



Total *en bloc* resection of primary and metastatic spine tumors

Elizabeth P. Howell¹, Theresa Williamson², Isaac Karikari², Muhammad Abd-El-Barr², Melissa Erickson³, Matthew L. Goodwin⁴, Jeremy Reynolds⁵, Daniel M. Sciubba⁴, C. Rory Goodwin²

¹Duke University School of Medicine, Durham, NC, USA; ²Department of Neurosurgery, ³Department of Orthopaedic Surgery, Duke University Medical Center, Durham, NC, USA; ⁴Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA; ⁵Oxford Spinal Unit, Oxford University Hospitals, Oxford, UK

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Correspondence to: C. Rory Goodwin, MD, PhD. Duke University Medical Center, Box 3807, 200 Trent Drive, Durham, NC 27710, USA.
Email: spineresearch@dm.duke.edu.

Abstract: Primary and metastatic tumors of the spine represent a significant cause of patient morbidity, and present a management challenge to treating providers. From a neurosurgical standpoint, resection surgery may be warranted in cases of spinal instability, progressive disease, neurological compromise, or intractable symptoms. Removal of a tumor “*en bloc*” offers a more aggressive modality over more conservative resection techniques. *En bloc* resection entails the removal of the entirety of a tumor without violation of its capsule, and may offer improved rates of local control and overall survival in appropriately selected patients. Conversely, this technique carries a higher complication rate, and requires a unique set of technical skills as compared to more traditional resection. Here, we describe the technical aspects of *en bloc* resection, as well as specific indications and considerations when employing this operative technique.

Keywords: Tumor; resection; *en bloc*

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Introduction

En bloc resection involves the surgical removal of the entirety of a tumor without violating its capsule, and requires resection of the lesion encased by a continuous margin of healthy tissue. An *en bloc* approach for tumors of the spine is accompanied by a unique set of anatomical considerations, and requires adaptation of surgical principles from both appendicular musculoskeletal and neurosurgical oncology. The *en bloc* technique was first coined by Enneking *et al.*, within the context of primary musculoskeletal sarcoma (1). In their description of a surgical staging system, the authors contrast intralesional resection—consisting of piecemeal debulking or curettage—against *en bloc* resections, with either marginal, wide, or radical resection of the tumor along with varying margins of normal tissue.

Boriani *et al.* adapted the Enneking staging system for

application in tumors of the spine. Their novel classification and staging of spinal tumors led to the Weinstein-Boriani-Biagini (WBB) staging system (*Figure 1*) (2). This system delineates 12 radiating zones in the axial plane of the vertebral body, five concentric layers of tumor involvement surrounding the dural sac, and accounts for the number of vertebral levels involved (2). Gross and histologic evaluation can further classify the operation as “intralesional” if the mass has been cut, “marginal” if the pseudocapsule has been dissected out, and “wide” if the tumor has been removed with a continuous margin of normal tissue (2). This system accepts that “radical” margins are unattainable in spinal lesions contiguous with the epidural space whilst creating a platform from which to plan complete resection without tumor breach. The WBB system has been clinically validated (3) and seems to accurately predict intraoperative margins in a majority of patients (4). This classification

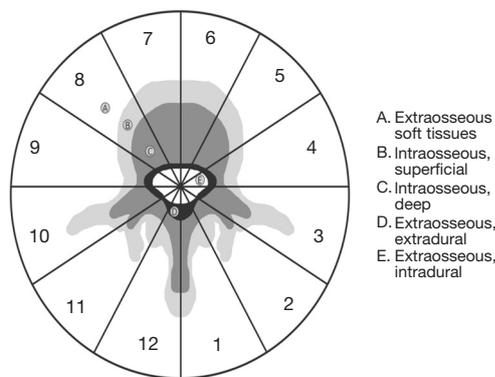


Figure 1 The Weinstein-Boriani-Biagini (WBB) anatomic classification system for spinal tumors. The location of the lesion is described using twelve radiating zones [1–12] in the axial plane of the vertebral body, and 5 concentric layers (A-E) of tumor involvement.

system lends to more informed preoperative planning and allows for total *en bloc* resections to be performed in a growing number of cases (5).

The term “total *en bloc* spondylectomy” was first coined by Tomita *et al.* Their description of this procedure specifically entailed an *en bloc* laminectomy and posterior instrumentation followed by a total vertebrectomy and anterior column reconstruction for tumors contained solely within the vertebral body (6). Since its first description, this technique has been increasingly employed with successful outcomes in a variety of patient populations (4,5,7-11). Generally, *en bloc* resections are appropriate in patients whose lesions do not invade adjacent viscera nor adhere to adjacent major blood vessels (12), and thus require careful patient selection and surgical planning.

En bloc resection in the spine is generally indicated for malignant primary tumors as well as aggressive benign tumors (1,4). This technique can also be employed for amenable solitary metastatic lesions including hormone secreting and radio-insensitive tumors (13-16). However, *en bloc* resection often involves a technically demanding procedure, and carries a high rate of complications. Improvements in tumor-related mortality must be balanced against procedure-related morbidity, and local lesion control against preservation of function (1,8). Due to the relative complexity of this surgical procedure, much of the *en bloc* literature consists of case reports and series. This review seeks to summarize the existing body of evidence

regarding the indications and utility of *en bloc* resection of primary and metastatic spinal tumors.

Survival & recurrence

In keeping with oncologic principles, removal of the tumor in its entirety without violation of the capsule should confer lower rates of future recurrence. Several studies have borne this out, showing recurrence rates to be higher in intralesional than *en bloc* surgeries (4,12,17-20). Furthermore, marginal *en bloc* resections are at higher risk of recurrence than wide *en bloc* resections (4). However, it is worth noting that wide resections are often unattainable in the spine, owing to its anatomical complexity.

Successful *en bloc* resection appears to especially improve recurrence-free and overall survival for aggressive primary tumors (4,21). A recent review estimated disease-free survival following *en bloc* resection to be 92.6%, 63.2%, and 43.9% at 1, 5, and 10 years, respectively, in a primary tumor cohort (5). Ten-year overall survival in the same cohort was estimated to be 71%, and 5-year survival was assessed to be 84.4% (5,22). However, it is worth noting that within this category there exists significant variability in baseline expected survival, recurrence rates and surgical morbidity, and any improvement following *en bloc* resection must be considered within the context of the primary pathology. Survival and recurrence rates by tumor type are detailed in a later section of this review.

Similarly, prognosis for metastatic lesions following *en bloc* resection varies widely based on primary pathology and systemic disease status. A recent review in this population estimated disease-free survival at 1, 5, and 10 years to be 61.8%, 37.5%, and 0%, respectively (5). Overall survival was undefined for that cohort, but mean survival has been estimated by other studies to range between 15 and 27 months (23,24). Local recurrence rates following *en bloc* resection for metastases have been reported to be as low as 11% (16).

For both primary and metastatic lesions, prior radiation therapy has been identified as a risk factor for local recurrence (16). This may be due to radiation-related changes to the peritumoral tissue, which can lead to indiscriminate tumor boundaries. Intraoperative dural tear and tumor occupancy rate of >50% of the spinal canal also predict future local recurrence (16). Unsurprisingly, recurrence rates have been reported to be higher in cases of reoperation, and if performed at a non-tertiary center (4,25).

Complications

Despite the benefits of *en bloc* resection in appropriately selected patients, this demanding technique nonetheless has significant risks (26). The high morbidity of spinal oncologic resections in general has been previously well-described (27–29). A demarcation zone between neoplastic and healthy tissue can be evasive or nonexistent, further complicating this technique. The potential also exists for tumor cell contamination of the surrounding structures during resection (12). Overall, *en bloc* resection carries an increased complication rate when compared with intralesional resection (8). Institutions who have more recently begun performing *en bloc* resections have published complication rates as high as 76% (23), highlighting the importance of surgeon comfortability with undertaking this procedure.

Several operative factors have been shown to affect complication rates. Anterior-posterior combined approaches independently increase the incidence of both major and minor complications as compared to a posterior-only approach (4,8). This finding is unsurprising given the likelihood that a combined procedure be used in cases with more complex anatomical involvement, and may have higher associated blood loss and procedural morbidity. Prior surgery or open biopsy also appears to confer increased risk of major complications as delineated by the McDonnell classification (4,8,30). Prior radiation therapy increases rates of infection, but not overall complication rate (8). Increased number of levels also increases risk of complications (4).

Primary spine tumors

Primary spine tumors account for 11% of primary musculoskeletal tumors, less than 5% of all spinal tumors, and only roughly 0.4% of all malignancies (14). *En bloc* resection has proven effective in improving prognosis and decreasing local recurrence for primary aggressive spinal lesions (12,20,31). Amendola *et al.* recently performed a prospective cohort study of 103 patients who underwent *en bloc* resection of primary benign and malignant spine lesions (4). *En bloc* resection was associated with decreased risk of local recurrence and overall tumor-related mortality. At mean follow-up of 100 months, 69 patients (67.0%) showed no evidence of recurrence. Of note, the risk of local recurrence following *en bloc* resection was significantly higher in patients who previously underwent an operation—either intralesional excision or open biopsy—than patients

with no prior surgery [hazard ratio (HR) =3.45, 95% CI, 1.38–8.63]. Forty-three patients (41.7%) presented with a total of 75 postoperative complications; in accordance with the McDonnell classification, 40 major and 35 minor complications were observed (4). Smaller case series have borne out similarly positive results (12).

With respect to specific primary tumor types, the role of *en bloc* resection has largely been investigated via case series and reports. Chordomas are slow-growing yet malignant primary bony lesions that can affect the spine. *En bloc* resection can offer a surgical technique for controlling locally aggressive chordomas, or those that threaten nearby viscera or vasculature. A 2018 systematic review concluded that *en bloc* excision remains the gold standard for the management of chordomas, and emphasized the importance of multimodal adjuvant therapy for these tumors (32). Recent analysis of the AOSpine Knowledge Forum Tumor database showed improved overall survival (8.4 vs. 6.4 years, $P=0.023$) in patients resected in keeping with Enneking principles, as compared to Enneking-inappropriate patients. Additionally, Enneking-inappropriate resection conferred a greater risk of local recurrence (HR, 7.02, 95% CI: 2.96–16.6, $P<0.001$) (17).

Chondrosarcoma is a malignant osseous neoplasm that accounts for only 10% of all primary bone tumors (14). These tumors are rare in the axial skeleton, with an estimated 2–12% of all chondrosarcomas arising in the spinal column (21). Chondrosarcoma of the spine is notoriously difficult to treat and has proven resistant to both radiation therapy and chemotherapy (9,33,34). Surgical resection correlates with overall survival benefit, and *en bloc* resection has been touted as the optimal surgical option for these lesions (9,14,35–38). Notably, a recent analysis of the Surveillance, Epidemiology, and End Results Registry (SEER) registry analyzed 973 cases of chondrosarcoma of the spine (37). Of these cases, the surgical cohort demonstrated overall and disease-free survival benefits over both the radiotherapy alone and adjuvant radiotherapy cohorts. Importantly, this review did not explicitly analyze extent of resection, due to limitations of the surgical data available via the SEER database (37). Ambispective cohort analysis of 111 patients with primary spinal chondrosarcoma demonstrated an improvement in local recurrence rates following Enneking appropriate resection (18). Finally, a recent review of 84 cases of primary chondrosarcoma of the spine calculated patients receiving non-*en bloc* resection to have a 9.4 times hazards ratio for death compared with those receiving an *en bloc* resection (95% CI: 2.6–34,

P=0.001) (39).

En bloc resection can also provide local control for several subtypes of sarcoma occurring in the spine. Recent analysis of 58 patients who underwent surgical treatment for primary spinal osteosarcoma demonstrated that *en bloc* resection in accordance with Enneking principles conferred increased survival and decreased local recurrence over intralesional resection (38). Promising results have also been reported following *en bloc* resection of synovial sarcomas—a soft tissue tumor with reported cases in the axial skeleton—though these results are limited to case reports and series (40-42).

Giant cell tumors (GCTs) comprise another primary bone tumor for which *en bloc* resection may be employed. These tumors often occur in the vertebral body, and 1.4–9.4% occur above the sacrum, in the mobile spine (25). Boriani *et al.* found that *en bloc* resection conferred a survival benefit: average time to local recurrence following *en bloc* excision was 197 months, versus 91 months in an intralesional excision cohort (P=0.03) (25). Recurrence rates are higher in GCTs involving the posterior elements, as well as in lesions with extra-osseous or paraspinal extension (43). Recent analysis of the AOSpine Knowledge Forum Tumor database supported these findings: *en bloc* resection with wide margins conferred a significantly reduced likelihood of local recurrence as compared to intralesional resection (P=0.029) (19). Some authors have suggested that preoperative denosumab may further facilitate the feasibility of complete resection of GCTs (44-46).

Metastatic spine tumors

Spinal metastases represent the most common type of spine tumor, occurring over 20 times more frequently than primary spinal neoplasms (47). The spine is the most common site for skeletal metastasis, with lesions of the axial skeleton representing roughly 39% of all bony metastases (27). Cord compression secondary to spinal metastases occurs in 5–10% of all cancer patients, and up to 40% of patients with existing nonspinal bone metastases (48). Spinal metastases subsequently represent a significant source of pain and disability, and a potential opportunity for surgical intervention and improvement of quality-of-life. Despite the prevalence of spinal metastases, there exists a paucity of data assessing the efficacy of *en bloc* resection in this patient population.

Breast, prostate, and lung cancers classically represent the most common primary tumors with propensity to

metastasize to the bony spine (49). *En bloc* resection has been reported to be an appropriate surgical option with appropriate patient selection and favorable status of systemic disease (13-15,50). However, systemic burden of oncologic disease often determines morbidity and mortality in this population. Therefore, the benefits of an aggressive *en bloc* resection technique may not always outweigh the risks, and consideration of all patient characteristics is imperative in determining optimal extent of resection.

A recent analysis of 91 patients who underwent *en bloc* resection for metastatic spine lesions demonstrated a local recurrence rate of 11%, at a mean follow-up duration of 27.4 months (range, 4–66 months) (16). A history of prior radiotherapy (P=0.04), intraoperative dural tear (P=0.03), and tumor occupancy rate of >50% of the spinal canal (P=0.02) were found to be predictive of future local recurrence. Sakaura *et al.* studied twelve patients who underwent *en bloc* resection of solitary thoracic metastases. *En bloc* resection provided long-term control to several patients within their cohort, with seven patients surviving for an average of 61 months (10). Similarly, Huang *et al.* recently reported outcomes of nine *en bloc* resections for solitary metastases to the lumbar spine (51). Five patients remained disease-free at the time of most recent follow-up (mean follow-up 41.2 months). Another analysis demonstrated average survival following *en bloc* resection to be 15 months for patients with metastatic lesions, compared to 47.6 months in patients with primary spinal tumors (23). The benefits of *en bloc* resection, therefore, may be less dramatic in a metastatic population, but remain non-negligible.

En bloc resection may provide particular benefit to patients with radioresistant metastases. Classically, renal, hepatocellular, colon, thyroid, and non-small cell lung carcinomas and melanoma are considered to be less responsive to radiation therapy (52) (Figure 2). Even in an era of increasingly precise radiosurgery, the epidural space and spinal cord represent important dose-constraining structures, and therapeutic doses to these tumor types may not be attainable in the spine. Without radiation as a useful adjunct for these lesions, *en bloc* resection may provide a better chance at local control than a more conservative resection. Case series have previously described successful *en bloc* removal of renal cell, non-small cell, thyroid, and hepatocellular carcinomas (24,53-56).

In the case of patients with secretory spinal metastases, *en bloc* resection can provide a uniquely useful surgical option. This technique has been described in the setting

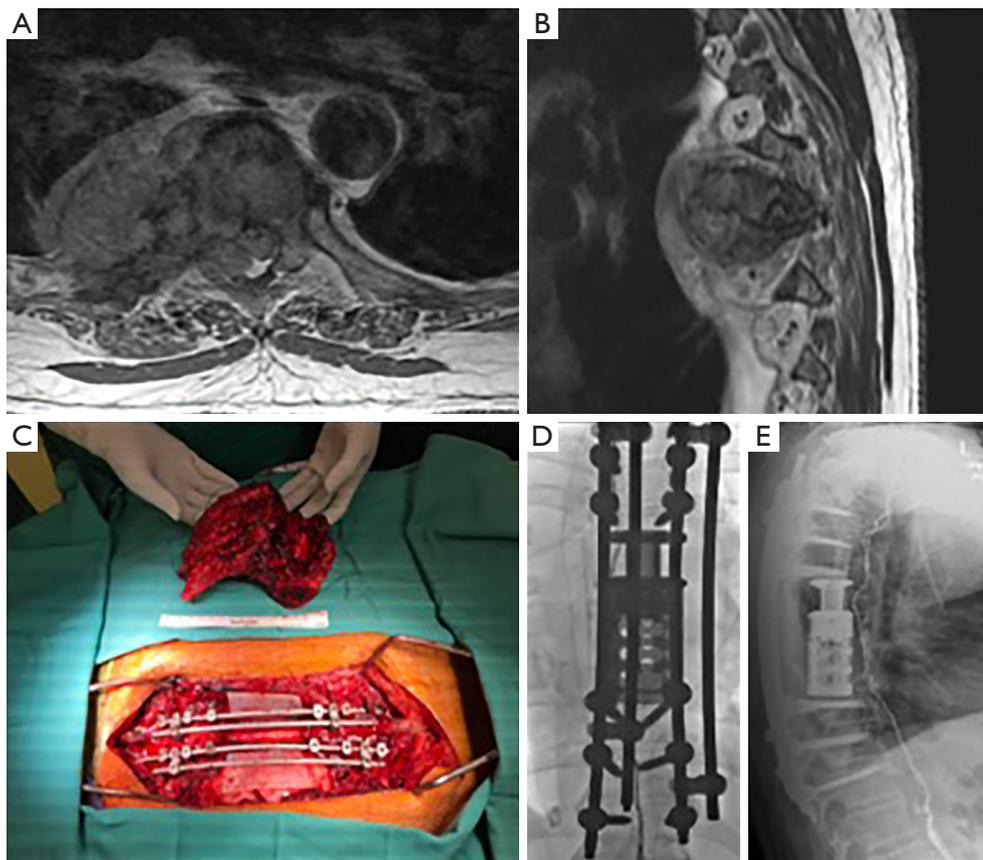


Figure 2 A 66-year-old male presented with metastatic renal cell carcinoma to the T5, T6, and T7 vertebral bodies. The patient underwent T5–7 corpectomy with *en bloc* resection, as well as partial resection of right ribs 5–7, followed by cage spacer placement and PSF T2–T10. The patient required 3 days of ICU admission, and was discharged to a SNF on POD13. (A,B) Preoperative imaging of the lesion demonstrating canal stenosis, paravertebral and chest wall extension; (C) intraoperative image following posterior instrumentation and resection; (D) intraoperative and (E) postoperative imaging demonstrating T2–T10 construct. PSF, posterior spinal fusion; POD, post-operative day; ICU, intensive care unit; SNF, skilled nursing facility.

of pheochromocytoma, carcinoid, paraganglioma, choriocarcinoma, and fibroblast growth factor 23-secreting phosphaturic mesenchymal tumors (15,57-59). These tumor types may uniquely benefit from *en bloc* resection, as this approach theoretically eliminates the functional ability of the lesions and provides improved symptom control over a subtotal resection (60).

Finally, several rare tumor types have been demonstrated to be amenable to *en bloc* resection. Cases have been reported of optimal long-term outcomes in metastatic epithelial-myoepithelial carcinoma (61), renal cell carcinoma of the spine (24), leiomyosarcoma (62), metastatic osteosarcoma (63), and acinic cell carcinoma (64), among others. However, due to the rare nature of these

tumor types in the context of spinal metastases, little can be definitively concluded about the overall superiority of *en bloc* resection in these cases.

Surgical technique and anatomic considerations

Single posterior approach

A single posterior approach can be an appealing surgical option in patients with concurrent comorbidities that preclude more extensive or staged procedures (65). This approach can also be employed in cases of prior surgery, prior radiotherapy, or unresectable anterior paraspinous tumor or scar tissue (12,65,66). A posterior-only approach may provide an ideal option for especially muscular

or obese patient populations (67). Posterior approach involves excision of the posterior elements, which allows hemostasis of the epidural venous plexus, sectioning of the posterior longitudinal ligament and annulus fibrosis, as well as posterior stabilization (2). A major disadvantage to this technique is a lack of direct visualization of ventral structures (5).

Combined posterior anterior-posterior approach

A combined anterior and posterior approach can increase the likelihood of obtaining an *en bloc* resection without violation of the tumor capsule, but poses additional challenges and necessitates greater coordination of surgical resources and skill. A combined spondylectomy may be performed as staged or simultaneous procedures. A non-staged approach allows for simultaneous anterior and posterior stabilization, but also demands the technical ability to achieve posterior reconstruction with the patient in lateral decubitus (5,68).

Cervical

The location of a lesion along the spinal column can drastically affect the surgical approach and feasibility of an *en bloc* resection. Employing this surgical technique in the cervical spine presents a unique set of considerations. The presence of the vertebral arteries within the transverse foramina poses an anatomical challenge to resection. If *en bloc* resection cannot be achieved while preserving bilateral vertebral arteries, a balloon-test occlusion can assess the collateral capacity of the Circle of Willis and the safety of sacrificing one vertebral artery (69). Digital-subtraction angiogram of the cerebral vessels can also assess the safety of vessel sacrifice (70). Endovascular vertebral artery occlusion may be performed prior to surgical ligation (71), though many authors recommend occluding after posterior instrumentation due to the potential risk of injury to the contralateral artery.

Posterior, anterolateral, retropharyngeal, and lateral *en bloc* approaches to tumors of the cervical spine have previously been described (72,73). A combined transmaxillary and transmandibular *en bloc* approach has also been described for a C1 chordoma (74). Hsieh *et al.* detail a staged procedure for cervical chordoma resection, with the first stage comprised of release osteotomies, posterior tumor

dissection, placement of instrumentation, posterolateral arthrodesis, and any required nerve root or vessel sacrifice, followed 2–5 days later by anterior dissection and *en bloc* resection (70).

Thoracic

The thoracic spine poses yet another set of distinct surgical considerations. Anterior access can be limited by the proximity of the esophagus and great vessels (75). The ribs and mediastinal structures may further impede thoracic access. Thoracic approaches often necessitate blunt dissection of the pleura from the ribs and vertebrae, and may require ligation of the intercostal vessels. Techniques of anterior, posterior, anterior followed by posterior, and posterior followed by anterior, have been identified and proposed for *en bloc* resection (75–79). A combined approach can facilitate dissection of the aortic branches, and may be preferable in cases involving the great vessels or at junctional locations. Sciubba *et al.* achieved *en bloc* resection of a T1–5 chordoma using a 5-level spondylectomy and bilateral chest wall resection, from which the patient recovered without neurologic complication (77). A simultaneous thoracoscopic and posterior approach has also been described to safely achieve resection of a T2–3 chordoma with paravertebral involvement (75). A similar technique has been used for resection of a T11 metastasis and a T5–6 osteogenic sarcoma (80) (*Figure 3*).

Lumbar

When *en bloc* resection is employed in the lumbar spine, additional care must be taken due to the anatomical proximity of the lumbar plexus and bowel, the vascular lumbar pedicles, and muscular insertions at the vertebral bodies. Some authors have suggested that a staged procedure is subsequently required to avoid complications (22,81). The utility of a single posterior approach is limited in the lumbar spine, due to the muscular insertions at the vertebral bodies (5). Still, some have suggested that a posterior-only approach is reasonable at the L3–5 levels (82).

Sacral

Sacral tumors that lend themselves to *en bloc* resection can either be approached via a combined or posterior-

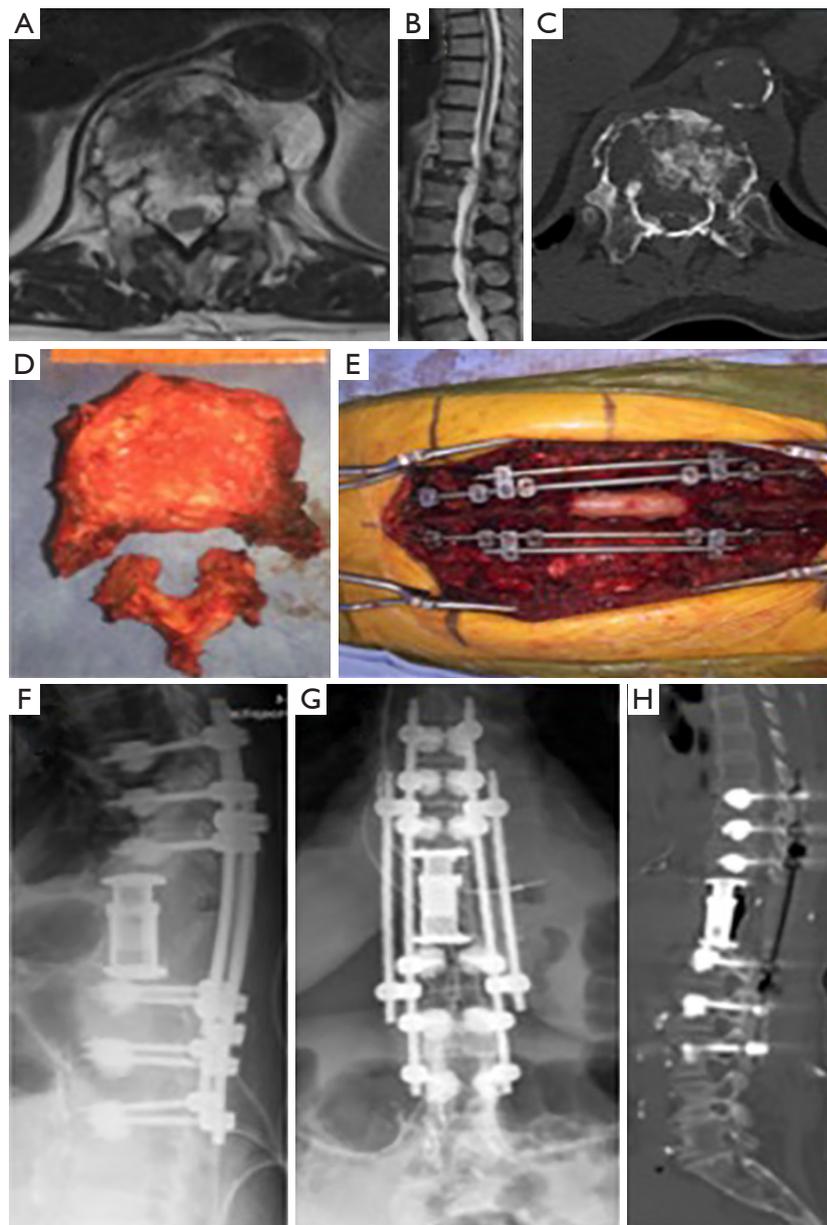


Figure 3 A 74-year-old woman presented with progressively worsening back pain. Imaging revealed an isolated lesion at T12 with some extension to T11. Biopsy revealed chordoma, and the patient underwent costotransversectomy with T11/T12 *en bloc* spondylectomy with cage placement, a “quad rod” construct, and instrumentation with fenestrated screws and cement from T8-L3. Given the extensive nature of the tumor on MRI, we prepared for a planned transgression of the tumor as our last step in *en bloc* resection. However, negative margins returned on final pathology. The patient remained neurovascularly intact both after surgery and on follow-up several months later, with repeat scans showing no evidence of disease. (A,B) Preoperative MRI demonstrating extensive tumor throughout T12 body and collapse of vertebral body; (C) CT image showing extensive destruction of bone at level of lesion; (D) resected specimen with single deliberate cuts through pedicles to minimize tumor spillage; (E) quadruple rod construct with visible thecal sac prior to closing; (F,G) upright AP and lateral images of final construct. Note the “lollipops” of cement at the tip of each screw to both improve strength of bone and decrease pull-out; (H) CT imaging of final construct.

only approach. Anterior access allows for mobilization and preservation of critical structures such as the rectum and internal iliac vessels. This approach also allows the surgeon to obtain a vascularized flap to aid in the closure of the posterior component. The combined anterior-posterior approach has been well-described (83-85). However, a posterior-only approach has been used by several groups, who emphasize the decreased morbidity of reducing without sacrificing *en bloc* principles (86-88).

Conclusions

- ❖ *En bloc* resection improves local control over intralesional resection for primary aggressive lesions (4,12,20,21,31). The associated improvement in overall survival may warrant the increased morbidity of surgery, as these tumor types are traditionally poor responders to adjuvant treatment options.
- ❖ *En bloc* may be an appropriate technique for carefully selected metastatic lesions—such as hormone-secreting tumors and solitary radioresistant tumors—but must be considered in the context of the patient's systemic disease status and the morbidity of surgery (13-15,50).
- ❖ Complication rates are higher following *en bloc* resection as compared to conventional resection techniques (76).
- ❖ Patients being considered for *en bloc* resection may be best managed by specialized surgeons in high-volume tertiary centers (23,25).

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Footnote

Conflicts of Interest: IO Karikari, MD; Consultant for Nuvasive, Depuy. Receives spine fellowship fund from Nuvasive; M Abd-El-Barr, MD, PhD: Consultant for Spineology; ML Goodwin, MD, PhD: Consultant for ROM3 Rehab, Augmedics; DM Sciubba, MD: Consultant for Orthofix, Globus, K2M, Medtronic, Stryker, Baxter; CR Goodwin, MD, PhD: Received grants from the Burroughs Wellcome Fund, North Carolina Spine Society, and the NIH/NINDS K12 NRC DP Physician Scientist Award, Robert Wood Johnson Harold Amos Medical Faculty Development Program. The other authors have no conflicts

of interest to declare.

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