Original Article

# Pelvic Bone Sarcomas: Controversies and Treatment Options

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**Key Words**
Pelvis, sarcoma, osteosarcoma, Ewing's sarcoma, chondrosarcoma

**Abstract**
Treatment of pelvic bone sarcomas remains one of the most challenging areas of orthopedic oncology for all members of the disease management team. Although considerable advances have been made in all aspects of sarcoma treatment, the prognosis for patients with primary sarcomas of the pelvis continues to be guarded, and therefore, much controversy exists regarding optimal surgical management, radiation therapy, and systemic therapy. This article summarizes the current treatment paradigms for the 3 most common bone sarcomas (osteosarcoma, Ewing's sarcoma, and chondrosarcoma), highlighting the unresolved issues in their management as they pertain to the pelvis. (*JNCCN* 2010;8:731–737)

Despite decades of success in the management of bone sarcomas, the pelvis remains an elusive anatomic site for all members of the bone sarcoma disease management team. Surgeons continue to struggle to obtain negative margins and reconstruct a functional limb; radiation oncologists wrestle to balance exposures that provide adequate local control while minimizing collateral damage to the surrounding vital organs; and medical oncologists toil to find novel targets for treatment as the limits of intensifying conventional chemotherapy have largely been met. Furthermore, considerable disagreement can exist among treating physicians as to the best method of obtaining local and distant control for sarcomas of the pelvis, especially as the long-term complications of individual and collective therapies emerge. This article summarizes the current treatment paradigms for the 3 most common sarcomas of the pelvis: osteogenic sarcoma, Ewing's sarcoma, and chondrosarcoma. The unresolved issues in the management of these difficult cases as they pertain to the pelvis are highlighted.

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## Osteogenic Sarcoma

Osteogenic sarcoma (also called *osteosarcoma*) is the most common primary tumor of bone, with approximately 900 cases diagnosed in the United States annually. Pelvic osteosarcoma accounts for 5% to 10% of all osteosarcomas. Most cases (~75%) occur in persons younger than 25 years. In this young population, 90% occur in the extremities in a de novo fashion (> 95%). A second age peak is seen in those older than 50 years, among which more than 50% of cases arise secondary to preexisting conditions such as Paget's disease and previous radiation. In this older population, up to 40% of tumors present in the pelvis, partly reflecting the natural history of conditions frequently treated with radiation therapy (RT). Within the pelvis, the ilium is the most common location for osteosarcoma, followed by the acetabulum then the ischium. Tumors frequently involve more than one part of the pelvis, and iliac tumors often infiltrate the sacrum (Figure 1).

Although the 5-year survival for localized extremity osteosarcoma approaches 70%, pelvic osteosarcoma portends a more dismal prognosis with a 5-year survival of approximately 30%.[1–3] The inferior survival of patients with pelvic osteosarcoma is multifactorial, including large tumor volume at presentation, difficulty in achieving adequate surgical margins, higher likelihood of metastatic status at presentation, inferior necrosis after preoperative chemotherapy, and presence of macro-

scopic tumor emboli in the large regional vessels.[2,4,5]

Resectable high-grade osteosarcoma is typically treated with multiagent chemotherapy combined with complete surgical resection of the tumor. Complete surgical resection is paramount to cure patients with osteosarcoma. Although advances in imaging techniques have played an important role in the surgeon's ability to plan complete resections, the complexity of pelvic anatomy coupled with the proximity of the genitourinary organs and sacrum makes margin-negative surgical resections exceedingly challenging. Intralesional resections (positive margins) are associated with high local recurrence (80%–92%),[2,6] as are even radical and wide resections (34%–50%). Most series fail to show a difference in survival for patients undergoing limb salvage surgery versus true hemipelvectomy (amputation).

High rates of local recurrence for pelvic osteosarcoma show the need for further local therapy. The role of RT in improving survival for patients deemed unresectable or for those with positive microscopic surgical margins is unresolved.[7] Historically, RT for osteosarcoma was not advocated because of its intrinsically high radioresistance based on early studies showing limited efficacy at doses less than 60 Gy.[8] However, with the advances in radiation delivery techniques, such as intensity-modulated RT and proton-based therapy, therapeutic doses exceeding 50 Gy can be delivered safely to most anatomic sites, including the pelvis, while minimizing exposure to the surrounding organs. Recent reports have shown improved local recurrence rates of 75% for patients with close or positive margins after definitive resection and up to 50% for patients who underwent biopsy alone without surgical resection.[9,10] The overall 5-year survival showed improvement, especially when radiation was administered after resection rather than for local recurrence. In addition, experience is emerging on the bone-seeking radioisotope samarium-153 and the use of concomitant radiosensitizing agents, such as gemcitabine, to supplement conventional radiation in the treatment of osteosarcoma.[11,12] Although optimal doses and delivery methods must be better defined, radiation plays a role in treating patients at highest risk for local recurrence. Clearly, the use of radiation in the management of osteosarcoma should be reinvestigated in light of the evolution of RT in the past 2 decades.

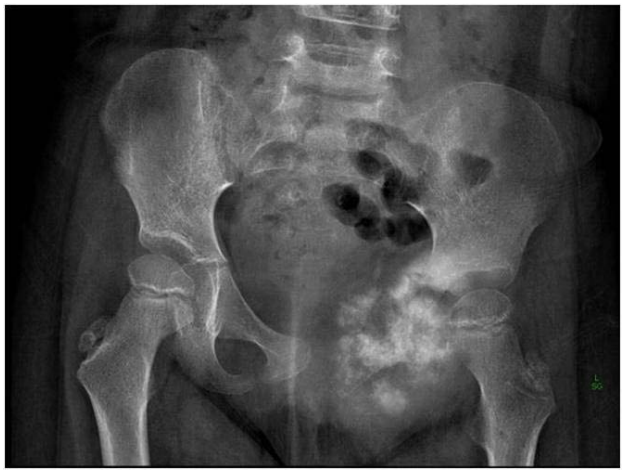

**Figure 1** Radiograph of an osteosarcoma of the pelvis. Bone-forming tissue is shown involving the acetabulum and ischium.

Patients with pelvic tumors are clearly at high risk for distant relapse and death. Tailoring systemic therapy based on risk stratification has not been an effective strategy for treating osteosarcoma. Intensification of current chemotherapy regimens has largely met its limit. Numerous investigative agents have been considered to supplement conventional chemotherapy. A recent large randomized trial[13] studying the novel immunomodulator muramyl-tripeptide-ethanolamine (MTP-PE) showed that although it improved overall survival for patients with osteosarcoma, those with pelvic primaries did not experience benefit. A large cooperative trial conducted by the European and American Osteosarcoma Group (EURAMOS) is randomizing postoperative systemic treatment to additional ifosfamide and etoposide, or interferon-α based on specimen necrosis. The benefit of this approach for treating patients with pelvic tumors is currently unknown.

## Ewing's Sarcoma

The Ewing's sarcoma family of tumors includes classic Ewing's sarcoma of bone. Ewing's sarcoma is the second most common variety of primary bone tumors in children and young adults, with approximately 400 cases diagnosed annually in the United States. Unlike osteosarcoma, Ewing's sarcoma has a high predilection for the axial skeleton (45%), with most axial tumors arising in the pelvis. Approximately 75% of patients will present with localized disease, and of those approximately 70% will experience a 5-year survival. Patients with metastatic disease at

presentation experience an inferior survival rate of 20% at 5 years, with those with nonpulmonary sites faring worse than those with lung-only metastases.[14] Several adverse prognostic factors have been consistently identified in Ewing's sarcoma, including advanced stage, tumor larger than 8 cm, older age (> 14 years), pelvic location, response to chemotherapy, translocation type, and detectable fusion transcripts in bone marrow.[15–20]

The general therapeutic approach to patients with localized Ewing's sarcoma consists of 3 segments: 1) cytoreductive therapy usually in the form of induction chemotherapy, 2) definitive local control that can be achieved by surgery or radiation alone or in combination, and 3) adjuvant chemotherapy. Vincristine, doxorubicin, cyclophosphamide, ifosfamide, and etoposide given in cyclic combinations are considered standard front-line treatment. The collective efforts of several national and international study groups have shown the efficacy of multiagent chemotherapy in improving survival from historical values of less than 10%.[21–24] The improved outcomes observed in Ewing's sarcoma are the direct result of patients being managed in worldwide cooperative trials.

An estimated 25% of Ewing's sarcoma presents in the pelvis, representing the most common bony location in most large series. The most common sites within the pelvis are the ilium followed by the pubis.[25] Patients with pelvic tumors often possess larger tumor volumes compared with extremity sites (Figure 2A) and more often have clinically detectable sites of metastatic disease at presentation. Furthermore, patients with pelvic primaries continue to relapse after 6 years, whereas nonpelvic primary sites usually plateau at 5 years.[26] Although patients with nonmetastatic extremity tumors can expect local and distant tumor control in 70% of cases, patients with pelvis tumors historically experienced 2- to 3-fold increased local failure and decreased survival. More recent series are reporting local and distant control rates for pelvic Ewing's sarcoma that are approaching those of nonpelvic.[18,24,27–29] The increased survival and local control rates in patients with pelvic disease is from the individual and combined improvements in systemic and local therapies. Optimizing chemotherapy doses and schedules, combined with improved supportive therapy, better radiation techniques, and more aggressive surgery, has led to significant progress overall most noticeably seen in pelvis tumors.

Perhaps the single most controversial topic in the management of Ewing's sarcoma is the modality through which to achieve local control, especially in the pelvis. No randomized controlled trials directly compare radiation and surgery. For decades, definitive RT was the standard local treatment for Ewing's sarcoma. As improvements in imaging have evolved and limb salvage techniques have been refined, surgery has become the preferred method of local control when negative margins and acceptable morbid-

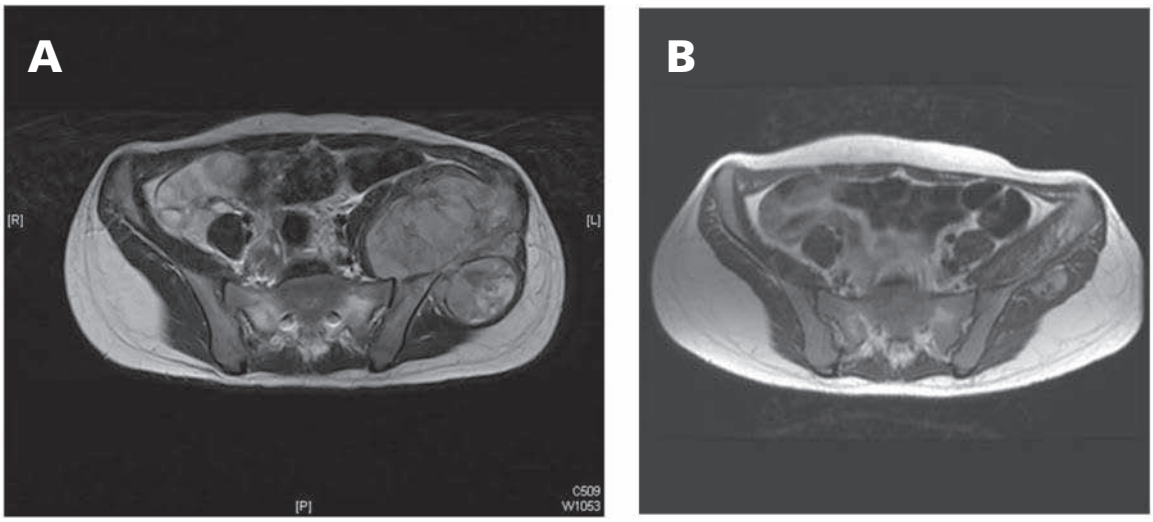


**Figure 2** (A) Ewing's sarcoma of the pelvis with intra- and extrapelvic extension of an associated soft tissue mass at presentation before cytoreductive chemotherapy. (B) The soft tissue extent of the tumor has decreased in size considerably after chemotherapy, facilitating definitive surgical resection.

ity can be expected. This trend is largely because of reports of higher rates of local failure in patients treated with radiation alone (30%) compared with those treated with either surgery alone or surgery combined with radiation (10%).[30–33] These observations are confounded by several factors: 1) a selection bias favors surgery, because patients who underwent radiation only usually had larger tumors in less-favorable locations, 2) these reports were from older series in which modern radiation techniques were not routinely used, and 3) in these older series, optimal systemic treatment regimens were still being elucidated that have since been shown repeatedly to have significant impact on local recurrence. For pelvic tumors specifically, the data are confusing, with some studies showing higher local recurrence and decreased event-free survival in patients treated with RT alone than in those treated with surgery alone or surgery in combination with RT,[34,35] and other investigations failing to show any difference among local control methods.[27]

Achieving negative margins while reconstructing a functional and durable limb in the pelvis represents the most challenging endeavor for orthopedic oncologists. Although patients with small pelvic tumors with greater than 90% necrosis that can be resected with negative margins will likely have an excellent outcome, this scenario unfortunately does not represent the typical patient with pelvic Ewing's sarcoma. Therefore, it is reasonable to conclude that surgery should be used in patients showing a good radiographic response to preoperative chemotherapy (Figure 2B) and when the surgeon expects to remove the tumor with negative margins without amputation. Radiation alone should be used when margin-negative resection is not achievable or surgery will result in unacceptable morbidity.

A combination of radiation and surgery is an effective strategy for tumors resected with a positive margin or close margins in the setting of poor chemotherapy necrosis. Although therapeutic doses, field size, and fractionation schedules have been established, these parameters are worthy of reinvestigation, especially given the long-term side effects of RT and the potential for secondary malignancies that occur with greater frequency in patients with a history Ewing's sarcoma.[36,37]

## Chondrosarcoma

Chondrosarcoma is the second most frequent malignant bone tumor. It usually affects middle-aged adults, with the pelvis representing the most common location. Unlike osteosarcoma and Ewing's sarcoma, chemotherapy and RT have not been shown to be reliable adjuvants for local and distant control in chondrosarcoma, and therefore surgery is the primary treatment. Chondrosarcoma of the pelvis is often high-grade, and is almost twice as likely to present with metastatic disease at presentation compared with high-grade extremity chondrosarcoma.[38] Furthermore, high-grade pelvic chondrosarcoma is associated with the highest local recurrence and worst prognosis.

The concept of low-grade pelvic chondrosarcoma is a great source of conflict. Evaluating the literature on pelvic chondrosarcoma is difficult because grading schemes for chondrosarcoma vary among institutions. In general, grading of chondrosarcoma relies on histologic interpretation and radiographic evidence, and has long been plagued with controversy.[39] The historic literature is even further contaminated by the term grade 1/2 chondrosarcoma previously used by some institutions to describe tumors that did not strictly fit the histologic criteria of grade I chondrosarcoma. These inconsistencies are magnified in the pelvis, where histologically grade I (and even grade 1/2) tumors behave clinically more aggressively.[40] Although patients with grade I chondrosarcoma of the extremity treated with intralesional excision combined with a local adjuvant experience good local control and long-term disease-free survival, grade I chondrosarcoma in the pelvis treated with intralesional or marginal excision is associated with unacceptably high rates of local recurrence, which tend to be a higher grade.[41] Furthermore, locally recurrent pelvic chondrosarcoma can be a surgical quagmire, unfortunately often without a solution. Although it has become evident that intralesional treatment of pelvic chondrosarcoma should be avoided regardless of grade, this approach is not uniformly accepted by all institutions.[42]

The role of RT in the treatment of chondrosarcoma remains unclear. As in all sarcomas, high doses are required for cure. For chondrosarcoma those doses exceed 60 Gy, which are difficult to deliver safely using conventional radiation methods. Radiotherapy using particles such as proton and heavy ions

(e.g., helium, carbon) is an attractive alternative because it allows delivery of therapeutic doses (> 60 Gy) while minimizing the exit dose to adjacent normal structures. Most of the literature on this topic pertains to chondrosarcoma of the skull base. Similar to the pelvis, the skull base represents an anatomic site in which achieving negative margins represents a significant surgical challenge. Preliminary reports show that proton therapy is effective for local control both as an adjuvant after surgical resection and as definitive treatment.[43] As particle therapy becomes more widely available and longer follow-up is reported, radiation is likely to play a more prominent role in the management of pelvic chondrosarcoma.

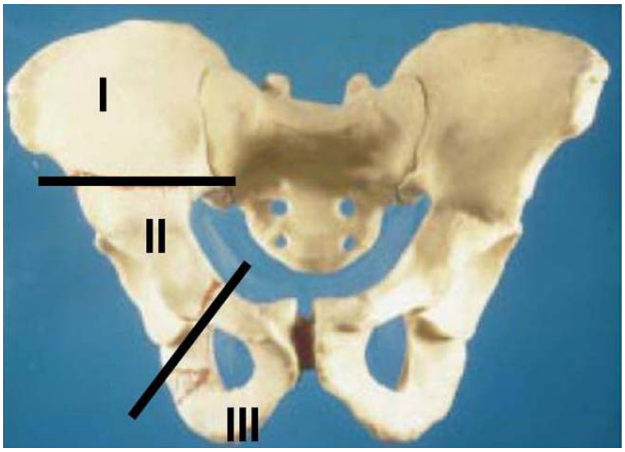


**Figure 3** The Enneking Classification of pelvic resections. Type I resections involve the ilium. Type II resections involve the acetabulum. Type III resections involve the ischium.

## Reconstruction Options After Surgery for Pelvic Sarcomas

Surgical treatment for sarcomas of the pelvis consists of amputations or limb-salvage pelvic resections. The term *hemipelvectomy* refers to an amputation through the sacroiliac joint. Modifications of the operation exist, including extended hemipelvectomy through the sacrum or amputation distal to the sacroiliac joint, maintaining portions of the pelvis.

The term *internal hemipelvectomy*, which refers to limb-salvage pelvic resections, is a misnomer; these operations should be called *pelvic resections*. Pelvic resections are often classified according to the system of Enneking (Figure 3). Type I resections remove all or part of the ilium with type I-S, including a portion of the sacrum. Type II resections remove the periacetabular area. Type III resections remove the ischium. Combinations such as a type II + III resection indicate that the acetabulum and ischium were removed en bloc. Resection of the entire innominate bone would be a type I + II + III resection. Intralesional excision of pelvic tumors, followed by placement of rebar-type constructs, has a limited role in the treatment of pelvic bone sarcoma. Although this procedure was once used to treat low-grade chondrosarcomas, the local recurrence rate is unacceptably high. Rebar-type constructs are still used for metastatic disease and in palliative settings.

All pelvic surgery has associated short- and long-term complications, with perioperative mortality rates of approximately 5% and perioperative morbidity rates easily exceeding 50%.[44] Common short-term complications include wound necrosis and deep infection. Long-term complications include implant failures and infection. These associated complications largely drive surgical decision making, namely amputation versus limb salvage and reconstruction options.

Treatment with hemipelvectomy versus limb salvage remains controversial. What constitutes a resectable tumor without amputation varies among surgeons, and what constitutes an acceptable functional result varies among patients. However, all would likely agree that resections that do not allow for adequate margins are best treated with hemipelvectomy. Tumors that involve a combination of the surrounding femoral vasculature, lumbosacral plexus, and acetabulum should be strongly considered for amputation. For tumors that can be treated with an effective adjuvant, such as RT in Ewing's sarcoma, hemipelvectomy is rarely considered. For tumors with no well-established adjuvant, such as chondrosarcoma, hemipelvectomy is more often considered to ensure complete surgical resection.

Regarding the optimal method of reconstruction after surgical removal of a pelvic sarcoma, there is probably no single topic of greater disagreement among orthopedic surgical oncologists. The ideal reconstruction method depends on a host of factors, including the resultant defect, desired functional outcome, use of adjuvant treatment, and age of the patient.

Type I resections may not require bony reconstruction if the pelvic ring can be maintained. When the ring is disrupted, reconstitution of the mechani-

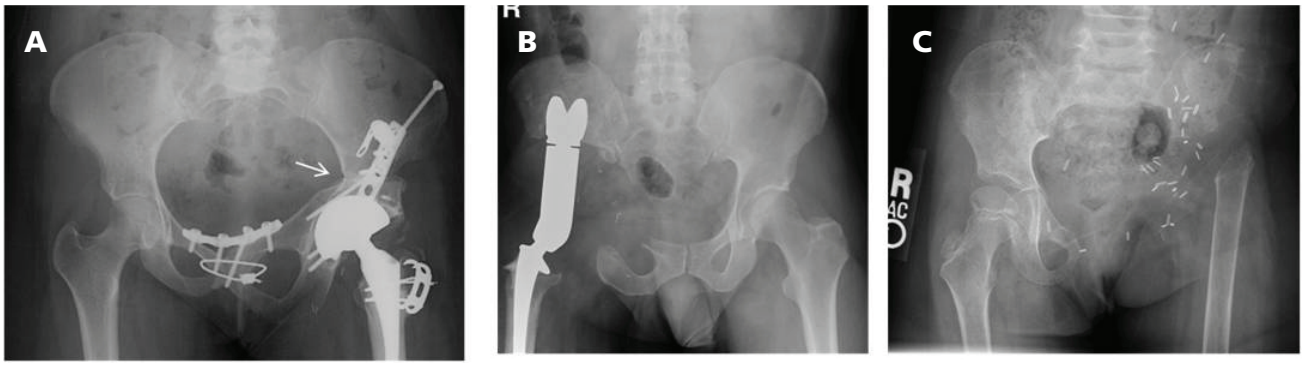


**Figure 4** Reconstruction options. (A) Allograft of the pelvis after a type II + III resection with a hemiarthroplasty of the hip. (B) Saddle prosthesis after type II resection. (C) Modified type I + II + III resection without reconstruction.

cal continuity is desired. This can be accomplished with vascularized and nonvascularized autografts and allografts and primary arthrodesis of the sacrum and periacetabular area. Type III resections typically do not require bony reconstruction. Patients experience loss of adductor strength but overall good function.

Reconstructions after type II resections and their associated combinations (types I + II, II + III, and I + II + III) are the most challenging and complicated. Options for reconstruction include biologic reconstructions with structural allografts, metallic implants, hip transposition, and iliofemoral or ischiofemoral arthrodesis (Figure 4A, 4B). All of these methods require considerable surgical expertise, a good soft tissue envelope, a lengthy recovery period, and acceptance by the patient and surgeon that complications may occur. Early and late infections are common. Joint instability and leg length discrepancy occur with moderate frequency. Ultimate implant failure is inevitable if the patient is fortunate enough to experience cure. Patients often require multiple surgeries to address the associated complications.

When these reconstructions fail for whatever reason, amputation is often performed. Because of the unavoidable complications associated with type II reconstructions, renewed interest has been shown in resection arthroplasty, or resection without reconstruction (Figure 4C). Those that support no reconstruction after pelvic resection argue that functional outcomes approach those of patients who have undergone reconstruction, without the need for repeated surgical intervention related to the complications of reconstruction. Long-term follow-up will help clarify what best serves theses complicated problems.

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