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REVIEW ARTICLE

Advances in the management of spinal metastases: what the radiologist needs to know

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ABSTRACT

Spine is the most frequently involved site of osseous metastases. With improved disease-specific survival in patients with Stage IV cancer, durability of local disease control has become an important goal for treatment of spinal metastases. Herein, we review the multidisciplinary management of spine metastases, including conventional external beam radiation therapy, spine stereotactic radiosurgery, and minimally invasive and open surgical treatment options. We also present a simplified framework for management of spinal metastases used at The University of Texas MD Anderson Cancer Center, focusing on the important decision points where the radiologist can contribute.

INTRODUCTION

According to the American cancer society, it is projected that about 1.9 million new cancer cases will be diagnosed by the end of 2021 in the USA.¹ Half of these cases will be due to cancers that frequently metastasize to bone.² Bone is the third most common site of distant metastases from cancer after lung and liver, and the spine is the most frequently involved osseous site of metastases.³ Spinal metastases can be associated with pain, pathological fractures, deformities, hypercalcemia, and compression syndromes such as spinal cord and cauda equina compression.⁴ Spinal cord compression, the most feared complication, develops in 10 to 20% of patients with spinal metastases.⁵

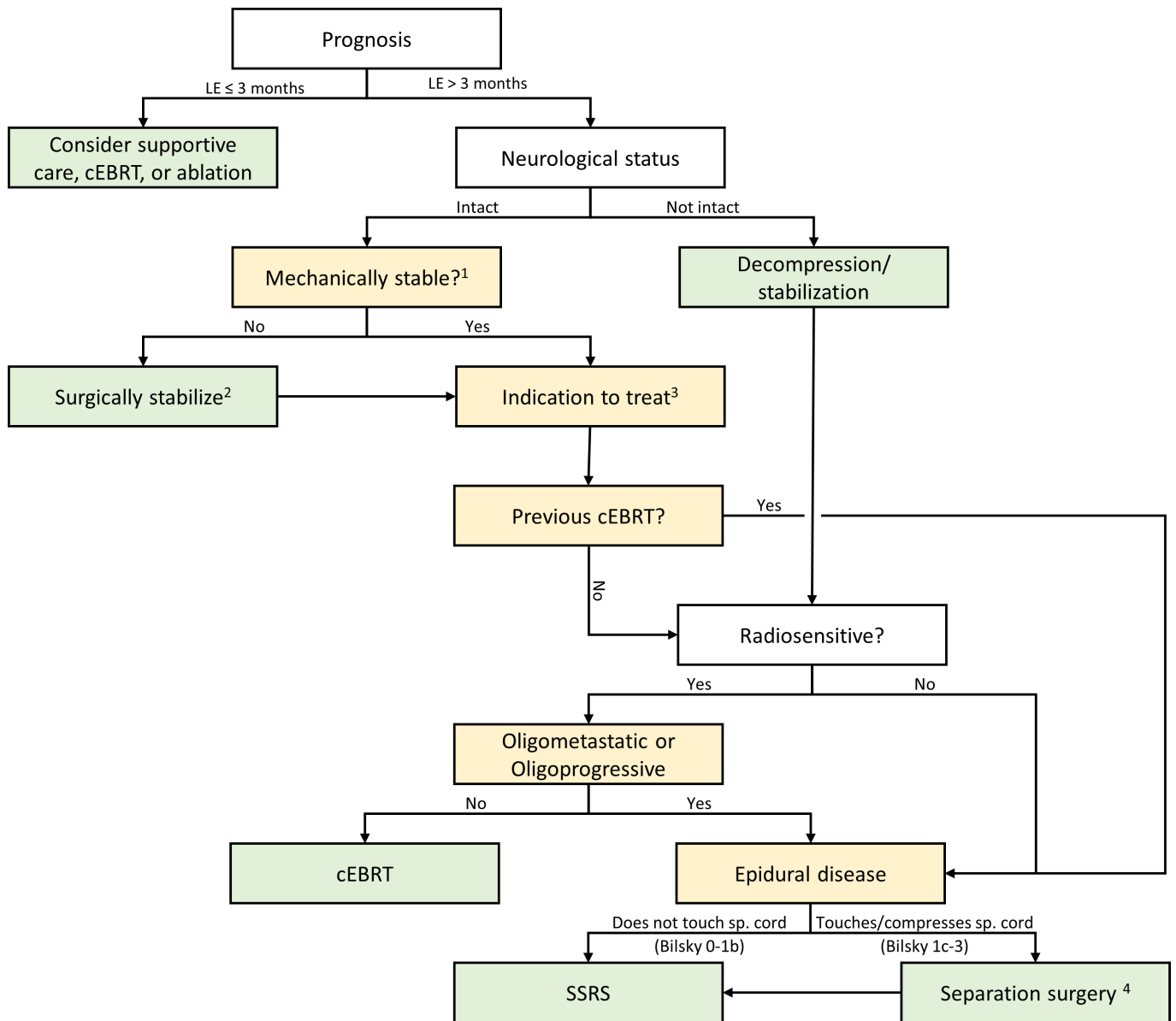
Historically, treatment of spinal metastases was focused on improving quality of life in patients with advanced cancer, through palliation of pain, prevention of pathological fractures and improvement of mobility and function.⁶ With improved disease-specific survival in patients with Stage IV cancer, durability of local disease control has become an important additional goal for treatment of spinal metastases,^{5,7} and in the case of oligometastatic disease, the intent of therapy is prolongation of long-term survival and even cure.^{8,9}

The management of spine metastases is multidisciplinary, involving medical oncologists, radiation therapists, spine surgeons and radiologists.¹⁰ A positive contribution from the radiologist requires familiarity with the different management options available to the patients. These include conventional external beam radiation therapy (cEBRT), spine stereotactic radiosurgery (SSRS), minimally invasive and open surgical treatment options, and systemic therapy. Prior to discussion of these modalities, it is vital to understand the considerations that determine their selection in a patient with a known primary source of metastasis who has completed staging assessment.¹¹⁻¹³

Management algorithm

Several frameworks have been developed to select the optimal management strategy for patients with spinal metastases.¹¹⁻¹³ No simple flow chart can account for all possibilities, and management schemes vary based on local factors such as expertise and resources. With the above caveats in mind, a simplified framework for management of spinal metastases used in The University of Texas MD Anderson Cancer Center (MDACC) is provided in [Figure 1](#), which illustrates important decision points that the radiologist needs to consider when reporting on spinal metastases.

Figure 1. MD Anderson Spine Metastasis Management Algorithm. Decision points requiring imaging input are highlighted in yellow. ¹ Mechanical stability is determined using SINS and presence of mechanical pain; ² Surgical stabilization may be performed using instrumented fusion or cement augmentation; ³ Indications to treat include presence of epidural disease and oligometastatic/oligoproliferative setting; ⁴ Separation surgery can be performed using percutaneous ablation (e.g. LITT) in specific cases. cEBRT, conventional external beam radiation therapy; SSRS, spine stereotactic radiosurgery.



The process starts with assessing the patient's life expectancy given performance status and availability of systemic therapy options. If prognosis is poor, the patient will not benefit from aggressive regimens focused on local control, but is best served by supportive care, and if needed, palliative cEBRT for pain control.¹⁴ Pain relief begins at approximately 2 weeks, continues to decrease over time following palliative radiation.¹⁵ Pain relief can be durable, with median pain relief duration ranging from 9 to 20 months.¹⁶

In patients with good prognosis, neurological status is assessed next. Patients with urgent neurological compromise are managed with decompressive surgery, which is aimed at

preventing neurological damage, rather than local control. With threatening epidural disease removed, these patients will then require consolidation radiation therapy, either cEBRT or SSRS depending on sensitivity of the tumor histology to cEBRT (See Radiosensitivity) and the overall disease burden (See Oligometastatic or Oligoproliferative Disease).

Patients with intact neurological status are then assessed for mechanical stability (See Stabilization), and stabilized as needed. The lesion of interest is then assessed for an indication to treat, which is typically presence of epidural disease, oligometastatic or oligoproliferative disease, or local failure following cEBRT. If there is an indication to treat in a previously untreated lesion, the lesion

is assessed for radiosensitivity to determine whether SSRS will be needed. SSRS is reserved for radioresistant histologies or for radiosensitive histologies in the oligometastatic/oligoprogressive setting. Lesions with epidural disease touching or compressing the spinal cord (e.g. Bilsky score 1c or higher¹⁷) will undergo surgery to separate the tumor from the spinal cord (See Separation Surgery) prior to SSRS. Lesions that have previously been treated with cEBRT are assessed for the presence of epidural disease to determine if separation surgery will be needed prior to SSRS.

The sections that follow will review the treatment modalities and the concepts introduced above.

Radiation therapy

Radiologists unfamiliar with management of spine metastases often elide the various radiotherapy modalities with abbreviations such as XRT or RT. However, differences in radiation delivery have important implications for patient management and outcome.

Conventional external beam radiation therapy

In cEBRT, high-energy X-rays are delivered to a target lesion using one or two beams (Figure 2). Therapy is prescribed in various doses and can be delivered in single dose but is often fractionated to allow for higher tumor lysis while reducing damage to adjacent tissues. Single, low-dose regimens have high rates of pain relief, but suffer from high incidence of local failure and need for retreatment, and are therefore reserved for patients with limited life expectancy, where pain relief and convenience supersede the need for durable local control.^{18,19}

The primary disadvantage of cEBRT is its broad radiation field, which usually includes a vertebral segment above and below the targeted level, as well as normal adjacent tissue including the spinal cord and bowel. The potential to injure non-target organs limits the effective dose that can be delivered to the metastasis and results in poor local control rates and minimal to no effective shrinkage of some (though not all) tumor histologies.

Figure 2. External Beam Radiation Therapy. cEBRT (left column) delivers high dose to the tumor, but also to adjacent structures, such as bowel and spinal cord. SSRS (right column) delivers high dose to the tumor, while avoiding high doses to adjacent structures such as the spinal cord and bowel. AT MDACC the tumor visible on imaging (gross tumor volume, blue outline) is treated with the highest dose, and the area around it that is assumed to have microscopic disease (clinical tumor volume, yellow outline) is treated with ~20% lower dose. cEBRT, conventional external beam radiation therapy; SSRS, spine stereotactic radiosurgery.

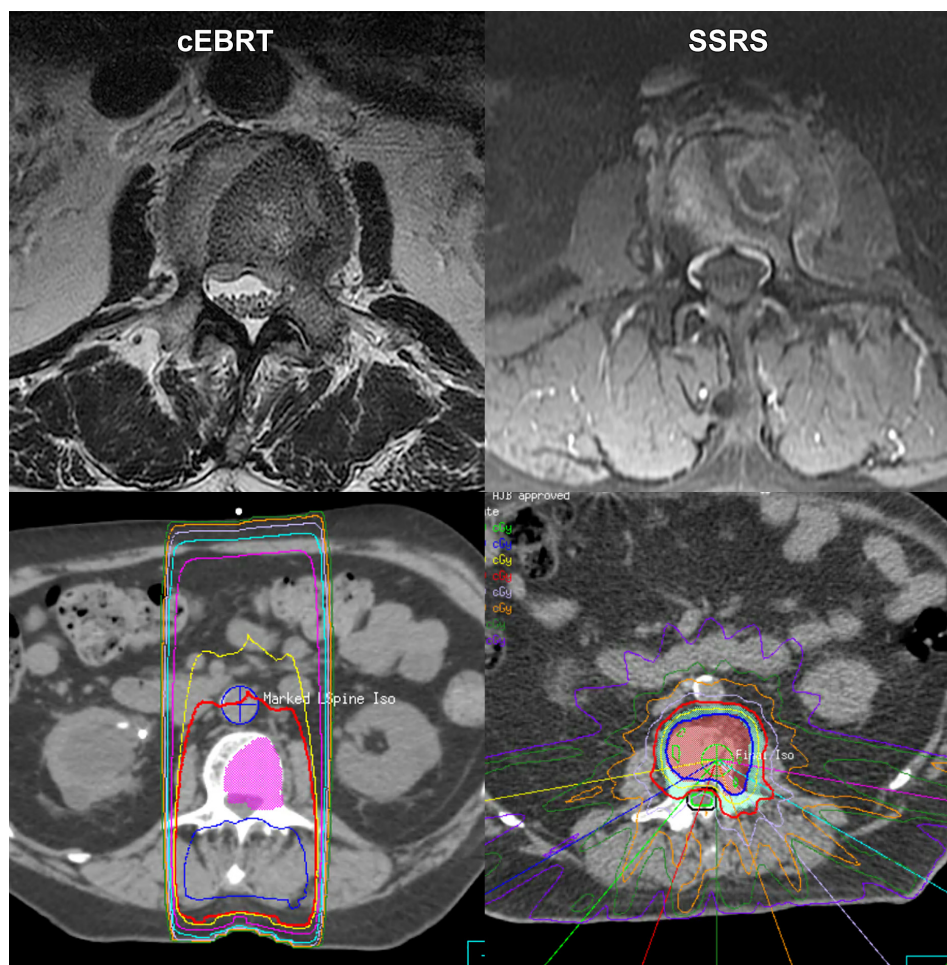


Table 1. Tumor radiosensitivity

Radiosensitive	Intermediate	Radioresistant
Lymphoma Plasmacytoma Seminoma Ovarian carcinoma Neuroendocrine carcinoma Small cell carcinoma Ewing sarcoma	Prostate cancer ^a Breast cancer ^a HPV+ squamous cell carcinoma	Sarcoma (except Ewing) Renal cell carcinoma Melanoma Non-small cell lung cancer Thyroid carcinoma Hepatocellular carcinoma Colorectal carcinoma

^aThese are typically considered radiosensitive in our institution.

Radiosensitivity

Variability of different tumor histologies in response to cEBRT is the basis of their division into radiosensitive and radioresistant (Table 1). Radiosensitive histologies include hematologic malignancies (*e.g.*, lymphoma and myeloma), as well as some solid tumors, such as seminoma, and ovarian cancer. Radioresistant histologies include common malignancies such as renal cell carcinoma, melanoma, hepatocellular carcinoma, non-small cell lung cancer, and some colorectal carcinomas. An intermediate group of tumors have mixed local control and shrinkage rates, and include prostate and breast cancer, although these are typically classified as radiosensitive at MDACC.^{13,20–23} Compared to radiosensitive histologies, radioresistant histologies have a shorter median response period (3 vs 11 months) and a shorter 2 year local control rate (30% vs 86%) in response to cEBRT.^{21,24}

Spine stereotactic radiosurgery

Over the last decade, SSRS has emerged as an effective modality for managing spinal metastases. SSRS uses high-resolution image guidance and intensity modulation to focus radiation on a target volume with a steep fall-off in radiation delivered to surrounding tissues (Figure 2). This allows for dose escalation to radioresistant tumors and limits radiation exposure to adjacent healthy tissue, the most important of which is the spinal cord.^{3,25} The precision targeting of tumor made possible by SSRS requires high-quality imaging and precise reporting to assist the radiation oncologist in prescribing the treatment field.²⁶

There may be slight institutional variations in dose prescriptions in order to achieve ablative stereotactic doses in 1 to 3 fractions. At our institution, the highest dose of radiation is delivered to disease visible on imaging (gross tumor volume, GTV) and a lower dose is delivered to the contiguous adjacent structures (clinical tumor volume, CTV), in a technique called single-field integrated boost.²⁷ Alternatively, the entire CTV and GTV may be treated to a single dose (single-field uniform dose).

As seen in Figure 1, the primary indications for use of SSRS instead of cEBRT include, radioresistant histologies (Table 1), oligometastatic or oligoprogressive disease, reirradiation of local failure following cEBRT (*i.e.* the reirradiation setting), and local control following decompressive surgery. SSRS in patients with radioresistant histologies and limited systemic disease provides local tumor control of 88% at 18 months with limited toxicity.²⁸

In the reirradiation setting, a biological effective dose greater than that of the previous radiation will often be required to

achieve local tumor control. However, the use of cEBRT is often problematic, because the radiation tolerance of the spinal cord precludes additional delivery of tumoricidal doses of radiation. Because SSRS allows for relative sparing of the spinal cord, it can be used safely and effectively in the event of treatment failure with cEBRT. Local tumor control rates in this setting range between 60 and 100% over a follow-up period of 6–21 months.^{20,29}

The main contraindication to SSRS is related to the more limited field of disease compared to cEBRT. Extensive disease that requires “cutting through” tumor results in poor local control. At MDACC, the craniocaudal limit is three contiguous levels, although exceptions can be made in specific cases.^{30,31} Lateral extent of disease, *e.g.* disease from pleura, rib, soft tissues, or retroperitoneal disease extending to the spine, can limit the ability of SSRS to control local disease. No general cut-off measurements are available for lateral extent, and the decision is often made on a case-to-case basis.

SSRS requires more complex planning than cEBRT, which can introduce delays in treatment compared to surgery and cEBRT. While cEBRT can typically start on the same or next day after the decision to treat, SSRS typically requires a week for planning. This includes more complicated planning for patient immobilization, dose delivery, and treatment set-up, as well as quality assurance and review by medical physicists and radiation oncologists.³²

Oligometastatic or oligoprogressive disease

Oligometastatic or oligoprogressive disease represents a special setting where de-novo or progressive disease is limited to a few sites, respectively. Patients with oligometastatic disease have been shown to have better prognoses than those with multiple metastatic sites, and patients with oligoprogressive disease can be maintained on their current effective therapy after control of progressive sites of disease has been achieved.^{9,33} The precise definition of “oligo” varies among and even within institutions and can depend on the proximity of lesions to one another, lesion location, and various patient factors, but is variably defined as fewer than five metastatic lesions.^{9,33} Patients with oligometastatic or oligoprogressive spinal metastases treated with SSRS benefit from high local control rates and low rates of toxicity and can achieve long-term survival and a long time before modification of systemic therapy is needed.^{9,33}

SSRS can also be delivered post-operatively following surgical decompression. In this setting, a high-dose, single-fraction radiation of 24Gy offers durable local tumor control that is

independent of tumor histology and can achieve a 1 year control rate of greater than 93%.³⁴

The main limitation of SSRS is in treatment of disease abutting or compressing the spinal cord. The spinal cord maximum tolerated dose is 10–14 Gy.³⁴ Even with high precision SSRS, treatment of tumor abutting the spinal cord would deliver higher than the maximum tolerated dose to the spinal cord. Two adjunct therapies (separation surgery and, more recently, laser interstitial thermotherapy) have been described to circumvent this limitation. These can be considered as neoadjuvant therapy for SSRS and are discussed in the sections below.

Surgery

The use of surgery for treatment spinal metastases dates back to the early 1900s and mainly consisted of laminectomy for posterior decompression and removal of accessible tumor.²⁰ Modern advances in surgical technique have significantly reduced post-operative complications and morbidity; however, even complete or *en block* resection is typically not able to provide durable local control for patients with spinal metastases. Therefore, surgery is often combined with radiation therapy.¹³ The current indications for surgery in patients with spinal metastases include stabilization of a mechanically unstable spine (performed percutaneously when possible), emergent decompression of the spinal canal in patients with spinal cord compression, removal of epidural disease to allow for SSRS (separation surgery), and, in rare cases, attempt at local disease control when radiation therapy cannot be safely delivered.^{13,25,35}

Stabilization and cement augmentation

Stabilization is typically indicated regardless of the radiosensitivity of the tumor or degree of epidural disease, and can be performed using combinations of instrumented fusion and cement augmentation (*i.e.* vertebroplasty and kyphoplasty).¹¹ The Spinal Instability Neoplastic Score (SINS) is a scoring system that can assist in the diagnosis of neoplastic instability using one clinical and five imaging criteria: pain, location, alignment, osteolysis, vertebral body collapse, and posterior element involvement.^{36,37} Stable lesions have a SINS of 0–6 and do not require surgery. Unstable lesions have a SINS of 13–18 and require surgical stabilization. Lesions with a SINS of 7–12 are considered potentially unstable and require further assessment to determine the need for surgery.^{36,37} Knowledge of the imaging components of SINS will enable the radiologist to assist in patient management.²⁶

Cement augmentation has been shown to reduce pain intensity scores and analgesic use in patients with pathological vertebral compression fractures.³⁸ It may be used in patients with spine metastases at the affected level to reduce pain or in conjunction with instrumented fusion at adjacent unaffected levels (prophylactic cement augmentation).³⁹ Selection of appropriate candidates for cement augmentation requires assessment of the posterior cortical integrity of the vertebral body to reduce the risk of epidural cement extrusion.²⁶ When the posterior cortex is disrupted, risk of cement extrusion can be reduced by inserting a metallic mesh or stent in the vertebral body prior to

cement augmentation, a novel technique broadly referred to as vertebral body stenting.^{40–42} Another method to decrease risk of cement leakage is the use of balloon kyphoplasty or expandable intravertebral implants, which attempt to restore vertebral height prior to injection of cement material.^{43–45} The question of whether cement augmentation at the affected level improves outcomes following SSRS is currently being investigated at MDACC.⁴⁶

Separation surgery

Separation surgery is so-called because it separates the tumor from the spinal cord.⁴⁷ The goal is to provide enough distance between the tumor and spinal cord (generally >2 mm) to allow for adequate radiation doses to be delivered to the tumor without resulting in spinal cord toxicity. Separation surgery combined with SRSS provides a 1 year local control rate of more than 91% regardless of tumor histology and radiosensitivity.⁴⁸ The primary disadvantage of separation surgery is morbidity associated with any surgical procedure, as well as the recovery time, which necessitates discontinuation of systemic chemotherapy. The latter is an important issue for patients with aggressive disease that is being controlled by chemotherapy and who risk progression if treatment is interrupted.

Laser interstitial ThermoTherapy (LITT)

Laser interstitial ThermoTherapy (LITT) in the spine addresses issues related to the morbidity and recovery time of separation surgery.^{49–51} By monitoring and controlling the heat delivered to the tumor and adjacent spinal cord, LITT can be used to safely treat epidural disease and serves as an alternative to separation surgery. The advantages of LITT over open surgery are reduced hospital stay and consequently short interruption of systemic treatment, low morbidity, and minimal impact on quality of life.^{25,52} Currently, LITT is limited to specific institutions that have expertise in the technique, and to lesions in the thoracic spine due to difficulty in treating the mobile cervical spine and the risk of cauda equina injury in the lumbar spine.^{52,53}

Radiofrequency ablation (RFA) and cryoablation

Radiofrequency (RFA) and cryoablation can be safely used for treatment of spinal metastases, with CT- and MR-guided monitoring of the ablation zone.⁵³

Data on the use of RFA and cryoablation alone for spinal metastases are limited to small series^{54,55} or those with end points such as pain relief,^{53,55,56} reduced analgesic use in the first 24 h following ablation,⁵⁷ length of hospital stay,⁵⁷ and reduction in tumor size following ablation.⁵³ Recent prospective trials have shown significant improvement in pain and quality of life up to 6 months post-RFA⁵⁶ and quality of life for more than 6 months post-cryoablation.⁵⁵

Ideally, spinal RFA and cryoablation, like LITT and separation surgery, would be used for improving recovery time and reducing the delay to initiation of radiation treatment to achieve durable local control. Unfortunately, data on this use of RFA and cryoablation are currently lacking.⁵⁸

CONCLUSION

We have reviewed the multidisciplinary management of spine metastases in order to provide the radiologist with an overview of the management options available to patients and referring medical, radiation, and surgical oncologists. We have also presented a simplified framework for management of spinal metastases used at our institution, focusing on the important decision points where the radiologist can contribute.

A companion paper²⁶ will delve into imaging details that the radiologist must be aware of in order to be a useful part of the multidisciplinary team.

CONFLICTS OF INTEREST

The authors have no conflicts of interest regarding the material in this manuscript.

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