysis after 8 months.

The bowel bag was contoured for PRV of the abdominal luminal organs, including the stomach, small intestine and colon. The internal margin was not added to the other organs.

The prescribed dose of the second SBRT course was 30 or 35 Gy in five fractions. The goal was to ensure that 95% of the PTV received 100% of the prescribed dose, provided that normal tissues satisfied the dose constraints. In addition, the maximum dose of the PTV was set to <170% of the prescribed dose. Dose constraints were set for the PRV_{cord} and cauda equina so that the maximum point dose was less than 15.5 Gy in five fractions (9). Dose constraints for the nerve roots and peripheral nerves outside the dura were not set (Fig. 1).

Evaluation and statistical analyses

The study endpoints were LF, OS and adverse effects (AEs). Pain response was not adopted as a study endpoint because the number of painful lesions was only four. LF was defined as tumor progression or any new tumors within the epidural space on MRI (or computed tomography [CT] in some situations) performed approximately every 3 months after SBRT (based on the Spine Response Assessment in Neuro-Oncology group recommendation (10)). OS was defined as the interval between the start date of SBRT and the most recent follow-up or death from any cause. AEs were evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 5 (11). Acute AEs were considered to arise within 90 days, and late AEs as those arising after 90 days of SBRT. Radiation myelopathy (RM) was diagnosed by radiologists based on T2 weighted images and enhanced T1 weighted images (12). RM was graded according to the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer radiation morbidity scoring system (13). Radiculopathy was judged based on focal neurologic deficit consistent with the irradiation site

without LF or RM. Vertebral compression fractures (VCFs) were defined as the development of new VCFs or progression of existing ones in SBRT-treated vertebral bodies based on MRI or CT.

Patient death without tumor recurrence was regarded as a competing risk factor. LF was estimated using the cumulative incidence function, adjusted for the competing risk of death. OS was estimated using the Kaplan–Meier method. All statistical analyses were performed using EZR software, version 1.54 (14).

Results

Patient and tumor characteristics

More than 700 patients were treated with bone SBRT at our institution, 17 (19 lesions) of whom satisfied the eligibility criteria. Patient and tumor characteristics are summarized in Table 1. Fourteen lesions (74%) were radioresistant tumors, including renal cell carcinoma (32%), thyroid cancer (26%), sarcoma (11%) and colorectal cancer (5%). The second SBRT course was delivered to the same spinal level as the first SBRT in 13 lesions and adjacent spinal level in 6. The prescribed dose of initial SBRT was 24 Gy in two fractions in all patients, and the dose constraints were set for the PRV_{cord} and cauda equina as 17 Gy in two fractions of maximum point dose for radiation-naïve patients (15), and 12.2 Gy for re-irradiation patients (9). In addition, three of these lesions (16%) were also initially irradiated with conventional EBRT before the first course of SBRT. The mean and median intervals between the initial and second SBRT were 24.8 and 23 months (range, 6–52 months), respectively. The targets compressing the spinal cord with Bilsky grade ≥ 2 (16) were present in five lesions (26%) at the second SBRT. SBRT doses of 30 and 35 Gy in five fractions were prescribed to 12 and 7 lesions, respectively. The median dose to 95% of the PTV was 26.7 Gy (range, 18.3–35.0 Gy).

Table 1. Patient and tumor characteristics

Characteristics	A total of 19 lesions in 17 patients
Sex	
Male/female	7/10
Mean age, years (range)	63 (24–84)
ECOG performance status 0/1/2/3–4	10/6/3/0
Lesion histopathology	
Renal cell	6
Thyroid	5
Breast	2
Sarcoma	2
Other	4 (one lesion each)
Levels treated*	
Cervical/thoracic/lumbar/sacral	3/9/7/1
Number of spinal levels 1/2/3/4	12/2/2/1
SINS	
0–6 (stable)	6
7–12 (potentially unstable)	12
13–18 (unstable)	1
2nd SBRT course at	
Same/adjacent spinal level	13/6
Interval after previous SBRT	
Mean/median, months (range)	24.8/23 (range, 6–52)
With history of conventional radiotherapy	3 (16%)
With fixation metal in the SBRT target	13 (68%)
Bilsky grade in second course of SBRT	
0/1 (no/dural compression)	5/9
2/3 (cord compression)	4/1
Prescribed dose of second SBRT	
30 Gy/35 Gy	12/7

ECOG, Eastern Cooperative Oncology Group; SBRT, stereotactic body radiotherapy; SINS, spinal instability neoplastic score.
*One lesion spanned two areas.

Clinical outcomes

The median follow-up after the second SBRT course was 19 months (range, 2–35 months). From the time of the second spine SBRT, two patients (11%) died at 2 and 9 months. For the entire cohort, the 1-year OS rate was 89% (Fig. 2). LF was confirmed in one case after 16 months, and the 12- and 18-month LF rates were 0% and 8%, respectively (Fig. 2).

RM, radiculopathy and VCFs were observed in zero (0%), four (21%) and two (11%) lesions, respectively. Among lesions at the C4-Th1 and L1-S2 levels, whose nerves control the motor and sensory capacities of the limbs, the occurrence rate of radiculopathy was 36% (4/11) (detailed information is shown in the next section and Table 2). Both VCFs were painless (grade 1). Acute grade 3 oral mucositis and late grade 2 radiation dermatitis were confirmed in one patient each. Other grade 3 or more severe acute and grade 2 or more severe late AEs were not encountered.

Detailed information of patients with radiculopathy

Table 2 shows detailed information of the four patients with radiculopathy. Three patients had received surgical decompression and posterior fixation for metastatic epidural spinal cord compression. Patient 1 had tibialis anterior muscle palsy (manual muscle test 3) since undergoing surgery 18 months ago, and no new neuropathy was found at the time of second SBRT. The other three patients had normal neurological functions at the second SBRT course. Three patients with radiculopathy experienced almost complete upper or lower limb paralysis. The neurological symptoms occurred 5–10 months after second SBRT.

Discussion

We performed a second SBRT course of 30 or 35 Gy in five fractions for 19 spinal lesions that had been treated with previous SBRT course of 24 Gy in two fractions. Excellent local control and absence of RM were confirmed, whereas four (21%) patients experienced radiculopathy.

Since spine SBRT of 24 Gy in two fractions for pain palliation became one of the standard treatment options based on the positive results of the SC.24 trial (5), the number of patients who are prescribed SBRT as a first treatment for spinal metastases will increase. Accordingly, the number of patients with LF who require re-irradiation after SBRT will also increase. However, few studies on salvage treatments after spine SBRT have been reported; hence, we reviewed our retrospective data.

The main strength of this study is that it only included patients with two uniform SBRT dose fraction schedules (30 Gy and 35 Gy in five fractions) and uniform dose constraints for the spinal cord

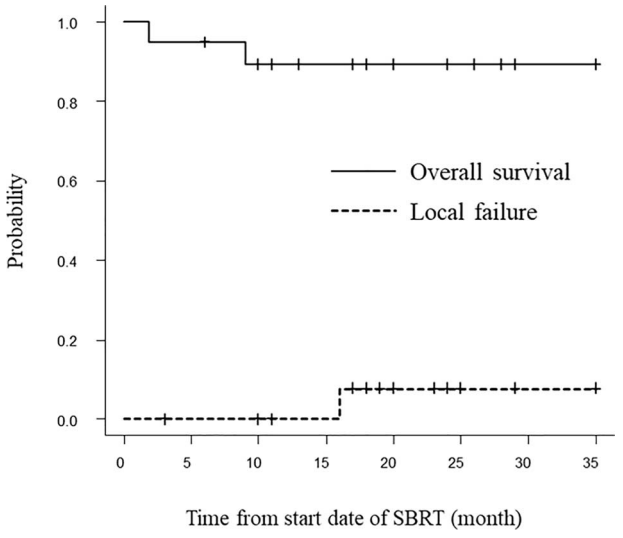

Figure 2. Kaplan–Meier curve of overall survival and cumulative incidence of local failure after stereotactic body radiotherapy. The 12-month overall survival rate was 89%. The 12- and 18-month local failure rates were 0% and 8%, respectively.

and cauda equina (maximum point dose of 15.5 Gy). Moreover, the initial SBRT dose was also unified to 24 Gy in two fractions. One of the most severe toxicities induced by spine SBRT is RM. Considering the low α/β of the spinal cord, we decided to deliver the treatment in five fractions, which is a large number of fractions relative to those used in other SBRT regimens. Although the appropriate dose constraint of the cord was unknown, a maximum point dose of 15.5 Gy in five fractions was adopted based on the report by Sahgal et al. (9), resulting in the absence of RM. Additionally, this regimen demonstrated a high local control rate despite the tumors being expected to be radioresistant because they had re-grown after initial SBRT. The prescribed dose and dose constraints used in the present study would be informative when performing the second SBRT course in daily clinical practice.

However, radiculopathy was confirmed in four (21%) patients in the current study. In a retrospective case series of 557 high-dose single-fraction SBRT for de novo spinal tumors, the overall peripheral nervous injury was only 2.5%, despite the dose constraint for the peripheral nerve not set (17). The same applies to re-irradiation SBRT after conventional EBRT. We previously reported that re-irradiation with SBRT after conventional EBRT caused radiculopathy in only 1.5% (2/133) of lesions (18). In contrast, the present study showed that the second SBRT course induced severe radiculopathy with a high probability. From the above, the tolerance dose of the peripheral nerves is presumed to be higher than the cumulative dose of conventional EBRT plus SBRT and lower than the cumulative dose of SBRT applied twice. Retrospective results of salvage second SBRT course to spinal metastases have been reported by Thibault et al. (19) Although good local control and the absence of RM observed in their study were consistent with ours, they did not confirm radiation-induced radiculopathy (Table 3). The reasons for this discrepancy are unclear. However, this may be attributed to differences in the following factors: survival time after SBRT (1-year OS: 48% vs. 89%), interval between SBRT, prescribed dose of SBRT, tumor localization and dose gradient inside the PTV.

Table 2. Patients with radiculopathy

No.	Age (years)/Sex	Type of cancer	Previous radiotherapy (time)	Second SBRT course	Maximum dose in first/second SBRT	Symptoms of radiculopathy	Time to onset (months)
1	75/Female	Clear cell renal cell carcinoma	30 Gy in 10 fractions at the L4–S1 level (48 months earlier) Separation surgery followed by SBRT of 24 Gy in 2 fractions at the L5 level (18 months earlier)	30 Gy in 5 fractions at the L5 level	30.0 Gy/42.0 Gy	Paralysis of the bilateral tibialis anterior muscles (L4 level, MMT 1) and extensor hallucis longus (L5 level, MMT 1)	8
2	57/Female	Follicular thyroid cancer	Decompression surgery and IORT of 20 Gy at the T2 level (74 months earlier) 24 Gy in 2 fractions at the C7–T1 level (6 months earlier)	35 Gy in 5 fractions at the C6 level	33.4 Gy/56.0 Gy	Paralysis of the right wrist flexors (C6-T1 level, MMT 2), flexor pollicis longus (C7–8 level, MMT 2), and finger flexor (C7-T1 level, MMT 2)	5
3	79/Male	Follicular thyroid cancer	Separation surgery followed by SBRT of 24 Gy in 2 fractions at the C5–C6 level (22 months earlier)	35 Gy in 5 fractions at the C5 level	31.0 Gy/56.0 Gy	Paralysis of the bilateral deltoid muscles (C5 level, MMT 1–2), biceps (C5 level, MMT 1–2), and triceps (C7 level, MMT 2). Power of wrist extensor (C6 level) was undocumented.	8
4	58/Male	Prostate adenocarcinoma	24 Gy in 2 fractions at the L3 level (41 months earlier)	30 Gy in 5 fractions at the L3 level	28.6 Gy/49.8 Gy	Numbness of the right femur (L3 level). No muscle weakness	10

IORT, intraoperative radiotherapy; MMT, manual muscle test; SBRT, stereotactic body radiotherapy.

Table 3. Stereotactic body radiotherapy literature review narrowed down to the terms 're-irradiation' and 'spine'

Author (year)	Study type	No. of same/adjacent spinal level	Median 1st SBRT dose (range)	Median 2nd SBRT dose (range)	LF at 1st/2nd year	OS at 1st/2nd year	RM	Radiculopathy	VCF	Other AEs ≥ Grade 3
Thibault et al. 2015 (19)	Retrospective	56/0	24 Gy/2 fx (20–35 Gy/1–5 fx)	30 Gy/4 fx (20–35 Gy/2–5 fx)	19/29%	48/18%	0	0	0	0
Present study	Retrospective	13/6	24 Gy/2 fx	30 or 35 Gy/5 fx	0/8%	89/89%	0	4 (21%)	2 (11%)	1 (5%)

AEs, adverse effects; fx, fractions; Gy, gray; LF, local failure; OS, overall survival; RM, radiation myelopathy; SBRT, stereotactic body radiotherapy; VCF, vertebral compression fracture.

Because the pedicle is a frequent site of spinal metastases, an SBRT plan avoiding the nerve roots cannot cover the gross tumor with sufficient dose. Additionally, it is impossible to detect the nerve roots separately from the spinal tumor using MRI in the case of mass-type metastases. Thus, it is difficult to prevent radiculopathy during treatment with the second SBRT course, especially in cases with metastases at the C4-Th1 and L1-S2 levels. In contrast, if no salvage irradiation is administered, recurrent tumors invade the nerve roots and cause radiculopathy. The therapeutic strategy should be decided based on the advantages and disadvantages of the second SBRT course. The present results would be useful for such decision-making.

This study has some limitations. First, this study had a small sample size and a small number of radiculopathy events; hence, it was insufficient to reach conclusive results. Second, dosimetric data of the nerve roots were not shown because it was difficult to delineate the nerve roots separately from the spinal tumors. Although the exact dose to the nerve roots was unknown, nerve roots were estimated to be irradiated with a dose close to the maximum dose of PTV (Table 2). If the peripheral nerve is >5 mm away from the gross tumor, we can technically delineate the nerve roots and reduce the irradiated dose. To establish a safer method, we are conducting a phase II clinical trial assessing the second course of spine SBRT (the University hospital Medical Information Clinical Trials Registry as UMIN000043319).

In conclusion, we performed a second course of salvage SBRT using 30 or 35 Gy in five fractions for patients who had been treated with spine SBRT of 24 Gy in two fractions, resulting in excellent local control and no RM. However, a high occurrence rate of radiation-induced radiculopathy was confirmed, and it was suggested to be the characteristic AE in repeat SBRT.

Acknowledgements

None.

Funding

No funding was received for this study.

Conflicts of interest

None declared.

Availability of data and material

The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

Ethics approval

This study was approved by the ethics review board (approval number 2312) of our institution.

Consent to participate and publication

Written informed consent was obtained from all patients.

References

1. Lutz S, Balboni T, Jones J, et al. Palliative radiation therapy for bone metastases: update of an ASTRO evidence-based guideline. *Pract Radiat Oncol* 2017;7:4–12. https://doi.org/10.1016/j.prro.2016.08.001.
2. Husain ZA, Sahgal A, De Salles A, et al. Stereotactic body radiotherapy for de novo spinal metastases: systematic review. *J Neurosurg Spine* 2017;27:295–302. https://doi.org/10.3171/2017.1.SPINE16684.
3. Yamada Y, Katsoulakis E, Laufer I, et al. The impact of histology and delivered dose on local control of spinal metastases treated with stereotactic radiosurgery. *Neurosurg Focus* 2017;42:E6. https://doi.org/10.3171/2016.9.FOCUS16369.
4. Myrehaug S, Sahgal A, Hayashi M, et al. Reirradiation spine stereotactic body radiation therapy for spinal metastases: systematic review. *J Neurosurg Spine* 2017;27:428–35. https://doi.org/10.3171/2017.2.SPINE16976.
5. Sahgal A, Myrehaug SD, Siva S, et al. Stereotactic body radiotherapy versus conventional external beam radiotherapy in patients with painful spinal metastases: an open-label, multicentre, randomised, controlled, phase 2/3 trial. *Lancet Oncol* 2021;22:1023–33. https://doi.org/10.1016/S1470-2045(21)00196-0.
6. Ito K, Sugita S, Nakajima Y, et al. Phase 2 clinical trial of separation surgery followed by stereotactic body radiation therapy for metastatic epidural spinal cord compression. *Int J Radiat Oncol Biol Phys* 2022;112:106–13. https://doi.org/10.1016/j.ijrobp.2021.07.1690 Epub October 26 2021.
7. Cox BW, Spratt DE, Lovelock M, et al. International spine radiosurgery consortium consensus guidelines for target volume definition in spinal stereotactic radiosurgery. *Int J Radiat Oncol Biol Phys* 2012;83:e597–605. https://doi.org/10.1016/j.ijrobp.2012.03.009.
8. Redmond KJ, Robertson S, Lo SS, et al. Consensus contouring guidelines for postoperative stereotactic body radiation therapy for metastatic solid tumor malignancies to the spine. *Int J Radiat Oncol Biol Phys* 2017;97:64–74. https://doi.org/10.1016/j.ijrobp.2016.09.014.
9. Sahgal A, Ma L, Weinberg V, et al. Reirradiation human spinal cord tolerance for stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys* 2012;82:107–16. https://doi.org/10.1016/j.ijrobp.2010.08.021.
10. Thibault I, Chang EL, Sheehan J, et al. Response assessment after stereotactic body radiotherapy for spinal metastasis: a report from the SPIne response assessment in neuro-oncology (SPINO) group. *Lancet Oncol* 2015;16:e595–603. https://doi.org/10.1016/S1470-2045(15)00166-7.
11. US Department of Health and Human Services Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Available via DIALOG. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf. Accessed November 21, 2021.
12. Khan M, Ambady P, Kimbrough D, et al. Radiation-induced myelitis: initial and follow-up MRI and clinical features in patients at a single tertiary care institution during 20 years. *AJNR Am J Neuroradiol* 2018;39:1576–81. https://doi.org/10.3174/ajnr.A5671.
13. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the radiation therapy oncology group (RTOG) and the European Organization for Research and Treatment of cancer (EORTC). *Int J Radiat Oncol Biol Phys* 1995;31:1341–6. https://doi.org/10.1016/0360-3016(95)00060-C.
14. Kanda Y. Investigation of the freely available easy-to-use software "EZR" for medical statistics. *Bone Marrow Transplant* 2013;48:452–8. https://doi.org/10.1038/bmt.2012.244.
15. Sahgal A, Weinberg V, Ma L, et al. Probabilities of radiation myelopathy specific to stereotactic body radiation therapy to guide safe practice. *Int J Radiat Oncol Biol Phys* 2013;85:341–7. https://doi.org/10.1016/j.ijrobp.2012.05.007.
16. Bilsky MH, Laufer I, Fourney DR, et al. Reliability analysis of the epidural spinal cord compression scale. *J Neurosurg Spine* 2010;13:324–8. https://doi.org/10.3171/2010.3.SPINE09459.
17. Stubblefield MD, Ibanez K, Riedel ER, et al. Peripheral nervous system injury after high-dose single-fraction image-guided stereotactic radiosurgery for spine tumors. *Neurosurg Focus* 2017;42:E12. https://doi.org/10.3171/2016.11.FOCUS16348.
18. Ito K, Ogawa H, Nakajima Y. Efficacy and toxicity of re-irradiation spine stereotactic body radiotherapy with respect to irradiation dose history. *Jpn J Clin Oncol* 2021;51:264–70. https://doi.org/10.1093/jjco/hyaa178.
19. Thibault I, Campbell M, Tseng CL, et al. Salvage stereotactic body radiotherapy (SBRT) following in-field failure of initial SBRT for spinal metastases. *Int J Radiat Oncol Biol Phys* 2015;93:353–60. https://doi.org/10.1016/j.ijrobp.2015.03.029.