Stereotactic Radiosurgery for Vertebral Metastases

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Introduction and Epidemiology

The bone is the third most common site of metastasis (after the lungs and liver), with the spine being the most common site for bony metastasis. It is estimated that >40% of all cancer patients will develop spinal metastases during the course of their disease [1]. Incidence is increasing due to both longer survival and the advent of more effective systemic therapies. Clinical manifestations of spinal metastases vary from asymptomatic disease detected on imaging workup to progressive axial pain with nocturnal aggravation, compression fracture, and neurological symptoms (ranging from radiculopathy to spinal cord compression). Together with the use of these newer targeted and immunotherapeutic agents, more sensitive diagnostic imaging has led to an increased incidence of spinal metastases; in the overwhelming majority, spinal metastasis represents either isolated metastases or oligometastatic disease. Therefore, previously considered a terminal stage disease restricted to palliative treatment, spinal metastases has a new landscape with new therapeutic options, especially in the oligometastatic setting. However, this evolving paradigm must account for various aspects of disease presentation such as neurological status, pain, location, stability, and systemic dissemination of the disease. The management approach for spinal metastases should be multidisciplinary, and various prognostic scoring systems and frameworks have been developed for better decision-making.

Anatomy and Historical Perspective

Most spinal metastases are extradural (>90%), while 5% are intradural and <1% are intramedullary [2]. The posterior half of the vertebral body is the most commonly involved segment due to high vascularity, followed by the anterior body, lamina, and pedicles [3]. Due to the proximity and tolerance of the spinal cord, conventional external beam radiotherapy with palliative radiation doses has historically been the mainstay of treatment. Various conventional radiotherapy dose fractionation schedules ranging from 8 Gy in a single fraction to fractionated 20–40 Gy in 5–20 fractions have been proposed; all regimens have largely revealed similar palliative efficacy, although the retreatment rate has shown to be higher in shorter fractionation regimens [4–7]. With the advent of newer image guidance techniques and precision radiation delivery technologies such as stereotactic body radiotherapy (SBRT) (also known as stereotactic ablative radiotherapy [SABR]) and stereotactic radiosurgery (SRS),

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it is now possible to treat spinal metastases with ablative doses, with the goal of achieving superior local control.

Spinal Metastasis: Management Approach

Multimodality approaches involving neurosurgeons, neuroradiologists, supportive care, and medical and radiation oncologists are essential for management of spinal metastases. Treatments include local therapies such as surgery and radiation therapy, as well as systemic therapy and pain management. Surgery is often preferred for immediate decompression in symptomatic patients with neurological symptoms related to spinal cord or nerve root compression. Discussion of various surgical techniques is beyond the scope of this chapter. The use of radiation therapy varies from mere palliation to the more ablative SRS in the setting of systemically controlled oligometastatic disease.

Radiological Assessment

Magnetic resonance imaging (MRI) is the recommended method for diagnosing spinal metastases, with high sensitivity and specificity compared to computed tomography (CT) for evaluating cortical destruction, bone marrow deposits, epidural extension, and cord/nerve root involvement [8, 9]. Assessment of the severity of epidural disease is crucial in determining the most suitable treatment. Bilsky et al. proposed an MRI-based 6-grade epidural spinal cord compression (ESCC) scale that has been clinically validated and is now widely used among spinal oncologists [10]. The ESCC scale consists of six grades: grade 0, bone involvement alone; grade 1, epidural impingement; grade 2, the retention of cerebrospinal fluid visible despite spinal cord compression; and grade 3, cerebrospinal fluid not visible due to marked spinal cord compression. Grade 1 is classified into three subgroups: grade 1a, epidural impingement without deformation of the thecal sac; grade 1b, compression of the thecal sac without spinal cord abutment; and grade 1c, deformation of the thecal sac with spinal cord abutment in the absence of spinal cord compression. In the absence of mechanical instability, patients with low-grade ESCC such as grade 0 (bone involvement only) and grade 1 (epidural impingement without spinal cord compression) can be addressed with SRS/SBRT, while those with higher-grade compression may be better managed by surgical decompression followed by radiation therapy [11].

Oligometastatic Disease

Oligometastases represent a subset of patients with limited metastatic disease, usually <5 sites, and represent an intermediary cancer state where the cancer has not progressed to widespread metastatic disease [12]. Patients with oligometastatic disease could potentially benefit from aggressive local therapy, leading to improved progression-free survival and possibly overall survival advantages. The SABR-COMET trial, a recent landmark multi-institutional phase II study, randomized 99 patients with oligometastatic cancers (1–5 lesions) to standard-of-care palliative therapy alone (33 patients) versus SABR plus standard of care palliative therapy (66 patients). The SABR arm was associated with an improvement in overall survival (41 vs 28 months; $p = 0•09$) and progression-free survival (12 vs 6 months; $p = 0•0012$) [13]. One of the keys to improved outcomes in these patients has been the accurate identification of oligometastatic disease with advanced imaging techniques (i.e., MRI, positron emission tomography [PET]), as well as the development of cancer-specific imaging strategies (i.e., prostate-specific membrane antigen [PSMA]-PET).

Spine Metastasis and Sterotactic Radiosurgery

Stereotactic radiosurgery (SRS) allows delivery of high ablative radiation doses with extreme precision, conformality, and accuracy. SRS of the spine has been accomplished using refined

image-guidance systems that allow sparing of the spinal cord and cauda equina. Image-guided spinal SRS (1-fraction) as well as SBRT using 2–5 fractions offers a radiobiological advantage of delivering high biological effective dose (BED), providing durable rates of local tumor control and pain relief with minimal toxicities. The BED, calculated using the linear-quadratic model, is as high as 37.5–81.6 Gy_{10} in SRS delivering 16–24 Gy in a single fraction and 43.2–51.3 Gy_{10} for spinal SBRT delivering 24–27 Gy in three fractions, compared with 14.4–39 Gy_{10} in conventional external-beam radiotherapy (EBRT) (8 Gy in single fraction to 30 Gy in 10 fractions). This increase in BED leads to high radiation-induced cell death through direct (DNA damage) and indirect mechanisms, combined with less elucidated changes in the vascular environment and immune microenvironment. There is growing evidence to suggest that spinal SRS of the non-collapsed spine is clinically effective and independent of histology, with lower levels of marginal failures [14–16]. There is increasing preference toward SRS for stable spinal metastases, especially for patients with oligometastatic disease with radioresistant histologies.

Patient Selection for Spinal SRS

SBRT is more resource intensive and is associated with the practical challenges of high cost and potential risks from high radiation doses. Careful patient selection is essential in order to avoid unnecessary treatment of those who may not benefit. To this end, a prognostic classification system can be an essential clinical tool for identifying patients who would most benefit from spine SRS. Chao et al. performed a recursive partitioning analysis (RPA) on 174 patients, which was recently validated in a larger patient group of 444 patients, showing that patients with RPA class 1 (Karnofsky Performance Scale (KPS) >70 with controlled systemic disease, class 2 (neither class 1 or 3), and class 3 (KPS ≤70 and age <54 years or KPS ≤70 age ≥54 years and presence of visceral metastases) had a median overall survival of 26.7 months, 13.4 months, and 4.5 months, respectively [17, 18]. Spine SBRT/SRS is most cost-effective in patients with an expected survival ≥11 months; therefore, the recommendation from this study is to limit spine SRS to class 1 and some class 2 patients [19]. As described above, patients with low-grade ESCC (such as Bilsky grade 0–1) without mechanical instability should be considered for spinal SBRT versus surgery [10].

Several decision-making frameworks have been developed to provide key principles and guidance to radiation oncologists and spine surgeons to help determine the optimal treatment modality, such as the 4-point NOMS (neurological, oncological, mechanical instability, and systemic framework) and LMNOP (location of disease in the spine, mechanical instability, neurology, oncology, and patient fitness, prognosis, and response to prior therapy) frameworks [20, 21]. The International Spine Oncology Consortium Report similarly proposes a multidisciplinary MNOP (mechanical, neurological, oncological, preferred treatment) algorithm for the management of spine metastases, utilizing similar principles to guide management [22].

Histology

In a large population-based study of 15,367 patients with metastatic spinal cord compression, the common histologies were lung cancer (25%), prostate cancer (16%), and multiple myeloma (11%) [23]. SBRT offers greater radiobiological advantage in radioresistant histologies (renal cell carcinoma, melanoma, and sarcoma). In renal cell carcinoma specifically, local control at 1 year has been reported to be >80% [24, 25]. For highly radiosensitive histologies (hematologic malignancies or small cell lung cancer), however, treatment with conventional radiotherapy may offer similar benefit.

Clinical Application of Spinal Sterotactic Radiosurgery/ Stereotactic Body Radiotherapy

Primary Treatment in Unirradiated Patients

As depicted in Fig. 16.1, spinal SRS is an effective modality to be considered for oligometastatic disease or symptomatic radioresistant disease. Various studies have reported excellent tumor and/or pain control of 80–100% in patients treated with SRS/SBRT for spinal metastases in unirradiated patients. The median duration of tumor/pain control was 6.5–13.3 months [14, 26–29].

Postoperative SBRT

Upfront surgery is warranted in patients with high-grade ESCC and/or mechanical instability. The goals of surgery are primarily stabilization and tumor debulking, which leads to high rates of local recurrence (>60%) with limited surgical options at recurrence; therefore, postoperative radiation therapy is justified [30]. Although postoperative radiotherapy has traditionally been delivered with conventional techniques, SBRT is increasingly being used in this setting with good tolerance and excellent disease control of 81–94.4%, compared with 60% in conventional EBRT patients [31, 32]. Timing between spinal SRS and surgery should be at least 1 week to minimize wound complications [33–35]. Skin sparing with SRS/SBRT makes it possible to start SBRT much sooner after surgery than with conventional EBRT.

Use of spinal SRS in the setting of significant epidural disease is challenging, given the spinal cord constraints limiting tumor coverage adjacent to the spinal cord. This can lead to marginal failure after spinal SRS/SBRT, most commonly within this epidural space. Minimally invasive "separation surgery," initially reported in a pilot study by Moulding et al. [36], has emerged as a treatment strategy by which the epidural tumor is selectively removed by limited posterolateral

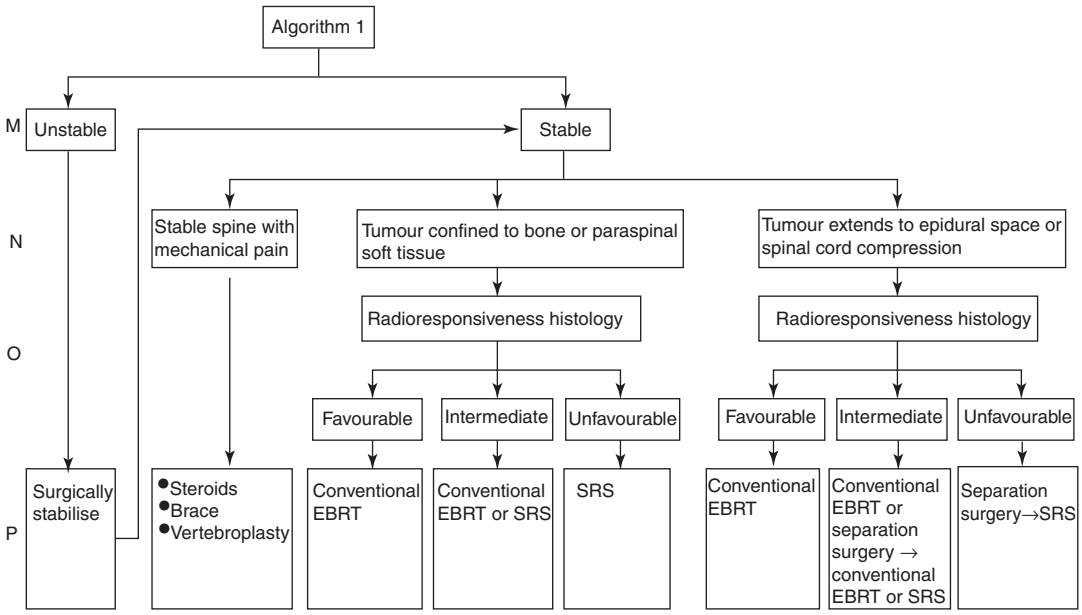

Fig. 16.1 Mechanical, neurological, oncological, preferred treatment (MNOP) algorithm for spinal metastasis management per the International Spine Oncology Consortium. MNOP mechanical, neurological, oncological, preferred treatment; EBRT external-beam radiotherapy; SRS stereotactic radiosurgery. (From Spratt et al. [22], with permission Elsevier)

tumor resection and posterior segmental instrumentation prior to postoperative stereotactic body radiotherapy (SBRT). Following this type of resection, the remaining disease is treated with spinal SRS. In a study of 186 patients of separation surgery combined with postoperative SRS/SBRT, Laufer et al. reported a 1-year local failure rate of 9.5–16.4% (6.3–9% for 24 Gy single fraction), with an excellent toxicity profile and no myelopathy [31].

Reirradiation Utilizing SBRT

Local recurrence following radiation treatment for spinal metastases is a challenging clinical scenario. Several trials have reported that within the first 3–6 months, about 20% of patients will need retreatment for failed treatment efficacy after initial conventional EBRT regimens [37]. Historically, reirradiation for spinal metastases has been limited to palliation, surgical decompression, or low-dose conventional EBRT due to concerns about radiation myelopathy. The Canadian Clinical Trials Group reported that for patients with a previous history of conventional radiotherapy for painful bone metastases, reirradiation with 8 Gy in single fraction or 20 Gy in 5–8 fractions resulted in an overall pain response rate of ~30% and a complete pain response rate of 8% [38]. Spinal SBRT offers a safe and effective noninvasive salvage approach, with several studies of reirradiation for spinal metastasis using SBRT reporting pain response rates of 65–81% and 1 year local control rates of 66–93% [39–46].

Treatment

Simulation and Immobilization Patients must be positioned in a stable supine position capable of reproducibility from simulation to treatment. A variety of rigid patient immobilization systems may be utilized, including vacuum bags, alpha cradles, or stereotactic frames that surround the patient on three sides with large rigid pillows (conforming to patient's external contours). In addition, for cervical spine or cervicothoracic junctional areas, a rigid head and neck immobilization mask should be used. Coordinate systems between imaging delivery systems should be precisely aligned for spine radiosurgery/SBRT.

CT simulations are performed in axial acquisitions with the gantry at 0 degrees, with a recommended slice thickness of 1–2 mm. The planning CT is the primary image platform for targeting and treatment planning. Intravenous contrast is recommended, as this will help delineate the tumor and adjacent normal tissues. CT images are co-registered with a recent MRI of the spine, ideally acquired within the previous 2 weeks.

Target and Spinal Cord Delineation/Contouring Image co-registration between MRI (gadolinium contrast T1-weighted and T2-weighted images) and simulation CT is required for delineation of both the soft tissue tumor component and the spinal cord. It is recommended but not required that MRIs are obtained with the simulation position. However, in a situation where the simulation CT and MRI images are done in different patient positions and spine curvatures are not well aligned, special attention should be given to fuse the target spine to be treated. A T1 series with gadolinium contrast is helpful in identifying paraspinal or extraosseous disease, and T2 weighted images are helpful in delineating the spinal cord. In the postoperative setting, where hardware artifact may obscure contour of the spinal cord, CT myelogram is generally recommended, as it is beneficial for visualizing this organ at risk.

Target Volume Definition per the Radiation Therapy Oncology Group (RTOG) 0631 and International Spine Radiosurgery Consortium Consensus Guidelines [47, 48]

Gross Target Volume The gross target volume (GTV) includes the complete extent of the gross metastatic tumor using all available clinical information and imaging modalities, including MRI, CT, myelography, plain films, and func-

tional imaging studies such as PET CT. All epidural and paraspinal components of the tumor should be included as a component of the GTV.

Radiosurgery Target Volume or Clinical Target Volume The clinical target volume (CTV) should include abnormal bone marrow signal suspicious for microscopic invasion adjacent to the GTV and also include adjacent physiologic appearing bone marrow spaces that may harbor subclinical disease and could potentially serve as a nidus for a local recurrence. An epidural lesion is included in the target volume if there is a ≥3 mm gap between the spinal cord and the edge of the epidural lesion. A paraspinal mass ≤5 cm in greatest dimension that is contiguous with a spine metastasis is included in the target volume. The International Spine Radiosurgery Consortium has published consensus specific details, recommendations, and guidelines for target delineation in spine SBRT based on expert opinion with ten representative cases [48].

No extraosseous CTV expansion (specifically in the epidural or paraspinal soft tissue spaces) was necessary beyond the GTV in cases of bone-only disease. However, for postoperative SRS/SBRT, the post-op bed at high risk of recurrence should be included in the CTV. An international group of experts generated consensus contouring guidelines for postoperative spine SBRT [49]. Circumferential or "donut-shaped" CTVs encircling the cord should be used only in cases where the vertebral body, bilateral pedicles/lamina, and spinous process are all involved or when there is near circumferential involvement of the epidural space with metastatic disease.

Planning Target Volume Radiosurgery does not assume setup errors. However, depending on the radiosurgery system, a planning target volume (PTV) margin of between 0 and 2 mm may be applied to account for setup error, image fusion errors, contouring uncertainty, potential intrafraction motion, and mechanical errors associated with image-guided radiotherapy (IGRT) system to meet the adequate dose coverage of the target. This margin can be reduced to 0–1 mm at the area of the spinal cord to meet the spinal cord dose constraints. Per the SRS International Consortium, PTV can be modified such that it never overlaps with the spinal cord or cauda equina but still encompasses the entire GTV and CTV [48]. Spine SRS treatment plan is considered acceptable as long as ≥90% of the target volume receives the prescribed radiosurgery dose.

Examples of SRS target volumes per RTOG 0631, the phase III randomized trial of conventional EBRT vs. SBRT for patients with 1–3 sites of spinal metastases [47], are illustrated in Fig. 16.2. Solid black represents the tumor

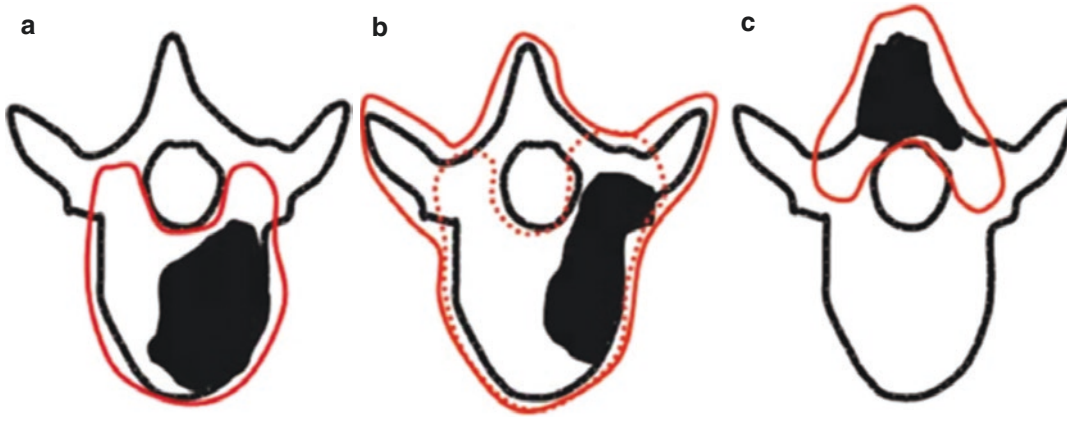

Fig. 16.2 Target volume definition for lesions in different locations in the spine per the Radiation Therapy Oncology Group (RTOG) [47]. (**a**) Metastases involving vertebral body; (**b**) metastases involving vertebral body and pedicle, solid and dotted lines both acceptable; (**c**) metastases involving spinous process and laminae

that can be seen on the imaging studies. Most of the spine metastases involve the vertebral body and the gross tumor seen on MRI or CT scan, as shown in Fig. 16.2a. This is the most common type of spine metastasis. The radiosurgery target volume includes the involved vertebral body and both pedicles (*solid red line*). Metastatic lesions can be more extensive, involving the pedicles (Fig. 16.2b). The target volume can be more generous (*dotted line* of Fig. 16.2b) or the target volume can include anterior and posterior elements of the spine (*solid red line* of Fig. 16.2b). The target volume may be chosen at the discretion of the treating radiation oncologist based on the extent of tumor involvement. When the metastasis involves only the posterior elements, the target volume includes the spinous process and laminae (*solid red* line of Fig. 16.2c). In any circumstance, when there is an epidural or paraspinal soft tissue tumor component, the visible epidural or paraspinal tumors are included in the target volume. The International Spine Radiosurgery Consortium published detailed consensus guidelines for target volumes for spine radiosurgery which are freely available online (Table 16.1) [48].

Table 16.1 Contouring guidelines for GTV, CTV, and PTV in spinal stereotactic radiosurgery, per International Spine Radiosurgery Consortium Consensus Guidelines. (From Cox et al. [48], with permission Elsevier)

Target volume	Guidelines
GTV	Contour gross tumor using all available imaging Include epidural and paraspinal components of tumor
CTV	Include abnormal marrow signal suspicious for microscopic invasion Include bony CTV expansion to account for subclinical spread Should contain GTV Circumferential CTVs encircling the cord should be avoided except in rare instances where the vertebral body, bilateral pedicles/lamina, and spinous process are all involved or when there is extensive metastatic disease along the circumference of the epidural space without spinal cord compression
PTV	Uniform expansion around CTV CTV to PTV margin ≤3 mm Modified at dural margin and adjacent critical structures to allow spacing at discretion of the treating physician unless GTV compromised Never overlaps with cord Should contain entire GTV and CTV

CTV Clinical target volume, *GTV* gross tumor volume, *PTV* planning target volume

Dose/Fractionation Various dose fractionation schedules are used, depending on factors such as treatment volume, proximity to the spinal cord, previous radiation, prior surgical resection, localization and image-guidance/IGRT, and risk of compression fracture. Common fractionation schemes include 16–24 Gy in a single fraction, 24 Gy/2 fractions, 24–30 Gy/3 fractions, 30 Gy/4 fractions, and 30–40 Gy/5 fractions. Large tumors may warrant 4–5 fraction courses. Single fractions of 15 Gy are effective; however, they may be related to increased toxicities such as vertebral compression fracture, pain flare, and myelopathy.

Normal Tissues Dose Constraints Table 16.2 summarizes the common practical dose constraints as per RTOG 0631 [47] and the American Association of Physicists in Medicine (AAPM) Task Group 101 [50] for SBRT.

Planning and Dosimetry RTOG 0631 dosing guidelines recommend that the plan is acceptable as long as >90% of the target volume receives the prescribed radiosurgery dose. Typically, the 80–90% isodose line can be used as a prescription line, which can vary depending on the delivery system. Coverage of <80% of the target volume is considered unacceptable. Unlike a conventional EBRT plan, dose inhomogeneity within the target volume is acceptable. Hot spots outside PTV should be <105% and should *not* be critically close to the spinal cord. Figure 16.3 illustrates target delineation and dose-volume histogram of a case of oligo-metastatic renal cell carcinoma involving T8 vertebral body treated at our institution.

Image Verification Keys to successful spinal SBRT/SRS include accurate on-board image verification after patient setup at treatment delivery,

Table 16.2 Normal tissue dose constraints for spinal SRS/SBRT per Radiation Therapy Oncology Group (RTOG) 0631 [47] and American Association of Physicists in Medicine Task Group (AAPM TG) 101 [50]

		RTOG 0631	AAPM TG 101		
		Single-fraction	Single-fraction	3-fractions	5-fractions
Normal tissues	Critical volume	D_{max} (Gy)	D_{max} (Gy)	D_{max} (Gy)	D_{max} (Gy)
Spinal cord	≤0.35 cc	10	10	18	23
	≤10% of partial spinal cord	10	10	18	23
	<1.2 cc	–	7	12.3	14.5
	Point dose[a]	14	14	21.9	30
Cauda equina	<5 cc	14	14	21.9	30
	Point dose[a]	16	16	24	32
Sacral plexus	<5 cc	14.4	14.4	22.5	30
	Point dose[a]	18	16	24	32
Esophagus	<3 cc	11.9	11.9	17.7	19.5
	Point dose[a]	16	15.4	25.2	35
Trachea/larynx	<4 cc	10.5	10.5	15	16.5
	Point dose[a]	20.2	20.2	30	40
Brachial plexus	<3 cc	14	14	20.4	27
	Point dose[a]	17.5	17.5	24	30.5
Skin	<10 cc	23	23	30	36.5
	Point dose[a]	26	26	33	39.5

[a]Point dose = 0.03 cc in RTOG 0631 and 0.035 cc in AAPM TG 101

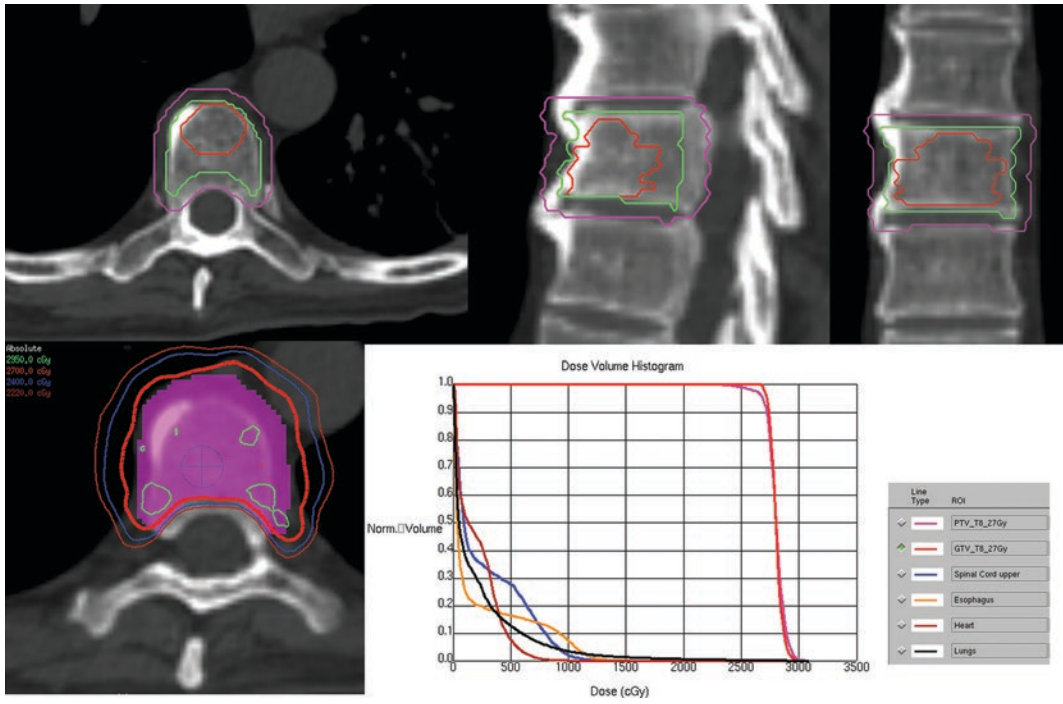

Fig. 16.3 Patient with oligo-metastatic renal cell carcinoma involving T8 vertebral body, status post immunotherapy. First row shows target delineation: *Red line* represents the gross target volume (GTV), *green* is clinical target volume (CTV), and *pink line* is planning target volume (PTV). The second row shows the planning, with respective isodose line (dose prescription: 27 Gy in 3 fractions), and the dose-volume-histogram

which is commonly done using a cone-beam CT (CBCT) aligned to target spine or surrogate fiducial markers and/or surgical clips. The multi-leaf collimator (MLC)-based linear accelerator (LINAC) system uses a hexapod robotic couch (Medical Intelligence, Schwabmuenchen, Germany) that can facilitate setup correction with 6 degrees of freedom. Other image verification techniques include CT-on-rails, MRI-LINAC, and CyberKnife® (Accuray, Sunnyvale, California) tracking. The CyberKnife® uses robotic arms to manipulate the LINAC position in real time according to the orthogonal image acquired by floor mounted stereoscopic KV X-rays. The MRI-LINAC offers superior soft tissue visualization using a single T1/T2 combination sequence MRI (0·35 Tesla, Varian Medical Systems, Palo Alto, California; and 1·5 Tesla, Electa AB, Stockholm, Sweden), online adaptation to daily changes in target and organ position, and real-time tumor respiratory gating based on MRI acquired during treatment delivery. Triggered kV imaging is a new capability of the TrueBeam® delivery system (Varian). This technique allows the user to define the frequency of triggered kV images based on various criteria such as elapsed time, monitor units delivered, gantry angle, or breathing motion of the patient. For gated SBRT, image acquisition can be set either for a particular breathing phase or "Continuous at Beam On," which can take a kV image every time the patient's breathing enters the respiratory gating window during the treatment delivery. Therefore, triggered imaging allows real-time verification that the target motion is maintained throughout the treatment delivery. With various options of IGRT systems available, the institution's IGRT systems must demonstrate <2 mm agreement between simulation/planning and treatment, as well as at the end of treatment.

Toxicities and Management

Spinal SBRT is well tolerated, and significant acute toxicity is relatively uncommon. Late toxicities include vertebral compression fracture and, rarely, radiation myelitis.

Pain Flare

Pain flares manifest as transient increase in pain immediately (1–7 days) after radiation. While pain flares occur in approximately a third of patients after conventional spinal radiotherapy [51], there is a reported incidence of 14–68.3% after spine SBRT [52, 53]. The pathophysiology of this phenomenon is unclear, but some have postulated that nerve compression or the release of inflammatory cytokine mediators secondary to radiotherapy-induced transient edema may be responsible. Pain flares are thus managed by short courses of dexamethasone [54]. The use of prophylactic dexamethasone is not routinely recommended and is an active area of investigation [55].

Post-SBRT Vertebral Compression Fractures

Vertebral compression fracture (VCF) is caused by a combination of tumor-induced demineralization through abnormal bone turnover and architectural changes, as well as radiation-induced intense inflammatory effects leading to collagen damage, weakening of bony matrix, and osteoradionecrosis of bone and tumor tissue [56]. VCF is more likely to occur with high BED spinal SRS/SBRT (11–39%), compared to approximately 3–5% after conventional radiotherapy [56–59]. The median time to VCF peaks at around 2.5–4 months post-treatment, with a second peak around 14 months post-treatment [57, 59–61]. Predictive factors for VCF include both patient-/disease- and treatment-related factors; these include tumor location at or below T10, lytic lesions involving >40% of the vertebral body, spine malalignment, dose ≥20 Gy per fraction, age >55 years, pre-existing fracture, baseline pain, or high Spinal Instability Neoplastic Score (SINS) [62]. Risk of VCF at 24 months for patients in the high SINS group has been reported as high as 66.3%, compared to 21.3% for those in the low SINS group [63]. Therefore, it is recommended that patients with

intermediate/high SINS should be considered for surgical stabilization of the spine prior to spinal SBRT/SRS.

Asymptomatic patients with only radiographic evidence of fractures may not need invasive treatment and are managed with conservative approaches with physical therapy while avoiding rigorous exercise and weight-lifting. Surgical management for VCF includes percutaneous cement augmentation procedures such as vertebroplasty and kyphoplasty. Open stabilization is generally required in one-third of patients with radiographic and symptomatic VCFs.

Radiation Myelopathy

Radiation myelopathy (RM) is a late, rare, but dreaded complication of spinal SBRT, with an incidence rate of ~0.4% [64]. Sahgal et al., in a logistic regression model yielding estimates for the probability of RM following SBRT, showed that with two fractions, a point maximum dose of 12.5, 14.6, 15.7, 16.4, and 17.0 Gy yielded an estimated risk of 1, 2, 3, 4, and 5% of myelopathy, respectively.

In the reirradiation setting, for SBRT given at least 5 months after conventional EBRT, a cumulative thecal sac point maximum BED of 20–25 $Gy_{2/2}$ (calculated and normalized to 2 Gy per fractions or EQD2, utilizing an α/β of 2) was safe, provided that the point maximum EQD2 does not exceed 70 Gy, and the SBRT EQD2 to the thecal sac comprises no more than approximately 50% of the cumulative dose [65].

Follow-Up and Response Assessment

Response assessment following spine SBRT is challenging, especially using traditional Response Evaluation Criteria in Solid Tumours (RECIST) criteria. This is because of the pseudoprogression (PP) phenomenon (changes in radiographic appearance on MRI secondary to radiation-related changes) that is reportedly seen in 14–37% post-SBRT [66–68]. PP incidence is reported to be higher and predictive in lytic (vs. sclerotic) tumors, confined to the 80% isodose line and earlier time to tumor enlargement [66–68]. To standardize response assessment after spine SBRT, international expert consensus devised the SPIne response assessment in Neuro-Oncology (SPINO) [69]. Progression is defined as visible increase in tumor volume, or development of new tumors in epidural space, and/or neurologic deterioration due to known epidural disease. To distinguish questionable PP vs true progression, serial MRI imaging and consideration of tissue biopsy should be made.

Future Directions

Tremendous progress in the radiotherapeautic approach to spine metastases has been made, and rigorous investigation continues, particularly in the new landscape of targeted systemic therapies, oligometastatic disease, and longer survival in patients with metastatic disease. Current ongoing studies are focused on increasing efficacy and reducing cost of spine SRS/SBRT, which has become increasingly popular as the results of the abovementioned literature have emerged. Improved image guidance (e.g., MRI-LINAC) will improve the thereapeutic window between treatment efficacy and toxicity, while new treatment platforms are capable of treating multiple lesions in a single session quickly, improving both patient convenience and workflow in the clinic [70]. For oligometastatic patients, many of whom are receiving biologic agents or immunotherapies, this short course treatment modality will help minimize any future interruptions to a systemic approach of controlling micrometastatic disease.

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