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Safety and Local Control of Radiation Therapy for Chordoma of the Spine and Sacrum:

A Systematic Review

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Abstract

Study Design—Systematic literature review.

Objective—To assess the toxicity, common radiation doses, and local control (LC) rates of radiation therapy for chordoma of the spine and sacrum and identify the difference in LC and toxicity between adjuvant, salvage, and primary therapy using radiation.

Summary of Background Data—Chordoma of the spine is typically a low-grade malignant tumor thought to be relatively radioresistant with a high rate of local recurrence and the potential for metastases. Improved results of modern radiation therapy in the treatment of chordoma support exploration of its role in the management of primary/de novo chordoma or recurrent chordoma.

Methods—We conducted a systematic literature review using PubMed and Embase databases to assess information available regarding the toxicity, LC rates, and overall survival (OS) rates for adjuvant, salvage, and primary radiation therapy for spinal and sacral chordoma.

Results—A total of 40 articles were reviewed. Evidence quality was low or very low. The highest rates of LC and OS were with early adjuvant RT for primary/de novo disease. Salvage RT for recurrent disease has very small cohorts and thus strong conclusions were not able to be made.

Conclusion—The use of pre- and/or post-operative photon image-guided radiotherapy (IGRT), proton or carbon ion therapy should be considered for patients undergoing surgery for the

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treatment of primary and recurrent chordomas in the mobile spine and sacrum, since these RT modalities may improve local control. Preoperative evaluation by the surgeon and radiation oncologist should be used to formulate a cohesive treatment plan.

The use of photon IGRT or carbon ion therapy as the primary treatment of chordoma, when currently in its developmental stage, shows promise and requires clear delineation of toxicity profile and long-term local control.

Keywords

carbon ion therapy; chordoma; convention radiation therapy; intensity modulated radiation therapy; photon therapy; proton therapy; radiation therapy; sacrum; spine; stereotactic radiosurgery

Chordoma is a rare and relentless tumor of the cranium, axial spine, and sacrum with an overall incidence of less than 1 in 1,000,000 persons.¹ Surgical resection of spinal and sacral chordoma remains the standard for control of macroscopic disease; however, it is associated with significant morbidity and reduction in ambulation, which could have significant repercussions for patients.² Surgical margins are defined according to the Enneking classification system as intralesional, marginal, wide, and radical. An intralesional margin resection is created if the tumor is entered to resect the tumor. A marginal margin resection occurs if the dissection extends into or through the reactive zone that surrounds the tumor but does not violate the tumor and a wide margin occurs if the reactive zone is not entered and the entire dissection is performed through healthy tissues. Lastly, a radical margin is created when the entire bony or myofascial compartment containing the tumor is resected.³ In the axial spine and sacrum, *en bloc* resection to achieve wide margins has been advocated as the best method to achieve a cure and offers the best chance of local tumor control.⁴ Wide or marginal margin resection rates for sacral chordoma range from 35% to 75%^{5–9} and only 21% in the mobile spine¹⁰ because of a higher likelihood of epidural involvement.¹¹ Specific to the sacrum, a wide or marginal resection of a tumor associated with the bilateral S1–2 nerve roots responsible for bladder and rectal function would likely to result in a substantial new deficit and reduction overall quality of life.^{2,12} The challenges of achieving wide margins are compounded for locally recurrent disease where tissue planes are disrupted, tumor seeding may have occurred, and anatomy can be distorted. Thus, there are typically four treatment modalities to address spinal chordomas: (i) surgery alone/ gross total resection with wide or radical margins, (ii) gross total resection with wide or marginal margins and RT, (iii) subtotal resection with intralesional margins and RT, and (iv) radiation therapy alone.

Although surgery is an effective therapy for macroscopic disease control and the quality of surgical margin is the most important factor for local control and overall survival,^{13–15} effective radiation therapy (RT) may have a role in addressing microscopic disease. Therefore, the combination therapy of surgical resection and radiation therapy may be associated with higher rates of local control and overall survival.¹⁶

To address lack of clarity regarding the toxicity and local control rates with radiation therapy for chordoma, we have proposed the following research questions:

1. What are the toxicity and local control rates for adjuvant postoperative radiation therapy for spinal and sacral chordoma?
2. What are the toxicity and local control rates for salvage radiation therapy for spinal and sacral chordoma?
3. What are the toxicity and local control rates for primary therapy for spinal and sacral chordoma?

MATERIALS AND METHODS

We conducted a systematic review of the English language literature by searching PubMed and Embase databases from 1974 to March 2016. Search terms included:

1. Chordoma
2. Radiation Therapy
3. Spine OR Sacrum

Exclusion criteria were as following: case reports, studies that focused on skull base chordomas, studies that focused on surgery for chordoma without a significant cohort who underwent RT, studies that did not report toxicity or local control rates, studies that did not report the radiation dose delivered or the modality of delivery, and review articles.

(Box 1).

Box 1

How to Use and Interpret GRADE Recommendations.³²

Strength of Recommendation	Interpretation
Strong	Can be confidently applied to all or almost all patients.
	Clinicians apply an intervention in all or almost all circumstances without a thorough review of the evidence and factors, and with an informing, but not necessarily detailed discussion with the patient.
Weak	Can be applied to most patients, but not all patients.
	Clinicians consider fundamental variables such as the quality of evidence, risk and benefit of the intervention, their experience, cost-effectiveness, and most importantly, patient preferences, thus, often resulting in a shared decision-making process with the patient.

RESULTS

Systematic Review

The search yielded a total of 19 articles in PubMed and 36 articles in EmBase. Duplicates were removed and the abstracts of 40 articles were reviewed. Those that met our exclusion criteria were removed, leaving 25 articles that were ultimately included in this review. Summaries of these articles are included in Tables 1, 2, and 3, <http://links.lww.com/BRS/B204>.

Excluded articles were four case reports, three studies focused on skull base chordomas, three studies focused on surgery without a significant cohort of patient who underwent RT, and five review articles were excluded.

What Are the Toxicity and Local Control Rates for Adjuvant Radiation Therapy for Spinal and Sacral Chordoma?

Photon-based Intensity Modulated Radiation Therapy—Local recurrence and progression of disease occurs frequently even with optimal tumor resection because of the inability to achieve wide margins and the inability to account for microscopic satellite lesions. Hence, adjuvant treatment with radiation therapy (RT) may improve local control (LC) and potentially overall survival (OS).⁴ However, the tolerance dose of the many of the organs and tissues surrounding the spinal column results in limitation of total RT dose that can safely be delivered to the tumor using nonconformal radiotherapy. Thus, the majority of older publications that used conventional photon radiotherapy did not exceed 60 Gy and investigators report poor LC of spinal and sacral chordomas with radical surgery and conventional radiation at doses below 60 Gy.^{17,18} Numerous publications on the use of photon RT with doses less than 60 Gy have shown eventual recurrence rates of 50% to 100% and 5-year progression-free survival (PFS) rates of less than 25%.¹⁹ This poor LC is as a result of the relative radio-resistance of chordoma and the limitations of historically available technology to deliver adequately high doses to the tumor without exceeding dose safety limits for nearby normal tissues.

Intensity modulated radiation therapy (IMRT) is a technique that can custom modulate each photon beam to conform to the three dimensional characteristics of the tumor by minimizing the dose to surrounding tissues, thus concentrating the radiation exposure to tumor tissues and decreasing the risk of radiation toxicity to surrounding tissues. IMRT has allowed dose escalation to tumors that were previously only achievable with proton beam treatment. In one series, 34 patients with sacral chordoma were treated with IMRT, with a median dose to target volume of 54 Gy in 1.8 Gy (Table 1, <http://links.lww.com/BRS/B204>). Of the 17 patients treated with adjuvant IMRT after their primary diagnosis 8 of the 17 patients (47%) demonstrated LC with a median follow up of 4.5 years and an OS of 76% over that follow-up period.²⁰ Interestingly, they found that local control was significantly higher in doses >60 Gy compared with total doses <60 Gy with only moderate side effects of radiotherapy and patients receiving >60 Gy showed a significantly improved overall survival (85% vs. 43%, $P < 0.01$).²⁰ From their mixed cohort of 34 patients (contained primary and recurrent chordomas) treated with IMRT, this group actuarial local control was projected to be 79%, 55%, and 27% after 1, 2, and 5 years, respectively. In addition, the overall survival projected to be 97%, 91%, and 70% at 1, 2, and 5 years, respectively. In the study of Bergh *et al.*²¹ local chordoma progression was significantly associated with an increased risk of metastasis and tumor-related death, thus improved local control may result in improved systemic control and survival.

Early primary adjuvant RT after surgery has higher rates of disease control than patient referred for salvage treatment of recurrent disease. One retrospective comparative cohort series found a 5-year LC of 88% with early adjuvant therapy compared with 9% in patient

who underwent salvage therapy.²² The median radiation dose delivered was 70 Gy relative biologic effectiveness (RBE) (range: 56–78 Gy RBE) delivered in 2 Gy per daily fraction. Higher recurrence rates were found with sacral tumors (84.6% vs. 15.4% of nonsacral tumors, $P = 0.004$), a higher surgery to RT interval (median time of 24.75 months), and gross disease present at the time of RT.²²

High-dose Single-fraction or Hypofractionated Photon Therapy—The use of image-guided technology coupled with IMRT has allowed for a very high dose of RT to the spine and sacrum in a single fraction or hypofractionated (<5 fractions) manner. Single fraction spine RT, also known as radiosurgery, can provide long-term LC in greater than 90% of cases for typically radioresistant metastatic tumors such as renal cell carcinoma (RCC) and melanoma.²³ Single fraction RT for chordoma has shown promising preliminary results for LC. In one series of 24 patients with an overall median follow-up of 2 years, 23 patients (95%) demonstrated LC with stable or reduced tumor burden based on serial imaging.²⁴ The one patient (4%) in this series without local control demonstrated radiographic progression of tumor at 11 months after the initial therapy.²⁴ Eight patients (33%) died during this 2-year interval with 5 of these patients dying from their disease (20%). The spinal cord, defined on a simulation CT myelogram, was constrained to a maximum dose of 1400 cGy to a single voxel and the median prescribed dose was 2400 cGy (1800–2400 cGy) to the selected tumor volume. The long-term LC from high-dose single-fraction RT is largely unknown and this report had a relatively heterogeneous patient population, with treatment delivered in the neoadjuvant and adjuvant setting on *de novo*, recurrent, and metastatic tumors. Nevertheless, this report does show the safety of using high dose single-fraction or hypofractionated RT.

Single-fraction and hypofractionated RT offers biological advantages for the treatment of chordoma. Higher doses per fraction result in irreparable and lethal DNA damage, which is important for the treatment of chordoma considering its relative radioresistance is thought to be because of its ability to repair radiation injured DNA.²⁵ In addition, high-dose hypofractionated RT causes increased endothelial cell apoptosis, a phenomenon only seen with high dose per fraction therapy.²⁶

Proton Beam Therapy—The major goals of optimal RT are to deliver targeted very high doses of radiation to a specific tumor bed with minimal toxicity to surrounding tissues. As previously stated, this a particularly challenging goal for the irradiation of chordomas because of their proximity to critical structures that are relatively sensitive to radiation such as the sacral nerve roots and the fact that the sacrum and mobile spine are structures consistently under significant mechanical stress and at higher risk for fracture. Thus, high-dose radiation that is not limited to only the tumor bed with minimal exposure to surround tissues can result in significant morbidity and injury from RT. In cases of concern for satellite lesions, these must also be included in the treatment volume, increasing the amount of normal tissue that must receive therapeutic doses of radiation. Proton radiation therapy aims to address this challenge by delivering a small dose to uninvolved normal tissue for any specified dose for a target.^{27–29} This allows a higher radiation dose to be delivered to the tumor target, with a lower risk of radiation toxicity to neural tissues. In a long term phase II

study of patient with primary spine column tumors treated with combined high dose photon/proton RT, patients with sacral tumors received a median of 19.8 Cobalt Gy Equivalent [CGE = 1.1 x Gy Relative Biological Effectiveness(RBE)] whereas patients with tumors received a median of 50.4 CGE (at 1.8 GyRBE daily) perioperatively (thoracolumbar tumors received all 50.4 CGE preoperatively whereas sacral tumors received 19.8 perioperatively and another 30.6 after wound healing).³⁰ The patients then received a second round of radiation of 19.8 CGE in 11 fractions for R0 resections (no cancerous cells seen within the margins of the resected specimen), and a 7.2 CGE boost for those with R1/R2 resections (cancerous cells seen within the margins of the resected specimen). Thus, a total median of 70.2 GyRBE was given to tumors with R0 resections and 77.4 CGE for tumors with R1/R2 resections.³⁰ Remarkably, they report a >90% local control rate at median 7.3 year follow up for primary chordomas with only 1 out of the 23 (4.3%) patients treated for primary chordoma developing a local recurrence.³¹ More interestingly, none of the seven patients who had a R0 resection developed a local recurrence, substantiating the importance of surgical resection to obtain optimal local control.

However, not all reports have such remarkable local control rates. Staab *et al*³² retrospectively analyzed 40 patients with chordoma of C-, T-, and L-spine and sacrum with a mean prescription dose of 72.5 CGE (range, 59.4–75.2) and a median follow up of median follow up of 3.6 years (range, 2–7.6). They report 13 of the 40 (32%) patients developed local recurrence resulting in actuarial 5-year local control rate of 62% for the entire cohort and OS rate of 80%. This study reported an actuarial 5-year LC rate of 100% in 19 patients who did not have surgical stabilization before their proton beam therapy; however, they report a 30% actuarial 5-year LC rate with spinal stabilization hardware (57% of patients instrumented experienced a local recurrence).³² The presence of titanium-based metal inside the target volume can potentially affect accuracy of RT by impairing the physician's ability to delineate the target volume accurately and reduce the homogeneous target coverage to the tumor.³² The Delaney group also found this increase in the rate of local recurrence with spine stabilization hardware with 5 of 16 patients (31%) with spine stabilization hardware suffered LF *versus* 6 of 34 (18%) patients without ($P=0.277$).³¹ A difference in the materials used for instrumentation and reconstruction may explain why the Delaney group does not have such a reduction in local control with surgical stabilization as the Staab group.^{30,33} Lastly, the Rotondo *et al*¹⁶ and Indelicato *et al*³⁴ articles also show comparable LC rates with preoperative and postoperative radiation therapy with a 68% 5-year LC rate (82% 5-year OS rate) and 88% 4-year LC rate (83% 4-year OS rate), respectively. Of note, metal can greatly affect the effective radiation dose given to a tumor bed. Thus, surgical hardware will often greatly increase the range uncertainty, and surgical instrumentation should be minimized as much as possible to lessen the impact of hardware on postoperative proton radiation therapy. Close collaboration between surgeons and radiation oncologists are recommended in these situations.

Heavy Ion Particle Radiation Therapy—Compared with protons, carbon ions have a biological advantage because of their increased relative biological effectiveness (RBE), likely because of complex double-stranded breaks.^{35–39} Carbon ion beams deliver a larger mean energy per unit length of their trajectory, known as the linear energy transfer (LET),

than protons and photons. In addition, the LET of carbon ion beams increases steadily from the initial value at the entrance point as it passes through the body, reaching its maximal value at the end of its range. Thus, carbon ion beam enables operators to avoid radiation-induced injuries to critical organs and to apply enough doses to control tumor and the higher LET and RBE of the carbon ion beam may contribute to the control of radioresistant tumor.

The Uhl group in Heidelberg,⁴⁰ Germany reports a retrospective analysis of 56 patients with sacral chordomas of which 41 patients received carbon radiation therapy as part of the primary treatment after biopsy ($n = 20$), R2 resection ($n = 11$), or R0/1 resection ($n = 10$). The cohort of 41 patients with primary sacral chordomas received either carbon ion radiation or a combination of IMRT with a carbon ion boost, with a median of dose of 75 GyRBE (range, 68.8 to 82.5 Gy) with a median follow-up of 25 months.⁴⁰ Primary chordoma treatment resulted in an 85% 2-year LC rate, which is marginally less than what is reported for single-fraction photon RT (>90% at 2 years)²⁴ and proton/photon combination RT (>90% at 5 years).³¹ Nevertheless, promising LC rate have also been seen in other independent retrospective analysis, with carbon ion RT have LC rates greater than >88% and an OS rates greater than > 80% at 3 to 5 years follow up.^{41–43}

When carbon ion RT is compared with surgery only, the LC rates and OS rate could support better outcomes with carbon RT. One retrospective analysis of 17 patients treated for sacral chordoma, 10 patients were treated with surgery only and seven patients were treated with carbon RT.⁴⁴ The carbon ion RT cohort received a median of 70.4 Gy (range, 54–73.6) and a median follow up of 4 years. Although the surgery only group had a median follow up of 6.3 years.⁴⁴ The LC at 5 years was 62.5% for the surgery and 100% for the carbon ion RT group.⁴⁴ Though the cohort of this study is very small it does highlight the potential to treat sacral chordomas with radiation only, without any surgical intervention. In particular, this study states that all seven patients had no late neurologic toxicity and maintained their urinary-anorectal function posttreatment. This is particularly interesting considering IGRT for a sacral tumor does not spare the canal, whereas IGRT for mobile spine typically targeted to spare the spinal cord.

Currently, there are no data directly comparing proton therapy with carbon ion therapy for spinal chordoma. However, there is currently an ongoing Phase II trial comparing the toxicity of both proton therapy and carbon ion therapy with a goal to construct a randomized phase III trial comparing hypofractionated proton and carbon ion irradiation.⁴⁵ At this time, adjuvant carbon-ion RT, proton beam RT, and single fraction photon RT have similar LC rates and OS rates. Comparison of toxicity profiles and long-term tumor control will be required to determine comparative safety and efficacy of these RT modalities for chordoma.

What Are the Toxicity and Local Control Rates for Salvage Radiation Therapy for Recurrent Spinal and Sacral Chordoma?

Most of the studies on RT for spine chordomas have mixed cohorts of primary chordoma and locally recurrent chordoma. However, primary chordomas are usually managed very differently from recurrent chordomas. For example, surgical resection is typically not an effective option to address macroscopic disease for locally recurrent chordoma. Thus, radiation plays an even more important role in obtaining significant disease control. Second,

the tumor biology of the recurrent disease is likely different from the initial disease. A recurrent chordoma composed of cells that have a higher intrinsic ability to repair double stranded breaks and thus these recurrent chordomas are likely even more radioresistant than primary chordomas.

Salvage therapy for the treatment of recurrent chordoma has significantly lower rates of LC, however no significant decrease in OS rates. The Zabel-du Bois *et al*²⁰ study (Table 2, <http://links.lww.com/BRS/B204>) shows a LC rate of 47% at 4.5 years, which decreases to 24% with salvage IMRT. However, both primary RT and salvage RT for chordoma results in a 74% OS rate at 4.5 years. This low 5-year LC rate for recurrent chordoma of approximately 20% using salvage IMRT is seen in other independent chordoma studies that used variable treatment modalities for recurrent sacral chordoma.²¹

Multiple groups have explored treatment of recurrent chordoma using proton beam therapy with or without photon RT. Macdonald *et al*⁴⁶ investigated the outcome of treating recurrent chordoma with proton therapy, and reported a 2-year LC and OS of 85% and 80%, respectively, for a cohort of 16 patients. Of note, this cohort of patients received at least one prior course of RT to the primary tumor site and all but one had at least one surgical resection before re-irradiation. Half of the tumors were clival and the remaining eight originated from the mobile spine or sacrum.

Current evidence suggests that the rates for LC with proton beam RT and carbon ion RT are higher than for photon RT. For salvage proton beam RT, though there are some studies with low LC rates,³⁶ most studies report a 70% to 80% 2-year LC rate and 40% to 50% 5-year LC rate.^{31,32,47} With salvage carbon ion RT and fast neutron RT, Uhl *et al*⁴⁰ focally reports a 47% 5-year LC rate and Breteau *et al*⁴⁸ reports a 54% 4-year LC rate, respectively. Nevertheless, these LC rates are notably better than the compared with approximately 30% 2-year LC rate and 24% 5-year LC rates with IMRT.²⁰

The LC and OS rates of single-fraction photon RT for recurrent chordoma remain unclear. However, there is optimism around single-fraction using 2400 cGy as a single-fraction to treat chordoma. Though this study has a mixed cohort of primary, metastatic, and recurrent chordomas and a short follow-up period (median follow up of 24 months), their report a >95% 2-year LC rate should prompt further investigation on the use of single-fraction photon RT as a viable option for recurrent chordoma.²⁴

What Are the Toxicity and Local Control Rates for Primary Radiation Therapy for Primary/de novo Spinal and Sacral Chordoma?

The use of radiation therapy as a primary treatment for chordoma could save patients from the morbidity and recovery from surgery. However, there is no evidence comparing primary RT and surgery with adjuvant RT. Nevertheless, the use of single-fraction photon RT as a neoadjuvant treatment has shown encouraging results, with seven of 13 (53.8%) patients who underwent single-fraction SRS as a planned preoperative neoadjuvant treatment never proceeding to surgery after SRS based on radiographic and clinical stability and patient preference over a 2-year follow-up period.²⁴

Chen *et al*⁴⁹ (Table 3, <http://links.lww.com/BRS/B204>) used proton beam RT with photon RT in a cohort of 24 patients with unresectable sacral chordomas to achieve a very favorable 90.4% 3-year LC rate (79.8% 5-year LC rate) and 91.7% 3-year OS rate (78.1% 5-year OS rate).

A Japanese trial with primary carbon ions irradiation without previous surgery showed comparable LC rates after treatment of inoperable sacral chordoma⁴¹ (Table 3, <http://links.lww.com/BRS/B204>). This group analyzed 95 patients were treated with 16 fractions carbon ions over 4 weeks with a median total dose 70.4 Gy (range, 52.8 to 73.6). At 5 years, they report an OS rate and LC rate were 86% and 88%, respectively.⁴¹

From both the proton beam RT studies and the heavy ion RT studies the data shows a clear trend towards optimal LC rates with primary RT for *de novo* chordoma only when the dose deliver is >70 GyRBE in 16 fractions. However, such a treatment modality is also associated with higher toxicity rates and adverse effects (Table 4, <http://links.lww.com/BRS/B204>). The majority of patients with toxic effects had radiation dermatitis; however, mucositis/esophagitis was reported for after cervical RT, urinary-anorectal dysfunction was reported after sacral RT. However, there is a trend towards a reduced amount of toxicity by using a hyperfractionated schedule of >30 fractions.⁴³

CONCLUSION

Though there is limited literature comparing the effectiveness of various radiation therapy modalities to achieve maximal LC and OS, there are promising trends specifically with doses >70 GyRBE. Proton beam and carbon ion therapy both show to have higher LC rates than conventional IMRT, however OS rates are not significantly different. This is likely because even after optimal local control is obtained, systemic and metastatic disease must be addressed to substantially change the overall survival for patient with chordoma. In other words, progressive local disease can cause increased morbidity and decreased functionality for the patient, but it is ultimately distant metastasis that results in progressive multiple system deterioration and death.

This review is not intended to discuss the differences in LC rate with wide margin/marginal margin en bloc resection (Enneking Appropriate surgery) *versus* intralesional surgical resection (Enneking Inappropriate surgery), but instead to concentrate on the various modalities of radiation therapy for chordoma. Nevertheless, the available literature on radiation therapy contains a very heterogeneous mixture of surgical resections, with some patient receiving Enneking Appropriate surgery and some receiving Enneking Inappropriate surgery. Currently there is some evidence to showing that adjuvant (post-operative) radiation therapy and neo-adjuvant (preoperative) radiation therapy is helpful in improving LC rates and OS rates irrespective of the surgical margins achieved at the time of resection. In other words, any surgery whether Enneking appropriate or inappropriate, when combined with radiation therapy will likely result in a higher LC rates, then surgical resection alone.

RECOMMENDATIONS

The use of adjuvant high dose conformal radiation therapy should be used for patients undergoing surgery for the treatment of *de novo* chordomas when surgical margins are concerning, and all recurrent chordomas in the mobile spine and sacrum.

- Recommendation strength: Strong.
- Quality of evidence: Low.

The use of adjuvant high dose conformal radiation therapy may be used for patients undergoing surgery for the treatment of primary (*de novo*) chordomas in the mobile spine and sacrum.

- Recommendation strength: Weak.
- Quality of evidence: Low.

High dose conformal radiotherapy should be considered for the treatment of primary (*de novo*) chordomas in the mobile spine and sacrum when surgery is not feasible.

- Recommendation strength: Strong.
- Quality of evidence: Low.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points

- The use of adjuvant high dose conformal radiation therapy should be used for patients undergoing surgery for the treatment of *de novo* chordomas when surgical margins are concerning, and all recurrent chordomas in the mobile spine and sacrum.
- The use of adjuvant high dose conformal radiation therapy may be used for patients undergoing surgery for the treatment of primary (*de novo*) chordomas in the mobile spine and sacrum. High-dose conformal radiotherapy should be considered for the treatment of primary (*de novo*) chordomas in the mobile spine and sacrum when surgery is not feasible.
- As radiation therapy continues to improve to allow for a high radiation dose targeted to a specific tumor bed with minimal toxicity to surrounding tissues, it will become a more viable option for the treatment of primary (*de novo*) and locally recurrent chordomas.