Finding the ‘right’ care for spine tumors

A Message from Edward C. Benzel, MD

Between 1 and 2 million cases of cancer are diagnosed annually in the United States. Roughly one-third of these will develop spinal metastases, with 20 percent developing spinal cord compression. Spine involvement with cancer, hence, is commonplace.

So often, patients with complex medical problems, such as a spine tumor, are misdiagnosed or channeled through a myriad of clinician portals and associated diagnostic and therapeutic options before the ‘right’ option is ‘discovered.’ This usually happens when specialists refer to specialists in an unstructured clinical environment.

What if a ‘structured’ clinical environment were available? What if a ‘system’ could provide a truly multidisciplinary approach to clinical care? What if this system could provide ‘state-of-the-art’ care — such as stereotactic radiosurgery and the many clinical advantages associated with such technology? What if it could offer an approach similar to a tumor board for evaluation and consultation, in which all medical specialties that potentially could be involved in the decision-making process are involved?

Oftentimes with complex clinical problems, the patient and family are left in the dark regarding what should be done. The patient and family feel ‘out there’ — not knowing who to trust or where to go. They too often hear the statement “I have nothing to offer and cannot help you” — and are offered no meaningful alternatives. This should happen infrequently when a program utilizes a multidisciplinary approach. A system that provides ‘one-stop shopping’ is obviously desirable. Such a system does not tell the patient that “I have nothing to offer and cannot help you.”

Long-term follow-up is almost always needed after initial diagnosis and treatment. This can be provided by either the tertiary center or by the referring physicians and their teams. Either may be appropriate, depending on the circumstances. Cleveland Clinic’s Center for Spine Health Spine Tumor Team facilitates both options, depending on the circumstances and the desires of the patient and referring physician, as well as the patient’s needs.

Referrals to our Center for Spine Health Spine Team come from the greater Cleveland metropolitan area, the surrounding states, and far beyond — including a significant number of international clientele. A truly multidisciplinary team can and, in the case of the Center for Spine Health Spine Tumor Team, does provide one-stop shopping and comprehensive coor-
An Evaluation of Literature Regarding Management of Metastatic Spinal Disease

By Thomas E. Mroz, MD

The most efficacious treatment for patients with spinal metastasis has been debated for decades. Spinal surgery for metastatic disease is never curative and is always palliative. The ultimate goal of either nonsurgical or surgical management is to optimize the patient’s functional outcome and, if possible, to improve survival. There are three main avenues of care for metastatic spinal lesions: corticosteroids, radiotherapy (RT) and surgery. The development of metastatic epidural spinal cord compression (MESCC) — a major threat to all cancer patients that can lead to paraplegia — is a factor in determining appropriate treatment. It is important in these instances to promptly recognize and treat MESCC.

Corticosteroids helpful pretreatment therapy, but carry side effects

Steroids are a helpful bridge to definitive therapy for patients with MESCC, and most studies have demonstrated clinical efficacy. Sorensen and colleagues performed a randomized clinical trial on the utility of high-dose corticosteroids versus no steroid treatment prior to radiation therapy in patients with MESCC. Gait function after treatment was defined as a success, and was obtained in 81 percent of patients who received steroids, compared with 63 percent of patients who did not. There was no intergroup difference in median survival. The side effects of high-dose steroids are considerable, however, and have been reported by several authors. Data from Heimdal and colleagues indicate that side effects can be minimized and clinical efficacy maintained with lower doses of corticosteroids. Based upon the available literature, an IV dose of 10 mg dexamethasone followed by a maintenance dose of 4 mg to 6 mg every six to eight hours usually is sufficient for most patients with MESCC prior to RT.

Radiotherapy alone suboptimal

Radiotherapy (RT) is a common treatment for patients with MESCC. In regards to radiation dosage regimens, Rades and colleagues conducted a large retrospective study. They reported on 1,304 patients with MESCC treated with five different radiation dosing regimens, comparing their motor function, ambulatory status and in-field recurrences. Of those who were not ambulatory before RT (477 patients), twenty-six percent (126 patients) regained the ability to walk after treatment; there was no significant differences found between dose schedules. On a multivariate analysis, the RT schedule was found not to be significantly associated with functional outcomes; however, age, performance status, primary tumor histology, involved number of vertebrae, interval from cancer diagnosis to MESCC, pretreatment ambulatory status and time of developing motor deficits were significantly associated with functional outcome and with survival. Others have similarly identified the number of involved vertebrae, time of motor deficit development before RT and tumor histology to be of prognostic value.

RT’s use as a sole treatment, while a standard for patients with MESSC, has shown suboptimal statistics overall. Less that 50 percent of patients with MESCC treated with RT alone ever walk again, and the likelihood of paraplegic patients recovering the ability to walk after RT is quite small. It is clear that conventional RT has a major role in the treatment of patients with spinal metastasis who are not at risk for pathologic fracture. In patients who do have pathologic fractures or who are at risk of developing them, the value of RT as a sole treatment regimen (i.e., without surgical reconstruction and stabilization) should be considered carefully.
Radiotherapy with surgery produces better outcomes than RT alone

A topic of particular controversy has been the relative value of surgery combined with RT vs. RT alone in treating spinal metastasis. The largest randomized, controlled clinical trial to date was published by Patchell et al. in 2005. One hundred and one patients were enrolled who had a tissue-proven diagnosis of cancer, evidence of MESCC, ≥ one neurologic sign or symptom, but not totally paraplegic for ≥ 48 hours, and expected survival ≥ three months. Of note, radiosensitive tumors were excluded, including lymphomas, multiple myeloma and germ-cell tumors. Fifty patients were randomized to circumferential decompression/stabilization surgery within 24 hours of randomization and 3 Gy X 10 fractions of radiotherapy within 14 days postoperatively; the other fifty-one patients were treated only with RT.

Primary outcomes included ability to walk and secondary outcomes were urinary incontinence, Frankel scores (functional status), maintenance of motor function (ASIA score), need for corticosteroids, opioids and survival time. The results indicated that more patients treated with surgery were able to walk compared with the RT group (84 percent vs. 57 percent, P=0.001). Surgically treated patients were also able to walk longer (median 122 days vs. 13 days, P=0.003). Patients treated surgically also had a longer survival time (126 vs. 100 days, P=0.033), a reduced need for narcotics (P=0.002), less need for corticosteroid use (P=0.009), better maintenance of continence (156 vs. 17 days, P=0.016), and better maintenance of functional ability as assessed by the Frankel score (566 vs. 72 d, P=0.0006) and of neurological function as assessed by the ASIA score (566 vs. 72 d, P=0.001). The authors concluded that for patients with spinal cord compression due to metastatic disease, surgery plus radiotherapy resulted in better outcomes compared with patients treated with radiotherapy alone.

Surgery: circumferential approach reported better outcomes than laminectomy

The surgical goal of improved patient outcome primarily is achieved by the resection of epidural tumors and stabilizing the spine, both of which may serve to diminish pain and restore neurological function and/or to prevent neurological deterioration. Indications for surgery include metastatic lesions that result in structural decompensation (e.g., pathological fracture) or neurological deterioration due either to a pathological fracture and/or to epidural compression by tumor in a patient who is a candidate for surgery.

The surgical outcomes reported by Patchell et al., who employed circumferential decompression and stabilization, are in stark contrast to the reports of others who used laminectomy alone as the index surgical procedure. These studies and others like them underscore the natural history of spinal metastatic disease and the biomechanical principles of the spine. More than 85 percent of metastatic spinal lesions will occur in the vertebral body, which is anterior to the spinal canal. As a tumor grows, it most often results in ventral neurologic compression, and in many cases erosion of the anterior column of the spine, which supports about 80 percent of physiologic axial load of the spine. Laminectomy not only fails to directly decompress the spinal cord or cauda equina, it also destabilizes the posterior column of the spine in an instance of anterior insufficiency due to bony destruction by tumor. This often can lead to pathologic fracture, kyphotic deformities and, in such cases, increased pain and neurological demise. The circumferential approach to patients with MESCC results in an adequate neural decompression coupled with stabilization, both of which are required for optimal treatment.

Clearly, several factors for each patient with metastatic spine lesions must be taken into account in designing the most efficacious method of treatment(s). The tumor type, degree of spinal involvement, neurologi-
cultural status, co-morbidities, life expectancy, nutritional status, the risks and benefits of surgical intervention and the realistic expectations of the treating physicians and the patient all must be carefully considered when delivering care for these complex patients.

Thomas E. Mroz, MD, is a spine surgeon with Cleveland Clinic’s Center for Spine Health. His specialty interests are minimally invasive spinal surgery, complex cervical spine surgery, cervical deformity, cervical spondylotic myelopathy, cervical radiculopathy, cervical disc arthroplasty and spinal tumors.

REFERENCES


Vertebral Augmentation for Spinal Metastases

By Isador Lieberman, MD, and Krzysztof B. Siemionow, MD

For those cancer patients who develop symptomatic spinal metastases and spinal cord compression, the tumor-induced osteolysis may lead to pain, dysfunction and, ultimately, vertebral collapse. Unfortunately, pathologic fractures resulting from vertebral destruction are frequently the first presentation of a new cancer.

Furthermore, osteolytic destruction of the spinal column has become even more of a clinical issue because recent advances in oncologic management have prolonged patient survival. This is due to improvements in oncologic management, which coincidentally may predispose the patient to further bone loss and vertebral body collapse.

Typically, the diffuse osteolytic involvement results in painful, progressive vertebral compression fractures at multiple levels over time. Treatment with bed rest, bracing and analgesics were the standard of care for most of these patients and have proven to be of limited benefit, especially when considering the progressive spinal kyphosis and its consequences.

Given the detrimental effects of non-operative care and the morbidity associated with open surgical reconstruction and internal fixation of osteolytic vertebral compression fractures, there is a need to address these issues in a less invasive and equally effective fashion.

Vertebral augmentation has been used successfully in the treatment of all forms of metastatic disease and multiple myeloma involvement of the spine. Probably the most significant clinical issue when considering treatment for these patients is the increasing survival time associated with improvements in chemotherapy and radiotherapy. The majority of morbidity and mortality is caused by skeletal failure because of bone destruction. Therefore, timely intervention with effective, less invasive skeletal reconstruction is of ever-increasing importance. As we have gained experience with the technique and have witnessed the early and sustained clinical improvement in pain and function, we now advocate early treatment of any fractured or collapsing vertebral body. This philosophy should avoid the structural and debilitating functional effects of a progressive spinal kyphotic alignment, and obviate the need for more invasive surgical intervention.
Cement augmentation stabilizes spine and relieves pain

Cement augmentation of the vertebral body has been used for the relief of pain in the spine as a result of tumor involvement since it was first described by Gallibert in 1984.1 This technique of vertebroplasty involves the injection of low-viscosity liquid bone cement (poly-methylmethacrylate [PMMA]) into the damaged vertebral body via a percutaneous approach under image guidance. This technique has been shown to stabilize the fractured vertebral body and to relieve pain caused by tumor.

If multiple vertebral levels collapse, global spinal deformity becomes more of an issue. This is common when there is generalized spinal involvement as in multiple myeloma. Under these circumstances, the kyphoplasty technique of vertebral augmentation can be used to stabilize the spine and correct the deformity. Kyphoplasty involves the percutaneous placement of a trochar into the vertebral body. This allows the passage of a balloon-like inflatable bone tamp (IBT) into the vertebral body. The inflation of the IBT under image guidance is designed to produce a cavity within the vertebral body and to restore lost vertebral height. The cavity is then filled with bone cement after the IBT is removed.

Concerns: cement leakage, dissemination and infection

Even though bisphosphonates have resulted in a significant decrease of skeletal morbidity, skeletal damage already sustained at the time of diagnosis as well as the pain resulting from these events limits mobility and, thus, increases morbidity and possibly mortality. Vertebral augmentation in the setting of osteolytic collapse is a safe and effective procedure; however, like any intervention it may have unwanted consequences. The most significant consequence of vertebroplasty or kyphoplasty is symptomatic cement leakage. If the cement is not confined to the margins of the vertebral body, it may embolize to the lungs or may impinge on the neurological structures. To avoid this complication, we advocate the strict adherence to patient selection criteria for use of these techniques, the use of biplanar fluoroscopy with continuous screening during actual insertion of cement, and the use of advanced techniques such as multiple layered injections to re-establish a posterior cortex.

Some osteolytic lesions of the spine are soft and can be quite vascular. The near-fluid consistency of the tumor makes it easy for thick cement to displace it and results in impressive cement filling of the vertebra. One concern however, is the further dissemination of tumor with these techniques. The effects of this dissemination, of what is an already widespread disease, are still not known. We do not suspect any significant systemic effects and our clinical experience with multiple myeloma supports this. One further concern is the risk of infection in these debilitated patients. To date in our experience, immediate post-operative infection of the cement block has

Vertebral augmentation has been used successfully in the treatment of all forms of metastatic disease and multiple myeloma involvement of the spine.

Need Caption for images.
not been seen. We have seen some late (greater than six months after the procedure) hematogenous seeding, which, as expected, was a difficult entity to treat.

**Allows for concurrent oncologic treatment**

One of the most significant advantages of these vertebral augmentation techniques is that we were also able to proceed safely in most patients simultaneously with any chemotherapy or radiotherapy, provided their WBC count was adequate and coagulation profile was normal. This is by virtue of the fact that there is nothing that must heal. The skin incision is a 2 mm stab incision and once the cement cures, the vertebral body is stabilized. These vertebral augmentation techniques provide for spinal stability while the concurrent chemotherapy or radiotherapy provide for tumor control.

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Isador Lieberman, MD, is Chairman of the Medical, Interventional and Surgical Spine Center at Cleveland Clinic in Florida. His specialty interests are minimally invasive spine surgery, disc replacement surgery, scoliosis, spine tumors, osteoporosis, spine fractures, spinal deformity, kyphosis and spondylolisthesis.

Krzysztof B. Siemionow, MD, is a resident in the Department of Orthopaedics.

**REFERENCE**

Intradural Spinal Cord Tumors: Diagnosis and Treatment

By Richard P. Schlenk, MD

Intradural spinal cord neoplasms vary in their presentation, natural history and treatment, depending upon their pathology and anatomical location. While accounting for only a minority of all spinal tumors, early diagnosis is of great importance. Any delay in treatment, as with many spinal tumors, can lead to loss of strength and sensation, resulting in significant loss of independence and permanent disability.

Extradural tumors more common than intramedullary

Intradural tumors are classified by anatomical location as either intramedullary (within the spinal cord) or extramedullary (outside the spinal cord but within the dura mater).

Extradural tumors are most commonly neoplasms of the intradural locale (85 percent). These tumors by definition originate within the dura, yet outside the confines of the spinal cord. They are typically slow growing and can distort and compress the spinal cord, causing significant loss of neurological function below their location. These tumors rarely invade the spinal cord proper. The three most common neoplasms are schwannoma, neurofibroma and meningioma, and collectively comprise approximately 80 percent of all extramedullary neoplasms. Schwannomas and neurofibromas originate from different regions of the intradural component of exiting nerve roots, but both are, in large part, benign. Meningiomas arise from the dura mater lining and most typically arise from the dorsal-lateral region.

Intradural tumors are more variable, aggressive neoplasms than extramedullary types. The most common are astrocytomas, ependymomas and hemangioblastomas. Overall, they are relatively uncommon tumors, comprising only 2 percent of all spinal neoplasms. However, they do account for 10 percent of pediatric central nervous system neoplasms. In adults, 85 percent to 90 percent of intramedullary tumors are the glial subtypes, astrocytoma or ependymoma. Ependymomas account for approximately 60 percent to 70 percent of all spinal cord tumors found in adults. In children, 55 percent to 65 percent of intramedullary spinal cord tumors are astrocytomas. Hemangioblastomas account for only 5 percent of intramedullary tumors, and paragangliomas, oligodendrogliomas and gangliogliomas account for the remaining lesions.

Present with variable symptoms

The symptoms related to intradural tumors are usually insidious in onset and secondary to the slow-growing nature of the vast majority of these neoplasms. Signs and symptoms may be present for months or years prior to the time of diagnosis. Depending upon the location and pathology of the tumor type, the initial presenting complaints vary.

Extradural spinal cord tumors of nerve-sheath origin commonly present with pain related to nerve-root irritation. Later, as spinal cord compression becomes more prominent, nerve sheath tumors may begin to cause myelopathic symptoms, which, when left untreated, may become severe. Meningiomas most commonly present with symptoms related to myelopathy. Patients with intramedullary spinal tumors of glial origin (i.e., ependymomas, astrocytomas) present with variable symptoms. It often takes many months or years to present with symptoms. Back pain may present at the level of the lesion. Objective deficits on physical examination secondary to intramedullary tumors commonly includes sensory loss and weakness (often mild even with large lesions). Symptoms may be quite similar to those of syringomyelia or cervical spondylotic myelopathy.

Patients with ependymoma display a slight female predominance and present on average in the early fifth decade. Pain may be nocturnal and dyesthetic. Patients with low-grade astrocytomas tend to experience symptoms over a mean duration of many years. Patients with malignant astrocytomas have a much shorter duration of four to six months between symptom onset and diagnosis. Hemangioblastomas
present usually by the fourth decade of life and one-third of patients have a familial disorder, such as von Hippel-Lindau disease. Hemangioblastomas have a predilection for the posterior columns and often present with associated neurological complaints.

**MRI useful in diagnosis**

Magnetic resonance imaging (MRI) is the study of choice for the diagnosis of spinal cord tumors. The usage of intravenous contrast can greatly assess the anatomic boundaries of tumor growth. Many intramedullary tumors have an associated syringomyelia or have a cystic component, which MRI can assist in delineating.

Cat scan myelography can be a useful tool when MRI is not obtainable and can help differentiate between intra- and extradural tumor pathology. Cat scan myelography is not particularly helpful in defining intramedullary pathology. Occasionally spinal angiography may be helpful when MRI suggests that the pathology may be hemangioblastoma. However, it usually is not indicated in the workup of spinal cord tumors.

**Surgery most common treatment**

Surgery is the mainstream of treatment for the vast majority of symptomatic intradural spinal cord tumors. The goals of surgical intervention are to preserve or restore neurological function and to provide a cure in most cases of spinal cord tumors.

Intradural tumors are in large part approached through a midline posterior spinal approach. Surgical resection of extramedullary nerve sheath tumors often involves removal of a significant amount of bone to avoid any retraction of the spinal cord. Many nerve sheath tumors are both extradural and intradural. Removal of a large component of bone may be necessary for safe and aggressive surgical resection. Often this necessitates spinal fusion. Nerve sheath tumor resection usually involves removal of the parent nerve root, which, in 90 percent of patients, can be done without motor deficit.

Meningiomas usually arise from the dorsal and lateral aspects of the dura. These tumors can be resected with preservation of the underlying dura mater. In general, neurofibromas, schwannomas and menigiomas can be successfully removed with a low recurrent rate and without the need for adjuvant therapy. Patients who present with radicular pain or early myelopathy typically have resolution of presenting symptoms.

Tumors of the intramedullary location pose a different set of challenges and risks. Resection requires a laminectomy for bony exposure. Due to the location of these tumors, a midline myelotomy is almost always required to gain access to the neoplasm (unless the tumor is visible at the surface). Intramedullary tumor resection is dependent upon the presence of a cleavage plane between the tumor and the surrounding spinal cord. The presence of syringomyelia
can actually assist with the identification of the plane that separates cord from tumor. Due to the more aggressive histopathology and anatomical location of intramedullary tumors, a surgical cure is obtainable, but in general less so than compared with extramedullary types.

Postoperative complications differ markedly between tumors of the intra- vs. extramedullary types. Extramedullary tumor resection is uncommonly associated with worsening of neurological deficit immediately after surgery. Deterioration of neurological function after resection of intramedullary tumors usually occurs and must enter into the preoperative discussions with patients. However, neurological recovery occurs in 80 percent of these patients. The remaining patients have permanent deficits after surgery. In general, patients who present with severe deficits are most likely to sustain further loss from surgery and are less likely to recover.

Radiation treatment is controversial

The use of postoperative radiation therapy is not indicated for benign tumors in the extramedullary location. The role for radiation therapy in patients with gross total resection of intramedullary neoplasms remains controversial. Often radiation is withheld and serial spinal MRIs are performed to assess for tumor recurrence. However, radiation may assist with tumor control in cases of incomplete resection of intramedullary neoplasms. A multidisciplinary team consisting of radiologists, medical and radiation oncologists, and surgeons is suggested to assist in the decision-making process.

Advances in radiographic imaging are responsible for earlier diagnosis and precise surgical planning for aggressive treatment of intradural tumors. The use of intraoperative microscopic techniques, electrophysiological tools, advancement in spinal instrumentation and radiation techniques has all led to an increased capability to successfully treat the most common intradural tumor pathology. Malignant tumors remain difficult to cure with surgical resection. However, advances in the understanding of tumor biology and adjuvant treatment will offer much hope in the battle to improve outcomes and survival.

Richard P. Schlenk, MD, is a neurosurgeon with Cleveland Clinic’s Center for Spine Health and Vice Chairman for Education of Neurosurgery. His specialty interests are complex spinal reconstruction, spinal deformities, spinal tumors, traumatic spinal surgery and the surgical treatment of osteoporotic compression fractures.
Contemporary Techniques for Spinal Reconstruction Following Tumor Excision

By Michael P. Steinmetz, MD

Spine surgeons often are asked to evaluate patients whose cancer has metastasized to the spine for the treatment of intractable pain or spinal cord compression caused directly or indirectly from the metastatic lesion or lesions. Untreated, these tumors can lead to paresis or paraplegia.

Early literature concluded that surgery plus radiation is no better than radiation alone for the management of metastatic spinal disease (see article on page 2). This has resulted in surgery only being used as salvage therapy. Patients often undergo radiation therapy upfront and surgery is used only if there is tumor progression or neurological decline. With advances in ventral spine surgery and instrumentation, however, surgery has proven to be very effective, perhaps better than radiation in certain circumstances. These include metastasis with spinal cord compression, pathologic fracture and/or spinal instability.

**Early surgery did not provide full decompression and stability**

Surgery for spinal metastasis in the 1970s and early 1980s consisted of decompressive laminectomy alone. Simple laminectomy fails to address key issues paramount to the management of spinal metastasis. First, the tumor is most often located ventrally in the vertebral body. Laminectomy does not allow significant resection of the tumor and full decompression of the spinal cord from the ventral mass. Second, decompression often resulted in instability following surgery, which resulted in neurologic deterioration and/or pain. This is evidenced in multiple studies that failed to find superiority of surgery plus radiation to radiation alone.1,2

**Current strategies allow for surgery as first-line therapy**

Recently, ventral, ventrolateral and dorsolateral approaches to the spine have become popular in addressing ventral spine pathology for the reconstruction of the weight-bearing anterior column and the placement of ventral instrumentation. These approaches allow complete resection of the tumor, reconstruction of the anterior column of the spine and instrumented stabilization. With the familiarity with ventral approaches, advances in spinal instrumentation and increased understanding of the pathophysiology of spinal metastasis, some have
argued that in select cases, surgery should be offered as first-line therapy as opposed to a salvage operation. These cases include single or possibly multiple spinal metastasis with spinal cord compression (even with no or mild neurologic deficit), pathologic fracture and/or spinal instability.

**Ventral and ventrolateral approaches allow tumor removal and reconstruction**

Ventral and ventrolateral approaches allow direct access to the vertebral bodies and tumor. In the thoracic spine, this may be accomplished through a corridor in the chest, or thoracotomy. The lung may be retracted aside to expose the entire side of the spine. The thoracic spine from approximately T3 through T12 may be easily exposed through this approach (see figures 1 and 2). For T12 and L1, the diaphragm may be incised and the retroperitoneal space entered. The approach affords the surgeon access into the chest for the thoracic spine and the retroperitoneal space for the lumbar spine. For tumors of the lumbar spine, L1 through L4, a retroperitoneal flank exposure may be used. The peritoneal sac may be mobilized to expose the ventrolateral aspect of the spine. For L5, often a pure anterior approach is used, either retro- or transperitoneal. The tumor is removed and the spinal cord and/or cauda equine is completely decompressed.

The removed vertebral body may easily be reconstructed through this approach. Choices of material for this reconstruction include the patient’s own bone, rib or iliac crest; cadaver bone, femur or humerus; cages, PEEK (medical-grade plastic), carbon fiber or titanium; and polymethyl methacrylate. The spine may be stabilized with ventrolateral plates or rod constructs. The choice of reconstruction largely depends on type of tumor and life expectancy. For example, a patient with breast cancer and a single metastasis to the spine may be expected to have a life expectancy greater than one year. A surgeon will likely use a bone product to obtain a fusion and long-term stability. If the patient has poorly controlled lung cancer with metastasis to other organs, including the spine, a surgeon would likely use methyl methacrylate to provide immediate stability, but fusion with a bone product would not be required due to a likely few month life expectancy.

**Dosolateral approaches allow reconstruction and instrumentation placement through same incision**

Dosolateral approaches permit ventral decompression of the spinal cord, reconstruction of the anterior column and instrumentation, all through the same dorsal incision. A variety of approaches have been described, including transpedicular, costotransversectomy and lateral extracavitary. All provide an increasingly lateral exposure of the spinal cord,
respectively. The advantage of this type of approach over pure ventral approaches is the ability to place dorsal instrumentation (i.e., pedicle screws) through the same incision. (see figures 3 and 4). The disadvantage is the limited visualization of the ventral spinal cord. At times, complete decompression may be difficult.

**Studies of ventral procedures report better outcomes than laminectomy**

Many studies using these ventral procedures have reported excellent outcomes. The results have been superior as compared with decompressive laminectomy alone. The authors have concluded that modern tumor surgery with approaches that permit ventral decompression of the spinal cord and stabilization permit a reduction in pain and recovery time or preservation of neurologic function following surgery. Many have begun to use these surgical strategies as first-line therapy and not only when radiation has failed. A recently released, multicenter randomized study has also confirmed these conclusions. In a highly select group of patients with metastasis to the spine, modern spine surgery (emphasizing ventral decompression) was found to be superior to radiation alone. The authors recommended that, in certain clinical situations, surgery be viewed as first-line therapy.

**Michael Steinmetz, MD, is assistant professor in Cleveland Clinic’s Center for Spine Health. His clinical interests are spinal oncology, adult deformity, reconstructive spine surgery and minimally invasive surgery. His research interest is in spinal cord regeneration and plasticity.**

**REFERENCES**


The management of spinal metastases has undergone a profound paradigm shift in the 21st Century. Until recently, many patients were offered only conventional radiation, with no other options if this treatment failed.

The new millennium, however, has ushered in novel and successful treatment options for these patients, including greater acceptance and proven effectiveness of surgical treatments, minimally invasive surgical decompression and stabilization procedures, more effective chemotherapy for many primary malignancies, and a novel treatment option known as stereotactic spine radiosurgery as a stand-alone treatment or an adjunct to other treatment modalities.

At Cleveland Clinic, we offer Novalis® Shaped-Beam (BrainLAB, Inc.) stereotactic spine radiosurgery for the treatment of spinal metastases. Stereotactic spine radiosurgery is a ground-breaking, non-invasive treatment that allows for the accurate and precise delivery of a highly selective dose of conformal radiation to the spine. Stereotactic spine radiosurgery is made possible through recent advances in radiation delivery systems, digital imaging, computer processing, spine immobilization and motion-tracking devices. With as little as a single session given on an outpatient basis, a limited volume encompassing the tumor can be very exactly targeted (see figure 1). This technique allows a highly selective radiation dose to be delivered to the tumor, resulting in effective pain or tumor control while at the same time minimizing the radiation dose to adjacent critical structures such as the spinal cord. This decreases both acute and delayed morbidity related to treatment.

The most common indication for spine radiosurgery is pain, which is reported in more than 80 percent of patients with spinal metastases. Pain relief is rapid, durable and achieved in greater than 85 percent of patients after stereotactic radiosurgery, often within a few days to weeks. Other indications for the procedure include:

• Initial tumor treatment
• Treatment after surgery for residual tumor
• Radiation boost following conventional treatment for more radio-resistant tumors
• Progression after other treatment modalities such as surgery, conventional radiation and chemotherapy have failed

Spine radiosurgery results in several distinct and significant advantages. It is a non-invasive outpatient procedure with proven safe and effective treatment outcomes; it involves a short treatment time, no patient discomfort and no convalescence; and it is independent of the patients’ clinical status or medications. Given the negligible dose of radiation to the fascia and skin, radiosurgery can be undertaken soon after open surgery. Furthermore, this single treatment modality results in little hospital-based treatment time for patients who often can be quite debilitated and have a limited life expectancy.

Most importantly, the data clearly supports that most patients achieve rapid and significant pain improvement. Figure 2 shows prospectively collected pain outcome measures in fifty patients with metastatic spine tumors. There is statistical improvement in patient pain scores in as little as one week — a truly meaningful outcome in quality of life for patients with disabling pain.

Thus, stereotactic spine radiosurgery is an exciting and novel treatment for tumor control, palliation of pain, prevention of pathological fractures prior to ex-
cessive metastatic destruction of the vertebral body and for stopping the progression or reversing certain neurological deficits due to benign or malignant spine tumors. This new and effective treatment is an important option in our ability to effectively treat patients with spine tumors and rapidly is becoming an important part of the treatment Cleveland Clinic provides to patients with spine tumors.

Lilyana Angelov, MD, is head of spinal radiosurgery at Cleveland Clinic. She is a neurosurgeon who specializes in neuro-oncology, with a particular interest in brain and spine metastatic disease and stereotactic radiosurgery.

**Figure 1:** Spine radiosurgery treatment plan for a patient with breast metastasis to the spine. Complete pain relief was achieved in one month.

**Figure 2:** Improvement in pain scores in 50 patients with painful spinal metastases treated with stereotactic spine radiosurgery.

The most common indication for spine radiosurgery is pain, which is reported in more than 80 percent of patients with spinal metastases.
Intrathecal pumps in metastatic spinal pain

By Milind Deogaonkar, MD

Intrathecal opioid infusion using implantable and programmable pumps is an established therapeutic option that has been in use for the last three decades. It is extremely effective in pain control in selected patients with malignant and non-malignant tumor pain, and pain due to metastatic spinal disease, as well as for complex regional pain syndrome, failed back syndrome, neuropathic pain, mechanical back pain, arachnoiditis, post-stroke pain, spinal cord injury pain and peripheral neuropathy.

While oral opioids remain effective in controlling most types of pain, their efficacy is limited by the central nervous system and gastrointestinal side effects. Because intrathecal infusion is directed to the receptors in the spinal cord, smaller doses of opioid are required than with oral or intravenous methods. Typically, the intrathecal to oral morphine dose conversion is 1:300, with the lower dose resulting in reduced systemic effects from the drug.1

Metastatic spinal disease pain can be tumor-related or treatment-related

The pain syndromes in metastatic spinal disease are secondary to tumor-related pain and treatment-related pain. Tumor-related pain can be due to a nociceptive stimulus in patients where the tumor is affecting the mechanical stability of spine, or it can be neuropathic pain if the tumor is causing entrapment of sensory nerves. The pain also can be due to increased cerebro-spinal fluid (CSF) concentrations of inflammatory modulators like IL-8 and PGE2 released by the vertebral metastatic tumor load.

Treatment-related pain includes post-surgical pain, post-radiotherapy pain and pain related to post-chemotherapy syndromes such as myelopathies and distal extremity neuropathies.

Pumps block pain projection

Five distinct subtypes of opioid receptors have been identified, three of which seem to have analgesic properties (mu, delta and kappa), and are present in the spinal cord and brain. Mu receptors are the most effective; their activation leads to the release of an intermediate intracellular protein called G-protein, which in turn activates associated K+ channels, which results in an efflux of K+ in the cell, leading to hyperpolarization and membrane stabilization. These modulations are most prominent in laminae II and III of the spinal cord (also known as substantia gelatinosa). Stabilization of cells at this central station in pain pathways leads to blocking of pain projection in the neuraxis, as postulated by the ‘gate control theory.’ Opioids administered intrathecally are carried in the CSF cranially and caudally before achieving a stable CSF concentration.

Morphine is the most common medication used in intrathecal pain pumps; it is used in 70 percent of pumps.2-4 Other medications used in intrathecal pumps are hydromorphone, sufentanil, fentanyl, meperidine, bupivacaine, clonidine, Zoconotide and methadone.

Pumps beneficial when other analgesics fail

The World Health Organization’s analgesic ladder directs cancer pain management to begin with non-opioid analgesics, then extends to mild opioid anal-
analgesics. When these therapies fail or are limited due to systemic side effects, intrathecal pain pumps can be used as a therapeutic alternative. The selection criteria for cancer patients considered for intrathecal drug delivery are described by Krames in the Journal of Pain and Symptom Management as follows:

- strong opioids have been prescribed in adequate doses and the patient is on around-the-clock dosing, not as-needed dosing;
- the patient experiences inadequate pain relief or intolerable side effects from systemic opioids;
- the patient has a life expectancy greater than three months;
- rule out tumor encroachment of the thecal sac.

Pump implanted using two-staged approach

The most commonly used implantable, programmable drug delivery system is the Medtronic SynchroMed® Infusion System (Medtronic, Minneapolis, Minn.). This system has been commercially available since 1988 and consists of an implantable, programmable pump, an intrathecal catheter and an external programmer (see figure 1).

Implantation of a drug infusion system generally is done in two stages. The first stage is a trial or screening test of intraspinal morphine administered via a lumbar puncture or percutaneous catheter, either by bolus injection or continuous infusion. The clinician evaluates the patient’s response to therapy by assessing pain relief using the visual analog scale (VAS), as well as activity levels. If the patient reports at least a 50 percent reduction in pain with tolerable adverse effects, it is considered a positive response and the patient is selected for the implantation of a drug delivery system.

Implantation of the catheter and pump usually is done under general anesthesia. The patient is placed in a lateral position with the side the pump is to be placed facing up. Fluoroscopy is used to identify the appropriate intraspinal intervals. A Tuohy needle is inserted and the catheter is placed in the appropriate spinal location corresponding to the patient’s pain pattern (see figure 2). Once the catheter is in place, a skin incision is made around the entry site of the needle and the catheter is anchored to the underlying fascia after confirming the CSF flow and withdrawing the needle. An abdominal incision is then made to create a subcutaneous pocket for the pump (see figure 3). The catheter is tunneled to the pump pocket and

Figure 2: Technique of implantation of intrathecal catheter
connected to the pump, which is then placed in the pocket and secured. An external programmer is used to communicate with the pump to change parameters to optimize pain control.

**Pump implantation leads to decreased pain and drug toxicity scores**

In a study by Hassenbusch et al. in patients with cancer pain, long-term epidural infusions of morphine sulfate have produced satisfactory pain relief in more than 80 percent of patients. Mean pain ratings decreased from 8.6 before pump placement to 3.8 at one month after pump placement and remained relatively stable thereafter. Mean systemic morphine equivalents likewise decreased from 77.7 mg per day pre-implantation to 27.9 mg per day at one month post-implantation with stable doses thereafter, but with increasing mean spinal infusion rates from 20.7 mg per day at one month after pump placement to 49.3 mg per day at nine months.

In another intrathecal infusion trial in cancer pain patients, pain scores and drug toxicity scores were reduced by 27 percent (p = 0.011) and 51 percent (p < 0.0001), respectively. Various other studies have shown similar improvement in VAS and pain scores after intrathecal pump implantation for metastatic and cancer-related pain.

**REFERENCES**


*Milind Deogaonkar, MD, is a neurosurgeon with Cleveland Clinic’s Center for Neurological Restoration. His specialty interests include deep brain stimulation for movement disorders, surgical treatment for refractory chronic pain and headaches, spinal cord stimulation, intrathecal pumps, lesioning procedures, surgical treatment of spasticity and peripheral nerve surgery.*

**Figure 3: Technique of making a subcutaneous pocket for the pump placement**
Evaluating and Diagnosing Spine Tumors

By Glen Stevens, DO, PhD, and Lilyana Angelov, MD

Back pain is a common problem in the population, and is due mostly to degenerative conditions. As spine care professionals, however, we must analyze all cases of back pain with an index of suspicion for spine tumors.

This is true in the case of patients with no prior cancer diagnosis as well as for patients with known metastatic disease and new back pain. Even a slight delay in spinal tumor diagnosis can, at times, be devastating for patients, as it can lead to an increased risk of morbidity and mortality related to progressive neurological dysfunction.

Back pain, especially in the middle or lower back, is the most common symptom of both benign and malignant spinal tumors. Back pain that worsens at night, is not relieved by over-the-counter medications and is not activity-related raises concern for a neoplastic process. Other symptoms of spinal tumors may include motor weakness, sensory changes, gait disturbance, increased muscle tone and spasticity or bowel and bladder dysfunction. Initial complaints often may be subtle, such as stiffness, fatigue or difficulty walking on an incline. Progressive focal neurologic deficits and change in bowel and bladder function require immediate medical attention.

Tumor classification determined by location

Spinal tumors usually are classified by location in the spine. Vertebral bodies in the spinal column are the most common site for spinal metasases. Prostate, breast, lung and renal cancers are the most likely to metastasize to this site. Intradural extramedullary tumors arise from the arachnoid membrane, nerve roots or filum terminale and include meningiomas, schwannomas and ependymomas. Intramedullary tumors (the least common type of spine tumors) arise from within the spinal cord and include astrocytomas and ependymomas. However, metastatic tumors, although rarely, can be seen in this area as well.

Certain genetic disorders such as neurofibromatosis type II and von Hippel-Lindau disease carry an increased risk of spinal tumors, so routine screening should be employed with spinal MRIs in these cases. It is important to remember that lymphoma can present in any of the described locations.

A critical issue in spine tumor management, however, is clinical evidence of a neurological deficit — a finding that often mandates urgent intervention.

Need Caption for image.
Evaluating a patient for a suspected spinal tumor often can be challenging and complex. Noninvasive spinal imaging techniques have resulted in earlier detection and improved neurological outcomes and overall survival in many patients. MRI is the preferred imaging technique for the diagnosis of spinal tumors and provides the most sensitive and specific screening imaging tool available. CT can be helpful when evaluating boney changes or when patients cannot have MRIs. Myelograms are rarely employed, but can be used to identify compressed nerve and obstructions. Once an abnormality has been identified, the need for tissue diagnosis prior to treatment needs to be made.

**Imaging vital to diagnosis**

Optimal management of spine tumors involves a multidisciplinary approach that takes into account a variety of factors, including the area and extent of spine tumor involvement, evidence of mechanical spine instability, availability of appropriate surgical options, sensitivity of the tumor to treatment modalities such as radiation therapy or chemotherapy, the patient’s systemic status and any associated significant medical conditions. A critical issue in spine tumor management, however, is clinical evidence of a neurological deficit — a finding that often mandates urgent intervention. For this to be appropriately handled, a well-functioning, interdisciplinary team is extremely helpful in determining the best treatment.

**Multidisciplinary care highly beneficial for treatment**

An extension of this team management system used at Cleveland Clinic is our interdisciplinary spine tumor board, which meets weekly to review the cases of spine tumor patients with benign and malignant, intramedullary and extramedullary spine tumors. Such a team approach offers the most advantageous upfront care, as well as further management of these very complex cases.

Glen Stevens, DO, PhD, holds joint appointments in Cleveland Clinic’s Taussig Cancer Institute and Brain Tumor and Neuro-Oncology Center. His specialty interests are adult neuron-oncology, EMG and neurofibromatosis.

Lilyana Angelov, MD, is head of spinal radiosurgery at Cleveland Clinic. She is a neurosurgeon who specializes in neuro-oncology, with a particular interest in brain and spine metastatic disease and stereotactic radiosurgery.
Finding the ‘right’ care for spine tumors

directed care to all patients, regardless of the distance traveled for their consultation.

Cleveland Clinic’s Center for Spine Health Spine Tumor Team offers consultations via eCleveland Clinic electronic services and via the Spine Tumor Board (nearly 400 case reviews since the inception of the spine tumor board in May 2006) prior to a patient’s visit to Cleveland Clinic. This structure can be used as a mechanism to determine if travel to Cleveland Clinic is indeed necessary, to confirm the recommendations of prior consultations (second opinion), or simply as a preliminary opinion regarding management. Subsequent management can be delivered locally or at Cleveland Clinic and the Center for Spine Health. This decision should be patient-centric, with multiple variables coming into play.

In these pages that follow, a collection of articles depicting the foundation of a model multidisciplinary spine tumor program, such as the Center for Spine Health’s program, are presented. Dr. Mroz begins with an in-depth discussion regarding the many management options available for treatment of metastatic spine tumors. This is followed by a discussion that focuses on the employment of minimally invasive kyphoplasty approaches to the management of vertebral column tumors by Drs. Lieberman and Siemionow. Dr. Schlenk and Dr. Steinmetz follow with a dissertation on intradural spine tumors and their management and with a review of spinal reconstruction techniques after tumor excision, respectively. Dr. Angelov then provides a description of stereotactic radiosurgery options in the overall management scheme. A review of pain pump technology to cancer pain is provided by Dr. Deogonakar and the volume is concluded with Drs. Stevens and Angelov’s discussion of the multidisciplinary approach to spine tumor care.

The employment of any or all options, as indicated, is the hallmark of the ‘ultimate’ multidisciplinary team and is the modus operandi at Cleveland Clinic’s Center for Spine Health. Our extensive experience with spine tumor care — more than 100 operations and 75 stereotactic radiosurgery procedures are performed here annually — and our structured approach to diagnosis and care provide significant advantages.

You can use this volume of Spinal Column as a guide to the decision-making process for spine tumors — a guide that provides information, as well as direction. Please read and enjoy.

FOR MORE INFORMATION
To learn more about the Center for Spine Health, please contact Dr. Benzel at 216.445.5514 or our administrator, Kathy Huffman, at 216.445.8442. To refer patients, call 216.444.2225 or 800.553.5056, ext. 42225.
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Co-Editor:
Edward C. Benzel, MD
Director, Cleveland Clinic
Center for Spine Health

Co-Editor:
Daniel J. Mazanec, MD, FACP
Associate Director, Cleveland Clinic
Center for Spine Health
Head, Section of Spine Medicine

Guest Medical Editor:
Isador Lieberman, MD, MBA

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