

# Management of spinal metastasis

## Tratamento das metástases da coluna vertebral

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### ABSTRACT

This is a brief revision about the actual concepts on the treatment of metastatic lesions of the spine with the personal experience of the author and the protocol of treatment on the subject.

**KEYWORDS:** Spinal neoplasms/ surgery; Spinal Neoplasms/therapy; Neoplasm metastasis

### INTRODUCTION

Each year, approximately 1.4 million new cases of cancer are diagnosed in the United States. It is estimated that greater than 550,000 of these new cases will die from their disease<sup>1</sup>. Despite significant advances in the overall management of cancer in the past decades, the major cause of death in most cases remains metastatic disease and its complications. The three most common sites for metastasis are the lungs, the liver and the skeletal system. Within the skeletal system, the spine is the most common site metastasis. Based on autopsy studies, approximately 5-30% of patients with cancer will develop spinal metastasis with 20% of these patients developing epidural compression<sup>2-7</sup>.

The management of spinal metastasis continues to evolve. Currently, radiotherapy, chemotherapy and a variety of surgical options constitute the primary treatment options available for patients with spinal metastasis. Identifying the appropriate management plan for each individual patient with spinal metastasis can be challenging. This paper will review the common management strategies for these patients.

### EPIDEMIOLOGY

Metastatic tumors are the most common tumors affecting the spine. The most common primary sites of origin for a spinal metastasis are breast, lung, prostate and the hematopoietic system. In most clinical series these primary sites alone account for one half to two thirds of all metastasis to the spine. However, approximately 10% of patients with symptomatic spinal metastasis present without a known primary site<sup>8</sup>.

### RESUMO

Neste artigo é apresentada uma breve revisão acerca dos conceitos atuais do tratamento das metástases da coluna vertebral acompanhada da experiência pessoal e da filosofia de tratamento do autor no âmbito desse tema.

**DESCRITORES:** Neoplasias da coluna vertebral/cirurgia; Neoplasias da coluna vertebral/terapia; Metástase neoplásica

Although the lumbar spine represents the most common site for spinal metastasis, approximately 70% of symptomatic lesions involve the thoracic spine, 15% involve the lumbosacral spine and 15% involve the cervical spine. The majority of these tumors occur in the extradural space with most originating within the vertebral body. Approximately 5% of spinal metastatic tumors are intradural and extramedullary while 3% are localized to the intramedullary space (Figure 1)<sup>8</sup>.

The route of spread to the spine has been demonstrated by Batson who noted that during periods of increased intra-abdominal/intrathoracic pressure, the abdomino-pelvic organs are drained preferentially via the valveless vertebral venous plexi<sup>9</sup>. This is the primary mechanism of spread by which tumors of the abdominal and pelvic organs embolize to the vertebrae. Spinal metastasis may also result from lo-



Figure 1  
Sagittal MRI demonstrating an intramedullary metastatic melanoma at the C2 level

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cal spread of tumor such as is the case with the extension of rectal carcinoma to the sacrum. The vertebrae, with their rich vascular network and cancellous bone interstices offers a fertile ground for implantation of tumor cells. This preferential affinity for bone tissue by tumor cells has been termed "osteotropism"<sup>6</sup>.

## CLINICAL PRESENTATION

Approximately 90-95% of patients with spinal metastasis present with pain as their chief complaint<sup>5, 10-16</sup>. The pain may have been present for a period of several weeks to a year, with a mean duration of eight weeks. The nature of the pain may be axial, radicular or referred depending on the extent of tumor involvement. A smaller percentage of patients may present with neurological deficits including sensory, motor, bowel or bladder dysfunction. In all patients with cancer who present with back pain, neck pain or symptoms of spinal cord compression, the working diagnosis should be spinal metastasis until proven otherwise.

The natural history of untreated spinal metastasis is generally one of relentless progression towards paralysis as well as loss of bowel and bladder function. Early diagnosis in these patients is critical since the results of treatment are dependent, to a large extent, on the neurological status of the patient immediately prior to treatment. Advances in neuroradiologic imaging have greatly facilitated the ability to make an early and accurate diagnosis in many of these patients.

The prognosis of these patients is directly related to three factors: 1) The biology of the tumor, 2) The pretreatment neurological status and 3) The treatment given<sup>17-19</sup>. Identifying the location and extent of the spinal metastasis and initiating treatment prior to the loss of ambulatory function is the primary goal in these patients. However some patients may present with the rapid onset of neurological deficit necessitating urgent surgical decompression without the benefit of a full clinical and radiological assessment. This early surgery is generally associated with a greater morbidity and less than optimal results<sup>20</sup>. Every effort should be made to stabilize the patient with conservative measures in order to allow for the proper planning of any indicated surgical approach.

## CONSERVATIVE MANAGEMENT

The management of spinal metastasis continues to evolve. Current treatment options include chemotherapy, radiation therapy, surgery or a combination of these options. Although many metastatic tumor types respond very well to radiation therapy and chemotherapy, others do not. The wide variety of tumor types, the tumor location, the degree of neurological involvement and the overall extent of systemic disease necessitates that each patient have an individualized treatment plan. Developing this individualized plan requires a thorough understanding of all conservative as well as surgical options available.

Chemotherapy typically involves the use of steroids to reduce the vasogenic edema that can affect the spinal cord in these patients. In addition to reducing tumor related edema, steroids can also act as an oncolytic agent to diminish the

mass of some tumors (i.e. lymphomas or neuroblastomas)<sup>21-22</sup>. However, the use of high dose steroids can also result in the development of gastric ulcers, glucose intolerance and poor wound healing. Therefore, when steroids are used, a gastric mucosal protecting agent is also administered and the serum glucose is closely monitored.

Radiation therapy is often considered the primary option for treating most cases of spinal metastasis<sup>15, 18, 22-24</sup>. The reasons for this include the fact that spinal metastasis typically occurs in the setting of widespread systemic disease with a relatively limited life expectancy. Approximately half of the patients treated with radiation therapy can be expected to achieve pain palliation and neurological improvement with the median duration of response lasting 3-6 months. Patients with radiosensitive tumors and those who are ambulatory when radiation therapy begins are more likely to remain ambulatory after treatment. Radiosensitive tumors include breast, prostate, lymphoma, germ cell tumors and myeloma. Radioresistant tumors include lung, renal cell carcinoma and sarcoma.

Radiation therapy techniques typically use a single posterior portal with one or two vertebral margins. This can result in unequal radiation dosage particularly for anteriorly located tumors. Most standard fractionation techniques use a course of 3000 Gy given in 10 fractions over two weeks. Smaller daily dose rates may allow a higher total dose to be given.

A recent development of radiation therapy for spinal metastasis is stereotactic radiosurgery. This technique uses precise localization technology to help deliver a higher, more focused dosage of radiation to the tumor bed. By focusing multiple, lower dose radiation beams directed from different angles onto the tumor bed, a much higher overall dosage can be applied without increasing radiation injury to the surrounding tissues. Initial radiosurgery techniques involved percutaneously attaching an external frame to the spine adjacent to the tumor. The frame functioned both as a reference point for tumor bed localization as well as a means to immobilize the patient during delivery of focused beam radiation. Hamilton used a modified LINAC radiation therapy system combined a skeletal fixation frame to treat patients with spinal metastasis<sup>25</sup>. Although the results were promising in many patients, the skeletal frame was cumbersome, the procedures were long and fractionated delivery of radiation therapy was not feasible.

These difficulties led others to develop a frameless method of spinal radiosurgery. The Cyberknife (Accuray Inc., Sunnyvale, CA) is a therapeutic LINAC device mounted on an industrial robotic arm that directs the treatment beam via computer control and a radiographic imaging feedback system. The imaging system consists of two orthogonally aligned x-ray cameras. During treatment, the imaging system acquires radiographs of anatomic target landmarks. The stereotactic image-guidance system analyzes these real-time radiographs and can register the landmarks to a treatment planning study to determine the target's position in six dimensions<sup>26</sup>. Control signals are then sent to the robot to adjust the planned treatment beam trajectories to

accommodate any changes in target position. This feedback system eliminates the need for a skeletal frame to rigidly immobilize the patient. The LINAC device mounted on the robotic arm then delivers radiation treatment beams from nearly anywhere around the patient according to the generated plan. The process is completely anatomic and can be easily repeated at defined intervals during treatment. Near real-time target updating aligns the radiation dose to the treatment volume with millimetric precision<sup>27-28</sup>.

A large number of patients with spinal metastasis are initially evaluated by an oncologist or a neurologist. For this reason, many of these patients are referred for radiation therapy without any surgical consultation. This can lead to the inappropriate use of radiation therapy as the initial management option in a large number of patients. This typically occurs in the setting of a patient with spinal instability secondary to vertebral body collapse or progressive spinal kyphosis. (Figure 2) In this setting, a higher degree of local control can be achieved by using radiation therapy after surgery in order to eradicate any tumor residual<sup>29</sup>.

A randomized, prospective study to assess the clinical effects of surgery and radiation therapy versus radiation therapy alone was recently completed. Patients with cord compression due to spinal column metastasis were randomly assigned to one of two treatment groups. Fifty patients received surgery for decompression and spinal stabilization within 24 hours of presentation followed by a course of fractionated radiotherapy (30 Gy at 3 Gy/day). A second group of fifty-one patients received only the course of radiotherapy. Both groups received the same corticosteroid protocol. At the study midpoint, an interim analysis revealed that the criterion of a predetermined early completion rule had been met.

In this study, those patients treated with surgery and radiation retained the ability to walk significantly longer than those treated with radiation therapy alone. The surgery patients also maintained continence and functional Frankel and American Spinal Injury Association scores significantly longer than patients receiving only radiation therapy. The surgery



Figure 2  
Sagittal MRI demonstrating metastatic involvement of C2 vertebrae with collapse and anterior angulation



Figure 3  
Sagittal MRI demonstrating significant collapse and kyphosis at C7-T2 due to extensive metastatic disease

patients required significantly less steroids and narcotics. The duration of survival was not significantly different between the two groups although there was a trend towards more survival time in the surgery group. The study concluded that for the management of spinal metastasis, a combination of early surgery followed by radiation therapy provided significantly better clinical outcomes than radiation therapy alone<sup>30</sup>.

## SURGICAL MANAGEMENT

The surgical management of spinal metastasis has undergone an extensive evolution over the last several decades. The earlier surgical management option for this condition was typically a laminectomy without spinal stabilization. However, the indiscriminate use of laminectomy resulted in an overall poor clinical outcome with a high rate of postoperative complications<sup>31</sup>. Numerous studies subsequently demonstrated that the combined use of laminectomy and radiation therapy had no demonstrable advantage over radiation therapy alone<sup>5,31-32</sup>. This led to a reduced interest in surgery for the management of these patients.

In 1978, Kakulas et al. studied the pathologic anatomy of spinal metastasis finding tumor destruction of the vertebral body in the majority of specimens examined. The vertebral body collapse was noted to be generally asymmetrical with the anterior border of the vertebrae compressed more than the posterior elements. This produced an angulation of the spine that created a maximal impact on the ventral spinal cord<sup>33</sup>. This study concluded that, in a majority of patients with spinal metastasis, laminectomy alone was an inappropriate surgical option. (Figure 3)

Several studies have assessed the clinical outcome of patients undergoing laminectomy for metastatic disease. Wright noted that laminectomy in patients with anterior column involvement produced only half as many favorable results compared to laminectomy in patients with no anterior involvement<sup>34</sup>. Brice and McKissock noted that none of the 26 patient with anterior column involvement in their series had neurological improvement following laminectomy<sup>35</sup>. Findlay reported that patients with vertebral collapse generally has a reduced prospect for preserving or regaining ambulation as well as an increased risk of neurological deterioration and postoperative spinal instability<sup>36</sup>. The word "laminectomy" unfortunately became synonymous with all forms of surgery, resulting in the widespread use of radiation therapy in these patients regardless of their clinical status or the nature of the compression.

These anatomic observations as well as improvements in surgical approach and spinal fixation options subsequently led to the increased use of anterior approaches for spinal metastasis. In 1985, Siegal et al reported a prospective series evaluating the effects of anterior spinal surgery for metastasis. Vertebral body resection was performed for patients with lesions anterior to the spinal cord and a laminectomy was performed for patients with lesions posterior to the spinal cord. Surgical patients were compared to a second group treated with radiation

therapy alone. Only 30% of patients treated with radiation therapy alone retained or regained ambulation compared to 40% of the laminectomy patients and 80% of the vertebrectomy patients. The operative mortality was similar for both surgical approaches but postoperative complications were more common in the laminectomy group, usually because of poor wound healing following radiation therapy<sup>3</sup>.

Several surgical strategies are currently available for the management of spinal metastasis. In general, surgical options will vary according to the type of tumor, the overall prognosis of the patient, the clinical status of the patient, the location of the tumor, the sensitivity to radiation therapy and the presence or absence of spinal instability. Surgical approach options include percutaneous biopsy, laminectomy, anterior corpectomy with reconstruction, posterolateral decompression with reconstruction or a combination of these options. (Figure 4) The selection of an appropriate surgical technique is individualized to each patient.

Although en bloc tumor resection is an appropriate surgical strategy for the management of many primary spinal column tumors, it is less commonly used for spinal metastatic lesions. These tumors are typically removed through a less aggressive intralaminar approach. The proximity of these tumors to neural and vascular structures limits the ability to obtain sufficient tumor margins during resection. (Figure 5) Furthermore, the general condition and overall prognosis of these patients frequently makes the en bloc approach unrealistic and prone to a significant surgical morbidity.

## INDICATIONS FOR SURGERY

In most patients with pathologies other than metastasis, the presence of neural compression and spinal instability typically warrants aggressive surgical intervention with

early decompression and stabilization. However, the shortened life span of patients with metastasis coupled with "quality of life" issues necessitates the use of a different set of criteria to assess the need for surgery. Although decompression and stabilization may preserve or restore neurological function and ease the pain of segmental instability, they do not prolong life from an oncological standpoint and may actually cause undue morbidity and mortality. These facts lead to a specialized set of indications for surgery in the patient with spinal metastasis.

As surgical options for the management of spinal metastasis have evolved so have the indications for surgery in these patients. It is important to have a clear rationale for surgery and to base the selected procedure on the expected goals of therapy as well as the location of the tumor and the overall prognosis of the patient. In general, indications for surgery include:

- 1) Establishing a tissue diagnosis when a needle biopsy is unsuccessful or contraindicated,
- 2) Failure of radiation therapy (radioresistant tumors) or progression of neurological deterioration during or following radiation therapy,
- 3) Spinal instability due to vertebral collapse or progressive spinal deformity
- 4) epidural compression secondary to bone fragments from a vertebral fracture. While these indications are relatively easy to identify, they need to be adjusted according to a variety of clinical, radiographic and anatomic factors that may be affecting the individual patient with the spinal metastatic lesion.

Tokuhashi et al proposed a scoring system using six parameters: 1) general condition of the patient, 2) number of extraspinal bone metastasis, 3) number of vertebral metastasis 4) metastasis to internal organs, 5) the primary tumor site and 6) the severity of the neurological deficits. Each parameter is given a score of 0 to 2 points with a maximum of 12. Aggressive surgery was recommended for patients having a score of 9 or more and palliative surgery reserved for patients with scores of 5 or less.<sup>37</sup> While this approach may simplify the decision-making in these patients the real difficulty lies with those patients who have an indeterminate prognosis.

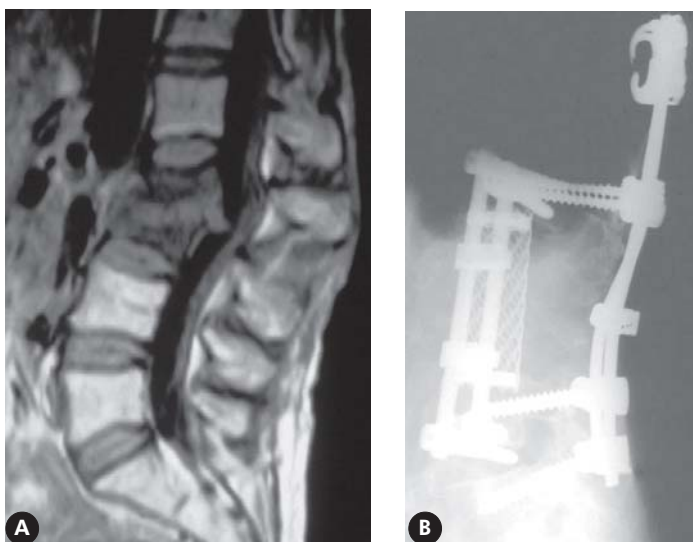


Figure 4  
A) Sagittal MRI demonstrating metastatic tumor at L2-3 with a significant compromise of the anterior spinal column. B) Lateral radiograph following L2-3 corpectomy with anterior and posterior fixation

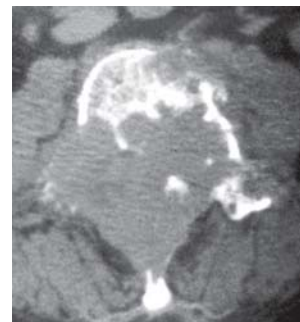


Figure 5  
Axial CT image demonstrating significant metastatic involvement of a lumbar vertebrae with extension into the epidural space

When a radiographic and clinical evaluation of the patient fails to identify the type of tumor affecting the patient, a needle or trocar biopsy can be attempted typically with the use of computed tomography (CT) guidance. For many patients with spinal metastasis, this may be the only procedure required. Not infrequently however, the anterior or epidural location of a metastatic lesion may preclude this percutaneous procedure or the biopsy obtained may be of insufficient quality and amount to establish a diagnosis necessitating an open surgical biopsy. (Figure 6). This open biopsy approach is frequently combined with a decompressive procedure with or without internal fixation.

Surgery is also indicated in patients with radioresistant tumors and in patients whose neurological deficits continue to progress during or following radiation treatments. A common scenario is that of a patient undergoing radiation treatments in the setting of spinal instability. Since it can frequently be difficult for even a spinal surgeon to identify and quantify spinal instability, it is not unusual for a neurologist or oncologist to begin radiotherapy in this setting.

Unfortunately, in the metastatic spine, there is little consensus on what constitutes instability except in the obvious cases of fracture-dislocation, vertebral translation or significant kyphosis.

Kostuik and Weinstein attempted to base stability in the setting of spinal metastasis using the three column model originally proposed by Denis for thoracolumbar trauma.<sup>38</sup> For spinal metastasis, each of the three components of the spinal column (anterior, middle and posterior) are divided into two halves creating a total of six zones. They proposed that spinal instability in the setting of tumor existed if three or more of these zones in the axial plane were destroyed by tumor.<sup>39</sup> (Figure 7)

Siegel et al proposed a number of criteria that contributed to spinal instability in the setting of metastasis. These criteria included 1) anterior and middle column involvement or >50% collapse of vertebral body height, 2) middle and posterior column

involvement or shearing deformity, 3) three column involvement, 4) involvement of same column in two or more adjacent vertebrae and 5) iatrogenic which includes laminectomy in the setting of anterior and/or middle column disease or resection of >50% of vertebral body.<sup>19</sup>

Harms suggested that the spine be considered as a mobile two-column structure with an anterior articulation through the intervertebral disc and a posterior articulation through the facet joints. The spinal column is viewed as a load-sharing system with 80-90% of the axial load passing through the anterior column and the remaining load through the posterior column. Although most tumors affect the anterior and middle columns, anterior reconstruction alone may not be sufficient to restore torsional stability or tensile strength if the posterior elements are also involved. (Figure 8) This requires a combined anterior and posterior reconstruction.<sup>40</sup>

Surgery is also indicated when epidural compression in a patient with a significant or progressive neurological deficit related primarily to bone compression. This is the case with a tumor related vertebral body fracture or deformity. While epidural compression secondary to tumor mass frequently responds to radiation therapy, bone compression does not.<sup>13</sup> (Figure 9)

**CONCLUSION**

The management of a patient with spinal metastasis is frequently a challenging task. While conservative management is appropriate for a majority of these patients, surgical options continue to evolve playing a greater role in treating this problem. The indications for surgery in this patient population are varied and at times complex. The specific indications outlined above need to be tailored to the individual patient. The risks and benefits of a surgical approach should be balanced with the patient's overall condition and prognosis and the goals and expectations for surgery should be realistic.



Figure 6  
Axial CT / myelography image demonstrating a metastatic tumor at the T2 level. The tumor is confined to the epidural space. An open biopsy, as opposed to a needle biopsy, is indicated

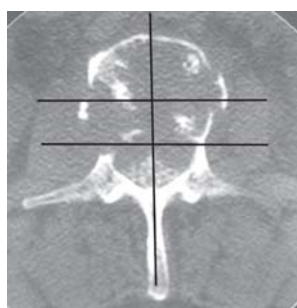


Figure 7  
Axial CT image with schematic overlay demonstrating a method for determining spinal instability in a patient with spinal metastasis. The axial plane of the involve vertebrae is divided into six zones. Lytic destruction of three or more of these zones indicates spinal instability



Figure 8  
Sagittal MRI demonstrating anterior and posterior column involvement of the mid-thoracic spine. A combined anterior and posterior reconstruction is indicated



Figure 9  
Sagittal MRI demonstrating metastatic involvement of C3 vertebrae with expansion of posterior vertebral bony cortex into the epidural space. Compression of the neural elements by bone will not respond to radiation therapy

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