Feasibility of achieving planned surgical margins in primary spine tumor: a PTRON study

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OBJECTIVE Oncological resection of primary spine tumors is associated with lower recurrence rates. However, even in the most experienced hands, the execution of a meticulously drafted plan sometimes fails. The objectives of this study were to determine how successful surgical teams are at achieving planned surgical margins and how successful surgeons are in intraoperatively assessing tumor margins. The secondary objective was to identify factors associated with successful execution of planned resection.

METHODS The Primary Tumor Research and Outcomes Network (PTRON) is a multicenter international prospective registry for the management of primary tumors of the spine. Using this registry, the authors compared 1) the planned surgical margin and 2) the intraoperative assessment of the margin by the surgeon with the postoperative assessment of the margin by the pathologist. Univariate analysis was used to assess whether factors such as histology, size, location, previous radiotherapy, and revision surgery were associated with successful execution of planned resection.

RESULTS Three hundred patients were included. The surgical plan was successfully achieved in 224 (74.7%) patients. The surgeon correctly assessed the intraoperative margins, as reported in the final assessment by the pathologist, in 239 (79.7%) patients. On univariate analysis, no factor had a statistically significant influence on successful achievement of planned margins.

CONCLUSIONS In high-volume cancer centers around the world, planned surgical margins can be achieved in approximately 75% of cases. The morbidity of the proposed intervention must be balanced with the expected success rate in order to optimize patient management and surgical decision-making.

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KEYWORDS wide; intralesional; margins; primary spinal tumors; surgery; spine
Primary spine tumors are rare, accounting for 4.2% of all spine tumors.\(^1\) Resection according to Enneking principles has been associated with the best chance of achieving local control or even a cure.\(^2\)\(^-\)\(^5\) En bloc resection aims to remove a tumor in a single piece encased by healthy tissue.\(^6\)\(^,\)\(^7\) However, without a description of the pathologic margin, “en bloc resection” can be misleading because it refers to only an attempt to remove the tumor in one piece. Margins can be defined as intralesional, marginal, or wide. Intralesional margin means that the plane of dissection has transgressed into the lesion.\(^6\) Marginal margin refers to dissection within the pseudocapsule or reactive zone.\(^6\) Lastly, wide margin denotes a plane of resection within normal tissue.\(^6\)

Resection of primary spine tumor harbors several challenges due to proximity to critical neurovascular structures and complex vertebral column reconstructions.\(^8\) Pioneering work by Boriani et al. has shown that the stages and methods of en bloc resection are applicable to primary spinal tumor.\(^8\)\(^,\)\(^9\) A specific resection margin based on the Enneking stage is recommended to optimize outcome. Meticulous preoperative planning is essential to achieve a given surgical margin.\(^1\)\(^,\)\(^6\)\(^-\)\(^8\)\(^,\)\(^10\) When oncological resection is the goal, failure to achieve the desired margin could expose the patient to unnecessary surgical morbidity without the survival advantages and decrease in local recurrence.\(^1\)\(^,\)\(^3\)\(^,\)\(^6\)\(^-\)\(^11\)\(^-\)\(^15\) In other words, planned intralesional resection could be achieved with less morbidity and potentially the same rates of local control and survival as planned en bloc resection with histological intralesional margin; however, this scenario has not been evaluated.

Even in the most experienced hands, the execution of a rigorously drafted plan sometimes fails.\(^8\) Two case series from experienced spine oncology centers reportedly achieved the planned surgical margins in 82% and 86% of patients, but are these results generalizable?\(^9\)\(^11\)\(^,\)\(^12\) Furthermore, some factors, such as tumor location and size, may impact the feasibility of en bloc resection. Knowing which patients are at high risk for failure to achieve planned surgical margins would significantly impact the shared decision-making process, especially given recent advances in radiotherapy and systemic therapies. Intralesional resection with neoadjuvant or adjuvant therapy could be considered for some patients, in order to avoid the high morbidity rates of aggressive resection, especially if this resection has a high risk of positive margins.

The goal of this study was to utilize prospective multicenter data to determine how successful experienced surgical teams are at achieving planned surgical margins and how successful surgeons are in intraoperatively assessing tumor margins. The secondary objective was to identify factors associated with successful execution of planned margins.

**Methods**

**Data Source**

This study was part of a multicenter international prospective registry for the management and outcomes of primary tumors of the spine called the Primary Tumor Research and Outcomes Network (PTRON). This study was registered with the ClinicalTrials.gov database (registration no. NCT02790983).\(^16\) PTRON was designed and led by the AO Spine Knowledge Forum Tumor and has established an international network of 16 spine oncology centers in North America, Europe, and Asia that are dedicated to prospective research of patients diagnosed with primary tumor of the spine. Demographic, clinical, diagnostic, and therapeutic variables are collected on a shared, web-based research application (REDCap v6.5.2, Vanderbilt University) and are used to answer specific questions pertinent to primary spine tumors. Patients from all 16 spine centers starting from the inception of the registry (May 4, 2016) until the date of data extraction (November 24, 2020) were eligible for inclusion in this study. Ethics approval was obtained at each participating center, and informed consent was obtained from all patients.

**Study Population**

Patients diagnosed with primary tumor of the spine who received medical and/or surgical treatment were enrolled in PTRON. Patients were included in this analysis if they 1) underwent prospective surgical treatment and 2) had data about the preoperatively planned, intraoperative, and pathological margins documented in the database at the time of extraction. Both patients with previously treated and those with untreated tumors were included. Patients who had a diagnosis of metastatic tumor of the spine, primary spinal cord tumor, and peripheral nerve sheath tumor were excluded. Patients who underwent planned intralesional resection were also excluded because their inclusion would have guaranteed success and biased the results. As such, we assessed only the successful achievement of marginal and/or wide margins in this study.

**Description of Variables**

The planned margin and intraoperative assessment of the margin by the surgeon were recorded in the PTRON database as 1) intralesional, 2) intralesional with planned focal transgression, 3) marginal, 4) wide with marginal at dura mater; and 5) wide. The pathologists’ assessments of the overall margin and those of the soft tissue, bone, and dura mater were documented as 1) intralesional, 2) intralesional with planned focal transgression, 3) marginal, and 4) wide. Pathologist assessments that were categorized as wide at all tissues except marginal at the dura mater were classified as wide with marginal at dura mater. For the analysis, pathological diagnosis was categorized as 1) chordoma/chondrosarcoma, 2) osteosarcoma/Ewing’s sarcoma, 3) giant cell tumor/aneurysmal bone cyst, 4) osteoid osteoma, 5) osteoblastoma, and 6) other. Tumor location was classified as 1) C0–2; 2) C3–6; 3) C7–T2; 4) T3–12; 5) L1–5; and 6) S1–5. An untreated tumor was defined as a primary spine tumor that has not received treatment with any prior open procedure, including open biopsy and/or previous surgery. Furthermore, the number of surgical stages (categorized as 1 or ≥ 2) and surgical approach (anterior, posterior, or simultaneous) of each procedure were collected and analyzed as potential predictors.
Endpoints

The primary endpoints of this analysis were used to compare 1) the planned surgical margin and 2) the intraoperative assessment of the margin by the surgeon with the postoperative assessment of the margin by the pathologist. For the first endpoint, success was defined as achievement of the planned surgical margins or better, as confirmed by the pathologist assessment. For the second endpoint, success was defined as appropriate intraoperative assessment of the margin by the surgeon when compared with the postoperative histological assessment by the pathologist. Pathological review of the specimens was done by experienced musculoskeletal oncology pathologists at each center; however, this review was not standardized across centers.

Statistical Analysis

Continuous variables were described using mean (SD), median (IQR), and range. Categorical variables were described as counts and percentages. The primary endpoints were analyzed using the chi-square test and Fisher’s exact test for two-group comparisons and the Cochran-Armitage trend test for trend analysis. The statistical analysis was performed using R version 4.0.2.

TABLE 1. Patient demographic characteristics (n = 300)

| Characteristic                  | Value          |
|--------------------------------|----------------|
| Age, yrs                       |                |
| Mean (SD)                      | 45.3 (19.6)    |
| Median (IQR)                   | 46.0 (27.0–61.5)|
| Range                          | 4.0–83.0       |
| Sex                            |                |
| Female                         | 111 (37.0)     |
| Male                           | 189 (63.0)     |
| CCI (n = 283)                  |                |
| Mean (SD)                      | 2.0 (1.1)      |
| Median (IQR)                   | 2.0 (2.0–2.0)  |
| Range                          | 0.0–7.0        |
| Smoking history (n = 300)      |                |
| Nonsmoker                      | 247 (82.3)     |
| Current smoker                 | 20 (6.7)       |
| Former smoker                  | 33 (11.0)      |
| ECOG Performance Status (n = 292)|        |
| 0*                             | 124 (42.5)     |
| 1†                             | 126 (43.2)     |
| 2‡                             | 27 (9.2)       |
| 3§                             | 14 (4.8)       |
| 4¶                             | 1 (0.3)        |
| 5**                            | 0 (0.0)        |

CCI = Charlson Comorbidity Index; ECOG = Eastern Cooperative Oncology Group.

Columns are shown as number (%) unless indicated otherwise.
* Fully active and able to perform all predisease activities without restriction.
† Restricted in physically strenuous activity, but ambulatory and able to carry out work of light or secondary nature (e.g., light housework, office work).
‡ Ambulatory and capable of all self-care, but unable to perform any work activities (up and about for > 50% of waking hours).
§ Capable of only limited self-care and confined to bed or chair for > 50% of waking hours.
¶ Completely disabled, cannot perform any self-care, and totally confined to bed or chair.
** Dead.

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Statistical Analysis

Continuous variables were described using mean (SD), median (IQR), and range. Categorical variables were described as counts and percentages. The primary endpoints were analyzed using the chi-square test and Fisher’s exact test for two-group comparisons and the Cochran-Armitage trend test for trend analysis. The statistical analysis was performed using R version 4.0.2.

TABLE 2. Tumor characteristics

| Characteristic                          | Value          |
|----------------------------------------|----------------|
| Prior open procedure (n = 295)         |                |
| Untreated                              | 214 (72.5)     |
| Treated                                | 81 (27.5)      |
| Primary tumor histology according to pathologist (n = 293) |            |
| Chordoma/chondrosarcoma                | 135 (46.1)     |
| Osteosarcoma/Ewing’s sarcoma           | 29 (9.9)       |
| Giant cell tumor/aneurysmal bone cyst  | 30 (10.2)      |
| Osteoid osteoma                        | 5 (1.7)        |
| Osteoblastoma                          | 19 (6.5)       |
| Other                                  | 75 (25.6)      |
| Primary tumor metastasis (n = 187)     |                |
| No                                     | 181 (96.8)     |
| Yes                                    | 6 (3.2)        |
| Primary tumor location (n = 296)       |                |
| C0–2                                   | 20 (6.8)       |
| C3–6                                   | 16 (5.4)       |
| C7–T2                                  | 19 (6.4)       |
| T3–12                                  | 71 (24.0)      |
| L1–5                                   | 87 (29.4)      |
| S1–5                                   | 83 (28.0)      |
| Total vertebral levels w/ tumor (n = 300)|            |
| Mean (SD)                              | 2.2 (1.4)      |
| Median (IQR)                           | 2.0 (1.0–3.0)  |
| Range                                  | 1.0–7.0        |
| Vol of primary spine tumor, cm³ (n = 156)* |            |
| Mean (SD)                              | 309.5 (1070.8) |
| Median (IQR)                           | 75.7 (28.0–163.4) |
| Range                                  | 0.1–9839.5     |
| Postop pathology (n = 93)              |                |
| Mean (SD)                              | 3.19 (2.0)     |
| Median (IQR)                           | 75.7 (10.0–163.4) |
| Range                                  | 0.1–9839.5     |
| Preop radiation therapy (n = 300)      |                |
| No                                     | 243 (81.0)     |
| Yes                                    | 57 (19.0)      |
| Preop chemo (n = 179)                  |                |
| No                                     | 128 (71.5)     |
| Yes                                    | 51 (28.5)      |
| Preop biopsy (n = 300)                 |                |
| No                                     | 33 (11.0)      |
| Yes                                    | 267 (89.0)     |
| Preop embolization (n = 300)           |                |
| No                                     | 222 (74.0)     |
| Yes                                    | 78 (26.0)      |
| Estimated blood loss, ml (n = 299)     |                |
| Mean (SD)                              | 1828.6 (2605.0) |
| Median (IQR)                           | 1000.0 (500.0–2300.0) |
| Range                                  | 0.0–32,400.0   |
median (IQR), and range values. Categorical variables were described as number (percent). Continuous parameters were analyzed using the standard t-test for normally distributed data. The Wilcoxon rank-sum test for nonnormally distributed data was used. Categorical data were tested with the chi-square test or with the Fisher’s exact test in the case of rare events. Univariate regression models were used to identify factors that influenced the execution of planned margins. Factors included in the regression models were chosen on the basis of the best available evidence and clinical expertise. All statistical tests were 2-sided with a predefined significance level of 5%. The kappa statistic was performed to assess agreement between the surgeons’ intraoperative assessments of the margins and the pathologists’ assessments. Statistical analysis was performed with SAS software version 9.4 (SAS Institute).

Results
A total of 300 patients from 16 centers located in North America, Europe, and Asia were included in the analysis (Table 1). The median (IQR) age was 46.0 (27.0–61.5) years. The majority of patients were male (63.0%). The majority of patients were fully active or restricted in physically strenuous activity (Eastern Cooperative Oncology Group Performance Status 0 or 1).

A total of 81 (27.5%) patients had undergone a prior open procedure (biopsy or resection). The most common histological diagnosis was chordoma or chondrosarcoma (46.1%) (Table 2). Six patients had metastasis at the time of treatment (3.2%). The most common locations of primary tumor were the lumbar (29.4%), sacral (28.0%), and thoracic (24.0%) spine. The median (IQR) tumor volume on preoperative imaging was 34.1 (10.0–122.0) cm³. Fifty-seven patients received preoperative radiation therapy (19.0%), and 51 received preoperative chemotherapy (28.5%). Seventy-eight patients received preoperative embolization (26.0%). Two hundred nineteen patients underwent a single-stage surgical procedure (73.0%), and 76 (25.3%) underwent surgery in two stages. For those who underwent a multistage surgery, a posterior approach was most commonly performed as the first stage (196 [65.8%] patients), followed by both anterior and posterior approaches (72 [24.2%]). Finally, the median (IQR) operative time of single-stage procedures was 398.5 (220–585) minutes, and the median (IQR) estimated blood loss of all procedures was 1.0 (0.5–1.6) L.

The planned margins were successfully achieved in 224 (74.7%) patients (Table 3). Overall, marginal or wide margins were attained in 261 (87.0%) patients (Table 4). The surgeon correctly determined the intraoperative margins in 239 (79.7%) patients according to pathologist assessments (Table 5). Margins identified as marginal or wide were adequately evaluated as such intraoperatively in 261 (87.0%) patients. The rate of agreement between the intraoperative assessments of the surgeons and the pathologist assessments of the surgical margins was moderate (weighted kappa statistic 0.52, 95% CI 0.44–0.60; SE 0.04).

In univariate analysis, no factors had a statistically significant association with successful achievement of surgical margins (Table 6). Tumor size (p = 0.088), previous radiation therapy (p = 0.066), and the number of involved vertebral bodies (p = 0.064) showed borderline associations. However, fewer involved vertebral levels was significantly associated with adequate perception of the intraoperative margins by the surgeon (p = 0.029). None of the other analyzed factors, including revision or primary surgery, tumor location, use of preoperative chemotherapy, tumor histology, and estimated blood loss, significantly impacted successful achievement of planned margins.

Discussion
In this study, the surgical plan was successfully achieved in 224 of 300 (74.7%) patients. Furthermore, wide or marginal margins were achieved in 87.0% of resections. Surgeons were adequately able to identify the intraoperatively achieved margin in 79.7% of patients. Interestingly, no factor was significantly associated with successful achievement of preoperatively planned margins. However, some factors, such as tumor size, previous radiation therapy, and number of involved vertebrae, were close to reaching statistical significance with successful achievement of planned margins. On the other hand, fewer involved levels was associated with adequate intraoperative assessment of the surgical margins by the surgeon. It appears reasonable to hypothesize that some of these factors may have reached significance with a larger sample size. These find-
ings from an international, multicenter cohort of patients add to our understanding of and to the decision-making process for these rare tumors.

Planned resection margins are typically chosen on the basis of a combination of factors. First, resection margin based on the Enneking stage of the tumor is recommended to increase local control and potentially survival. Second, the feasibility of achieving that margin should be assessed according to Weinstein-Boriani-Biagini (WBB) classifications. Lastly but most importantly, patient preferences and acceptance of potential morbidity, neurological deficit, and medical comorbidities should be combined when making the final surgical plan. Achievement of this surgical plan is crucial to maximizing outcomes and minimizing unnecessary morbidity.

There are few reports on this topic in the literature. Other studies have analyzed the reliability of achieving disease-free margins by comparing expected margins based on preoperative surgical planning with postoperative histological margins. Fisher et al. used WBB staging to accurately plan and predict the achieved margins in 73% of patients with primary spinal tumor who underwent tentative curative resection. In this study, wide or marginal margins were attained in 88% of patients. In a prospective cohort of similar patients, Amendola et al. accurately predicted the achieved margins in 75.7% of patients. Wide or marginal margins were attained in 82.4% of patients. Lador et al. compared surgeons’ intraoperative perceptions of margins with histopathological evaluations. Surgeons tended to underestimate the achievement of clear margins. However, margins evaluated intraoperatively as clear were contaminated in 10% of cases. Thus, the findings of the present study are very similar to those of published studies. However, the inclusion of an international, multicenter cohort in the present study improves generalizability. It also confirms that surgeons are able to accomplish their preoperative surgical plans in as many as 75% of patients.

In the current analysis, no factors were associated with successful achievement of planned margins on univariate analysis. Interestingly, the location of the tumor in the spine did not affect the success rate, contrary to the findings of previous reports. Molina et al. reported on 16 patients who underwent en bloc resection of cervical chordoma. Upper cervical (C1–2) tumors had the most violated margins compared with subaxial cervical tumors (43% vs 11%). This was believed to be due to increased proximity to vital structures. The incidence of local tumor recurrence was more than twice as high for C1–2 tumors (29%) than subaxial tumors (11%). Despite the higher rates of tumor violation and complications in patients with upper cervical tumor, overall survival was similar between the two groups. In the present study, it is possible that high cervical tumors were deemed more appropriate for planned intralesional resection, and as such, positive margins were deemed successful. Another explanation may be that this study is underpowered to detect differences based on tumor location. Consequently, it is hard to exclude tumor location as a potential predictor of successful achievement of planned margins. Similarly, tumor size, previous radiation therapy, and number of involved

### Table 4. Comparison of planned surgical margin versus pathologist assessment

| Planned Surgical Margin | Pathologist Assessment |
|-------------------------|------------------------|
|                         | Intralesional | Intralesional Planned Focal Transgression | Marginal | Wide w/ Marginal at Dura Mater | Wide | Total |
| Intralesional planned focal transgression | 10 (43.5) | 6 (26.1) | 1 (4.3) | 1 (4.3) | 5 (21.7) | 23 (7.7) |
| Marginal | 7 (13.7) | 1 (2.0) | 29 (56.9) | 2 (3.9) | 12 (23.5) | 51 (17.0) |
| Wide w/ marginal at dura mater | 11 (14.1) | 1 (1.3) | 17 (21.8) | 26 (33.3) | 23 (29.5) | 78 (26.0) |
| Wide | 3 (2.0) | 0 (0.0) | 18 (12.2) | 8 (5.4) | 119 (80.4) | 148 (49.3) |
| Total | 31 (10.3) | 8 (2.7) | 65 (21.7) | 37 (12.3) | 159 (53.0) | 300 (100.0) |

All values are shown as number (%).

### Table 5. Comparison of intraoperative assessment of surgical margin vs pathologist assessment

| Intraoperative Assessment | Pathologist Assessment |
|---------------------------|------------------------|
|                          | Intralesional | Intralesional Planned Focal Transgression | Marginal | Wide w/ Marginal at Dura Mater | Wide | Total |
| Intralesional | 11 (68.8) | 1 (6.3) | 0 (0.0) | 1 (6.3) | 3 (18.8) | 16 (5.3) |
| Intralesional planned focal transgression | 7 (33.3) | 6 (28.6) | 2 (9.5) | 1 (4.8) | 5 (23.8) | 21 (7.0) |
| Marginal | 4 (8.2) | 1 (2.0) | 29 (59.2) | 3 (6.1) | 12 (24.5) | 49 (16.3) |
| Wide w/ marginal at dura mater | 8 (10.5) | 0 (0.0) | 18 (23.7) | 26 (34.2) | 24 (31.6) | 76 (25.3) |
| Wide | 1 (0.7) | 0 (0.0) | 16 (11.6) | 6 (4.3) | 115 (83.3) | 138 (46.0) |
| Total | 31 (10.3) | 8 (2.7) | 65 (21.7) | 37 (12.3) | 159 (53.0) | 300 (100.0) |

All values are shown as number (%).
vertebral bodies were all almost significantly associated with successful achievement of planned margins, and their importance to successful surgical planning remains to be determined. Further subgroup analyses are required to assess the impacts of specific tumor locations and histological characteristics.

The best available evidence supports margin-appropriate en bloc surgery to decrease local recurrence and improve survival. However, this is not always possible given the proximity to vital structures, such as the spinal cord, nerves, and vasculature. Given their proximity to vital structures, between 35% and 65% of sacral chordoma/chondrosarcoma, osteosarcoma/Ewing's sarcoma, giant cell tumor/aneurysmal bone cyst, osteoid osteoma, osteoblastoma, other, primary tumor location, largest tumor dimension, number of surgical stages, number of vertebral spine levels, preop radiation therapy, and values are shown as number or number (%) unless indicated otherwise.

* Wilcoxon rank-sum test.
† Chi-square test.
‡ Based on history of open biopsy or previous surgery.
§ Fisher’s exact test.

| Factor                      | Failure (n = 76) | Success (n = 224) | p Value |
|-----------------------------|------------------|-------------------|---------|
| Age, yrs                    | 76               | 224               | 0.141†  |
| Mean (SD)                   | 48.1 (19.4)      | 44.3 (19.6)       |         |
| Median (IQR)                | 49.0 (31.5–64.5) | 44.0 (26.0–60.5)  |         |
| Range                       | 10.0–82.0        | 4.0–83.0          |         |
| Sex                         | 76               | 224               | 0.428†  |
| Female                      | 31 (40.8)        | 80 (35.7)         |         |
| Male                        | 45 (59.2)        | 144 (64.3)        |         |
| Preop primary tumor status‡ | 73               | 222               | 0.372†  |
| First tumor surgery         | 50 (68.5)        | 164 (73.9)        |         |
| Recurrence tumor surgery    | 23 (31.5)        | 58 (26.1)         |         |
| Histology of primary tumor, n (%) | 75             | 218               | 0.213§  |
| Chordoma/chondrosarcoma     | 29 (38.7)        | 106 (48.6)        |         |
| Osteosarcoma/Ewing's sarcoma| 8 (10.7)         | 21 (9.6)          |         |
| Giant cell tumor/aneurysmal bone cyst | 11 (14.7) | 19 (8.7)          |         |
| Osteoid osteoma             | 0 (0.0)          | 5 (2.3)           |         |
| Osteoblastoma               | 3 (4.0)          | 16 (7.3)          |         |
| Other                       | 24 (32.0)        | 51 (23.4)         |         |
| Primary tumor location      | 76               | 220               | 0.136†  |
| C0–2                        | 5 (6.6)          | 15 (6.8)          |         |
| C3–6                        | 7 (9.2)          | 9 (4.1)           |         |
| C7–T2                       | 2 (2.6)          | 17 (7.7)          |         |
| T3–12                       | 13 (17.1)        | 58 (26.4)         |         |
| L1–5                        | 27 (35.5)        | 60 (27.3)         |         |
| S1–5                        | 22 (28.9)        | 61 (27.7)         |         |
| Largest tumor dimension, cm | 74               | 219               | 0.088*  |
| Mean (SD)                   | 6.9 (4.0)        | 5.9 (3.6)         |         |
| Median (IQR)                | 5.9 (3.8; 8.3)   | 5.4 (3.4; 7.7)    |         |
| Range                       | 1.7–21.2         | 0.4–31.3          |         |
| No. of surgical stages      | 76               | 224               | 0.886†  |
| 1                           | 55 (72.4)        | 164 (73.2)        |         |
| ≥2                          | 21 (27.6)        | 60 (26.8)         |         |
| No. of vertebral spine levels | 76               | 224               | 0.064*  |
| Mean (SD)                   | 4.9 (2.7)        | 4.3 (2.7)         |         |
| Median (IQR)                | 5.0 (3.0–7.0)    | 4.0 (2.0–6.0)     |         |
| Range                       | 1.0–10.0         | 0.0–15.0          |         |
| Preop radiation therapy     | 76               | 224               | 0.066†  |
| No                          | 67 (88.2)        | 176 (78.6)        |         |
| Yes                         | 9 (11.8)         | 48 (21.4)         |         |
domas and approximately 21% of mobile spine chordomas are amenable to en bloc resection with negative surgical margins.34–36 Even when resection is feasible, microscopic satellite spread outside the planned resection site or failure to achieve surgical margins may lead to increased recurrence.2 This has pushed some groups to rely more heavily on neoadjuvant and adjuvant treatment and to try to limit the surgical footprint. Nevertheless, even when neoadjuvant and adjuvant therapies are used, the addition of en bloc resection seems to confer an advantage in local control.34 However, major advances in radiation therapy techniques and adjuvant chemotherapy are challenging this concept.35,36 Jin et al. reported that the 5-year overall survival rate was 84.3% for patients with primary spinal chordoma treated with single-fraction, high-dose stereotactic radiosurgery.2 In this report, extent of surgery was not predictive of overall survival or local recurrence–free survival, but rather of surgical toxicity.2 However, when considering the morbidity and health-related quality of life (QOL) of these patients, it is important to note that the health-related QOL returns to normal in long-term survivors and that local recurrence, as opposed to aggressive surgical intervention, is the most important factor that negatively impacts QOL at long-term follow-up.2,20,37–40 Consequently, every effort should be deployed toward achieving the best strategy to decrease local recurrence, even if more aggressive.

To our knowledge, this is the largest series to assess successful achievement of surgical margins for primary spinal tumors. The multicenter nature of this study also increases the external validity of these results. However, it must be noted that all included patients received care from experienced surgeons at high-volume oncology centers. Although this is the largest series on this matter, inherent limitations are present given the retrospective nature of this study, such as selection and information bias. Multivariate analysis was not possible because of the low number of events for both objectives. Therefore, it is plausible that this study was not sufficiently powered to identify factors predictive of successful resection. Because no factors were associated with successful achievement of surgical margins, rigorous preoperative assessment of feasibility and planning cannot be emphasized enough to improve success rates. Future studies need to assess the specific and individual effects of factors such as location, histology, number of levels, use of preoperative radiation therapy, and instrumentation and reconstruction techniques on successful achievement of surgical margins. Furthermore, pathological assessments of margins may vary between pathologists and between centers, and this assessment was not standardized in this study. Moreover, adverse events were not analyzed, and no conclusion can be made about the association between morbidity and successful surgery. Moreover, the goal of this study was not to determine the correlation between surgical margin and local control, but strictly to answer the question: how successful are surgeons at achieving their plans?

Conclusions

Using a prospective international registry, we showed that the planned surgical margin can be achieved in as many as 75% of patients at high-volume cancer centers. The morbidity of the proposed intervention must be weighed against the expected rate of successful achievement of the surgical margin in order to optimize patient management and surgical decision-making. Moreover, this critical piece of information will help with patient counseling.

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References

1. Chan P, Boriani S, Fourney DR, et al. An assessment of the reliability of the Enneking and Weinstein-Boriani-Biagini classifications for staging of primary spinal tumors by the Spine Oncology Study Group. Spine (Phila Pa 1976). 2009;34(4):384–391.
2. Jin CJ, Berry-Candelario J, Reiner AS, et al. Long-term outcomes of high-dose single-fraction radiosurgery for chordomas of the spine and sacrum. J Neurosurg Spine. 2020;32(1):79–88.
3. Boriani S, Saravanja D, Yamada Y, et al. Challenges of local recurrence and cure in low grade malignant tumors of the spine. Spine (Phila Pa 1976). 2009;34(22)(suppl):S48–S57.
4. Charest-Morin R, Fisher CG, Sahgal A, et al. Primary bone tumor of the spine-an evolving field: what a general spine surgeon should know. Global Spine J. 2019;9(1)(suppl):108S–116S.
5. Fisher CG, Saravanja DD, Dvorak MF, et al. Surgical management of primary bone tumors of the spine: validation of an approach to enhance cure and reduce local recurrence. Spine (Phila Pa 1976). 2011;36(10):830–836.
6. Lador R, Gasbarrini A, Gambarotti M, et al. Surgeon’s perception of margins in spinal en bloc resection surgeries: how reliable is it? Eur Spine J. 2018;27(4):868–873.
7. Dea N, Gokaslan Z, Choi D, Fisher C. Spine oncology—primary spine tumors. Neurosurgery. 2017;80(3S):SI24–SI30.
8. Yamazaki T, McLoughlin GS, Patel S, et al. Feasibility and safety of en bloc resection for primary spine tumors: a systematic review by the Spine Oncology Study Group. Spine (Phila Pa 1976). 2009;34(22)(suppl):S31–S38.
9. Boriani S, Weinstein JN, Biagini R. Primary bone tumors of the spine. Terminology and surgical staging. Spine (Phila Pa 1976). 1997;22(9):1036–1044.
10. Enneking WF. A system of staging musculoskeletal neoplasms. Clin Orthop Relat Res. 1986(204):9–24.
11. Fisher CG, Keynan O, Boyd MC, Dvorak MF. The surgical management of primary tumors of the spine: initial results of
Disclosure

Dr. Fisher is a consultant for Medtronic and NuVasive, receives royalties from Medtronic, and receives fellowship support paid to an institution from Medtronic and AO Spine. Dr. Bettgowda is a consultant for DePuy Synthes and Bionet Labs. Dr. Sciubba is a consultant for DePuy Synthes, Medtronic, Stryker, and Baxter. Dr. Rampersaud receives royalties from Medtronic. Dr. Chou is a consultant for and receives royalties from Globus. Dr. Hornicek is a consultant for Stryker Medical and is a board member of ISOLS. Dr. Laufer is a consultant for DePuy Synthes and Brainlab. Dr. Dea is a consultant for Stryker and Medtronic, owns stock in Medtronic, and is on the speakers bureau for Baxter.

Author Contributions

Conception and design: Dea, Fisher, Rhines, Boriani, Gokaslan, Clarke, Laufer, Sahgal. Acquisition of data: Dea, Dandurand, Lazary, Kawahara, Rampersaud, Chou, Shin, Hornicek, Laufer. Analysis and interpretation of data: Dea, Dandurand, Fisher, Rhines. Drafting the article: Dea, Dandurand. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Dea. Statistical analysis: Dea, Dandurand. Administrative/technical/material support: Dea, Fisher, Rhines, Rampersaud, Chou, Shin, Hornicek, Laufer.

Supplemental Information

Previous Presentations

This work was presented virtually at the annual meeting of the Canadian Spine Society, February 2021.

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