Radiosurgery and radiotherapy for sacral tumors

IRIS C. GIBBS, M.D., AND STEVEN D. CHANG, M.D.

Departments of Radiation Oncology and Neurosurgery, Stanford University School of Medicine, Stanford, California

Sacral neoplasms are relatively rare. Those involving the sacrum fall into three major categories: primary benign or malignant lesions, metastatic lesions, or lesions that secondarily involve the sacrum by local extension. The majority are benign, with giant cell tumor of the sacrum representing 70% of all sacral tumors. Although the majority of malignant sacral tumors involve metastatic spread from nearby pelvic sites or distant sites, primary malignant tumors comprise a wide range of histologies including chordoma, osteosarcoma, chondrosarcoma, myeloma, lymphoma, and Ewing sarcoma. Chordoma is the most common primary malignant sacral tumor. Tumors secondarily involving the sacrum by local extension are predominantly of neural precursor, connective tissue, or supportive tissue origin. This group includes neurofibroma, schwannoma, ependymoma, epidermoid, and teratoma. We limit our discussion to the role of radiotherapy and radiosurgery in the management of the most common sacral tumors.

**RADIOTHERAPY**

Initial complete removal of sacral tumors is rare because of their proximity to neural and vascular structures. Therefore, radiotherapy plays a central role in their management. The goal of any radiation-based treatment is to allow maximal destruction of the tumor while minimizing the effects on normal tissue. The optimal therapeutic ratio is determined by maximizing tumor obliteration while minimizing normal tissue complications. By allowing for repair of sublethal damage in normal tissues, radiation fractionation enhances the therapeutic ratio. For example, it is estimated that a conventionally fractionated course of radiotherapy of 45 Gy in 22 to 25 fractions minimizes the risk of radiation-induced myelopathy to an acceptable level of less than 0.2%, and higher doses significantly increase the risk. For sacral metastases, radiotherapy may be the initial treatment of choice, whereas in some cases of primary sacral tumors, conventional radiotherapy is used in conjunction with surgery for adequate treatment of the lesion.

**Radiotherapy for Sacral Metastases**

Spinal metastases will develop in 5 to 10% of all cancer patients during the course of their illness. Metastatic tumors represent the majority of malignant sacral tumors. These metastases generally arise by hematogenic dissemination of tumor cells from primary breast, lung, renal, thyroid, and prostate carcinomas. In addition to hematogenic spread, it is not unusual for locally recurrent pelvic tumors such as rectal adenocarcinoma or advanced prostatic tumors to invade the sacrum by local extension. Although the most common presenting symptom is pain, the most catastrophic outcome is neurological compromise causing loss of bowel control, urinary incontinence, and lower-extremity weakness.

Palliative radiotherapy as a first-line intervention for spinal metastasis has been the mainstay of management since the late 1960s after several authors compared radio-
therapy with laminectomy and found no significant difference in patient outcome.3–10,20,28,42,44 More recently, a prospective trial of 209 patients with metastatic spinal cord compression were evaluated after radiotherapy and steroid treatment of the spinal metastases.27 The authors reported that pain was alleviated in 82% of patients, ambulatory ability was regained or maintained in 76%, and sphincter dysfunction was improved in 44%. Based on a thorough review of patient outcomes presented in the literature, Loblaw and Laperrriere26 concluded that radiotherapy is an appropriate first-line therapy unless osseous instability or acute paraplegia necessitate surgical intervention.

Radiotherapy for Benign Sacral Tumors

The most common benign tumors that affect the spine include hemangioma, osteoid osteoma, osteoblastoma, osteochondroma, aneurysmal bone cyst, and GCT.36 Although excision and curettage are the mainstay of treatment in most patients with benign lesions, radiotherapy has been performed for aggressive osteoblastoma, aneurysmal bone cyst, and GCTs.2,3,4,5 Because of the concern for malignant transformation, radiotherapy is generally not recommended in the initial management of these lesions. The incidence of radiation-induced malignancy after treatment of benign bone tumors has been reported to be as high as 27%.3 In modern series in which improved radiation techniques are used, the reported incidence has been lower.39,41 Even though less aggressive surgical techniques such as intraslesional excision and cementation have evolved as preferred treatment of GCT, it may be impractical to expect a good functional outcome for some aggressive sacral lesions. In such cases, radiotherapy is recommended. Local control rates with radiotherapy for aggressive recurrent GCT have been reported to range from 70 to 90% in contemporary series involving conventional doses of 35 to 68 Gy. There are data that support the contention that local control of GCT is improved at doses greater than 40 Gy. Consequently, the recommended dose for conventional radiotherapy of these lesions is 40 to 45 Gy.31

Radiotherapy for Primary Malignant Sacral Tumors

Although multiple myeloma is the most common bone tumor in adults, chordoma is the most common primary neoplasm to involve the sacrum.3,36 Sacral chordoma comprises 50% of all spinal chordomas. Chordoma is a histologically benign tumor originating from remnants of the notochord. Although it is a slow-growing tumor, it is locally aggressive with a high propensity for local recurrence and rare potential for cure.40 Radical resection is the initial treatment of choice. When this is possible, it extends the time to local recurrence compared with subtotal excision. A recent retrospective review of 27 patients with sacral chordomas treated at M.D. Anderson Cancer Center, York, et al.,19 demonstrated a statistically significant difference in the disease-free interval after radical resection of sacral chordomas compared with subtotal excision (2.27 years and 8 months, respectively) Furthermore, the addition of radiotherapy in cases of subtotally resected lesions prolonged the disease-free interval to 2.12 years compared with 8 months without radiotherapy.

Radiation doses of 30 to 50 Gy are indicated for palliation and the risks are minimal. Cummings, et al.,10 reported no differences in survival, duration of symptomatic response, and progression-free survival in a heterogeneous group of patients who underwent 50- to 60-Gy radiotherapy compared with conventional fractions to less than 50 Gy or by a hyperfractionated regimen of 44 Gy delivered in 1-Gy fractions, four times daily for 14 days. Much higher doses of 60 to 70 Gy are likely required for potentially curative intent.3

To achieve these higher doses, specialists at the Massachusetts General Hospital and Harvard Cyclotron Laboratory use a combined treatment of x-ray and proton-beam irradiation.19 Although the biological properties of protons are not significantly different from x-rays, their physical characteristics exhibited by a finite range of energy deposition with only minimal exit dose beyond the target region are significantly advantageous. These advantages are particularly important in achieving high-dose delivery to sacral chordomas. Using this approach of x-ray and proton beam therapy combined with optimal surgery, improved local control was achieved at doses greater than 77 CGE (cobalt Gray equivalent).19

Radiotherapy Techniques

Conventional radiotherapy for spinal metastasis is delivered through simple portals to doses of 30 to 40 Gy in 2- to 3-Gy fractions. For isolated sacral lesions, an opposed anterior–posterior field is typically used, encompassing one or two vertebral segments above and below the lesion. Alternatively, a three-field arrangement with two lateral portals and a single posterior field is used to spare anterior pelvic structures. A single posterior field arrangement is generally avoided for sacral lesions, particularly if lower energy beams are used, because the treatment depth will vary along the sacral hollow. More complex radiation-beam arrangements can be achieved using three dimensional conformal radiotherapy. Three-dimensional conformal therapy is particularly useful when the extraosseous component of tumor is irregularly shaped or extends into the region of normal sensitive tissues of the rectum, small bowel, and bladder. This modality involves an array of radiation beam arrangements with each field shaped according to the beam’s eye view around the target volume. In this way, normal tissue is optimally shielded for the primary radiation beam. The use of IMRT can potentially spare even more of normal structures by incorporating inhogeneous beam intensities directed at target lesions from multiple beam directions.

STEREOTACTIC RADIOSURGERY

For most sacral tumors, radiotherapy is a treatment option; however, concern regarding radiation dose to surrounding normal structures may limit treatment doses to suboptimal levels.22 The incidence of radiation-induced injuries to the lumbo-sacral plexus appears to increase with an escalated dose,30 and relapses within the radiation fields are not uncommon. Sacral lesions also often have complex topology, making conformal dose delivery difficult,40 even with the development of IMRT.

Confining radiation doses strictly to a target volume within or around the sacrum should, theoretically, enhance
lesion control while decreasing the risk of injury to the adjacent normal structures. Delivering radiation with a steep dose gradient is possible if accurately targeted. Such accuracy is difficult when using conventional radiotherapy because manual positioning of the patient, which involves attaching surface markers to the skin, limits precision and is not reproducible. With radiosurgery, single-stage sacral treatments are possible in many cases. In the event that lesions size or radiation dose to critical structures prevents single-stage treatment, multiple stereotactic treatments (staged radiosurgery) are feasible and have advantages over conventional radiotherapy because each stage allows irradiation of the target volume in a highly precise and reproducible manner. Frameless image-guided radiosurgery systems such as the CyberKnife, which allows both spatially precise treatment delivery and reproducible multiple doses, allow treatment of lesions throughout the spine, even at the level of the sacrum.

**Technological Basis of Spinal Radiosurgery**

Conventional intracranial SRS involves using a rigid frame to reference the target lesion to a known location in space. In stereotactic targeting in the brain it is assumed that the target has a fixed relationship with respect to the cranium. Because spinal lesions generally have a fixed relationship to the osseous spine, stereotactic methods involving spinal fixation are analogous to frame-based stereotactic localization of intracranial lesions.

The first spinal stereotactic surgery is attributed to Worschiloff in 1874. He used a spinal localization device attached to sinus processes to make precise cord lesions for in vivo electrophysiological studies. In 1972, Nadvornik used a similar method of open spinal fixation to perform radiofrequency ablation of the cord. Clark is said to have modified the attachment to the lamina for more accurate localization later that year. Nadvornik, et al., later modified the Worschiloff system to perform stereotactic lesioning of the lumbar spinal cord. Lax, et al., proposed an external stereotactic frame that enclosed the body from the head to the middle femoral area with foam pad stabilization, which was not rigid and permitted patient movement.

Hamilton with Lulu and colleagues developed a spinal SRS system that involved a modified LINAC and a skeletal fixation frame. In the Hamilton–Lulu extracranial stereotactic frame the patient was placed in a rigid box. Immobilization was achieved by fixing the frame to spinous processes of the patient after induction of general anesthesia. The results were promising in many patients; however, the fixation was cumbersome, resulted in long procedures, and was not feasible for fractionated delivery. Image-guided SRS was developed to deliver nonframe-based treatment with the precision of frame-based systems. This technology has three fundamental differences from conventional frame-based radiosurgical systems. 1) Referencing is based on internal radiographic features such as skeletal anatomy or implanted fiducials. 2) Near real-time radiographs are required to evaluate changes in target location and to adapt the treatment delivery to accommodate these motions. 3) Fixed isocenters are not required, which allows for irregular dose shapes and homogeneity.

**The CyberKnife System**

The CyberKnife (Accuray Inc., Sunnyvale, CA) is a 6-MV therapeutic LINAC mounted on a robotic arm that directs the treatment beam via computer control and incorporates an x-ray imaging feedback system. During treatment, the imaging system, which consists of two orthogonally aligned x-ray cameras, acquires radiographs of target landmarks. The image guidance process analyzes these real-time radiographs and can register landmarks to the treatment planning study to determine the target's position in six dimensions. The process then sends control signals to the robot to adjust the originally planned treatment beam directions to accommodate any changes in target position. This feedback eliminates the need for rigid immobilization. The LINAC then delivers radiation treatment beams from nearly anywhere around the patient according to the previously generated plan. This process is completely automatic and repeated at defined intervals during treatment. Near real-time target updating aligns the dose to the treatment volume with millimeter precision. Sacral lesions can be treated with minimal modification of standard hardware and software.

**Spinal Procedure**

**Simple Immobilization.** At our center patients with sacral tumors are fitted with an AlphaCradle (Smithers Medical Products, Inc., Akron, OH), a custom body mold filled with a plastic similar to styrofoam. This AlphaCradle maintains the general orientation of patients while simultaneously restricting motion during pretreatment scanning and during treatment.

**Fiducial Placement.** The current CyberKnife system requires implanted fiducial markers for all spinal lesion registrations. Fiducials are placed during outpatient procedures, typically lasting 15 minutes, and can be placed days to weeks before treatment. Four 2 × 6-mm surgical stainless-steel self-retaining tacks or self-tapping screws were placed through stab skin incisions under fluoroscopy in a noncoplanar pattern within the bone tissue of the sacrum.

**Treatment Planning.** Following AlphaCradle immobilization and fiducial placement, contrast-enhanced computerized tomography scans of the sacrum were acquired for treatment planning and to provide a basis for generating the digitally reconstructed radiographs used during position tracking. The treatment system uses an inverse planning solution. The plans are designed in the following manner: the volume of the lesion to be treated is defined; the desired prescription dose is specified; volumes of sensitive structures such as the spinal cord are defined and the maximum radiation doses to these critical regions are specified; and computed optimization then produces the best-fit treatment plans that conforms to the defined constraints.

**Treatment Delivery.** Patients with sacral lesions are typically treated in the supine position. The robotic arm moves the LINAC sequentially through the planned beam positions delivering the planned dose. At each position, the imaging system can check the target position and send corrective pointing directions to the robot. These position checks are performed approximately once a minute, although checks are made more frequently in patients with
more frequent movements. All patients are treated on an out-patient basis, with staged treatments given on consecutive days.

**Clinical Experience With Radiosurgery**

At Stanford University School of Medical, we reviewed our experience of 53 patients with spinal lesions treated with the CyberKnife. Three of these patients harbored lesions involving the sacrum. The first patient harbored a schwannoma of the L5–S1 nerve root; the neural foramen was widened secondary to local bone erosion along the superior edge of the sacrum. This patient received 18-Gy SRS to the 75% isodose line in two stages. The second patient had previously undergone surgery and radiotherapy for an L-3 ependymoma when follow-up magnetic resonance imaging revealed a new S1–2 ependymoma (drop metastasis). The lesion was treated with 18 Gy to the 80% isodose line in a single stage. A third patient underwent SRS for a large renal cell metastasis of the sacrum for which previous 40-Gy radiotherapy had failed (Fig. 1). This tumor received a dose of 18 Gy delivered in two stages to the 76% isodose line. There were no SRS-related side effects in any of the three patients. Gerszten, et al., reviewed their series of 56 spinal tumors treated in 46 patients. Four of the tumors (all metastases) were sacral and received single-stage doses up to 18 Gy. No radiation-induced side effects were noted.

**CONCLUSIONS**

Although sacral neoplasms represent only a small subset of spinal tumors, their treatment can be challenging because of their involvement with adjacent neural and vascular structures. Conventional radiotherapy has been performed for decades as either primary or adjunctive treatments for sacral tumors. More conformal forms of radiotherapy, including IMRT, have the potential to reduce complications by including lower volumes of normal tissue within treatment volumes. Stereotactic radiosurgery represents the most conformal treatment to date, and early experiences at several institutions have shown this modality to be effective for both primary and secondary sacral lesions.

**Acknowledgment**

We thank Beth Hoyte for assistance with production of the figures.

**References**

Radiosurgery and radiotherapy for sacral tumors


Address reprint requests to: Iris C. Gibbs, M.D., Stanford University Medical Center, Department of Radiation Oncology, Room A-095, Stanford, California 94305-5302. email: iris.gibbs@stanford.edu.