Neuro-Oncology Practice
7(S1), i25–i32, 2020 | doi:10.1093/nop/npaa056

# The importance of multidisciplinary care for spine metastases: initial tumor management

**William Christopher Newman, Ankur Patel, Jacob L. Goldberg, and Mark H. Bilsky**

*Department of Neurosurgery, Louisiana State University Health Sciences Center, Shreveport, Louisiana (W.C.N.); Department of Neurosurgery, Baylor University Medical Center, Dallas, Texas (A.P.); Department of Neurosurgery, New York Presbyterian/Weill Cornell and Memorial Sloan Kettering Cancer Center, New York, New York (J.L.G.); Department of Neurosurgery, Memorial Sloan Kettering Cancer Center, New York, New York (M.H.B.).*

**Corresponding Author:** Mark H. Bilsky, MD, Department of Neurosurgery, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, New York 10065 (bilskym@mskcc.org).

**Abstract**

Spine metastases are very common in cancer patients often requiring urgent assessment and the initiation of therapy. Treatment paradigms have changed exponentially over the past decade with the evolution and integration of stereotactic body radiotherapy, minimally invasive spine techniques, and systemic options including biologics and checkpoint inhibitors. These advances necessitate multidisciplinary assessments and interventions to optimize outcomes. The NOMS framework provides a mechanism for all practitioners to evaluate the 4 sentinel assessments required to make decisions in patients with spine metastases: Neurologic, Oncologic, Mechanical Stability, and Systemic disease. The NOMS framework is continuously updated with the integration of newer technologies and evidence-based medicine as they become available. This paper presents the current iteration of NOMS with a focus on the role of medical and neuro-oncologists in the assessment and treatment of metastatic spine tumors.

**Keywords**

decision making | NOMS | spine metastases | stereotactic radiosurgery

Spine metastases are a very common and potentially devastating complication affecting approximately 40% of cancer patients.[1–4] Despite these large numbers, the overall incidence of spine metastases is expected to continue to rise as targeted therapies and checkpoint inhibitors improve survival for virtually every tumor histology but are significantly more effective for visceral than for bone disease. The principal treatment goals for spine tumors are focused on achieving pain control, restoration or maintenance of neurologic function, ensuring spinal stability, improvements in health-related quality of life, and providing durable tumor control. To these ends, the greatest advance in the treatment of metastatic spine tumors over the past decade has been the development and integration of stereotactic body radiotherapy (SBRT). SBRT can deliver an ablative radiation dose, which has led to an exponential improvement in histology-independent local tumor control, a significant reduction in treatment-related morbidity, and even an improved overall survival when compared to systemic therapy alone for oligometastatic disease.[5] In addition to SBRT, the past decade has witnessed the development of numerous other technological advances both in surgery and interventional radiology that have also substantially improved outcomes. Advances in all domains of treatment have mandated a comprehensive assessment from multiple specialists including medical oncologists, spine surgeons, radiation oncologists, interventional radiologists, pain specialists, and physiatrists. The NOMS (Neurologic, Oncologic, Mechanical Stability and Systemic Disease) framework was developed to facilitate and standardize decision making by providing a common multidisciplinary assessment that has the flexibility to integrate new technologies and evidence-based medicine to optimize patient outcomes.[6] The 4 sentinel decision points incorporated into NOMS will help focus and simplify assessments and decision making by all physicians who treat these patients.

## Presentation

Primary care physicians, medical oncologists, and emergency physicians are often the gatekeepers for recognizing

relevant symptoms from spine metastases and obtaining appropriate diagnostic imaging. It is critically important for screening practitioners to recognize signs and symptoms of spine metastases in order to initiate timely and effective treatment based on the NOMS framework. The most common presenting symptom is back pain, which often presents weeks to months before the onset of neurologic symptoms. Practitioners need to maintain a high index of suspicion that new onset or a change in the quality of back pain in a cancer patient is metastatic disease until otherwise proven. Two predominant back pain syndromes occur in cancer patients: biologic and mechanical.[7] Biologic pain is the presenting symptom in nearly all patients harboring spine metastases. This pain presents at night persisting into the early morning and completely resolves with increased activity during the day. The genesis of biologic pain is thought to be related to the diurnal variation in endogenous steroid secretion. As steroid levels nadir at night, inflammatory mediators secreted by the tumor cause severe back pain. This pain typically resolves with ambulation commensurate with a rise in endogenous steroid levels and is also very responsive to exogenous steroids, such as dexamethasone. Definitive tumor treatment most often with radiation therapy (RT) resolves biologic pain.

In counter-distinction to biologic pain, mechanical pain is broadly defined as movement related and signifies a loss of structural integrity resulting, for example, from a vertebral-body burst fracture. As opposed to biologic pain, mechanical pain cannot be treated with radiation alone, but requires an intervention such as brace application, kyphoplasty or vertebroplasty, percutaneous pedicle screws, or open surgical instrumentation. Recognizing level-dependent pathognomonic pain syndromes is important for identifying patients with unstable pathologic fractures. In the subaxial cervical spine (ie, C3-C7), patients present with severe pain in flexion and extension. Atlantoaxial (ie, C1-C2) fractures present with flexion and extension pain, but also have a rotational component and one-third will have occipital neuralgia.[7] Patients with thoracic and lumbar fractures typically have pain on axial load such as sitting or standing; however, thoracolumbar junction instability pain is somewhat counterintuitive as it often presents in recumbency. These patients are very comfortable sitting or standing, which places the fracture in a kyphotic position. When the patient lies flat, the unstable kyphosis hinges into a straight position resulting in severe back pain. Patients will often give a history of sleeping in a recliner, unable to assume a flat position. Finally, unique to the lumbar spine is mechanical radiculopathy, described as axial load pain resulting in severe back and radicular pain. The pathogenesis of this pain is a fracture-related narrowing of the neural foramen, often from the pedicle wedging into the nerve root on standing or sitting.[8]

The initial presentation with biologic or mechanical pain may progress to neurologic symptoms including myelopathy and functional radiculopathy from epidural spinal cord compression (ESCC) or nerve root compression. Radiculopathy in the cervical or lumbar spine can cause pain or weakness in the classic dermatomal distributions. Thoracic radiculopathy occurs as band-like pain at a segmental level without motor deficits. Myelopathy often presents with a pin level secondary to compression of the spinothalamic tracts followed by motor loss related to corticospinal tract involvement. Loss of proprioception from involvement of the posterior columns is often a late finding in myelopathy, but its presence is a poor prognostic sign for a functional recovery. Autonomic dysfunction affecting the bowel and bladder is typically a late finding in myelopathy. The exception is compression at the level of the conus medullaris or diffuse sacral replacement, where autonomic dysfunction can be the primary finding in the absence of significant motor weakness. Neurogenic bowel and bladder symptoms are almost universally associated with perineal numbness. In the absence of sensory changes, one should seek other etiologies for urinary retention or bowel incontinence, such as side effects from narcotics, prostatic hypertrophy, or a response to laxatives.

## Imaging

The recognition of signs and symptoms related to spine metastases is fundamentally important to obtaining timely and appropriate imaging. Several imaging modalities play important roles in assessing spine metastases; however, MRI scans are the most sensitive and specific for identifying tumors and the degree of ESCC. Our practice is to obtain sagittal and axial images of the entire spinal axis rather than focusing solely on the symptomatic index level. Many patients have multiple discontiguous tumors throughout the spine and paraspinal regions that need to be accounted for in the final treatment plan. Gadolinium-DPTA is routinely given to assess for leptomeningeal and intramedullary metastases. On the sagittal screening, the most important sequences are the T1-weighted and T2-STIR (short-TI inversion recovery), in which tumors appear hypointense or hyperintense, respectively. The degree of ESCC is based predominantly on the T2-weighted images as well as T1-weighted postcontrast. An ESCC scoring system (also known as "Bilsky score") has been developed and validated to standardize reporting for clinical communication and outcomes studies.[9] ESCC is evaluated using a 6-point scoring system in which ESCC scores 0 to 1c range from bone only to progressive degrees of epidural impingement without spinal cord compression. ESCC scores 2 and 3 represent high-grade ESCC differentiated by the presence (2) or obliteration (3) of the cerebrospinal fluid space. Grade 3 is the MR radiographic equivalent of a complete block on myelogram (Figure 1)

Oncologists often rely on imaging changes to determine the efficacy of treatment; however, responses to RT or chemotherapy are difficult to assess in bone because of a delayed signal change on standard MRI sequences. On T1-weighted images, treated and viable tumors both appear hypointense relative to normal marrow signal. In a study of breast cancer patients, only 3% had a reduction in the volume or number of vertebral bodies involved on imaging, and there was no correlation between changes in signal intensity and clinical response to therapy.[10] In a palliative situation, clinical response to therapy, that is, resolution of biologic pain, may suffice despite the absence of radiologic changes. Dynamic contrast-enhanced MRI (DCE-MRI) specifically assessing plasma volume has

recently been added to the routine imaging sequences for spine tumors both pretreatment and at all subsequent follow-up studies (Figure 2). This modality has shown great promise in predicting and monitoring tumor response to SBRT[11] (see Figure 2). A precipitous drop in DCE-MRI values can be seen within 1 hour of SBRT administration, which reflects the impact of the radiation on the tumor vascularity and is predictive of long-term tumor control.[12] Alternatively, 2-[F-18] flouro-2-deoxy-D-glucose (FDG-PET) can be used to assess the viability of tumor posttreatment as well as serving as an effective imaging modality to stage the extent of disease. FDG-PET is not as sensitive for detecting osteoblastic compared to osteolytic disease.

## NOMS Decision Framework

The NOMS decision framework was developed to extract the critical components of the clinical presentation and imaging in making treatment decisions. The 4 sentinel

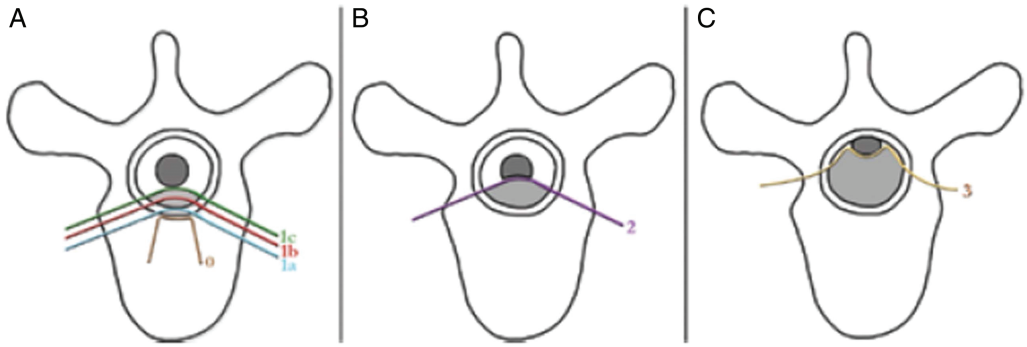


**Fig. 1** Schematic representation of the 6-point epidural spinal cord compression (ESCC) grading scale. Grade 0 indicates disease contained within the bone of the vertebrae. Grade 1a describes epidural extension without deformation of the thecal sac. Grade 1b lesions deform the thecal sac but have no spinal cord abutment, whereas grade 1c lesions have spinal cord abutment without cord compression. With grade 2 tumors, spinal cord compression is present with cerebrospinal fluid visible around the cord. Grade 3 describes tumors with spinal cord compression and no visible CSF around the cord. From Bilsky et al[9]; used with permission.

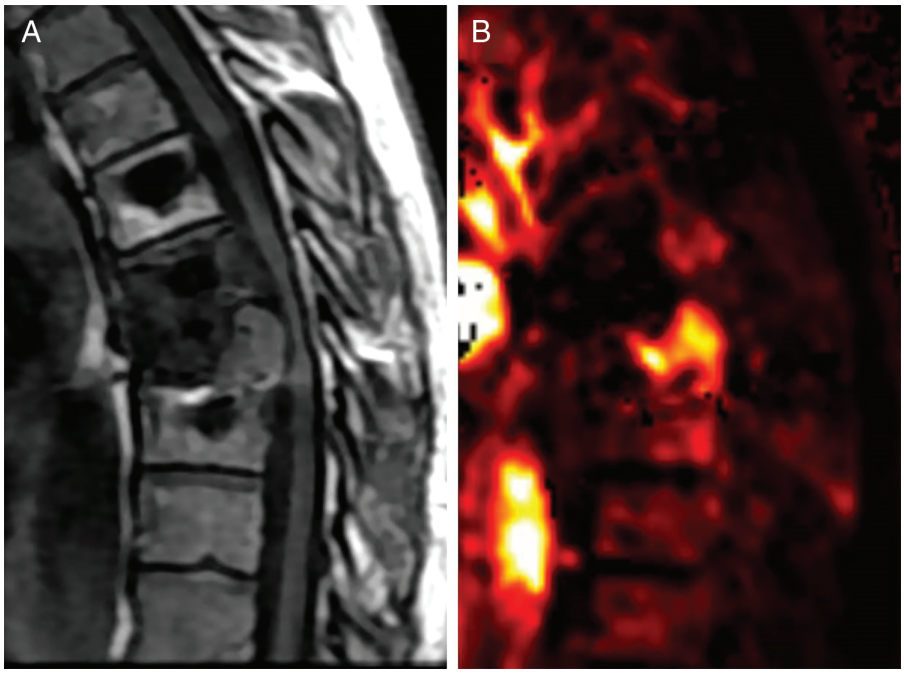


**Fig. 2** Sagittal T1 A, weighted and B, perfusion MRI of the spine in a 64-year-old man with metastatic hurtle cell carcinoma. Grade 2 epidural spinal cord compression is seen at T7 by a metastatic tumor that displays increased perfusion.

decision points in the NOMS framework are neurologic, oncologic, mechanical stability, and systemic disease. The neurological assessment takes into consideration the clinical presentation and radiographic parameters including the presence and severity both of myelopathy and functional radiculopathy, as well as the ESCC score. The oncologic consideration assesses the best method of achieving local-tumor control most commonly with radiation or systemic therapy. The neurological and oncological considerations are combined to determine the need for RT and/or surgery. Mechanical instability is a separate assessment based largely on the presence of mechanical pain correlated with radiographic criteria embedded in the Spine Instability Neoplastic Score (SINS).[13] As noted, determination of instability necessitates an interventional procedure because RT will not restore stability or provide pain relief for patients with unstable fractures. Finally, an assessment of systemic disease and medical comorbidities must be made to determine whether the proposed intervention can be tolerated and is rational in the context of the patient's disease (Figure 3)

## Neurological and Oncological Assessments

Treatment decisions for metastatic spine tumors are largely predicated on the combined assessment of neurological and oncological considerations. The neurological assessment is based on the severity of myelopathy and functional radiculopathy, but in the current iteration of NOMS, is largely based on the radiographic degree of ESCC. The oncological consideration is focused on optimizing local tumor control and typically is dependent on the radiation response. Outcome data assessing conventional external beam radiation therapy (cEBRT) (eg, 30 Gy in 10 fractions) over the past several decades led to a delineation of expected tumoral responses based on primary tumor histology and the organ of origin.[15] The limitation of cEBRT is the inability to deliver an ablative tumoral dose while remaining within the radiation-dose constraints of normal surrounding vital structures, such as the spinal cord; thus, tumoral responses are stratified into radiosensitive and radioresistant histologies. Radiosensitive histologies include hematological malignancies (eg, lymphoma and multiple myeloma) as well as selected solid tumors (eg, breast and prostate carcinoma). Even in the presence of high-grade ESCC, radiosensitive tumors can be treated with cEBRT, demonstrating excellent tumor control rates and maintenance of neurological function. Patients with myelopathy who have hematological malignancies typically respond well to cEBRT, with the expectation that the tumor will undergo apoptosis decompressing the spinal cord. However, breast and prostate carcinoma do not respond as reliably; thus, myelopathic patients with these tumor histologies are often offered initial surgical treatment to optimize the chances of neurological recovery. Most of the remaining solid tumors are radioresistant to cEBRT, including melanoma, sarcoma, renal cell, thyroid, non–small cell lung, and colon carcinoma. Radioresistant tumors have demonstrated response rates in the 20% to 30% range with a low probability of neurological recovery or durable control.[16,17]

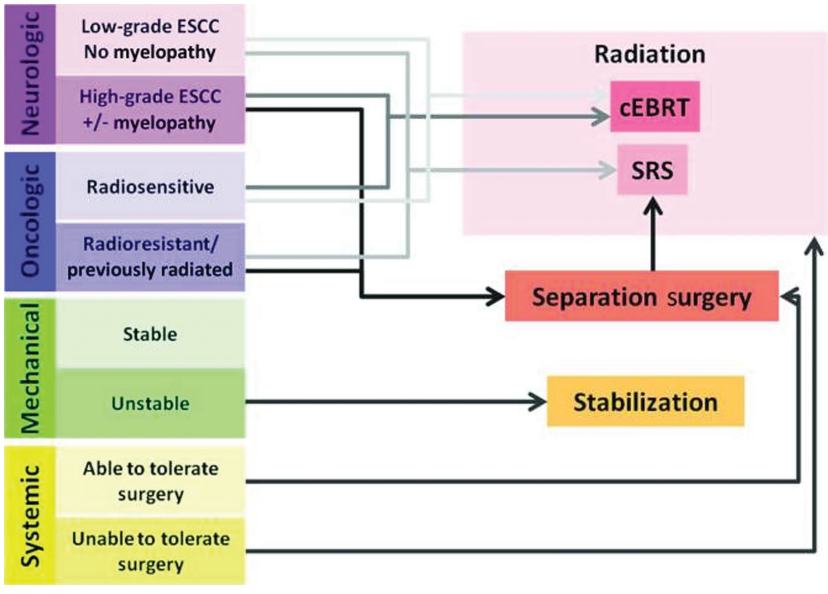


**Fig. 3** Schematic depiction of the neurologic, oncologic, mechanical, and systemic (NOMS) decision framework. cEBRT, conventional external beam radiation; SRS, stereotactic radiosurgery. From Laufer et al.[14]; used with permission.

## Stereotactic Body Radiotherapy as Ablative Therapy: Overcoming Radioresistance

The great advance in overcoming radioresistance to cEBRT was the development and integration of SBRT. SBRT is defined as high-dose hypofractionated photon radiation often delivered as 16 to 24 Gy in a single fraction or 24 to 30 Gy in 3 fractions. SBRT uses image-guide intensity-modulated radiation therapy to deliver highly conformal and very precise beam delivery. SBRT delivers a much higher biological equivalent dose than can be given with cEBRT; thus, SBRT overcomes radioresistance resulting in histology-independent response rates for all tumors.[18]

Yamada et al[18] reviewed a series of 811 patients undergoing single-fraction SBRT. All tumors had ESCC scores of 0 to 1c, and 82% were considered radioresistant to cEBRT. The prescription dose was analyzed as a continuous variable and an optimal cut point was used to establish a low-dose (LDC) vs high-dose cohort (HDC) with median doses of 16.4 Gy and 22.4 Gy ,respectively. At 1 year the incidence of local failure was 5% in LDC and less than 1% in HDC; however, at 4 years the incidence of local failure was 20% in LDC vs 2.1% in HDC. The only significant factor in the incidence of local failure was the dose of radiation. SBRT overcomes the radioresistance associated with cEBRT, rendering all tumors equally radiosensitive. Numerous centers have demonstrated excellent response rates with various hypofractionated SBRT regimens, which has led to widespread acceptance and a growing use of this technology. Whereas initially such therapy was confined to academic centers, currently most radiation oncology programs both in academic and private settings offer spinal SBRT.[19]

Currently, SBRT can be used very effectively as definitive treatment for radioresistant tumors with ESCC 0 to 1c; however, patients presenting with ESCC 2 and 3 (ie, high grade) and/or myelopathy require surgical decompression. For this reason, it is important to irradiate radioresistant tumors with ESCC 0 to 1c in a timely manner to prevent progression to high-grade spinal cord compression necessitating surgery (Figure 4). The surgical recommendation for radioresistant tumors with ESCC 2 and 3 is based both on radiation and surgical outcomes data. The major impediment to treating high-grade spinal cord compression with SBRT is a spinal cord constraint typically defined as a cord maximum dose of 14 Gy single fraction. Delivering an ablative SBRT dose (ie, 15-24 Gy) would potentially result in a treatment-related myelopathy, or intentionally underdosing the margin of the spinal cord would risk epidural progression.[20] In point of fact, Rao and colleagues used SBRT to treat high-grade ESCC, which resulted in a 20% risk of neurologic decline in the radioresistant tumors. Despite this disappointing first attempt, treating high-grade ESCC remains a work in evolution. Mounting evidence suggests that ESCC 2 can be treated with hypofractionated radiation (24-30 fractions), with local control rates approaching the treatment of ESCC 0 to 1c. Ultimately, ESCC 3 may be reasonable targets for SBRT, but this is dependent on redefining cord constraints and potentially augmenting local radiation effects. Both clinical and experimental evidence suggest that vascular endothelial growth factor–tyrosine kinase inhibitors (eg, axitinib) can act as radiosensitizers.[21] Also, the combination of checkpoint inhibitors and SBRT may improve the therapeutic window and local control.

Currently, the case for surgical decompression in patients harboring high-grade compression from solid (ie, radioresistant) tumors is largely predicated on a prospective randomized trial by Patchell et al that demonstrated a significant advantage in neurologic outcomes and survival comparing surgery and cEBRT to cEBRT.[22] Based on this and a number of other retrospective studies, an evidence-based Cochran review by Bilsky et al made a

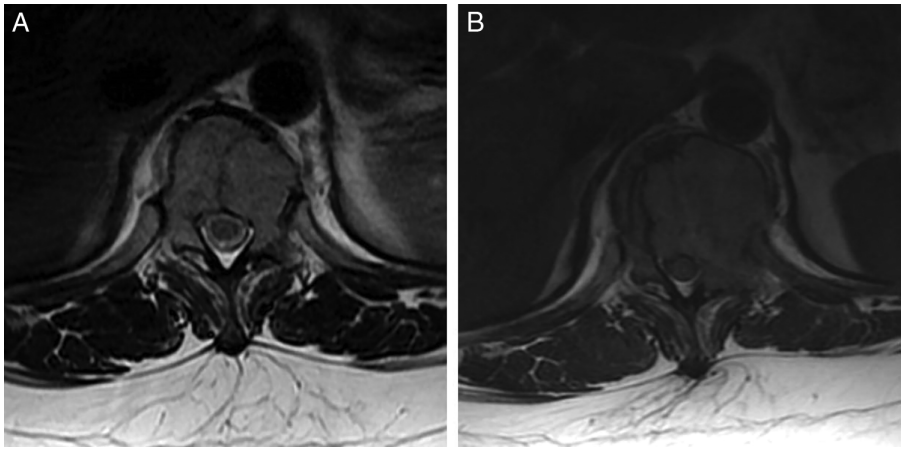


**Fig. 4** Axial T2 weighted MRI of the spine in a 48-year-old woman with metastatic pancreatic cancer. A, On her initial MRI, the metastatic tumor displayed grade 1a epidural spinal cord compression (ESCC) that progressed to B, ESCC grade 3 on a subsequent MRI 4 months later and Spine Instability Neoplastic Score consistent with mechanical instability.

strong recommendation based on low-quality evidence that patients with high-grade ESCC from radioresistant tumor undergo surgical decompression followed by radiation therapy[23]; however, the integration of SBRT as a postoperative adjuvant fundamentally changed the type and goals of surgery. The poor control rates associated with postoperative cEBRT led surgeons to attempt gross total or even en bloc resection. Despite these very aggressive and highly morbid surgeries, local control rates were only 30% at 1 year.[24] With the integration of postoperative SBRT, the oncologic goal of surgery changed from very aggressive resections to simply decompression of the thecal to create a 2-mm margin on the spinal cord to deliver an ablative radiation dose within normal spinal cord constraints. This concept is known as *separation surgery*, which involves a very simple posterolateral resection of the epidural tumor, leaving large paraspinal and vertebral-body tumors unresected. Patients require posterior screw-rod instrumentation but advances in cement-augmented screw fixation have reduced the traditionally long constructs to shorter segments. Neurologic outcomes, pain relief, and patient reported health-related quality of life are excellent. Laufer and colleagues reported tumor control employing the combination of separation surgery followed by SBRT, that is, hybrid therapy, in 186 patients of whom 77% harbored cEBRT-radioresistant tumors and 50% had failed prior local RT.[25] The cumulative incidence of failure was 16.4%; however, in the high-dose single (24 Gy) or hypofractionated (24-30 Gy in 3 fractions) cohorts, the failure rate was less than 10%. Failure was not associated with cEBRT-radioresistant tumors or previously failed radiation (Figure 5).

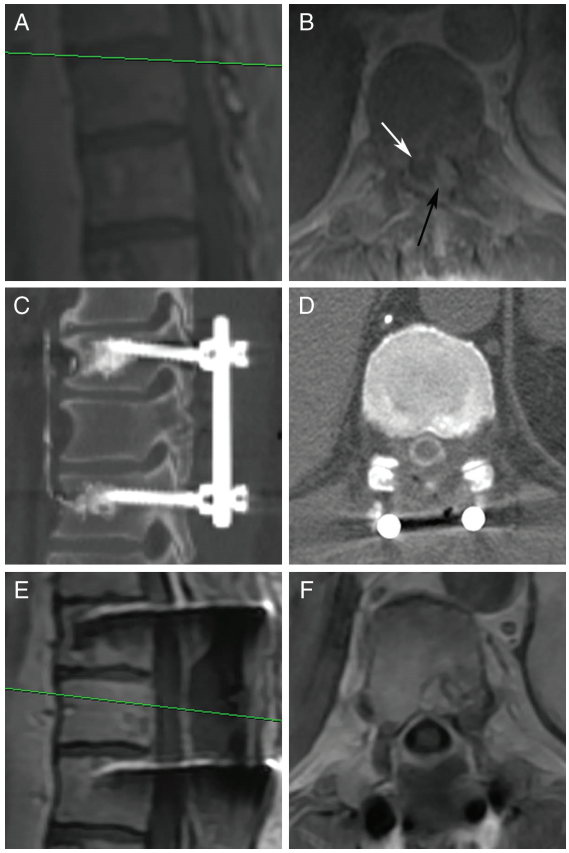


**Fig. 5** A 61-year-old man with metastatic renal cell carcinoma presented with left-side subscapular pain that worsened with recumbency consistent with mechanical instability. A, Sagittal and B, axial T1 weighted postcontrast MRIs of the spine revealed epidural spinal cord compression grade 3 of the spinal cord (white arrow) at T10 from a metastatic tumor (black arrow). The patient was treated with separation surgery followed by stereotactic body radiotherapy. C, Sagittal and D, axial images from a CT myelogram of the spine performed 5 days after surgery for radiation planning show pedicle screw fixation at T9 and T11 with cement augmentation as well as circumferential decompression of the spinal cord with reconstitution of the cerebrospinal fluid space. Three-month posttreatment E, sagittal and F, axial T1-weighted postcontrast MRIs of the spine confirm local control.

## Mechanical Instability

The third assessment in NOMS is mechanical instability. SINS is an instrument developed by the Spine Oncology Study Group to define instability resulting from pathologic fractures. SINS essentially validates radiographic correlates to these pain syndromes and consists of 6 assessments: spine location, quality of the bone lesion, spinal alignment, vertebral body fracture, posterior element involvement, and pain. The authors validated this scoring among spine surgeons and radiation oncologists; but there is no expectation that the gatekeepers should know the SINS scoring system. For the gatekeepers, recognizing the pain syndromes associated with instability are critical prompts for obtaining imaging studies and making referrals to spine surgeons or interventional radiologists. Percutaneous cement augmentation, that is, kyphoplasty or vertebroplasty, is the workhorse for painful thoracic and lumbar burst fractures. These procedures are somewhat controversial in osteoporotic fractures, but the CAFE study provides level 1 evidence that kyphoplasty improves both short- and long-term pain control from pathologic, tumor-related fractures.[26] Patients with vertebral body burst fractures with additional destruction of the facet joints have not responded well to standalone kyphoplasty or vertebroplasty and often require supplemental percutaneous cement-augmented pedicle-screw fixation.[27]

## NOMS Systemic Disease and Medical Comorbidities

The last question that needs to be addressed in the NOMS assessment is whether the patient can medically tolerate the proposed procedure and whether it makes sense in the context of his or her disease. In many respects, this is the most important question and is best assessed by the medical oncologist, who often has a much better sense of the pace of the disease and remaining treatment options. Many patients who would benefit from surgery based on the NOM assessment are excluded based on significant medical comorbidities, such as extensive pulmonary

or cardiac disease. Whereas it is hard to watch someone progress to paralysis, it is equally hard to take away remaining quality of life operating on someone who has no realistic expectation of meaningful recovery. Expected survival from cancer is a major determinant in recommending treatment, particularly surgical intervention. A number of models have been developed to predict survival in metastatic spine patients, such as the Tomita[28] and Tokuhashi[29] scores. These scores are largely based on tumor histology and extent of disease but fail to account for advances in systemic treatment that have extended survival for most tumor histologies. The Skeletal Oncology Research Group (SORG) nomogram is an externally validated assessment that was developed in the era of biologics and checkpoint inhibitors to predict survival for patients undergoing metastatic spine surgery.[30,31] Compared to other available models, the SORG nomogram is the best predictor of 3- and 12-month survival. The nomogram is available online to facilitate the expeditious systemic assessment of patients to optimize decision making and outcomes.

The most recent addition to the systemic disease assessment is predicated on local ablative treatment for spine metastases affecting systemic disease control and improving overall survival, which has now been demonstrated in a number of trials. The SABR-COMET trial is a phase 2, randomized, open-label trial comparing standard therapy to standard therapy and SBRT for oligometastatic tumors (ie, 1-5 tumors).[5] An overall survival advantage was seen in the SBRT cohort vs standard systemic therapy, 41 vs 28 months, respectively; however, there was a 20% risk of grade 2 or greater toxicity in the SBRT cohort. The second avenue of exploration uses the combination of SBRT and checkpoint inhibitors to induce the abscopal effect, in which local radiation affects systemic disease control. Postow et al described a patient with widespread melanoma on long-term ipilimumab who developed a progressive paraspinal tumor.[32] This tumor was irradiated at 24 Gy single fraction while continuing on the checkpoint inhibitors. Following SBRT, the systemic disease significantly regressed, which correlated with a 30-fold increase in antibodies to tumor-specific epitopes. Although there are limited data on the abscopal effect, many centers are now exploring ways to meaningfully employ this mechanism.[33]

## Conclusion

Spine metastases represent one of the most debilitating and complicated manifestations of cancer care. For the gatekeepers, recognizing signs and symptoms and obtaining timely imaging is critically important for initiating effective therapy. The NOMS framework provides a focused road map for all practitioners to recognize the 4 sentinel decision points that need to be addressed in every metastatic spine patient: neurologic, oncologic, mechanical stability and systemic disease. Major advances in technology and the development of evidence-based medicine have very heavily affected and changed the decisions made in the NOMS framework compared to 10 years ago and will continue to evolve over the next decade. SBRT has by far had the biggest impact on outcomes in spine metastases, but surgical and interventional radiology procedures have also significantly changed treatment paradigms. These domains will continue to improve, but the most interesting development may be the role that local spine SBRT plays in improving overall survival by providing truly ablative local therapy and possibly inducing the abscopal effect. The goals of treatment of spine metastases remain palliative, but recognition of the impact of SBRT on overall survival may change the ultimate impact of local therapy.

## Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

**Conflict of interest statement.** W.C.N., A.P., and J.L.G. have nothing to disclose. M.H.B. receives royalties from Globus and DePuy/Synthes.

## References

1. Hernandez RK, Adhia A, Wade SW, et al. Prevalence of bone metastases and bone-targeting agent use among solid tumor patients in the United States. *Clin Epidemiol*. 2015;7:335–345.
2. North RB, LaRocca VR, Schwartz J, et al. Surgical management of spinal metastases: analysis of prognostic factors during a 10-year experience. *J Neurosurg Spine*. 2005;2(5):564–573.
3. Sinson GP, Zager EL. Metastases and spinal cord compression. *N Engl J Med*. 1992;327(27):1953–1954; author reply 1954.
4. Wong DA, Fornasier VL, MacNab I. Spinal metastases: the obvious, the occult, and the impostors. *Spine (Phila Pa 1976)*. 1990;15(1):1–4.
5. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet*. 2019;393(10185):2051–2058.
6. Barzilai O, Laufer I, Yamada Y, et al. Integrating evidence-based medicine for treatment of spinal metastases into a decision framework: neurologic, oncologic, mechanicals stability, and systemic disease. *J Clin Oncol*. 2017;35(21):2419–2427.
7. Bilsky MH, Lis E, Raizer J, et al. The diagnosis and treatment of metastatic spinal tumor. *Oncologist*. 1999;4(6):459–469.
8. Moliterno J, Veselis CA, Hershey MA, et al. Improvement in pain after lumbar surgery in cancer patients with mechanical radiculopathy. *Spine J*. 2014;14(10):2434–2439.
9. Bilsky MH, Laufer I, Fourney DR, et al. Reliability analysis of the epidural spinal cord compression scale. *J Neurosurg Spine*. 2010;13(3):324–328.
10. Brown AL, Middleton G, MacVicar AD, Husband JE. T1-weighted magnetic resonance imaging in breast cancer vertebral metastases: changes on treatment and correlation with response to therapy. *Clin Radiol*. 1998;53(7):493–501.
11. Chu S, Karimi S, Peck KK, et al. Measurement of blood perfusion in spinal metastases with dynamic contrast-enhanced magnetic resonance

imaging: evaluation of tumor response to radiation therapy. *Spine (Phila Pa 1976).* 2013;38(22):E1418–E1424.
12. Lis E, Saha A, Peck KK, et al. Dynamic contrast-enhanced magnetic resonance imaging of osseous spine metastasis before and 1 hour after high-dose image-guided radiation therapy. *Neurosurg Focus.* 2017;42(1):E9.
13. Fourney DR, Frangou EM, Ryken TC, et al. Spinal Instability Neoplastic Score: an analysis of reliability and validity from the Spine Oncology Study Group. *J Clin Oncol.* 2011;29(22):3072–3077.
14. Laufer I, Rubin DG, Lis E, et al. The NOMS framework: approach to the treatment of spinal metastatic tumors. *Oncologist.* 2013;18(6):744–751. doi:10.1634/theoncologist.2012-0293.
15. Gerszten PC, Mendel E, Yamada Y. Radiotherapy and radiosurgery for metastatic spine disease: what are the options, indications, and outcomes? *Spine (Phila Pa 1976).* 2009;34(22 suppl):S78–S92.
16. Maranzano E, Latini P. Effectiveness of radiation therapy without surgery in metastatic spinal cord compression: final results from a prospective trial. *Int J Radiat Oncol Biol Phys.* 1995;32(4):959–967.
17. Mizumoto M, Harada H, Asakura H, et al. Radiotherapy for patients with metastases to the spinal column: a review of 603 patients at Shizuoka Cancer Center Hospital. *Int J Radiat Oncol Biol Phys.* 2011;79(1):208–213.
18. Yamada Y, Katsoulakis E, Laufer I, et al. The impact of histology and delivered dose on local control of spinal metastases treated with stereotactic radiosurgery. *Neurosurg Focus.* 2017;42(1):E6.
19. Pan H, Simpson DR, Mell LK, et al. A survey of stereotactic body radiotherapy use in the United States. *Cancer.* 2011;117(19):4566–4572.
20. Lovelock DM, Zhang Z, Jackson A, et al. Correlation of local failure with measures of dose insufficiency in the high-dose single-fraction treatment of bony metastases. *Int J Radiat Oncol Biol Phys.* 2010;77(4):1282–1287.
21. Rao SS, Thompson C, Cheng J, et al. Axitinib sensitization of high single dose radiotherapy. *Radiother Oncol.* 2014;111(1):88–93.
22. Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet.* 2005;366(9486):643–648.
23. Bilsky MH, Laufer I, Burch S. Shifting paradigms in the treatment of metastatic spine disease. *Spine (Phila Pa 1976).* 2009;34(22 suppl):S101–S107.
24. Klekamp J, Samii H. Surgical results for spinal metastases. *Acta Neurochir (Wien).* 1998;140(9):957–967.
25. Laufer I, Iorgulescu JB, Chapman T, et al. Local disease control for spinal metastases following "separation surgery" and adjuvant hypofractionated or high-dose single-fraction stereotactic radiosurgery: outcome analysis in 186 patients. *J Neurosurg Spine.* 2013;18(3):207–214.
26. Berenson J, Pflugmacher R, Jarzem P, et al; Cancer Patient Fracture Evaluation (CAFE) Investigators. Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial. *Lancet Oncol.* 2011;12(3):225–235.
27. Barzilai O, McLaughlin L, Lis E, et al. Utility of cement augmentation via percutaneous fenestrated pedicle screws for stabilization of cancer-related spinal instability. *Oper Neurosurg (Hagerstown).* 2019;16(5):593–599.
28. Tomita K, Kawahara N, Kobayashi T, et al. Surgical strategy for spinal metastases. *Spine (Phila Pa 1976).* 2001;26(3):298–306.
29. Tokuhashi Y, Matsuzaki H, Oda H, et al. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine (Phila Pa 1976).* 2005;30(19):2186–2191.
30. Paulino Pereira NR, Mclaughlin L, Janssen SJ, et al. The SORG nomogram accurately predicts 3- and 12-months survival for operable spine metastatic disease: external validation. *J Surg Oncol.* 2017;115(8):1019–1027.
31. Ahmed AK, Goodwin CR, Heravi A, et al. Predicting survival for metastatic spine disease: a comparison of nine scoring systems. *Spine J.* 2018;18(10):1804–1814.
32. Postow MA, Callahan MK, Barker CA, et al. Immunologic correlates of the abscopal effect in a patient with melanoma. *N Engl J Med.* 2012;366(10):925–931.
33. Macki M, Fakih M, Elmenini J, et al. Trends in the abscopal effect after radiation to spinal metastases: a systematic review. *Cureus.* 2019;11(10):e5844.