Management of primary and metastatic spinal tumors is complex and requires a multidisciplinary approach.

Surgical Management of Primary and Metastatic Spinal Tumors

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Background: The axial skeleton is a common site for primary tumors and metastatic disease, with metastatic disease being much more common. Primary and metastatic spinal tumors have a diverse range of aggressiveness, ranging from benign lesions to highly infiltrative malignant tumors.

Methods: The authors reviewed the results of articles describing the treatment and outcomes of patients with metastatic disease or primary tumors of the spinal column.

Results: En bloc resection is the mainstay of treatment for malignant primary tumors of the spinal column. Intralesional resection is generally appropriate for benign primary tumors. Low-quality evidence supports the use of chemotherapy in select primary tumors; however, radiation therapy is often used for incompletely resected or unresectable lesions. Surgical considerations for the treatment of metastatic disease are more nuanced and require that the health care professional consider patient performance status and the pathology of the primary tumor.

Conclusions: The treatment of metastatic and primary tumors of the spinal column requires a multidisciplinary approach in order to offer patients the best opportunity for long-term survival.

Introduction

The axial skeleton is a common site for primary tumors and metastatic disease, with metastatic disease being much more common. Both primary and metastatic spinal tumors have a diverse range of aggressiveness, ranging from benign lesions to highly infiltrative malignant tumors. This article will review a variety of primary and metastatic bony tumors of the spine,

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Submitted October 1, 2013; accepted November 13, 2013.

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Dr Vrionis receives grants/research support from Globus Medical, DePuy Synthes, and Spine360. He also is a consultant for Orthofix. Dr Gokaslan receives research grants from AO North America, the Neurosurgery Research and Education Foundation, Medtronic, Integra Life Sciences, Depuy Spine, and K2M. He receives honoraria from the AO Foundation and is a stock shareholder of US Spine and Spinal Kinetics. No significant relationship exists between the remaining authors and the companies/organizations whose products or services may be referenced in this article.
each of which display unique pathophysiological and histological properties that help determine current diagnostic and treatment modalities. We will also discuss a wide variety of surgical techniques, including advances in en bloc vertebrectomy, as well as recent advances in medical and stereotactic radiotherapy for the treatment of tumors within the vertebral column. Surgical treatments discussed include conventional debulking vs en bloc resection, conventional radiotherapy and radiosurgical techniques, and minimally invasive approaches.

The differential diagnosis for primary cancer in metastatic spinal tumors is wide and includes lung, breast, prostate, renal cell, and gastrointestinal neoplasms. Although rare, tumors from other areas of the body may also spread to the spine. The differential diagnosis of primary bony tumors of the spine may include chordoma, giant cell tumor, hemangioma, osteosarcoma, chondrosarcomas, synovial sarcoma, aneurysmal bone cyst, hemangioma, eosinophilic granuloma, osteoid osteoma, and osteoblastoma pathologies. Other lesions that may mimic primary spinal tumors include infection, metastatic disease, and, possibly, spontaneous or traumatic hematoma.

**Diagnosis of Spinal Tumors**

Patients who have spinal tumors commonly present with chronic and progressively worsening focal back pain. Depending on the morphological characteristics of the spinal tumor, tumor size, and infiltration to the surrounding neural and vascular structures, patients may have intractable radiculopathy, myelopathy, or cauda equina syndrome. Paraspinal pain is due to infiltration of the tumor into surrounding muscle and subcutaneous tissues, while radiculopathy is due to tumor extension into the neural foramen, compressing exiting nerve roots. Tumor burden extending within the spinal canal in the epidural space may cause compression of the spinal cord and neurological compromise.

On physical examination, patients with cervical spinal cord compression have signs of myelopathy, such as a positive Hoffman sign, spastic weakness as well as hyperreflexia in the upper and lower extremities, upgoing Babinski signs bilaterally, and gait instability. With further tumor extension, vascular supply to the spinal cord becomes compromised and the neural structures become compressed. Patients with severe spinal cord compression may present with quadriplegia with a sensory or motor level. Patients with lumbar sacral tumors with canal compromise may have weakness and/or numbness in one or both extremities, and evidence of perineal numbness and saddle anesthesia. Patients with lumbar sacral tumors with severe canal and foraminal involvement may present with low back pain and cauda equina syndrome with perineal numbness, bowel and bladder dysfunction, and/or lower extremity weakness.

Diagnostic modalities for tumors of the spine include computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) scans, and CT of the chest, abdomen, and pelvis. CT scans can help determine the extent of the tumor erosion within the vertebral anatomy as well as the extent of destruction from the anterior to the posterior columns of the spine. MRI scans (with and without contrast) are critical for observing tumors of the spinal column. Compared with CT, MRI can more clearly delineate the anatomy of the tumor and the extent of its enhancement. MRI will further identify regions of the tumor that may be cystic or necrotic without enhancement, as well as the extension of the tumor burden into surrounding tissues. In addition, MRI is important when identifying tumor burden within the epidural space and the extent of neural element compression or injury, either centrally or foraminally. PET scans are helpful in determining other areas of abnormal radioactive uptake of glucose throughout the body, signifying possible metastatic disease or tumor elsewhere. CT of the chest, abdomen, and pelvis (with and without contrast) is often obtained to rule out other areas of tumor burden to then rule out metastatic disease. Standard laboratory tests, including white and red blood cell counts, coagulation numbers, and electrolyte levels should be obtained to rule out infectious process and prepare the patient for possible surgical intervention.

If no other lesions are noted elsewhere based on CT, MRI, and PET scans, then core biopsy should be performed of an isolated spinal column lesion without acute deterioration to obtain a definitive diagnosis. The interventional radiology team can percutaneously perform this procedure using fluoroscopic guidance. For malignant lesions, the biopsy tract should be carefully marked and excised upon definitive surgical management. Open biopsy for malignant lesions should be avoided to reduce the risk of metastatic seeding. Once this is done and a diagnosis is obtained, the multidisciplinary treatment plan can be arranged. Determining whether the spinal column mass is a primary spinal tumor vs metastatic disease or infection is crucial before beginning surgical treatment. Metastatic disease is classically treated with intralesion resection due to tumor burden elsewhere, while en bloc resection for primary spinal tumors has improved patient outcome and survival rates over the last decade.

**Primary Tumors**

Primary spinal column tumors include malignant pathologies such as chondrosarcoma, osteosarcoma, Ewing sarcoma, and chordoma. For these pathologies, en bloc resection with adjuvant radiotherapy pro-
vides the best chance of cure.\textsuperscript{6-15} By contrast, benign primary tumors, such as aneurysmal bone cyst, giant cell tumor, and osteoblastoma, may be safely treated with intralesional resection, radiotherapy, or both to reduce the risk of surgical morbidity.\textsuperscript{16,17} This section will review the indications for en bloc resection and the advances in adjuvant therapy for primary tumors.

**En Bloc Resection of Primary Spinal Tumors**

Many studies validate the role of en bloc resection as the standard of care for primary spinal column tumors.\textsuperscript{7,18-23} The goal of en bloc tumor resection is to provide local oncological control and prevent the seeding of tumor cells into surrounding tissues. This strategy avoids dissemination of the tumor and ultimately leads to decreased local recurrence as well as prolonged disease-free and overall survival rates.\textsuperscript{11,18-22,24} However, anatomical considerations often limit the feasibility of this approach.

En bloc resection of cervical lesions is complex and is not without significant morbidity and mortality risks. For this reason, a preoperative understanding of patient pathology, involvement of neural and vascular structures, and intracranial vascular anatomy is important in determining patient outcomes. One such risk factor is injury to vertebral arteries. Depending on primary spinal tumor morphology and extension, the vertebral arteries may be encased with tumor on presentation, adding to the danger of surgical resection. Cranial anastomotic anatomy to the posterior circulation is critical in cases of bilateral or dominant vertebral artery injury or intraoperative and postoperative vasospasm. During vertebral artery manipulation, any neurological decline in neuromonitoring during temporary clipping necessitates artery preservation.

Although some studies have recommended a clear avoidance of en bloc vertebrectomy in the cervical spine due to the risk posed to the vertebral arteries and cervical nerve roots, others have published data demonstrating its safety and feasibility. Hoshino et al\textsuperscript{25} published a study of 15 patients undergoing unilateral vertebral artery ligation during en bloc resection of cervical spinal tumors and noted no adverse events affecting the brain stem, spinal cord, or cerebellum. In a meta-analysis by Cloyd et al,\textsuperscript{26} 8 of the 18 patients undergoing en bloc resection of primary cervical spinal tumors had unilateral vertebral artery ligation without complication. Other possible risk factors involved in en bloc resection of primary cervical spinal tumors include infection, significant bleeding, dysphagia, aspiration, spinal instability, seeding of tumor cells into surrounding tissues and into the cerebrospinal fluid if a dural tear is encountered, and spinal cord, nerve root, and large vessel injuries, including the internal carotid arteries, vertebral arteries, and internal jugular veins.\textsuperscript{26}

Careful preoperative planning may reduce complication rates for tumor resection at all levels of the spinal column. Tomita et al\textsuperscript{27} described the use of preoperative embolization of vessels supplying spinal tumors. A significant decrease was reported in intraoperative bleeding with preoperative embolization, meticulous blunt dissection, and tumor resection, as well as with the use of fibrin glue in the epidural venous plexus. In addition, use of a T-saw for pediculectomy or anterior column osteotomy was seen in a separate study.\textsuperscript{28} The researchers reported a decrease in tumor spread following the use of the T-saw. Postoperative considerations, such as reconstruction, are another cause for concern in patients undergoing en bloc resection. Specifically, for patients undergoing en bloc resection of the large mobile spine chordoma, generating a custom cage or construct may be necessary to facilitate adequate reconstruction. Similarly, in the sacral spine, resection of more than one-half of the sacroiliac joint requires reconstruction of the spinopelvic junction with bone grafts and instrumentation.\textsuperscript{21,29}

However, with advances in surgical technique, the benefit of en bloc resection has been independently demonstrated for various pathologies of primary vertebral tumor. In a landmark study by Boriani et al,\textsuperscript{30} recurrence rates following surgical resection in a group of 22 patients with spinal chordosarcoma were 21.4\% for patients with en bloc resection compared with 100\% for patients undergoing repeat curettage. Strike and McCarthy\textsuperscript{8} reported a cohort of 16 patients with predominantly low-grade chordosarcoma with total resection. This study reported that, despite 14 of 16 patients receiving total resection, the mean interval to death was 3.6 years, and 43.8\% of patients died from pulmonary metastases. Furthermore, 100\% of patients with subtotal resection developed metastases.\textsuperscript{8} Talac et al\textsuperscript{31} studied patients with primary sarcomas of the spine undergoing en bloc resection with negative margins, piecemeal resection with negative margins, and all resections with positive margins, reporting recurrence rates of 11\%, 33\%, and up to 70\% in these groups, respectively.

En bloc resection in chordoma has also been studied. Patient outcomes are classically reported using the cervical, mobile spine, and sacral levels of disease. One group reported five cases of en bloc chordoma excision in the cervical spine with a mean disease-free survival rate of 84.2 months.\textsuperscript{18} Cloyd et al\textsuperscript{26} performed a meta-analysis of the existing literature on cervical primary spinal tumors with en bloc resection. The analysis involved 10 articles comprising 18 cases. The authors identified a combined recurrence rate of 22\% in all published studies for primary cervical spine tumors, with a mean follow-up time of 47.4 months. The group then calculated disease-free survival rates of approximately 88\% and 76\% at 1 and 5 years, re-

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spectives. No factors were identified as predictive of recurrence in this meta-analysis. During a 5-year follow-up period, Carpentier et al.32 noted recurrence and mortality rates of 40% and 33%, respectively, in their study of 16 patients with occipitocervical chordoma undergoing intralesional resection. In addition, Barrenechea et al.33 studied 7 patients with intralesional piecemeal resections of cervical chordomas and noted a recurrence rate of approximately 30% over a median of 2 years of follow-up.

In the mobile spine and sacrum, en bloc resection of chordoma may prolong survival. In the largest study to date of patients with mobile spine chordoma, Boriani et al.34 reported superior outcomes in patients with en bloc resection and adjuvant therapy; 4 patients remained free of disease for a mean of 77 months. Furthermore, multiple studies of sacral chordoma have confirmed improved survival and decreased recurrence rates for patients undergoing en bloc resection.7,21,35-39

Surgical treatment of Ewing and osteogenic sarcomas of the spine has noted recent advances in the previous decade. Sciubba et al.14 published data with strong recommendations and moderate quality evidence of neoadjuvant chemotherapy, but with a weak recommendation with low evidence for en bloc surgical resection for Ewing sarcoma of the spine. They also reported that en bloc surgical resection provided improved local control but did not improve overall survival rates.

By contrast, for benign but aggressive lesions in the spine, intralesional resection is generally recommended.17,40-42 In one study, Harrop et al.17 reviewed the quality of evidence supporting surgical resection for an aneurysmal bone cyst, giant cell tumor, and osteoblastoma and concluded that gross resection is an appropriate therapy for these lesions. However, recurrence rates for these benign lesions are not negligible. Junming et al.41 analyzed 21 patients undergoing piecemeal resection of cervical giant cell tumors and noted a recurrence rate of 33% over a mean follow-up of 68 months. Further, Boriani et al.42 reported a case series of 51 patients with spinal osteoblastoma and found that en bloc resection was more effective for stage 3 lesions compared with those with stage 2 lesions.

Adjuvant Therapy for Primary Tumors
The role of adjuvant treatment along with chemotherapy and radiation is still unclear in the treatment of primary spinal tumors and varies by pathology. Chordomas are classically resistant to conventional radiation treatments at doses favorable to surrounding tissues at below 60 Gy.43 By contrast, proton beam radiotherapy (PBRT) utilizes ionizing radiation with reduced scatter in surrounding tissues and has demonstrable benefit in unresected or partially resected chordoma of the cervical spine, mobile spine, and sacrum.43-46 Further, in a cohort of 44 consecutive patients with chordoma and chondrosarcoma of the skull base, PBRT in combination with conventional photon radiotherapy resulted in 3-year local control rates of 83.1% for chordoma and 90% for chondrosarcoma.47 The use of radiotherapy to treat benign primary tumors, such as giant cell tumor, has been debated. In a retrospective review of 239 treated lesions, Leggon et al.48 reported that recurrence rates were not low for patients who had surgery and radiation versus a solitary modality. Another retrospective review of 25 patients with giant cell tumors in the axial and appendicular skeleton reported a 5-year overall survival rate of 91%.49 The study authors concluded that conventional radiotherapy was appropriate for unresectable giant cell tumors or as adjuvant therapy. However, complications associated with radiotherapy are not insignificant. Such complications include wound breakdown and infection (particularly if performed at least 2 weeks before surgical treatment), neurological decline from radiation necrosis, and radiation-induced malignancy.

Neoadjuvant chemotherapy for Ewing sarcomas and osteogenic sarcomas has shown to have benefits, along with radiotherapy for Ewing sarcoma. Expert consensus supports the use of radiation therapy alone or as adjuvant treatment for local control, although the evidence cited was very low.14 For patients with osteogenic sarcoma, the consensus supported a strong recommendation with moderate quality evidence favoring neoadjuvant chemotherapy. The consensus also strongly recommended (but with very low evidence) en bloc resection in order to provide improved local control and potentially improved overall survival rates. Chemotherapy with imatinib mesylate was shown in one study to benefit patients with spinal chordomas, although further studies are required.50,51

Metastatic Tumors
Spinal metastatic disease with cord compression occurs in 5% to 14% of patients with cancer and results in significant morbidity rates.52-58 The most common tumors to metastasize to the spinal column are lung, breast, prostate, renal cell, and gastrointestinal tumors. A rare subset of spinal tumors has no known primary site identified.59,60 In addition, the histological diagnosis and grade of metastatic tumor pathology is critical in diagnosis and management.

Indications for Surgery
Historically, surgical intervention for patients with spinal metastatic disease has been controversial due to poor prognosis. Limited palliative intervention with radiation was previously utilized to minimize pain for patients with a terminal illness and at the end of life. However, Patchell et al.63 published a nonrandomized
control clinical trial in 2005 of laminectomy plus radiation compared with radiation alone for the treatment of metastatic spine disease. The study was terminated early due to the overwhelming superiority of surgery with radiation versus radiation alone. Patients in the surgery plus radiation group were more likely to walk after treatment (odds ratio: 6.2) and retained the ability to walk for longer than their counterparts in the radiation-only group (122 vs 13 days). Further, the use of opiate and steroidal medications was reduced in the surgical cohort. Since the Patchell et al study, multiple studies have confirmed that surgery for spinal metastases improves patient quality of life.64,65

The outcome of surgical intervention for metastatic spinal cord compression is related to the preoperative clinical status of the patient. Patients who are severely disabled upon presentation may improve, but this likelihood decreases if their deficits are severe and have been present for a prolonged period of time prior to surgical intervention.66 Further, overall survival rates vary by pathology.67-70 Of note, the presence of visceral metastases does not appear to influence patient outcome68,71; thus, surgical decision-making varies depending on patient presentation, tumor type, and performance status.

To guide surgical decision-making, a variety of scoring systems have emerged such as the Spinal In- stability Neoplastic Score (SINS), Tokuhashi system, and the Tomita system.72-74 The 6-point SINS system considers instability based on the extent of vertebral body collapse, quality of pain, location of metastasis, alignment, radiographic appearance, and posterior element involvement.72 Tokuhashi et al74 devised a 15-point scale and later revised this system, taking into consideration Karnofsky performance score, extent of vertebral metastases, extent of extraspinal bone metastases, extent of visceral metastases, tumor histology, and neurological status. Based on the results of these studies, patients with a life expectancy based on the revised scoring scale of fewer than 6 months were recommended to undergo conservative treatment, while those with a life expectancy of 1 year or more were recommended to undergo excisional surgery. Those expected to survive 6 months or more were recommended to undergo limited palliative surgery. Tomita et al75 devised a 10-point scale taking tumor histology and extent of visceral and bony metastases into account in determining goals for surgery and prognosis.

The use of these scoring systems was critically evaluated in the literature.75,76 In their evaluation of the SINS system, Fourney et al76 studied 30 patients with spinal tumors and classified these patients into one of 3 categories (stable, potentially unstable, or unstable) and according to the SINS system (≥ 6 weeks apart on 2 occasions). The authors identified that the interobserver and intraobserver reliability rates were near perfect when determining the 3 levels of preoperative stability. Sensitivity and specificity rates of 96% and 80%, respectively, were reported for the potentially unstable and unstable cohorts.76

In a review of the Tomita and Tokuhashi scoring systems, the prognostic Tokuhashi score was found to be more useful than the Tomita score in predicting survival time and overall survival rate following an initial diagnosis among a prospective cohort study of 52 consecutive patients.75

**Surgical Approaches**

Surgical approaches include direct posterior decompression alone, posterior decompression with posterolateral fusion, posterolateral costotransversectomy with corpectomy and placement of cage graft with posterolateral fusion, thoracotomy with corpectomy and cage graft placement, retroperitoneal approaches for corpectomy and cage placement with or without posterolateral instrumentation and fusion, vertebroplasty/kyphoplasty alone or in combination with posterolateral fusion, and radiosurgery alone or as an adjunct to surgical treatment. Minimally invasive approaches to the spine for metastatic spinal disease have been performed with varying success.77 The goals of surgery must be discussed with the patient and the family so that everyone has an understanding of treatment and desired outcomes. Goals of surgery include deformity correction and stabilization, restoration of neurological function, pain control, and oncological control.54

Surgical decompression ranges from intratumoral curettage to wide margin en bloc vertebrectomy. Patients with metastatic disease to the anterior thoracic spinal column with epidural extension and spinal cord compromise with associated kyphotic deformity may be offered surgical decompression with circumferential instrumentation and fusion. These patients are likely to undergo corpectomy and tumor resection via a posterolateral or anterolateral approach with placement of a cage constructed of titanium mesh or polyetherketone, usually filled with allograft, along with posterolateral instrumentation and fusion for added stabilization. Thoracic tumors from T3 to T12 may be accessed via a posterolateral costotransversectomy approach for corpectomy with the ability to sacrifice the nerve roots from T3 to T12 without any significant neurological compromise. In some cases, sacrifice of the T12 nerve root may produce a pseudohernia that may or may not require surgical treatment.78,79

Tumors along the cervical or cranial–cervical junction may benefit from a transnasal, transcervi- cal, transoral, or endoscopic stereotactic transcervical approach toward accessing the anterior cervical region. Ventral access to the upper thoracic spine is complicated by the presence of the great vessels and
is generally deferred unless the tumor growth cannot be assessed any other way. If it is necessary, manubriotomy, sternotomy, or a trap-door approach may be performed to access the upper thoracic region. T5 to L1 can generally be accessed via a lateral/thoracotomy approach, while L2 to L5 may be accessed via a lateral retroperitoneal approach. These approaches may be performed by experienced neurosurgeons; the use of vascular surgeons for exposure may also be utilized.

Although true en bloc procedures are not possible for metastatic disease, vertebrectomy for “en bloc” resection of a solitary bony metastatic lesion has been reported. This approach is effective for patients with hormonally active tumors. For example, a patient with metastatic pheochromocytoma to the thoracic spine underwent treatment as well as a patient with a metastatic tumor to the spine that caused severe hormonally induced osteomalacia. En bloc vertebrectomy led to the resolution of osteomalacia and a decline in fibroblast growth factor-23 levels.

Complication rates vary by approach, but patient characteristics also influence postoperative complications. Over a period of 11 years, Jansson and Bauer studied 282 consecutive patients at a single institution with metastatic thoracolumbar disease undergoing surgical treatment. The primary surgical indication was neurologically deficit as opposed to pain. A total of 13% of patients had a single metastasis, 64% had multiple skeletal metastases, and 23% had nonskeletal metastases. Preoperatively, 64% were Frankel A to C (nonwalkers), 30% were Frankel D, and 8% were Frankel E (normal motor function). A total of 212 patients had posterior decompression and stabilization, 47 had laminectomy alone, and 23 had anterior decompression and stabilization. The authors noted a complication rate of 20%, with 70% of patients showing an improvement of at least one Frankel grade. In more than 80% of patients, the ability to walk was retained.

Lau et al studied 106 patients with a variety of metastatic spinal pathologies. The authors identified that patients above the age of 65 years had the greatest likelihood of complication (40.9%; \( P = .034 \)). Patients with diabetes mellitus were isolated as having a higher risk of complications than those without diabetes (42.9% and 18.5%, respectively; \( P = .039 \)). In this study, the authors noted an overall complication rate of 21.7%, with wound infections and deep venous thromboses being the most common. Furthermore, patients requiring more extensive surgery (> 7 instrumented levels) were more likely to have increased complications.

Conclusion
Management of primary and metastatic tumors is quite complex and requires a multidisciplinary understanding of tumor type, location, extension, and overall preoperative and neurological conditions. Precise and timely diagnosis with a history, physical examination, imaging, and biopsy are critical first steps. Meticulous preoperative planning for en bloc surgical resection of spinal tumors is necessary for improved patient outcomes as well as to minimize any intraoperative and postoperative complications.

References
26. Cloyd JM, Chou D, Deviren V, et al. En bloc resection of primary tu-


57. Meyer SA, Singh H, Jenkins AL. Surgical treatment of metastatic spi-