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# Disease outcomes for skull base and spinal chordomas: A single center experience☆,☆☆

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ABSTRACT

*Objective:* Chordomas carry significant morbidity due to their growth patterns and surgical constraints in resection. En bloc resection, when feasible, is the ideal treatment goal, but is associated with significant morbidity. We sought to elucidate the relationship between extent of surgery, location and radiotherapy in relation to overall disease and progression free survival (PFS).
*Methods:* We reviewed case records for all patients with a primary histopathological diagnosis of clival and spinal chordomas that was presented to our institution between 1978 and 2010.
*Results:* A total of 49 patients (location: $n = 30$, skull base/clival; $n = 12$ vertebral column; $n = 7$ sacrum) were identified with mean follow-up period of 6.3 years (range 0.25 months–33 years). Improved 5 year and 10 year survival rates were noted following gross total resection ($n = 8$, 5 year and 10 year survival = 88%) as compared to patients that underwent subtotal resection ($n = 41$, 55% and 31%, respectively), ($p$-value > 0.05, GTR versus STR). Adjuvant high-dose stereotactic fractionated radiotherapy (HS-FSRT) significantly improved 5 year PFS in craniocervical chordoma patients (70%, $n = 13$) as compared to standard dose radiation therapy (20%, $n = 16$; $p$-value = 0.03). Overall 10 year survival for craniocervical patients undergoing HD-FSRT (40%) was however not significantly different in comparison with conventional radiotherapy (45%). Sacral chordomas had the worst prognosis with 3 year survival of 28.6%.
*Conclusions:* GTR offers the best prognosis for improved long-term survival. Adjuvant HD FSRT for craniocervical/clival chordomas significantly improves disease free survival though the long-term benefits on survival have yet to be established. Sacral chordomas are associated with a worse prognosis and poor long-term survival.



## 1. Introduction

Chordomas are primary bone tumors that arise from remnants of embryonal notochord. They have an indolent, local growth pattern and a propensity for repeated recurrences. Although they can metastasize, their long-term outcomes are most dependent on the pattern of local recurrences that often require repeated surgical debulking and/or radiation therapy. Due to their poor ultimate prognosis and the potential for significant surgical morbidity especially at recurrence, most chordomas are treated by initial near total resection followed by post-operative radiation therapy [1–4]. Treatment failure following radiation therapy is often attributed to sub-optimal dosing due to adjacent critical neural structures like the optic chiasm or the brain stem [5]. Cytoreductive surgery, especially for skull base chordomas, is therefore critical for tumor debulking and decompression of these near-by critical normal structures [3,6].

Even though this is a rare disease entity, recent Surveillance, Epidemiology and End Results analysis revealed a higher reported incidence of chordoma in Iowa [7]. Given the relative higher incidence as well as a lack of consensus in treatment strategies, we undertook a retrospective review of our experience to assess clinical outcomes in chordoma patients. Clinical outcomes through

*Abbreviations:* HD FSRT, high dose fractionated stereotactic photon radiation therapy; GTR, gross total resection; STR, sub total resection; PFS, progression free survival.

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disease survival and interval to disease progression were assessed in relation to extent of surgical resection and use of adjuvant therapy. Given the limited availability of proton beam based radiotherapy, high-dose adjuvant stereotactic radiotherapy has been used at our institution for adjuvant therapy in skull base chordomas. We therefore evaluated disease outcomes for skull base chordomas treated with high-dose adjuvant stereotactic radiotherapy in comparison to conventional radiotherapy.

## 2. Materials and methods

We identified 49 patients with a histopathological diagnosis of chordoma through a retrospective search of the neurosurgery database at the University of Iowa Hospitals and Clinics, between January 1978 and January 2010. Patient records were reviewed for: (1) demographics, (2) clinical presentation, (3) surgical treatment, (4) radiation therapy, and (5) final clinical outcome. All patients underwent clinical and radiographic evaluation by the neurosurgery and radiation oncology services. The University of Iowa Human Subjects Office Institutional Review Board approved this retrospective study.

### 2.1. Radiation therapy

High dose fractionated stereotactic photon radiation therapy to 81 Gy has been used to improve disease control in clival and cervical chordomas at our institution since 1999. Patients are treated using a hyperfractionated regiment of 1.2 Gy twice daily (BID) to 60 Gy followed by a 21 Gy boost at 1.5 Gy BID. The median max and mean dose to the brainstem were 81 Gy (46.7–85.7) and 38 (6.7–58.1), respectively. The mean target volume was 22 $cm^3$ (60.5–193.3).

Progression free- and disease survival intervals were determined with the Kaplan–Meier method. Statistical associations were assessed using logrank Mantel Cox analysis using GraphPad Prism version 5.04 for Windows.

## 3. Results

A total of 49 patients (men = 26 and women = 23) with chordoma were included in the study population. These were classified by anatomical site of presentation into the following groups: skull base/clivus: $n = 30$, sacrum: $n = 7$, lumbar spine: $n = 5$, cervical spine: $n = 6$ and thoracic spine: $n = 1$.

### 3.1. Clival chordomas

There were 30 patients ($n = 30$, 61%) with clival chordomas. Sex distribution was equal ($n = 15$, 50%, respectively), Table 1. Mean age at presentation was 40 years (range: 7–69 years). Presenting symptoms consisted of neurological deficits due to cranial nerve palsy in 24 patients (80%); CN VI palsy in 10 patients, multiple (>1) cranial nerve palsies in 13 patients and myelopathy in 3 patients. Fifteen ($n = 15$, 50%) patients presented with headaches due to local tumor growth. The mean time from symptom onset to clinical presentation was 8.7 months (range 1–36 months).

Subtotal resection was undertaken in 27 patients ($n = 27$, 90%). Total resection was achieved and radiographically confirmed in 3 patients ($n = 3$, 10%). Nineteen patients experienced tumor recurrence (defined as radiographic or clinical progression) at mean interval of 14.5 months (range: 3–72 months) after the first surgery, Table 1. Of these, 14 (74%) underwent a repeat resection, 5 patients underwent radiotherapy and one patient elected to undergo chemotherapy with hydroxyurea. One patient elected for conservative management with clinical observation and serial imaging. Second recurrences were noted in 13 patients ($n = 13/30$, 43%) whereas 9 patients ($n = 9/30$, 30%) had multiple (>2) recurrences.

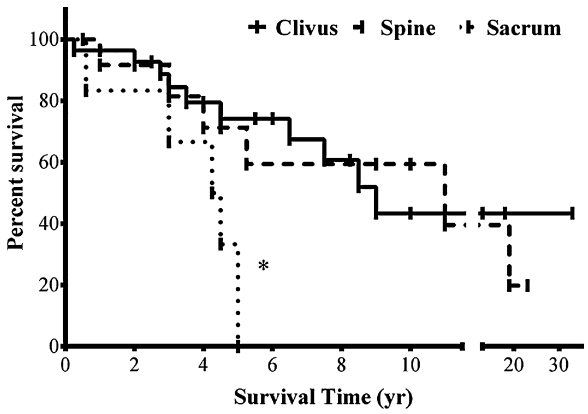


**Fig. 1.** Comparison of overall disease survival between chordoma patients with respect to anatomical site. Patients with sacral chordomas have significantly lower survival rate at 5 years ($p$-value < 0.001).

Adjuvant radiation therapy was recommended and instituted in 15 patients due to significant residual tumor following initial resection, Table 2. Of these, 13 patients received high-dose hyperfractionated stereotactic radiation therapy (HD-SFRT) with median dose of 81 Gy. Radiation therapy was used for treatment of recurrent diseases in nine patients ($n = 9$, 30%), Table 2.

One patient was lost to clinical follow up in the immediate postoperative period. The remaining 29 patients were followed for a mean follow up period of 6.4 years (range: 1–18 years). By final follow up, 18 patients were alive and 11 patients were deceased. Cumulative 5 year and 10 year survival rates for these patients were 73% and 44%, respectively (Table 1 and Fig. 1).

### 3.2. Vertebral and sacral chordomas

There were 12 patients with chordomas located within the mobile spine and 7 patients with tumor in sacrum ($n = 7$). There was equal sex distribution within patients with vertebral column based chordomas ($n = 6$, 50%). There was a male preponderance in sacral chordoma patients (male: $n = 5$, 71%; female: $n = 2$, 29%). Mean age at presentation for vertebral patients was 44 years (range: 12–80 years). Sacral chordoma patients were older with mean age at presentation of 70 years (range: 58–76 years), Table 1.

The predominant presenting symptom for both vertebral and sacral chordomas was localized pain, as noted in 11 patients (91%) with vertebral chordomas and all patients ($n = 7$, 100%) with sacral chordomas. Neurological deficits were the presenting symptoms in five patients within the vertebral group consisting of extremity paresthesias or weakness in three patients, bladder incontinence and cranial nerve (CN XII) palsy in one patient each. One patient ($n = 1$) with a sacral chordoma presented with urinary incontinence and saddle anesthesia. Mean interval from symptom to clinical presentation for vertebral chordoma patients (6.0 months, range: 1–12 months) was shorter than for sacral chordoma (19.3 months, range: 0–36 months).

Surgical treatment on primary presentation consisted of subtotal resection in eight patients ($n = 8/12$, 67%) with vertebral chordomas and six patients ($n = 6/7$, 86%) with sacral chordomas. Total resection was achieved in four patients ($n = 4/12$, 33%) with vertebral chordomas and one patient (14%) with a sacral chordoma. Tumor recurrence was noted in six patients ($n = 6/12$, 50%) with vertebral chordomas at a mean interval of 30 months after surgery (range: 3–96 months). Tumor recurrence was noted in five patients with sacral chordomas ($n = 5/7$, 71%) at a mean interval of 11.8 months (range: 2–30 months) from initial surgery. The mean