An integrated multidisciplinary algorithm for the management of spinal metastases: an International Spine Oncology Consortium report

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Spinal metastases are becoming increasingly common because patients with metastatic disease are living longer. The close proximity of the spinal cord to the vertebral column limits many conventional therapeutic options that can otherwise be used to treat cancer. In response to this problem, an innovative multidisciplinary approach has been developed for the management of spinal metastases, leveraging the capabilities of image-guided stereotactic radiosurgery, separation surgery, vertebroplasty, and minimally invasive local ablative approaches. In this Review, we discuss the variables that should be considered during the management of these patients and review the role of each discipline and their respective management options to provide optimal care. This work is synthesised into a practical algorithm to aid clinicians in the management of patients with spinal metastasis.

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Introduction

In the USA, nearly 300 000 adults have osseous metastatic disease,[1,2] with approximately 60% of the metastases being spinal metastases.[3] Similar to other bone metastases, spinal metastases can cause substantial pain, functional limitations, and worsening performance status depending on the location and extent of disease. Approximately 10% of patients with spinal metastases develop spinal cord compression—a severe and often permanently disabling condition that is an oncological emergency.[3] Partly for this reason, spinal metastases are viewed as complex bone metastases, distinct from simple bone metastases that cause pain but rarely cause permanent disability.

Historically, spinal metastases have been treated with invasive surgical approaches (eg, en-bloc resection), or low-dose palliative conventional external-beam radiotherapy (EBRT), or both. Unfortunately, en-bloc resection, which is used to achieve clear surgical margins, results in substantial patient morbidity and poor long-term local control.[4–6] Conventional EBRT improves pain in approximately 60% of patients with spinal metastases, with a median duration of less than 4 months.[7,8] As the number of patients with metastatic cancer living beyond 3 months increases, the need for durable palliation and long-term tumour control are becoming increasingly important to control.

The suboptimal outcomes of invasive surgery and conventional EBRT in the treatment of spinal metastases have led many cancer centres to explore the potential of spine stereotactic body radiotherapy (SBRT) or spine stereotactic radiosurgery (SRS) as an alternative therapeutic option for this subset of patients. These techniques allow for less invasive surgery to be performed, and demonstrate high rates of both durable pain control and local tumour control.[9] The incorporation of spine SBRT and spine SRS into oncological practice is fundamentally changing the treatment paradigm for spinal metastases. As such, patients with spinal metastases should be managed by an integrated, multidisciplinary team.

For simple bone metastases, a wealth of level 1 evidence (typically randomised trials) guides clinicians' decision making and care.[10] By comparison, there is a relative paucity of prospective, randomised data to guide the management of spinal metastases. Several frameworks have been developed that emphasise important concepts and decision points in the management of spinal metastases (eg, the neurological, oncological, mechanical, and systemic framework [NOMS], and the location of disease in the spine, mechanical instability, neurology, oncology, and patient fitness, prognosis and response to prior therapy framework [LMNOP]),[11,12] and are meant to provide key principals and general guidance to radiation oncologists and spine surgeons. These frameworks often simplify or omit important details (eg, available systemic therapy options) that are paramount to the treatment of patients with metastatic disease—a process that is often led by a medical oncologist, rather than a radiation oncologist or spine surgeon. To address this need for a framework and algorithm that takes all aspects of care into consideration, and builds on the existing frameworks, the Spine Oncology Consortium decided to evaluate, consolidate, and synthesise all available evidence into two multidisciplinary algorithms for the management of spinal metastases.

Data collection

Search strategy and selection criteria

To inform the recommendations provided in this Review, we performed a systematic literature search (figure 1) using MEDLINE (via PubMed), Cochrane Library, and Embase using the search terms "(surgery OR radiation) AND spine metastases." Search results were restricted to those published between Jan 1, 1980, and June 1, 2016, and to those published in English. Articles were selected for relevance to the multidisciplinary management of spinal metastases with surgery or radiotherapy, or both.

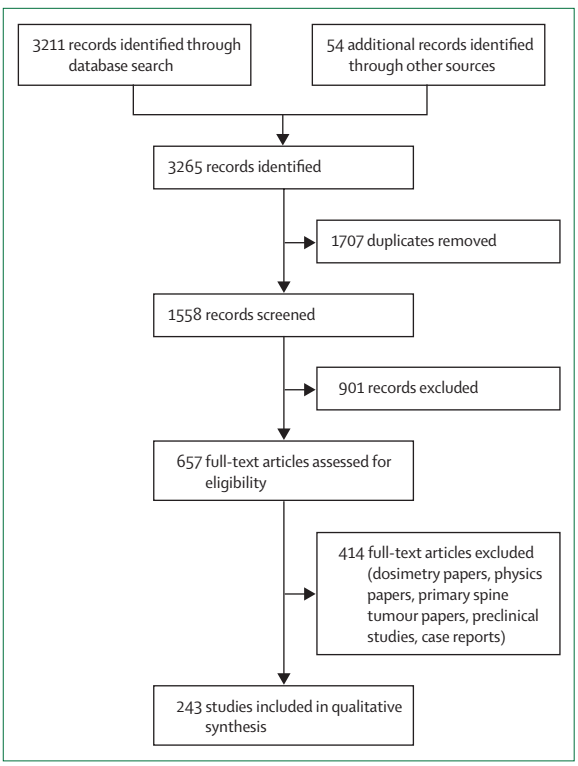

Figure 1: **PRISMA flow diagram**

After duplicates were electronically and manually removed, 1558 potentially relevant abstracts remained. Prospective studies, retrospective reviews of more than ten patients, systematic reviews, guidelines, algorithms, and consensus recommendation studies were included for discussion; case reports, commentaries, studies on primary spine tumours, preclinical studies, and dosimetric or physics studies were excluded. DES and NJS independently reviewed the abstracts and identified 243 publications relevant to the management of spinal metastases, of which 42 were prospective trials. 243 studies were included in the qualitative analysis and were discussed among seven members of the Spine Oncology Consortium (subgroup chosen for simplicity; ie, to focus the review), before being circulated among the remaining Spine Oncology Consortium committee members. In general, there were little prospective data for the management of spinal metastasis and the recommendations included in this Review are based largely on retrospective data, single-institution prospective single-arm trials, and expert opinion. Findings from our literature search and committee discussions are described below.

Assessment of patient and systemic options

Initial assessments of patient performance status, systemic burden of disease, and systemic treatment options are crucial in the management of patients with spinal metastases. As such, we developed a treatment algorithm to account for these measures (figure 2), each of which is more clearly described below.

Performance status

Patients with metastatic cancer are generally considered incurable, with highly variable but often limited life expectancies; therefore, the benefits of any potential treatment should be balanced against the risks and disease burden for each individual patient. The long-term benefits of an invasive, timely, or costly procedure might not manifest in patients with a short life expectancy. Furthermore, an overly aggressive treatment approach might cause more harm than benefit in patients who are frail and neurologically debilitated, or who are dying.

For patients with spinal metastases, an important prognostic factor is overall performance status, as assessed by the Karnofsky performance status or Eastern Cooperative Oncology Group scale.[13,14] Chao and colleagues[15] developed a recursive partitioning analysis (ie, a method by which to allocate patients into categories of an outcome of interest) for patients undergoing spine SBRT, based on time from primary diagnosis, Karnofsky performance status, and age. Median overall survival rates ranged from 2·4 to 21·1 months (recursive partitioning analysis class three to one). For patients whose overall performance status is poor (ie, Karnofsky performance status ≤40), spine SBRT is unlikely to provide clinically significant benefit over less complex forms of radiotherapy, and comes at an increased cost of time, resource use, and additional imaging studies. A single fraction of conventional EBRT is recommended to alleviate pain, and a five-fraction regimen can be used to treat symptoms of spinal cord compression.[16–18]

Patients with very poor performance status (Karnofsky performance status ≤40) should be given the opportunity to discuss goals of care with their family, treating physicians, and their palliative care team or multidisciplinary spine team, or both (figure 2).

Systemic burden of disease

A patient's systemic burden of disease could influence prognosis, treatment choices, and goals of care.[19] The presence of symptomatic disease in a crucial organ (eg, brain, liver, or lung) might decrease the need or urgency for treatment of a minimally symptomatic spinal metastasis. The presence of extensive systemic disease might push the clinician to consider short-course conventional EBRT, either to expedite the initiation of systemic therapy, or, if no effective therapies are available, to minimise side-effects while maximising quality of life. If spinal disease is widespread, it might be difficult to localise the culprit lesion for treatment or preclude safe hardware placement, or both. In the Prognostic Index for Patients with Spinal Metastases (PRISM) model, both the presence of metastatic disease outside of the spine and the number of organ systems involved were associated with worse overall survival after spine SRS.[20]

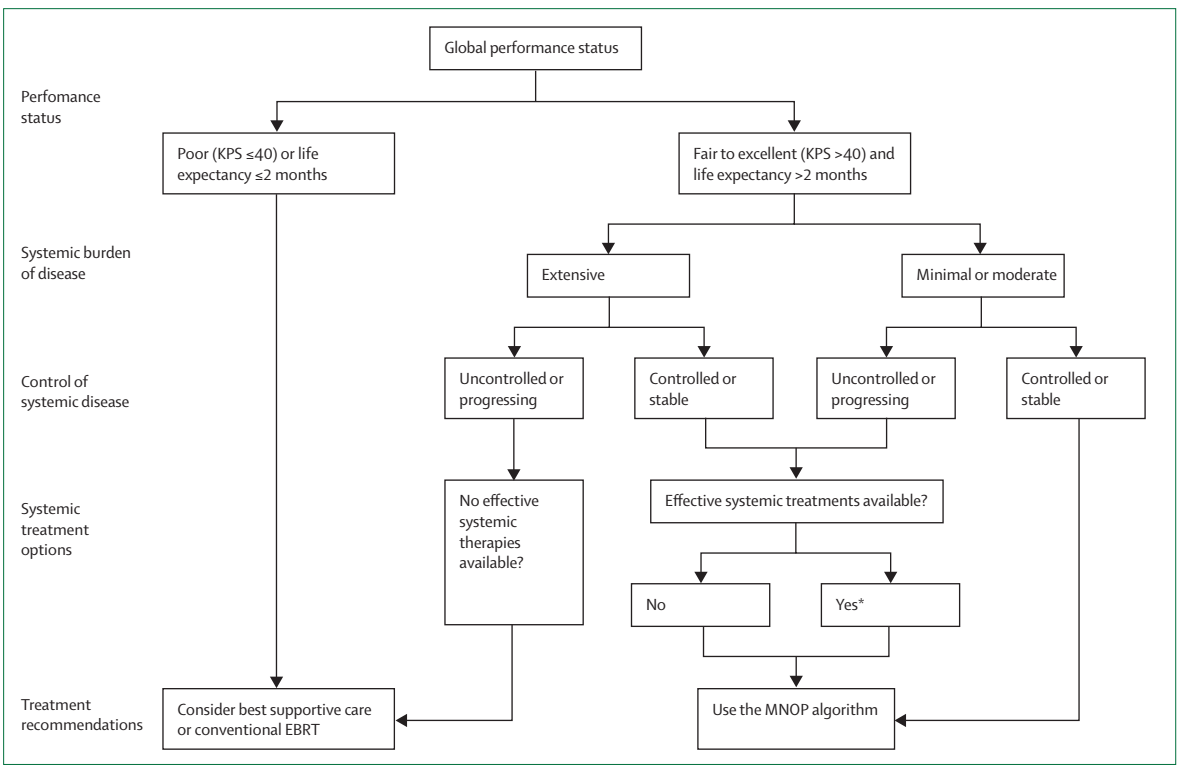

Figure 2: **Initial assessment algorithm for patients with spinal metastases: algorithm 1**
KPS=Karnofsky performance status. EBRT=external-beam radiotherapy. MNOP=mechanical, neurological, oncological, preferred treatment. *For select patient with effective systemic therapy treatment options, systemic therapy without the use of radiotherapy might be most appropriate.

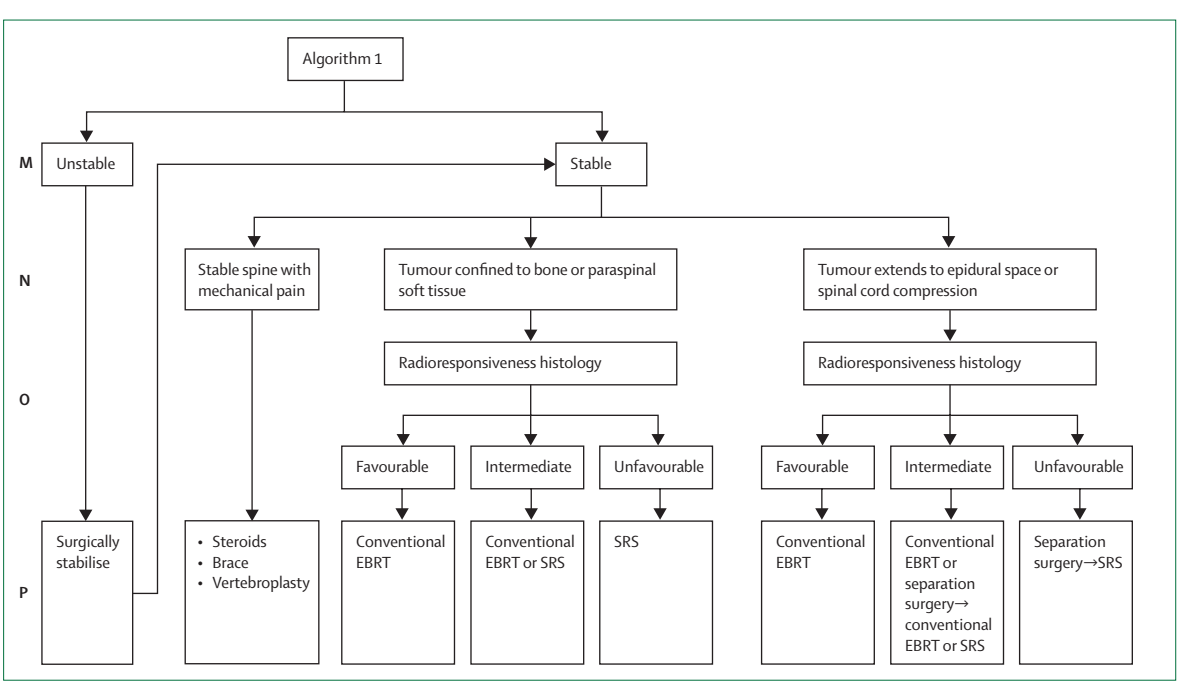

Figure 3: **MNOP algorithm for spinal metastasis management**
MNOP=mechanical, neurological, oncological, preferred treatment. EBRT=external-beam radiotherapy. SRS=stereotactic radiosurgery.

	SINS
Location within the spine	
Junctional (occiput–C2, C7–T2, T11–L1, L5–S1)	3
Mobile spine (C3–C6, L2–L4)	2
Semi-rigid (T3–T10)	1
Rigid (S2–S5)	0
Pain relief with recumbence and pain with movement or loading of the spine	
Yes	3
No (occasional pain but not mechanical)	1
Pain-free lesion	0
Bone lesion quality	
Lytic	2
Mixed lytic or blastic	1
Blastic	0
Radiographic spinal alignment	
Subluxation or translation present	4
De-novo deformity (kyphosis or scoliosis)	2
Normal alignment	0
Vertebral body collapse	
>50% collapse	3
<50% collapse	2
No collapse with >50% body involved	1
None of the above	0
Posterolateral involvement of spinal elements (facet, pedicle, or costovertebral joint fracture or replacement with tumour)	
Bilateral	3
Unilateral	1
None of the above	0

The SINS score is generated by adding all of the scores from the six individual components. A score of 0–6 is classified as a stable spine, and no action is needed. A score of 7–12 receives a classification of indeterminate, and indicates potential instability, which warrants surgical consultation. A score of 13–18 indicates spinal instability that warrants surgical consultation. Adapted from Fisher et al.,[32] with permission from Wolter Kluwer Health. SINS=Spine Instability Neoplastic Score.

Table 1: **Classification system for SINS**

The method of assessment for systemic disease should be driven by routine imaging for the primary tumour type. For example, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET plays a fundamental role in the staging of various tumour types, such as lymphoma and small-cell lung cancer. Typically, CT, PET, and bone scans are the most common methods to assess the burden of systemic disease, but new molecular imaging techniques and whole-body MRI are being actively investigated as additional options.[21,22]

Effective systemic treatment options

The availability of effective treatment options is equally as important as the absolute burden of systemic disease. Patients who develop epidural tumours often have late-stage, treatment-resistant disease; however, a subset of patients might develop spinal metastases early on in their disease course. With the advent of numerous effective biological targeted agents and the increased numbers of immunotherapies approved by the US Food and Drug Administration, patients with metastatic disease often have substantial and durable responses to therapy.[23,24] By contrast, for specific tumour histologies, systemic therapy might offer little efficacy. Therefore, the clinician should consider not only the burden of systemic disease, but also tumour histology and the availability and efficacy of treatment for each patient.

In select clinical scenarios, systemic therapy might be recommended over surgical or radiotherapeutic intervention for spinal cord compression; primarily, these can include Hodgkin's and non-Hodgkin lymphomas, germ-cell neoplasms, neuroblastoma, breast cancer, and prostate cancer.[25–30] When spine SRS and SBRT is recommended instead, systemic therapy is often held off because of concern for radiosensitisation near the spinal cord.[31] With few data guiding these decisions, the need for radiation and medical oncologists to communicate their preferences to one another and reach consensus on a treatment recommendation is paramount.

Mechanical stability, neurological risk, oncological parameters, and preferred treatment (MNOP) algorithm

After assessing performance status, systemic burden of disease, and systemic treatment options, the next crucial step for clinicians is to evaluate the spinal metastasis itself. This evaluation can be done according to the MNOP algorithm (figure 3).

Mechanical stability

Spinal instability contributes to pain, decreases quality of life, and can lead to devastating neurological injury. The Spine Oncology Study Group defines spinal instability as a "loss of spinal integrity as a result of a neoplastic process that is associated with movement-related pain, symptomatic or progressive deformity, and/or neural compromise under physiologic loads."[32] Numerous methods have been developed to assess the stability of a patient's spine. One of the most widely adopted systems that we, the Spinal Oncology Consortium, and others endorse is the Spine Instability Neoplastic Score—an easy-to-use scoring system specific to patients with cancer (table 1). The system is based on six radiographic or clinical categories that are weighted by their contributions to spinal instability, with total scores ranging from 0 to 18. The six component scores are combined and used to categorise spinal stability as either stable (0–6), potentially unstable (7–12), or unstable (13–18). In a study[33] examining the use of this system, interobserver and intraobserver reliability was high (0·846 and 0·886). The validity of this score was very good, with a specificity of 80% and sensitivity of 95%.[33] For ethical reasons, no instability scoring system will be prospectively validated to document the natural history of an unstable spine without receiving some form of stabilisation; thus, clinical judgment is required in the use of the Spine Instability Neoplastic Score system. Ultimately, if the

	Favourable	Intermediate	Unfavourable
Durable local control (radiosensitivity)	Radiosensitive (very high local control)	Mixed results (moderate to high local control)	Radioresistant (poor local control)
Rapid reduction of tumour size (radioresponsiveness)	Highly radioresponsive (likely to achieve rapid complete radiographic responses)	Moderately radioresponsive (possible to achieve rapid reduction in tumour size)	Less radioresponsive (unlikely to achieve rapid reduction in tumour size)
Example histologies	Chloroma, lymphoma, multiple myeloma, seminoma or germinoma, and small cell carcinoma	Prostate cancer, breast cancer, and HPV+ squamous cell carcinoma	Sarcoma, melanoma, NSCLC, renal cancer, and GI cancers

HPV+=human papillomavirus-positive. NSCLC=non-small-cell lung cancer. GI=gastrointestinal. EBRT=external-beam radiotherapy.

Table 2: **Effect of tumour histology on conventional EBRT outcomes**

spine is deemed unstable, the goal is to achieve a stable spine in some manner.

Neurological risk

Another important component of the Spine Oncology Consortium algorithm is a thorough assessment of neurological risk. This assessment includes both current neurological function (ie, signs or symptoms of myelopathy, radiculopathy, motor, or sensory deficits) and potential neurological compromise based on the amount of epidural disease or cord compression seen on MRI or a CT myelogram. Bilsky and colleagues[34] proposed a systematic grading of the degree of spinal cord compression, which is now widely used amongst spinal oncologists. The involvement of neuroradiology is crucial in the assessment of neurological risk because not all things in the epidural space are tumours; for example, retropulsion of bone, hardware, or artifact can be mistaken for soft-tissue tumour. The presence of acute, symptomatic spinal cord compression are oncological emergencies, and usually require prompt surgical decompression (except in the setting of a pure radiosensitive histology, which will be discussed in the next section of this Review).[35] The presence of bone-only disease poses little immediate risk to the patient's neurological status, and the treatment for these two situations—ie, spinal cord compression and bone-only disease—is appropriately different. Assessment of the degree of epidural disease is crucial to determine whether separation surgery is warranted for the safe and effective delivery of spine SBRT and SRS.

Oncological parameters

Generally, oncological assessment is based on tumour histology. There are three fundamental characteristics of tumour histology that affect treatment recommendations: radiosensitivity, radioresponsiveness, and vascularity (table 2). Radiosensitivity (ie, sensitive *vs* resistant) reflects the likelihood that durable local control from conventional EBRT will be achieved. This component primarily affects the type of radiotherapy selected (ie, conventional EBRT *vs* spine SBRT and SRS). Radioresponsiveness (ie, rapid *vs* slow) reflects how rapidly a tumour will decrease in size. This component primarily affects patients with epidural disease or spinal cord compression for whom the decision of surgical decompression versus conventional EBRT depends on the rapidity of tumour response. Radioresponsiveness should be viewed as distinct from radiosensitivity because although high rates of tumour cell death might be achieved in some tumours after conventional EBRT, the same tumours might take weeks or months to reduce in size so that decompression is achieved. Vascularity (ie, vascular *vs* non-vascular tumours) primarily affects surgical management and the need for preoperative tumour embolisation. Each of these three tumour characteristics have implications on treatment recommendations.

Preferred treatment

The section below discusses each of the components in the management of patients with spinal metastases.

Spinal metastasis treatment

Radiotherapy

The principal treatment of patients with spinal metastases is radiotherapy, which can be delivered alone, postoperatively, or in conjunction with neurointerventional procedures. Almost all patients with spinal metastases receive radiotherapy at some point during their care, unless they have an extremely chemosensitive malignancy (ie, a haematological cancer), poor prognosis, or very short life expectancy.[36] The two primary reasons that radiotherapy is given to patients with spinal metastases are pain control and durable local control to improve or prevent neurological compromise. Depending on the intent of treatment and other case-specific circumstances, radiotherapy can be delivered as conventional EBRT, spine SRS, or SBRT. These modalities are shown in figure 4 and compared and contrasted in the appendix.

See Online for appendix

Similar to other sites of bone metastases, spinal metastases are most often treated with conventional EBRT. The primary goal of conventional EBRT is to alleviate pain, and approximately 60–70% of patients have a partial or complete response with this technique.[8,37] After conventional EBRT, about 25% of patients report complete resolution in pain, typically for a duration of

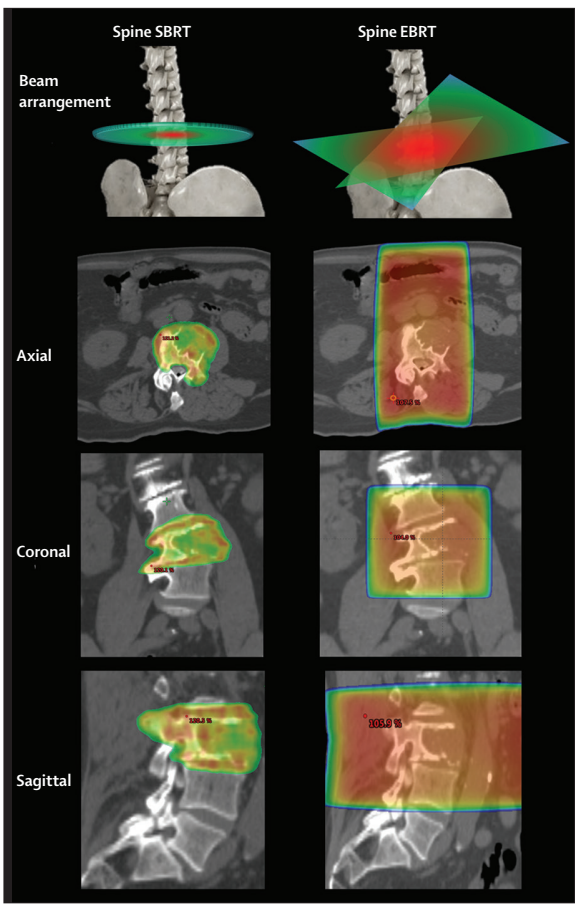

Figure 4: **Visual depiction of spine SBRT versus conventional EBRT**
Spine SBRT and SRS is a highly conformal therapy, typically delivered using multiple beams or arcs to target only the affected vertebral level(s), while the spinal cord and other organs are spared. Conventional EBRT is usually delivered using two opposed beams that deposit a near-full dose across the entire width of the patient (including the spinal cord and other internal organs). It is convention to include one uninvolved vertebral body superior and inferior to the affected vertebral level(s), given the rudimentary setup of these patients. SBRT=stereotactic body radiotherapy. EBRT=external-beam radiotherapy. SRS=stereotactic radiosurgery.

3–4 months, depending on histology.[37] Conventional EBRT can be delivered in many different dose and fractionation regimens, with the most common being 8 Gy in one fraction, 20 Gy in five fractions, or 30 Gy in ten fractions. Numerous prospective trials have shown equivalent efficacy (ie, decreased pain or decreased narcotic use) between these regimens, even for patients with vertebral body metastases.[7,17,38,39] However, a three-times greater likelihood of retreatment has been reported with a single-fraction regimen compared to a multifraction regimen.[37,38] In spinal disease, the benefits of single-fraction radiotherapy, such as its convenience and low use of resources, should be weighed against the risks of retreatment. The American Society for Radiation Oncology's bone metastases consensus guidelines recommend a single 8-Gy fraction for patients with painful spinal metastases and acknowledge the emerging data on the use of more advanced treatment techniques, such as spine SRS.[17]

Another important consideration for conventional EBRT is the likelihood of durable local control, which depends on tumour histology, radiosensitivity, and dose. For classically radiosensitive histologies, such as lymphoma, multiple myeloma, and germinoma, these tumours have favourable long-term local control.[40] For more radioresistant tumours, such as sarcomas and renal carcinoma, long-term local control rates are consistently less than 50%.[41,42] There is prospective evidence[18] that multifraction conventional EBRT (30 Gy in ten fractions, 37·5 Gy in 15 fractions, or 40 Gy in 20 fractions) improves 1-year local control compared with single-fraction conventional EBRT, and further efforts at dose escalation (eg, 3 Gy in 20 fractions) has been shown to afford excellent rates of local control based on single-institution data.[43] Sophisticated planning techniques, immobilisation, and image guidance are necessary when doses are escalated beyond spinal cord tolerance (45–50 Gy; appendix).

Spine SRS delivers high doses of radiation to tumours and spares adjacent healthy tissues, such as the spinal cord, nerve roots, and oesophagus. Typically, spine SRS is delivered in a single treatment, whereas spine SBRT is delivered as two to five treatments. The optimal dose and number of fractions is unknown. A biologically effective dose of spine SRS is approximately three-times higher than conventional EBRT, allowing for improved local control. Additionally, the high amounts of DNA damage elicited by spine SRS appear to obviate the histological dependence that exists for conventional EBRT to achieve local control, and multiple series have demonstrated 12-month local control rates of over 85% for even the most classically radioresistant histologies.[44–54]

The use of spine SRS is complex because it often requires a pretreatment MRI to evaluate the extent of metastatic disease with or without a spinal myelogram to visualise the proximity of disease to the spinal cord. Additionally, spine SRS often required special immobilisation to minimise target motion to less than 1 mm, computer-based inverse treatment planning, and adequate image-guidance for accurate daily alignment. With modern image-guidance techniques, various immobilisation techniques might be suitable. The generation of a spine SRS treatment plan is labour intensive and requires more quality assurance steps compared with conventional EBRT, which can technically be delivered without simulation or computer-based planning. Although bony landmarks (ie, the tops and bottoms of vertebral bodies used to set up patients for conventional EBRT) are principally used to define treatment fields in conventional EBRT, spine SRS requires an in-depth understanding of spinal anatomy to accurately define the volume treated. Even among spine SRS experts, there is a fair amount of variability in target delineation.[55–58] For this reason, the radiation

oncologist might wish to consult with a neuroradiologist or neurosurgeon, or both, to aid in target delineation for more difficult cases. When substantial epidural or intramedullary disease is present, SBRT is not recommended as first-line treatment; however, select reports of the safety and efficacy of SBRT in this context warrant further investigation.[59,60]

Surgery

The goal of surgery is to stabilise a mechanically unstable spine, decompress spinal cord compression, remove epidural disease to allow spine SRS and SBRT treatment, establish a histological diagnosis, and to provide local control when radiotherapy cannot be safely delivered.

The surgical procedure performed is directly related to the goals of care. The chosen procedure should take into account factors such as the mechanical stability of the spine, the neurological status of the patient, the adjuvant treatment taken, and patient preference. Because radiotherapy is often used to try to eradicate the tumour, the surgical focus should be on the optimisation of the ability to deliver effective postoperative radiotherapy.

The surgical treatment of metastatic disease is largely not oncological, meaning that surgery alone will not eradicate the disease with durable local control. In one neurosurgical case series,[61] the local recurrence rate was 96% at 4 years and there was no difference in overall survival between those who received complete versus incomplete surgical resections. The integration of spine SRS into the standard treatment process represents a paradigm shift from the years when extensive surgeries for gross-total resections were performed in an attempt to cure patients of metastatic disease. These invasive surgeries have largely fallen out of favour in institutions with multidisciplinary spine programmes because of high complication rates, and we do not recommend en-bloc resections in the palliation of patients with spinal metastases.[62] The different categories of surgical procedures and their corresponding objectives are listed in the appendix, from the least invasive to the most invasive procedures.

If stabilisation alone is used to treat spinal metastases, the type of stabilisation method should be tailored to overall treatment goals. Stabilisation without decompression can be accomplished with external bracing or minimally invasive approaches, such as percutaneous cement augmentation or percutaneous pedicle screw fixation. These procedures limit the interruption of systemic therapy and allow for the delivery of early radiotherapy.

The most minimally invasive surgical procedure used for spinal stabilisation is cement augmentation of a vertebral body. In our experience, patients who benefit most from stabilisation have a Spine Instability Neoplastic Score reflective of potential instability (ie, 7–12) and typically have a tumour isolated to the anterior portion of the spine. Patients with substantial posterior involvement of spinal elements, such as the facet joints, are unlikely to get pain relief from this procedure alone.[63,64] In patients with anterior vertebral body and posterior facet joint involvement, both percutaneous cement augmentation and pedicle screw fixation might be beneficial. Moussazadeh and colleagues[64] reported their experience with minimally invasive, short construct cement augmentation (one level above and below the affected level) in patients with both anterior and posterior involvement. Another group has shown[65] similar results with minimally invasive techniques and longer constructs (two to three levels above and below the lesion) without cement augmentation. These minimally invasive techniques give the advantage of starting adjuvant therapy as soon as 1 week after surgery, compared with adjuvant radiotherapy 1 month after traditional open surgery, which is usually done to allow time for adequate wound healing.

The term separation surgery was coined by Lilyana Angelov and Edward Benzel at The Cleveland Clinic, OH, USA, to designate a procedure in which tumour resection is limited to decompression of the spinal cord to create a gap to the tumour and provide a safe target for spine SRS. Such a technique helps to facilitate the delivery of an ablative dose to the residual tumour while sparing the spinal cord or cauda equina.[11] Although most neurosurgeons are trained in stabilisation, decompression, or more extensive tumour resections, they might not be familiar with the terminology of separation surgery if not trained at a programme with multidisciplinary spine management.

Fundamentally, spine separation surgery decompresses the spinal cord and allows spine SRS and SBRT to be safely delivered, which will ultimately provide more durable local control than if initially treated solely with conventional EBRT. The goal of surgical decompression is to achieve a 360° decompression that allows full re-expansion of the dura and affected nerve roots.[35] Different approaches have been used on the basis of the spinal level of the lesion, how much bone is involved, and surgeon preference, including the transpedicular approach, costotransversectomy, lateral extracavitary approach, transthoracic approach, or retroperitoneal approach. The transpedicular approach is by far the most versatile of these techniques, and can be safely used for a 360° decompression, minimising the number of procedures patients need.[66]

For a detailed technical description of classic separation surgery, see Wang and colleagues.[67] This technique continues to undergo modifications to make it less invasive. The essential elements of most separation surgeries include posterolateral decompression via a laminectomy and pedicle resection, with a partial corpectomy of the affected level (figure 5). This surgery will destabilise the spine; thus, a stabilisation procedure is always required in conjunction with the tumour

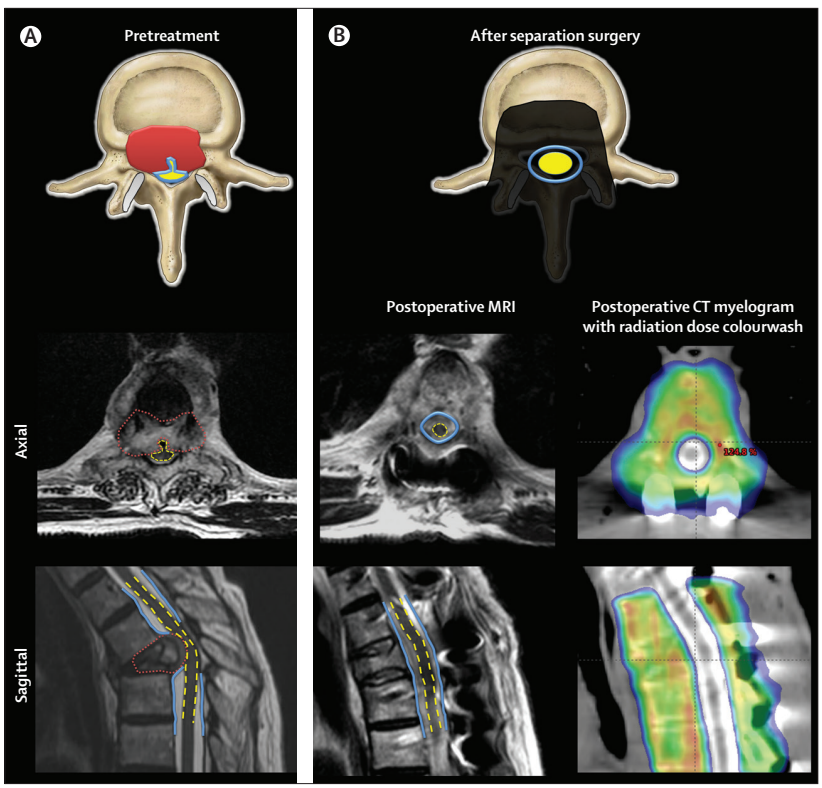

Figure 5: **Example of separation surgery followed by stereotactic spine radiotherapy in a patient with spinal cord compression**
(A) Pretreatment T2 MRI demonstrates the tumour causing spinal cord compression—the tumour is shown in red, the thecal sac in blue, and the spinal cord in yellow. The sagittal image demonstrates severe cord compression from tumour and bone retropulsion. (B) Postoperative MRI shows decreased canal stenosis and increased separation between the tumour and spinal cord. CT myelogram shows the stereotactic body radiotherapy dose distribution with sparing of the spinal cord. The thecal sac is shown in blue, and the spinal cord in yellow.

resection. There might be select cases in which a laminectomy might be appropriate for posterior tumours, especially in the thoracic spine.[66]

Neurointerventional procedures

Neurointerventional radiology has emerged as a key discipline in the multidisciplinary management of spinal metastases. There are several procedures performed by interventional radiologists, neurosurgeons, or orthopaedic spine surgeons that are helpful for the management of patients with spinal metastases. These procedures are provided at different times in a patient's care and include: CT-guided biopsy, spinal myelography, local ablative techniques, cement or device augmentation of the spinal column, and intra-arterial tumour embolisation.

The oncological risk assessment is based primarily on tumour histology, radiosensitivity, and radioresponsiveness, and is paramount in guiding appropriate management decisions. In many cases, when a patient presents with spinal metastases (ie, de-novo metastatic disease), the underlying tumour histological subtype is unknown. In these cases, it is crucial to achieve tissue diagnosis quickly and safely. Interventional radiologists can perform an image-guided biopsy, which is done under conscious sedation, and involves the placement of a biopsy needle into the area of abnormality using fluoroscopy, ultrasound, CT, or MRI for anatomical guidance.

A spinal myelogram is done under conscious sedation, and involves the placement of a fluoroscopy-guided needle into the thecal sac, and the injection of iodinated contrast dye into the subarachnoid space to visualise the spinal cord on conventional x-ray or CT. The procedure is commonly used in patients who have contraindications to undergoing MRI of the spine, and can also assess the extent of epidural disease. Additionally, CT myelography is routinely used in some centres to aid in spine SRS and SBRT treatment planning. An MRI can be registered to the planning CT scan, but this process can be associated with additional errors that must be accounted for, and is therefore less ideal than a myelogram.

Minimally invasive vertebral augmentation techniques, such as vertebroplasty, balloon kyphoplasty, and the Kiva treatment system (Benvenue Medical, Santa Clara, CA, USA), have been shown to be effective in the treatment of painful spinal bone metastasis, especially in the context of cancer-related vertebral compression fractures.[68,69] Malignant tumour infiltration of the vertebral body can cause a pathological compression fracture that leads to associated mechanical pain. Vertebral augmentation treats the pain and consolidates the weight-bearing bone. The cement used (ie, polymethylmethacrylate) creates an exothermic reaction that destroys tumour and nerve endings within a 3-mm radius of the cement.[49] Multiple groups have reported pain relief in 80–97% of cases who have had vertebral augmentation in patients with cancer.[70–83] However, percutaneous cement augmentation should not be used to control the tumour in lieu of effective radiotherapy treatment.

Image-guided spinal tumour ablation is another palliative treatment option for painful spinal metastases. Multiple types of locally ablative techniques can be performed by interventionalists, including radiofrequency ablation, microwave ablation, cryoablation, laser interstitial thermal therapy, and thermal ablation.[66,84,85] Local ablative techniques can be done as primary treatment, but are most commonly used as a salvage treatment option in cases where previous radiotherapy has been delivered and re-irradiation is unlikely to be safe or effective. One study showed that salvage radiofrequency ablation after previous radiotherapy decreased pain scores from 7·7 to 3·3 in 1 month, with approximately 50% of patients having a reduction in opioid usage.[86]

Preoperative transarterial embolisation of a hypervascular vertebral tumour with particles, glue, or ethylene vinyl alcohol can reduce intraoperative blood loss.[85] Furthermore, embolisation has an effective palliative role in controlling pain and neurological symptoms in patients with vertebral metastases.[87,88]

Cancer rehabilitation management

Rehabilitation interventions can provide substantial pain relief and improve stabilisation of the spine with less invasiveness and inherent risk to the patient than surgery or radiotherapy. For patients with a relatively stable spine and without neurological deficits or impending fracture, physiatrist-led cancer rehabilitation can reduce symptom burden and potentially prevent injury. For a detailed discussion of the interventions a rehabilitation team can provide, we recommend Raj and Lofton's review.[89]

For patients with an unstable or potentially unstable spine, surgery is often warranted. However, for patients who have contraindications to safely undergo surgery, or patients who wish to avoid a surgical intervention, rehabilitation provides two main options for spinal stabilisation: bracing and muscular strengthening. There is a wide range of bracing options, depending on the affected spinal region. In general, rigid bracing is ideal. The specific bracing option can be affected both by the degree of instability in the spine, and by how much it will affect function. The brace should be properly fitted to prevent skin breakdown, and patients should be educated in the proper spine precautions. In addition to bracing, exercises to stabilise core musculature might prevent injury and improve function.

Metastatic bone pain has been linked to decreased quality of life, physical function, and mood, and the adequate treatment of pain improves a patient's physical activity, mood, ability to work, and personal relationships.[90] Pain medications are usually prescribed in a ladder approach, starting with non-opioid agents (ie, non-steroidal anti-inflammatory drugs and paracetamol). For mild-to-moderate breakthrough pain, opioids such as codeine and tramadol are recommended. For severe breakthrough pain, opioids such as morphine, oxycodone, hydromorphone, and transdermal fentanyl should be started, slowly titrated, and rotated to ensure adequate analgesia, while minimising the risk for overdose. Adjuvants are added depending on the type of pain; for example, gabapentin or pregabalin for neuropathic pain, steroids for inflammatory pain, and bisphosphonates for bone pain.[91] Interventional spine procedures for palliation of pain, such as epidural steroid injections or facet medial branch blocks, should be considered in patients with radicular or mechanical pain symptoms.

When metastatic disease results in neurological damage (eg, neurogenic bowel or bladder, motor or sensory function loss), physical medicine and rehabilitation should be consulted to institute an efficient and effective plan to regain as much function as possible, and maximise patient independence.

Patients with malignant spinal cord compression might benefit from inpatient rehabilitation, though considerations should be made with respect to patients' care goals as they relate to life expectancy.[66]

Conclusion

Advancements in technology and multidisciplinary management have revolutionised the treatment of spinal metastases. Cases that once required radical surgical resection or low-dose conventional radiotherapy, or both, are now being managed with separation surgery or spine SRS, or both, with decreased morbidity, improved local control, and more durable pain control. Other cases might be optimally managed with interventional procedures, rehabilitation, or palliative care involvement, depending on the clinical scenario of the patient. Future efforts are needed to prospectively compare the effectiveness of these available treatment approaches, focusing primarily on outcomes of tumour control, treatment-related morbidity, and quality of life.

Contributors

DES and NJS conceived the project; DES, WHB, and NJS did the literature search; all authors contributed to the literature analysis and synthesis of expert opinions; DES, KCY, and NJS created the figures; KCY contributed to the physics component of the Review; DES, WHB, and NJS wrote the Review; and all authors were involved in editing the manuscript.

Declaration of interests

MB is a consultant for Globus and BrainLab and receives royalties from Depuy/Synthes. MD has received research funding and honoraria from Varian Medical Systems. KCY has received funding from Varian Medical Systems. All other authors declare no competing interests.

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