Recurrence After and Complications Associated With Adjuvant Treatments for Sacral Giant Cell Tumor

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Abstract

Background The best treatment of giant cell tumor of the sacrum is controversial. It is unclear whether adjuvant treatment with intralesional surgery reduces recurrences or increases morbidity.

Questions/purposes We therefore asked whether adjuvants altered recurrence rates and complications after intralesional surgery for sacral giant cell tumors.

Methods We retrospectively studied 31 patients with sacral giant cell tumors treated with intralesional surgery with and without adjuvants. Survival to local recurrence was evaluated using Kaplan-Meier analysis. The differences in survival to local recurrence with and without adjuvants were evaluated using multivariate Cox

regression analysis. Complications were recorded from clinical records and images. The minimum followup was 36 months (median, 108 months; range, 36–276 months). **Results** Overall survival to local recurrence was 90% at 60 and 120 months. Survival to local recurrence with and without radiation was 91% and 89%, with and without embolization was 91% and 86%, and with and without local adjuvants was 88% and 92%, respectively. Adjuvants had no influence on local recurrence. Mortality was 6%: one patient died at 14 days postoperatively from a massive pulmonary embolism and another patient had radiation and died of a high-grade sarcoma. Fifteen of the 31 patients (48%) had one or more complications: eight patients (26%) had wound complications and seven patients (23%) had massive bleeding during curettage with hemodynamic instability. L5-S2 neurologic deficits decreased from 23% preoperatively to 13% postoperatively; S3-S4 deficits increased from 16% to 33%.

Conclusions Adjuvants did not change the likelihood of local recurrence when combined with intralesional surgery but the complication rate was high.

Level of Evidence Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

This work was performed at the Istituto Ortopedico Rizzoli, University of Bologna, Bologna, Italy, and the ATTIKON University Hospital, Athens University Medical School, Athens, Greece.

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Introduction

The sacrum is the most common location of giant cell tumor in the axial skeleton and the third most common location after the knee and the radius [5, 8, 32, 35, 43]. Sacral giant cell tumors usually develop in an eccentric position but commonly extend to involve both sides of the midline [25] and into the presacral space [25, 26]. There is usually a thin cortical rim, which the soft tissue mass can

break through. In addition, these tumors have the propensity to cross the sacroiliac joints and intervertebral discs, which is unusual for many other spinal lesions and is a useful distinguishing feature of giant cell tumors [32]. Although generally considered a benign tumor, 5% to 10% are reportedly malignant, many of which are believed to be related to previous radiation therapy [5, 25, 26, 35, 43]. One to 9% of giant cell tumors metastasize to the lungs although the primary lesion is considered histologically benign [16].

The standard treatment for a giant cell tumor is aggressive curettage followed by adjuvant phenol, hydrogen peroxide, liquid nitrogen or argon beam therapy, and bone grafting or cementation [10, 15–17, 20, 21, 23, 24, 27] or wide excision [1, 3, 30, 31, 33, 36, 37]. Total or partial en bloc sacrectomy can enhance local tumor control and overall patient survival despite potential complications and neurologic dysfunction [37, 44]. Total sacrectomy is indicated when a malignant or aggressive benign lesion involves the proximal sacrum with anterior extension [6, 13, 18]. Partial sacrectomy is used for tumors with substantial involvement of the sacrum below the S2 segment because it can usually be resected with wide margins and allows patients to maintain bowel and bladder control without the need for lumbopelvic reconstruction. If complete resection cannot be easily achieved, preoperative or serial arterial embolization [10, 15, 17, 21, 24], intralesional curettage [16, 20, 27], cryosurgery [20, 27], or radiation therapy [16, 23] are alternatives. However, the best treatment for giant cell tumor of the sacrum is controversial and the role of adjuvant treatments is unclear [23]. Is recurrence different after adjuvant treatments and intralesional surgery or does it just add morbidity? The answer to this question is unclear perhaps in part because no single institution has a large experience with these uncommon tumors [23, 43].

We therefore asked whether adjuvants altered recurrence rates and complications after intralesional surgery for sacral giant cell tumors.

Patients and Methods

We retrospectively studied the medical records of 31 patients with giant cell tumors of the sacrum that were treated with intralesional surgery and adjuvant treatments at two institutions between 1986 and 2006. There were 22 females and nine males with a mean age of 29 years (range, 14–68 years). The tumor involved the S1 vertebra in 25 of the 31 patients: S1 in five, S1–S2 in five, S1–S3 in six, S1–S5 in nine, S2–S5 in four, and S3–S5 in two. In the remaining six patients, S1 was not involved. According to Enneking's classification for benign bone

tumors [11], 30 patients were classified as Enneking Stage 3 and one as Enneking Stage 2. No patients had lung metastases at presentation or multicentric tumors. Previous treatments included intralesional surgery in four patients and intralesional surgery with preoperative radiation therapy in one (Appendix 1; Supplemental materials are available in the online version of CORR). One patient (Patient 14) died 14 days after surgery as a result of a massive pulmonary embolism. The minimum followup of the surviving 30 patients was 36 months (median, 108 months; range, 36–276 months). No patients were lost to followup; all patients gave written informed consent and were included at the latest evaluation for the purpose of this study. This study has been approved by the Institutional Review Board/Ethics Committee of the authors' institutions.

Radiation therapy was administered preoperatively in one patient (total dose 47.5 Gy) and postoperatively in 20 patients (36–56 Gy). Initially, it was our practice to use radiation therapy as adjuvant treatment in every patient with a giant cell tumor of the sacrum to improve local control after surgery. However, this was reconsidered for the latest 10 patients given reports suggesting these treatments did not influence recurrences [23] and the possibility of radiation-induced sarcomas [4]. Preoperative selective arterial embolization was performed in 23 patients; in three of these patients, repeat embolization was performed because of the high vascularity of the tumors. Embolization was performed to reduce intraoperative blood loss and surgical field bleeding to improve curettage. The treatment plan was to perform preoperative selective embolization on all patients when possible. Embolization was not performed in cases in which angiography showed the lesion was not amenable to embolization because of insufficient vascular pathology of the tissue.

In all patients, we curettaged the lesion through an anterior (one patient), posterior (15 patients), or combined (15 patients) approach. Although our typical approach for intralesional sacral surgery was posterior, we used an anterior approach in patients with aggressive tumors and anterior extension. Through the anterior approach, we were able to ligate the hypogastric, internal iliac, and tumor vessels and separate the tumor from the rectum. Through the posterior approach, we used wide laminectomy and complete curettage with a curette and high-speed burr. The sacral nerve roots were identified and preserved. The S1 and S2 nerve roots are large and easy to identify and preserve; substantial and well-defined neurologic deficits from injury of the L5–S2 nerve roots were classified as major neurologic deficits. The S3 and S4 nerve roots are smaller and more difficult to identify and preserve; S3–S4 neurologic deficits including pain and hypesthesia in the outer perianal region and the penis or labia and inner perianal

pain and hypesthesia are subtle and were classified as minor neurologic deficits.

We used phenol in 14 patients, liquid nitrogen in one patient, and both in two patients (Appendix 1; Supplemental materials are available in the online version of CORR). Phenol and liquid nitrogen were applied as hemostatics during intralesional surgery to control bleeding and improve curettage. In cases in which close proximity of the sacral nerve roots was identified, neither phenol nor liquid nitrogen was applied.

Postoperative management included bed rest for 3 to 6 weeks, analgesic administration, and progressive mobilization of the patients, as tolerated. We attempted to mobilize the patients as soon as possible to prevent immobilization-related complications such as deep venous thrombosis and urinary infections. At discharge from the hospital, all patients were functionally independent; a spinopelvic brace or ankle and foot orthosis was not used in any of the 31 patients.

Followup routine evaluation was performed every 3 months for the first 3 years, every 6 months for the next 2 years, and then annually. Each followup evaluation included inquiry for sexual dysfunction; clinical examination of motor, sensory, bladder, and bowel deficit; and imaging evaluation, including CT scan and MRI of the pelvis. CT scan of the chest was performed annually. Intraoperative and postoperative complications were recorded. A complication was considered major if it was life-threatening or associated with L5-S2 neurologic

deficits; minor was considered a nonlife-threatening complication or S3-S4 neurologic deficits.

We determined the patients' survival after intralesional surgery with and without adjuvant treatments using the Kaplan-Meier analysis [19] with local recurrence as an end point. The differences in survival to local recurrence by additional treatment (with and without radiation therapy, preoperative selective arterial embolization, and local adjuvants) were estimated using the multivariate Cox-regression analysis; we used this analysis because we were simultaneously evaluating the effect of three variables on survival. The hazard represented the risk or probability of reaching the end point (eg, local recurrence or death) at a particular time [34]. The patient (Patient 14) who died postoperatively from a massive pulmonary embolism was excluded from the survival analysis.

Results

Overall survival to local recurrence was 90% (27 patients) at 60 and 120 months (Fig. 1). Three patients (10%) had local recurrence that was observed within 34 months from initial treatment. No patient developed metastases during the period of this study. At 60 and 120 months followup, survival to local recurrence after intralesional surgery was 91% with radiation therapy and 89% without radiation therapy (Fig. 2), with and without preoperative selective arterial embolization was 91% and 86%, respectively

Fig. 1 A graph showing the overall survival to local recurrence. The overall survival to local recurrence was 90% at 60 and 120 months.

Fig. 2 A graph showing the survival to local recurrence with and without radiation therapy. The survival to local recurrence with and without radiation therapy was 91% and 89%, respectively, at 60 and 120 months (95% confidence interval: 0.064–8.605).

Fig. 3 A graph showing the survival to local recurrence with and without preoperative selective arterial embolization. The survival to local recurrence with and without preoperative selective arterial embolization was 91% and 86% at 60 and 120 months, respectively (95% confidence interval: 0.068–8.449).

(Fig. 3), and with and without local adjuvants was 88% and 92%, respectively (Fig. 4). Although our data were limited for comparison of adjuvants treatments as an adjunct to surgery, and we did not control for confounding factors such as tumor volume, size, and aggressiveness, we found radiation therapy, preoperative selective arterial embolization, phenol, and liquid nitrogen had no influence on local recurrence (Table 1).

Two of the 31 patients (6%) died. One patient (Patient 14) died 14 days postoperatively from a massive pulmonary embolism and a second patient (Patient 12) who had radiation therapy subsequently died of a high-grade sarcoma. This patient had histologically proven local recurrence 34 months after intralesional surgery and radiation therapy (40 Gy), and repeat intralesional surgery and radiation therapy (30 Gy) was performed. Histologic

Fig. 4 A graph showing the survival to local recurrence with and without local adjuvants, including phenol and liquid nitrogen. The survival to local recurrence with and without local adjuvants, including phenol and liquid nitrogen, was 88% and 92% at 60 and 120 months, respectively (95% confidence interval: 0.153–20.180).

Table 1. Multivariate Cox regression statistical analysis of local recurrence by adjuvant treatments

Variable	Odd ratio	95% CI		p value
		Lower	Higher	
Radiation therapy	0.739	0.064	8.605	0.810
Preoperative selective embolization	0.760	0.068	8.449	0.824
Phenol and liquid nitrogen	1.755	0.153	20.180	0.653

CI = confidence interval.

sections of the biopsy specimen from the secondary tumor and the metastases showed a high-grade sarcoma.

Fifteen of the 31 patients (48%) had a perioperative complication. Eight patients (26%) had wound complications; two of these patients had minor wound dehiscence that did not require operative intervention and were treated with wound dressing changes, and six patients had major wound dehiscence that required wound revision. Seven patients (23%) had life-threatening massive bleeding during curettage with hemodynamic instability; in one of these patients (Patient 22), the operation had to be discontinued because intraoperative hemorrhaging was difficult to control by the anesthesiologists. This patient was reoperated on after 7 days. No patient developed cerebrospinal fluid leakage, pelvic instability, or infection. The number of patients with L5-S2 neurologic deficits decreased from seven of 31 (23%) preoperatively to four of 31 (13%) postoperatively. The number of patients with S3-S4

neurologic deficits increased from five of 31 (16%) preoperatively to 10 of 31 (33%) postoperatively.

Discussion

The best treatment of sacral giant cell tumors is controversial [23]. Many authors have reported intralesional surgery with and without radiation therapy, preoperative or serial selective arterial embolization, phenol or liquid nitrogen, bisphosphonates, and denosumab with variable results [1, 7, 16, 17, 21, 23, 24, 31, 35, 37, 40, 42–44]; in these studies, local recurrence rates were 20% to 43% [16, 17, 20, 21, 23, 27, 43] compared with 8% to 30% in other location [3, 5, 22, 23, 30, 33], and morbidity was substantial [2, 5, 6, 9, 13, 18, 23, 29, 41]. We performed this study of a relatively large number of patients with Stage 2 and 3 giant cell tumors of the sacrum and long-term followup to determine local recurrence rates and complications after intralesional surgery with and without adjuvant treatments, including radiation therapy, preoperative selective embolization, and phenol and liquid nitrogen.

We acknowledge several limitations. First is the lack of a control group of patients treated by wide resection that, although it is associated with substantial functional deficits, has consistently given better tumor control than curettage [5, 28, 39]. Second, perhaps given the relatively small sample size, we found no difference in survival to local recurrence with and without adjuvants; we acknowledge

the possibility of a Type II error. Third, when considering differences without and with adjuvants, we did not control for confounding variables such as how much tumor was left and the size and aggressiveness of the tumors that potentially could have influenced treatment choice and outcome. We presume the surgeons added adjunctive treatments to curettage when the size and stage of the tumor were increased, and almost all of these tumors are large, Stage 3, and difficult to access in the sacrum. Our exploratory regression analysis was intended to assess the differences in survival to local recurrence by additional treatment (with and without radiation therapy, preoperative selective arterial embolization, and local adjuvants) but in a mixed group of patients. Larger studies may determine some of these variables are influential. Fourth, we had no data on blood loss and numbers of transfusions, so we cannot say whether preoperative embolization reduced either.

Previous studies have reported survival to local recurrence after curettage, radiation, and embolization for sacral giant cell tumors ranging from 57% to 80% (Table 2) [16, 17, 20, 21, 23, 27, 43]. Radiation is typically combined with surgery for large sacral giant cell tumors [12, 14, 23, 38, 43]. Given the high vascularity and morbidity associated with surgical resection and/or radiation therapy, preoperative embolization provides for tumor devascularization and low local recurrence [10, 17, 21, 45]. Typically, surgery should be performed within 24 to 48 hours after embolization to prevent recanalization [45]. In this series, the overall survival to local recurrence was 90% at 60 and 120 months and the local recurrence rate was 10%. We

used radiation therapy in 21 patients and preoperative selective arterial embolization in 23 patients. Although we did not control for variables such as the volume, size, and aggressiveness of the tumors, of the factors we studied, none influenced the risk of local recurrence. This could be explained by the adequate exposure and approach and aggressive curettage performed. In our common practice, phenol and liquid nitrogen are applied as hemostatics during intralesional surgery to control bleeding and improve the curettage. In cases in which close proximity of the sacral nerve roots was identified, neither phenol nor liquid nitrogen was applied.

Intralesional surgery, partial and total sacrectomy are associated with substantial complications, including pelvic instability [6, 9, 13, 18], wound healing problems, infection, hemorrhage as well as vascular and visceral injuries [9] and necessitate sacrifice of sacral nerve roots, leading to motor deficits and bowel, bladder, or sexual dysfunction. Preserving both S1 nerve roots is important for maintaining the patient's normal gait and foot plantar flexion. Patients with bilaterally preserved S2 nerve roots will retain bowel and bladder function, but if only one S2 nerve root remains, bowel and bladder function will likely be lost [2, 29, 41]. However, if the sacral nerve roots are preserved, there is greater potential for leaving microscopic disease after gross excision and curettage. In this series, major neurologic preoperative deficits from tumor involvement of the L5-S2 nerve roots postoperatively improved because the L5-S2 nerves have large, easily identified nerve roots and are protected and preserved during curettage. Conversely, minor neurologic deficits increased postoperatively because

Table 2. Summary of reported cases on the treatment of giant cell tumors of the sacrum

Reference	Number of cases	Treatment	Followup (months)	Survival to local recurrence (months)
Guo et al. [16]	24	Intralesional surgery, intraoperative occlusion of the abdominal aorta	Mean, 58; median, 50; range, 25–132	69.6% at 60
Hosalkar et al. [17]	9	Serial selective arterial embolization	Mean, 107; median, 94; range, 46–254	78% at 108
Lackman et al. [21]	5	Serial selective arterial embolization	Mean, 90; range, 48–204	80% at 80.4
Leggon et al. [23]	10	Radiation therapy, intralesional surgery, and chemotherapy	Mean, 96; range, 11–254	80% at 36
Lin et al. [24]	18	Selective arterial embolization, intra-arterial cisplatin	Median, 105; range, 6–205	69% at 120, 57% at 180 and 240; no significant effect of cisplatin
Marcove et al. [27]	7	Cryosurgery and intralesional surgery and/or limited excision	Median, 147; range, 24–170	71.4% at 147
McDonald et al. [28]	14	Intralesional surgery	Mean, 84; range, 48–312	77% at 84
Turcotte et al. [43]	26	Intralesional surgery, radiation therapy	Mean, 94; range, 84–396	67% at 84
Ruggieri et al. [current study]	31	Intralesional surgery with and without postoperative radiation therapy, selective arterial embolization, phenol and liquid nitrogen	Mean, 118; median, 108; range, 36–276	90% at 60 and 120

distal roots (S2-S4) are more difficult to identify and preserve during curettage. Because we prefer the morbidity associated with an initially more aggressive surgical approach compared with the morbidity of possible local recurrence necessitating retreatment, we only recommend partial sacrectomy with wide margins for rare, small, distal giant cell tumors of the sacrum. Radiation therapy can have possible deleterious effects, including late pathologic fractures, fibrosis, neuritis, and radiation-induced sarcomas [4, 14, 23, 38, 43]. An incidence of 10% of radiation-induced sarcomas has been reported after radiation for sacral giant cell tumors [23]. One patient had radiation therapy and died of a high-grade sarcoma during this study; although we cannot ensure the sarcoma was radiation-induced, we recommend avoiding radiation to eliminate the risk of radiation-induced sarcomas [4]. Eight patients had wound healing problems with six of them requiring wound revision; seven patients had massive intraoperative bleeding with hemodynamic instability. Although we found no influence of preoperative embolization on recurrence, we recommend preoperative embolization for highly vascular tumors to reduce intraoperative blood loss despite our lack of data on blood loss and transfusions.

Although our study has limited power owing to small numbers and uncontrolled variables, the data suggest adjuvants do not change the likelihood of local recurrence when combined with intralesional surgery. The complication rate was high in this group of patients although the survival to local recurrence was high at 120 months.

References

- Althausen PL, Schneider PD, Bold RJ, Gupta MC, Goodnight JE Jr, Khatri VP. Multimodality management of a giant cell tumor arising in the proximal sacrum: case report. *Spine*. 2002;27:361–365.
- Biagini R, Ruggieri P, Mercuri M, Capanna R, Briccoli A, Perin S, Orsini U, Demitri S, Arlecchini S. Neurologic deficit after resection of the sacrum. *Chir Organi Mov*. 1997;82:357–372.
- Bini SA, Gill K, Johnston JO. Giant cell tumour of bone: curettage and cement reconstruction. *Clin Orthop Relat Res*. 1995;321:245–250.
- Cahan WG. Radiation-induced sarcoma—50 years later. *Cancer*. 1998;82:6–7.
- Campanacci M, Baldini N, Boriani S, Sudanese A. Giant-cell tumor of bone. *J Bone Joint Surg Am*. 1987;69:106–114.
- Capanna R, Briccoli A, Campanacci L, Gasbarrini A, Scarborough MT. Benign and malignant tumors of the sacrum. In: Frymoyer JW, ed. *The Adult Spine: Principles and Practice*. 2nd ed. Philadelphia: Lippincott-Raven; 1997:2367–2405.
- Chang SS, Suratwala SJ, Jung KM, Doppelt JD, Zhang HZ, Blaine TA, Kim TW, Winchester RJ, Lee FY. Bisphosphonates may reduce recurrence in giant cell tumor by inducing apoptosis. *Clin Orthop Relat Res*. 2004;426:103–109.
- Disler DG, Miklic D. Imaging findings in tumors of the sacrum. *AJR Am J Roentgenol*. 1999;173:1699–1706.
- Doita M, Harada T, Iguchi T, Sumi M, Sha H, Yoshiya S, Kurosaka M. Total sacrectomy and reconstruction for sacral tumors. *Spine (Phila Pa 1976)*. 2003;28:E296–E301.
- Eftekhari F, Wallace S, Chuang VP, Soo CS, Cangir A, Benjamin RS, Murray JA. Intra-arterial management of giant-cell tumors of the spine in children. *Pediatr Radiol*. 1982;12:289–293.
- Enneking WF, ed. *Clinical Musculoskeletal Pathology*. 3rd ed. Gainesville, FL: University of Florida Press; 1990:451–489.
- Gerszten PC, Ozhasoglu C, Burton SA, Welch WC, Vogel WJ, Atkins BA, Kalnicki S. CyberKnife frameless single-fraction stereotactic radiosurgery for tumors of the sacrum. *Neurosurg Focus*. 2003;15:E7.
- Gokaslan ZL, Romsdahl MM, Kroll SS, Walsh GL, Gillis TA, Wildrick DM, Leavens ME. Total sacrectomy and Galveston L-rod reconstruction for malignant neoplasms. Technical note. *J Neurosurg*. 1997;87:781–787.
- Goldenberg RR, Campbell CJ, Bonfiglio M. Giant-cell tumor of bone: an analysis of two-hundred and eighteen cases. *J Bone Joint Surg Am*. 1970;52:619–664.
- Gottfried ON, Schmidt MH, Stevens EA. Embolization of sacral tumors. *Neurosurg Focus*. 2003;15:E4.
- Guo W, Ji T, Tang X, Yang Y. Outcome of conservative surgery for giant cell tumor of the sacrum. *Spine*. 2009;34:1025–1031.
- Hosalkar HS, Jones KJ, King JJ, Lackman RD. Serial arterial embolization for large sacral giant-cell tumors: mid- to long-term results. *Spine*. 2007;32:1107–1115.
- Jackson RJ, Gokaslan ZL. Spinal-pelvic fixation in patients with lumbosacral neoplasms. *J Neurosurg*. 2000;92:61–70.
- Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc*. 1958;53:457–481.
- Kollender Y, Meller I, Bickels J, Flusser G, Issakov J, Merimsky O, Marouani N, Nirkin A, Weinbroum AA. Role of adjuvant cryosurgery in intralesional treatment of sacral tumors. *Cancer*. 2003;97:2830–2838.
- Lackman RD, Khoury LD, Esmail A, Donthineni-Rao R. The treatment of sacral giant cell tumours by serial arterial embolisation. *J Bone Joint Surg Br*. 2002;84:873–877.
- Larsson SE, Lorentzon R, Boquist L. Giant-cell tumor of bone: a demographic, clinical, and histopathological study of all cases recorded in the Swedish Cancer Registry for the years 1958 through 1968. *J Bone Joint Surg Am*. 1975;57:167–173.
- Leggon RE, Zlotecki R, Reith J, Scarborough MT. Giant cell tumor of the pelvis and sacrum: 17 cases and analysis of the literature. *Clin Orthop Relat Res*. 2004;423:196–207.
- Lin PP, Guzel VB, Moura MF, Wallace S, Benjamin RS, Weber KL, Morello FA Jr, Gokaslan ZL, Yasko AW. Long-term follow-up of patients with giant cell tumor of the sacrum treated with selective arterial embolization. *Cancer*. 2002;95:1317–1325.
- Llauger J, Palmer J, Amores S, Bagué S, Camins A. Primary tumors of the sacrum: diagnostic imaging. *AJR Am J Roentgenol*. 2000;174:417–424.
- Manaster BJ, Graham T. Imaging of sacral tumors. *Neurosurg Focus*. 2003;15:E2.
- Marcove RC, Sheth DS, Brien EW, Huvos AG, Healey JH. Conservative surgery for giant-cell tumors of the sacrum: the role of cryosurgery as a supplement to curettage and partial excision. *Cancer*. 1994;74:1253–1260.
- McDonald DJ, Sim FH, McLeod RA, Dahlin DC. Giant-cell tumor of bone. *J Bone Joint Surg Am*. 1986;68:235–242.
- Nakai S, Yoshizawa H, Kobayashi S, Maeda K, Okumura Y. Anorectal and bladder function after sacrifice of the sacral nerves. *Spine*. 2000;25:2234–2239.
- O'Donnell RJ, Springfield DS, Motwani HK, Ready JE, Gebhardt MC, Mankin HJ. Recurrence of giant-cell tumors of the long bones after curettage and packing with cement. *J Bone Joint Surg Am*. 1994;76:1827–1833.

31. Ozaki T, Liljenqvist U, Halm H, Hillmann A, Gosheger G, Winkelmann W. Giant cell tumor of the spine. *Clin Orthop Relat Res.* 2002;401:194–201.
32. Peh WC, Koh WL, Kwek JW, Htoo MM, Tan PH. Imaging of painful solitary lesions of the sacrum. *Australas Radiol.* 2007;51:507–515.
33. Persson BM, Ekelund L, Lovdahl R, Gunterberg B. Favourable results of acrylic cementation for giant cell tumors. *Acta Orthop Scand.* 1984;55:209–214.
34. Petrie A. Statistics in orthopaedic papers. *J Bone Joint Surg Br.* 2006;88:1121–1136.
35. Randall RL. Giant cell tumor of the sacrum. *Neurosurg Focus.* 2003;15:E13.
36. Raque GH Jr, Vitaz TW, Shields CB. Treatment of neoplastic diseases of the sacrum. *J Surg Oncol.* 2001;76:301–307.
37. Sar C, Eralp L. Surgical treatment of primary tumors of the sacrum. *Arch Orthop Trauma Surg.* 2002;122:148–155.
38. Shikata J, Yamumuro T, Shimizu K, Shimizu K, Kotoura Y. Surgical treatment of giant-cell tumors of the spine. *Clin Orthop Relat Res.* 1992;278:29–36.
39. Sung HW, Shu WP, Wang HM, Yuai SY, Tsai YB. Surgical treatment of primary tumors of the sacrum. *Clin Orthop Relat Res.* 1987;215:91–98.
40. Thomas DM, Skubitz KM. Giant cell tumour of bone. *Curr Opin Oncol.* 2009;21:338–344.
41. Todd LT Jr, Yaszemski MJ, Currier BL, Fuchs B, Kim CW, Sim FH. Bowel and bladder function after major sacral resection. *Clin Orthop Relat Res.* 2002;397:36–39.
42. Tse LF, Wong KC, Kumta SM, Huang L, Chow TC, Griffith JF. Bisphosphonates reduce local recurrence in extremity giant cell tumor of bone: a case-control study. *Bone.* 2008;42:68–73.
43. Turcotte RE, Sim FH, Unni KK. Giant-cell tumor of the sacrum. *Clin Orthop Relat Res.* 1993;291:215–221.
44. Wuisman P, Lieshout O, Sugihara S, van Dijk M. Total sacrectomy and reconstruction: oncologic and functional outcome. *Clin Orthop Relat Res.* 2000;381:192–203.
45. Yakes WFJ, Carrasco CH, Luethke JM. Embolization of lumbosacral lesions. In: Doty JR, Rengachary SS, eds. *Surgical Disorders of the Sacrum.* New York: Thieme; 1994:294–308.