The evolution of surgical management for vertebral column tumors

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Surgery for the resection of vertebral column tumors has undergone a remarkable evolution over the past several decades. Multiple advancements in surgical techniques, spinal instrumentation, technology, radiation therapy, and medical therapy have led to improved patient survival, function, and decreased morbidity. In this review, the authors discuss major changes in each of these areas in further detail.

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KEYWORDS spine tumor; primary tumor; secondary tumor; spinal radiosurgery; separation surgery; oncology

THE treatment of vertebral column tumors has undergone significant transformation over the past several decades. Advances in surgical techniques, chemotherapy, radiation therapy, and the incorporation of technological innovations into the operating room have led to an overall shift in the management of patients with spine tumors, all with the goal of minimizing treatment-related morbidity. Perhaps the most significant changes have been the recent advances in spinal radiosurgery and cancer immunotherapy and the incorporation of patient and tumor-specific genomic and molecular information to personalize cancer therapy, particularly for metastatic disease.

While the goal of surgery for metastatic spine disease remains palliative, the typical poor prognosis given to these patients is trending toward a more optimistic outlook. With each advance, traditional prognostic scoring methods for metastatic spinal disease are becoming less accurate. Unlike metastases, most primary spine tumors continue to be treated primarily with surgery, but advances in surgical techniques that have incorporated principles from the treatment of long bone tumors have led to decreased tumor recurrence rates and, in some cases, a potential for cure. Research into adjuvant therapy for primary tumors is progressing, with many recent promising

advances. In this review, we discuss the ongoing evolution of spine tumor treatment, particularly with regard to management of metastatic and primary spine tumors.

Advances in Surgical Strategies

The treatment of primary spine tumors remains primarily surgical. This simple fact belies the relatively recent change in how we resect these tumors. Principles for the treatment of long bone primary tumors developed and published by Enneking et al.¹⁹ in the 1980s were adapted for the spine by Weinstein and colleagues⁷ in the 1990s. The Weinstein-Boriani-Biagini system became an essential tool in presurgical planning for these tumors as it standardized the staging of primary spine tumors (Fig. 1). Specification of the exact tumor location in relation to the bony elements of the vertebra allows the surgeon to tailor the surgical approach, based on histology and location, which is particularly useful for tumors in which an en bloc resection is desired. While en bloc resection of primary spine tumors carries significant approach-related morbidity, the local recurrence rate and tumor-associated mortality can be significantly reduced.^{2,6} The Weinstein-Boriani-Biagini classification also standardized the terminology

ABBREVIATIONS EBRT = external-beam radiation therapy; NOMS = neurological, oncological, mechanical, and systemic; SINS = spinal instability neoplasia score; SRS = stereotactic radiosurgery.

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FIG. 1. Weinstein-Boriani-Biagini classification for spinal tumors. Reproduced with permission from Boriani S, Weinstein JN, Biagini R: Primary bone tumors of the spine. Terminology and surgical staging. *Spine (Phila Pa 1976)* 22(9):1036–1044, 1997. <https://journals.lww.com/spinejournal/pages/default.aspx>.

used when describing extent of resection, which allowed accurate comparison of treatment strategies between institutions and in the published literature.

Surgery for spinal metastases has perhaps undergone the most significant transformation in terms of surgical technique. Prior to the 1990s many surgeons were performing either simple posterior bony decompression or primary external-beam radiation therapy (EBRT) for patients with metastatic epidural spine disease, causing cord compression. Young et al.⁶¹ demonstrated that these 2 treatments had similar efficacy in terms of pain relief, ambulation, and sphincter function, leading many to question the utility of a simple decompression. In addition, it was noted that many patients who underwent a laminectomy would develop kyphotic deformity over time, leading to significant patient morbidity. The landmark trial of Patchell et al.,⁴⁷ published in 2005, which excluded radiosensitive tumors, demonstrated that a direct circumferential decompression of the spinal cord with postoperative EBRT had significant benefit in terms of the ability to regain or preserve ambulatory function and reduced the need for corticosteroids and opioid analgesics. Subsequently, there was an increased focus on the benefit of surgical intervention with surgeons performing circumferential decompression supplemented with vertebral column reconstruction and posterior segmental instrumentation in increasing numbers.

Concurrent to the Patchell trial, work was also being done to study the utility of a new spinal radiation modality: spinal stereotactic radiosurgery (SRS), which built off the success of radiosurgery for brain metastases. In 2007, Gerszten et al.²⁴ published the results of a series of 500 metastases to the spine in 393 patients who underwent spinal radiosurgery; they excluded patients with neurological deficits or spinal instability. The results were particularly encouraging, with high rates of long-term pain control (86%) and long-term tumor control (90%). Radiosurgery will be discussed in more detail below, but suffice it to say that these results led again to a change in treatment paradigm for patients with metastatic spine disease.

The success of SRS led to many metastatic spine tumor patients being treated with primary radiation therapy rather than surgical intervention. Currently, the 2 main indications for primary surgical intervention are decompression of the spinal cord and stabilization of the spine if there is evidence of instability. While the former had demonstrated utility thanks in large part to the study of Patchell et al.,⁴⁷ spinal instability had not been well defined for the metastatic spine disease population. There had been significant heterogeneity in the literature regarding who might benefit from stabilization surgery, and there were no consensus guidelines available. In 2010, the Spine Oncology Study Group published the spinal instability neoplasia score (SINS),²⁰ a scoring system to determine who may

TABLE 1. The SINS for scoring spinal instability in patients with spine tumors

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

CV = costovertebral.

The total score is used to classify a spine tumor as stable (0–6), potentially unstable (7–12), or unstable (13–18). Reproduced with permission from Fisher CG, DiPaola CP, Ryken TC, et al: A novel classification system for spinal instability in neoplastic disease: an evidence-based approach and expert consensus from the Spine Oncology Study Group. *Spine (Phila Pa 1976)* 35(22):E1221–E1229, 2010. <https://journals.lww.com/spinejournal/pages/default.aspx>.

benefit from surgical consultation for tumor-related spinal instability (Table 1). This system has been shown to be reliable among both surgeons and nonsurgeons.^{3,8,22}

To provide a treatment decision-making framework for spine oncology practitioners, Bilsky and Smith⁵ published the neurological, oncological, mechanical, and systemic (NOMS) system, which incorporates multiple factors, including 1) neurological examination, degree of spinal cord compression on imaging; 2) tumor sensitivity to radiation (oncological); 3) presence or absence of spinal instability; and 4) systemic burden of metastatic disease. This system has been refined,³⁷ incorporating both radiosurgery and the SINS classification system into its decision-making algorithm. Its ease of use has led to its widespread adoption at many institutions. Under the NOMS framework,

patients who should be considered for surgery are those who have high-grade spinal cord compression and/or spinal instability (Fig. 2). The high rate of local tumor control with SRS led to the concept of “separation surgery” in patients with high-grade metastatic epidural spinal cord compression.⁴⁶ The goal of separation surgery is to limit the amount of tumor resection needed by creating a tumor-free margin around the thecal sac and using postoperative SRS for the remaining spinal tumor. By minimizing tumor resection, the hope is that surgical morbidity can be reduced, although this needs further study. Recently, Tatsu et al.^{53,55} published their experience using spinal laser interstitial thermotherapy (sLITT) for separation surgery, combined with percutaneous instrumentation. This technique minimizes surgical morbidity by treating epidural tumor with LITT rather than resection. This may be particularly useful in patients who either are poor surgical candidates or need to be given systemic treatment for their metastatic disease with minimal delay to treatment after surgery.

Advances in Surgical Instrumentation and Technology

Technological innovation in industry and academia has led to the incorporation of many different surgical adjuncts to decrease patient morbidity and improve surgical efficacy. Some of these innovations have become widely adopted, including screw-rod constructs, expandable titanium cages, kyphoplasty/vertebroplasty, computer-assisted spinal navigation, and intraoperative 3D fluoroscopy or CT. The trend toward minimally invasive approaches has influenced the development trajectory in all these different areas.

Placement of surgical instrumentation in patients with vertebral column tumors is performed for the purpose of providing stability due to either pathologic fracture causing instability or tumor resection via a surgical approach that causes iatrogenic instability. Modern instrumentation today primarily consists of posterior screw-rod constructs^{15,49} and various forms of vertebral column reconstruction (Fig. 3). Hook placement and wiring strategies are sometimes utilized, but the screw-rod technique has become the primary means of posterior stabilization. Screw-rod instrumentation can span multiple spinal segments, provides 3-column support, and is safe to place with minimal risk of neurological or vascular morbidity.^{35,36}

Intraoperative imaging and integrated computer-assisted spinal navigation can reduce the risk of hardware malposition and the need for subsequent revision.^{44,56} Today's spinal navigation systems primarily use intraoperative 3D fluoroscopy¹ and CT⁶² to register the patient's spine to a fixed reference array attached to the patient. These systems are useful not only for assistance in screw placement but also can be useful during tumor resection. Spinal navigation can assist the spine surgeon in real time by defining the current extent of tumor resection in relation to surrounding bony structures. This is particularly useful in the event of significant distortion of normal anatomy by tumor. It is also possible with high-resolution imaging to identify

tumor margins when attempting gross-total resection. For primary spinal tumors, we have fused preoperative MR images with intraoperative CT scans to create a 3D tumor model that is used with navigation to identify tumor margins and avoid tumor transgression (results pending publication). Spinal navigation is also particularly useful during mini-open exposures, as the amount of exposed anatomy available for intraoperative reference by the surgeon is reduced. Integration of navigation can potentially reduce patient morbidity during these approaches by localizing normal neurovascular structures without necessarily exposing them and minimizing the amount of soft-tissue dissection necessary to visualize the pathology of interest.

There are a range of options for vertebral column reconstruction after tumor resection that have been developed over the last several decades, with many viable solutions, including various polymethylmethacrylate constructs,^{45,60} mesh cylindrical cages,¹⁷ strut grafts,⁴³ and expandable cages.^{18,52} Expandable cages, either titanium or polyetheretherketone (PEEK), have become perhaps the most popular method of vertebral column reconstruction following vertebral column tumor resection. Some advantages of expandable cages over other reconstruction options include their minimal insertion profile, ability to expand the cage in situ to create a solid fit in the bony defect, ability to correct sagittal plane deformity, and ability to insert autograft and/or allograft into the cage for osseous integration. Their smaller insertion profile allows relatively straightforward insertion from a posterior thoracic/lumbar approach,⁵² or mini-open thoracic/lumbar anterior approach,¹³ as well as an anterior cervical approach.

Another method of providing vertebral column support for pathologic vertebral body fractures is vertebroplasty or kyphoplasty. Vertebroplasty was first described in the late 1980s²³ followed by kyphoplasty a decade later.^{4,54} For each procedure, polymethylmethacrylate is injected into the fractured vertebral body via a percutaneous transpedicular approach. Kyphoplasty has the additional step of inflating a balloon in the vertebral body to create a cavity prior to cement injection, which can help reduce kyphotic deformity and increase the overall cement volume injected. Both procedures have been shown to improve pain scores (visual analog scale), reduce narcotic usage, and improve quality of life (SF-36).¹² These procedures can be particularly useful as an adjunct prior to SRS,²⁵ both to relieve mechanical back pain and provide mechanical stability. SRS has been shown to significantly increase the risk of vertebral body fracture at the treated level,⁵¹ particularly in patients with a high SINS score.³⁸ Prophylactic cement augmentation can be considered in these high-risk patients.

Advances in Radiotherapy

As previously mentioned, SRS has changed the overall treatment paradigm for vertebral column tumors. Up until the late 20th century, radiation for spine tumors was performed using EBRT.²⁷ While conventional EBRT is an effective modality for radiosensitive tumors such as lymphoma and myeloma, other solid tumors such as renal cell carcinoma do not respond as well.⁴¹ In 1995, Hamil-

FIG. 2. Neurological, oncological, mechanical, and systemic (NOMS) framework for treatment of spine metastases. cEBRT = conventional EBRT; ESCC = epidural spinal cord compression. Reproduced with permission of Wiley, from The NOMS framework: approach to the treatment of spinal metastatic tumors. Laufer I, Rubin DG, Lis E, Cox BW, Stubblefield MD, Yamada Y, Bilsky MH. *Oncologist* 18(6):744–751, 2013; permission conveyed through Copyright Clearance Center, Inc. Figure is available in color online only.

ton et al.²⁹ applied the principles of stereotactic radiation therapy developed by Lars Leksell to the treatment of 5 patients with spine metastasis using a linear accelerator and a spine-mounted frame. The encouraging early results led to further technological development to improve spine registration, tumor targeting, and radiation delivery accuracy. The CyberKnife system was the first advanced SRS platform applied to the treatment of spine tumors.⁵⁰ There have been many iterations of this technology since then, with impressive local tumor control rates of over 90% when used as the primary treatment modality for metastatic spine tumors.²⁴ For primary spine tumors, the results have been mixed, with most recommending SRS as either postoperative adjuvant treatment or primary therapy for those with unresectable or recurrent tumors.^{9,10,26,34}

Proton-beam radiotherapy and more recently carbon ion radiotherapy are 2 other potential treatment options for primary spine tumors today. Proton-beam radiotherapy can deliver a large dose of energy with a sharply localized peak (Bragg peak), which means less radiation to surrounding normal tissues.³⁹ This is particularly appealing for tumors of the spine, as it can be difficult to deliver high doses of radiation without injuring the spinal cord. Proton-beam radiotherapy has been shown to have local control rates for spinal chordomas and primary sarcomas at least as high or higher than that for photon-based radiotherapy.^{14,31,33} A recent meta-analysis comparing photon- and particle-based radiotherapy following surgery for chordoma suggested that proton radiotherapy may have an increased long-term overall survival compared with SRS.⁶³ Carbon ion radiotherapy, like proton radiotherapy, relies on charged particles to deliver energy to a target and has the same advantages as photon therapy in terms of dose drop-off. The primary advantage of carbon ion radiotherapy is the higher relative biological effectiveness versus both proton- and photon-based treatments. The

FIG. 3. Illustrative case of a 68-year-old woman with a thoracic spine metastasis causing epidural spinal cord compression seen on sagittal MRI of the thoracic spine with contrast (A). The patient underwent a posterior modified costotransversectomy with partial corpectomy, followed by posterior pedicle screw segmental instrumentation and expandable titanium cage vertebral column reconstruction. Postoperative sagittal CT scan of the thoracic spine showing the anterior reconstruction (B) and a 3D reconstruction showing both the anterior and posterior instrumentation (C). Figure is available in color online only.

5-year local control rates after carbon ion radiotherapy for patients with unresectable chordomas and sarcomas of the spine have been reported to be nearly 80%.^{32,42} Patients who undergo resection as the primary treatment may benefit from early postoperative particle radiation therapy versus salvage radiation therapy for recurrence.³¹

Advances in Medical Therapy

In the last decade, there have been multiple exciting developments in the medical treatment of cancer, particularly with development of monoclonal antibodies that affect signal transduction pathways and cellular checkpoints. Some tumors may be particularly susceptible to this approach due to their frequent infiltration with CD8-positive T cells, namely melanoma, lung, and kidney cancer.¹⁶ Several agents have significant tumor response rates and improved patient survival, namely inhibitors of *BRAF*,^{21,40} PD-1,²⁸ PD-L1,⁴⁸ and CTLA-4.³⁰ *BRAF* is a proto-oncogene that produces a protein involved in cell growth and is commonly mutated in melanoma patients. Patients with melanoma and a *BRAF* mutation (V600E) given a *BRAF* inhibitor have been shown to have significantly improved overall survival and progression-free survival versus traditional chemotherapy.^{11,21} Inhibition of CTLA-4 (cytotoxic T-lymphocyte antigen-4), an immune checkpoint, with the monoclonal antibody ipilimumab has been shown to improve survival in melanoma³⁰ and is being investigated for use in a number of other cancers. Agents that inhibit the PD-1 checkpoint, or its ligand PD-L1, have been shown to improve survival in patients with non-small cell lung cancer,⁴⁸ melanoma,²⁸ and renal cell carcinoma.⁵⁹

Cancer immunotherapy has altered how we view prognosis for patients with metastatic spinal disease, particularly for cancers previously thought to be resistant to either chemotherapy or radiation therapy. Scoring systems such as those by Tomita⁵⁸ and Tokuhasi⁵⁷ and their colleagues

utilize the primary tumor site as one of the factors in determining prognosis. Considering the last decade's immunotherapy advances, the utility of these systems should be viewed skeptically. As patients with metastatic disease live longer, surgery technical considerations for surgery, such as construct durability, should be a consideration to prevent long-term complications, such as hardware failure, that may become more frequent.

Conclusions

The incorporation of these advances has led to hope for many patients, with improved survival for some and decreased surgical morbidity. Technological innovations have been occurring rapidly, as have discoveries in cancer biology and targeted therapies. If the last several decades have taught us one thing, it is that the future of surgical treatment for vertebral column tumors will likely not resemble treatment today.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Gokaslan. Acquisition of data: Fridley. Drafting the article: Fridley. Approved the final version of the manuscript on behalf of both authors: Gokaslan.

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