

# Impact of the Spinal Instability Neoplastic Score on Surgical Referral Patterns and Outcomes

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## ABSTRACT

**Background** The Spinal Instability Neoplastic Score (SINS) was developed to identify patients with spinal metastases who may benefit from surgical consultation. We aimed to assess the distribution of SINS in a population-based cohort of patients undergoing palliative spine radiotherapy (RT) and referral rates to spinal surgery pre-RT. Secondary outcomes included referral to a spine surgeon post-RT, overall survival, maintenance of ambulation, need for re-intervention, and presence of spinal adverse events.

**Methods** We retrospectively reviewed CT simulation scans and charts of consecutive patients receiving palliative spine RT between 2012 and 2013. Data were analyzed using Student's t-test, Chi-squared, Fisher's exact, and Kaplan-Meier log-rank tests. Patients were stratified into low (<7) and high (≥7) SINS groups.

**Results** We included 195 patients with a follow-up of 6.1 months. The median SINS was 7. The score was 0 to 6 (low, no referral recommended), 7 to 12 (intermediate, consider referral), and 13 to 18 (high, referral suggested) in 34%, 59%, and 7% of patients, respectively. Eleven patients had pre-RT referral to spine surgery, with a surgery performed in 0 of 1 patient with SINS 0 to 6, 1 of 7 with SINS 7 to 12, and 1 of 3 with SINS 13 to 18. Seven patients were referred to a surgeon post-RT with salvage surgery performed in two of those patients. Primary and secondary outcomes did not differ between low and high SINS groups.

**Conclusion** Higher SINS was associated with pre-RT referral to a spine surgeon, but most patients with high SINS were not referred. Higher SINS was not associated with shorter survival or worse outcome following RT.

**Key Words** Palliative radiotherapy, spinal metastases, spinal surgery, spine radiotherapy, radiation, spinal instability neoplastic score

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## INTRODUCTION

Vertebral metastases are common in cancer patients and require a multidisciplinary approach involving radiation oncology, surgery, radiology, medical oncology, palliative care, and primary care physicians. The appropriate treatment decision must be based on imaging in addition to other patient and tumour characteristics, including patient health, prognosis, and tumour histology<sup>1,2</sup>. Treatment commonly includes external beam radiotherapy, which provides a palliative benefit to 50 to 80% of patients, with complete pain relief achieved in one-quarter of patients<sup>3</sup>. Surgical decompression can also be an important

component of treatment for some patients. There is evidence showing that patients with spinal cord compression have better functional outcomes when treated with surgical decompression and postoperative radiotherapy compared with radiotherapy alone<sup>4</sup>. Surgical referral is also generally recommended for selected patients with spinal instability, although there is less evidence to guide this recommendation<sup>5,6</sup>.

Assessing spinal stability is recognized as a challenge for spine surgeons and non-surgeons alike. The Spine Oncology Study Group has defined spinal instability as the loss of spinal integrity as a result of a neoplastic process that is associated with movement-related pain, symptomatic or

progressive deformity, and/or neural compromise under physiologic loads<sup>1</sup>. The Spinal Instability Neoplastic Score (SINS) was developed as a tool to help clinicians identify patients with unstable, or potentially unstable, spines in order to guide appropriate referrals for spine consultation<sup>1</sup>. The SINS assigns a score based on the spinal location of disease, the presence of mechanical or postural pain, spinal alignment, bone lesion quality, vertebral body involvement, and posterior element involvement. A total score out of 18 is generated. Patients with scores of 0 to 6 are classified as having stable spines, with no surgical referral recommended, those with scores of 7 to 12 as having potentially unstable spines, with consideration of referral recommended, and those with scores of 13 to 18 as having unstable spines, with surgical referral recommended. The SINS was developed by expert consensus<sup>1</sup> and has been shown to have good inter- and intra-rater reliability amongst spine experts<sup>7</sup>, radiologists<sup>8</sup>, and radiation oncologists<sup>9</sup>.

Recent retrospective studies have shown higher SINS to be associated with higher rates of referral to spinal surgeons<sup>10</sup>, higher rates of re-irradiation following palliative radiotherapy<sup>11</sup>, and higher rates of spinal adverse events following palliative radiotherapy<sup>12</sup>. These studies have been performed in tertiary referral clinics. It is uncertain whether the distribution of SINS scores and reported outcomes are representative of a general population of patients with vertebral metastases.

The aims of this investigation were to describe the distribution of SINS seen in a population-based patient cohort, to identify factors associated with referral to spinal surgery prior to palliative radiation (pre-RT), and to determine whether higher SINS is associated with worse outcome following palliative radiotherapy to vertebral metastases.

## MATERIALS AND METHODS

### Patient Selection

We performed a retrospective review of a population-based cohort of patients treated with palliative RT for vertebral metastases between February 2012 and November 2013 at the Vancouver Centre of the BC Cancer Agency. All radiotherapy in our region is publicly funded and organized in regional population-based catchment areas around cancer centres. Each cancer centre has a population-based referral base. This study was performed at a single centre, which serves a large urban region with no availability of private treatment facilities. Spinal surgery is available to all eligible patients in our region at a nearby hospital. Patients with spinal cord compression, previous surgical instrumentation within the radiation field, repeat treatment to the same spinal level, and pediatric patients were excluded from this study.

### Data Collection

The SINS were determined by one of the authors (SLu), based on CT simulation scan images accessed via the radiotherapy planning software, available diagnostic images, and review of patient charts. Patient charts were also reviewed for patient, tumour, and treatment factors. Patients were considered to have a referral to a spine surgeon if there was a written consult note in the chart, or documentation of a physician conversation with a spine surgeon (by phone or

in person). Patient prognosis at the time of radiation was estimated using the TEACHH model<sup>13</sup>, which is based on the type of primary tumour (lung and other vs. breast and prostate), Eastern Cooperative Oncology Group (ECOG) performance status ( $\leq 1$  vs.  $> 1$ ), age ( $> 60$  vs.  $\leq 60$ ), number of courses of prior palliative chemotherapy ( $< 2$  vs.  $\geq 2$ ), presence of hepatic metastases, and presence or absence of hospitalization within the prior three months.

### Outcomes

The primary outcomes were 1) the distribution of SINS in a population-based cohort (overall and by cancer type [breast, lung, prostate, and other]), and 2) referral rates to a spine surgeon pre-RT. Secondary outcomes included referral to a spine surgeon following radiotherapy (post-RT), overall survival, maintenance of ambulation, need for re-intervention (with surgery or RT), and presence of spinal adverse events (SAEs) as defined *a priori* based on the definition of Lam *et al.*<sup>12</sup> of: symptomatic vertebral body fracture, interventional procedure for pain control at the spine site, salvage spinal surgery, any new or deteriorating neurologic symptoms, cord or cauda equina compression, or hospitalization for site-related pain.

### Statistical Analysis

For patients treated with multiple courses of radiotherapy during the study period, only the first course of radiation was included in the analysis. Data were analyzed in SPSS version 14.0 (IBM Analytics, New York, USA). Univariate analyses were performed using Student's t-test, Chi-squared, or Fischer's exact test to assess factors which may be associated with pre-RT referral to a spine surgeon. Factors examined on univariate included SINS  $\geq 7$  vs.  $\leq 6$ , patient age, gender, ECOG  $\geq 2$  (vs.  $< 2$ ), primary tumour type, metastatic disease limited to bone (vs. visceral involvement), control of primary tumour, use of bisphosphonate, use of hormone therapy, use of chemotherapy, use of targeted therapy, epidural tumour component, paraspinal tumour, and estimated prognosis based on the TEACHH score. The SINS were stratified as low-SINS (stable, SINS 0 to 6) vs. high-SINS (unstable or potentially unstable, SINS 7 to 18) for actuarial outcome analysis. Scores of 7 to 18 were analyzed together because surgical referral should be at least considered for these patients and because there were relatively few patients in the SINS  $\geq 13$  category. Actuarial outcomes were analyzed using Kaplan-Meier curves and the log-rank test.

This study had Institutional Review Board approval.

## RESULTS

Two hundred and thirteen courses of palliative spine RT in 195 patients were reviewed. For patients with multiple courses of RT, only the first course was used in the analysis. Therefore, 195 patients were included in the study. The median (95% confidence interval [CI]) survival was 7.8 (5.1 to 10.5) months. Survival at 1, 2, and 3 years was 38.2% (31.1% to 45.2%), 21.8% (15.7% to 27.9%) and 14.4% (8.7% to 20.1%), respectively. Amongst the 41 patients still alive at last follow-up, the median (range) duration of follow-up was 25.9 (0.2 to 42.3) months.

## Distribution of SINS

The median SINS was 7 (Table I). The distribution of SINS is shown in Figure 1 and did not differ significantly between patients with breast, lung, prostate, or other primary tumours.

A single fraction of palliative RT was prescribed in 64 (33%) patients overall. Amongst the 102 patients with low (< 7) SINS, 36 (35%) were treated with a single fraction of RT. Amongst the 93 patients with high ( $\geq 7$ ) SINS, 28 (30%) were treated with a single fraction. The remaining patients were treated with fractionated RT.

## Surgical Referral Patterns

Eleven patients (5.6%) were referred for surgical opinion pre-RT. One of 66 patients (1.5%) with SINS 0 to 6 was referred for surgical consultation, 7 of 115 patients (6.1%) with SINS 7 to 12 were referred, and 3 of 14 patients (21.4%) with SINS 13 to 18 were referred. Surgical opinion was obtained in 5 of 48 patients (10.4%) with breast cancer, 3 of 43 patients (7.0%) with lung cancer, 0 of 30 patients with prostate cancer, and 3 of 74 patients (4.1%) with other primary cancers.

Amongst the 11 patients referred for surgical opinion pre-RT, surgery was not recommended in the patient with SINS 0 to 6. Surgery was performed in 1 of 7 patients (14.3%) with SINS 7 to 12, and in 1 of 3 patients (33.3%) with SINS 13 to 18. Lack of or mild neurological deficit ( $n = 5$ ), spinal stability on surgeon's assessment ( $n = 3$ ), and short estimated life expectancy ( $n = 2$ ) were the most commonly cited reasons for surgery being not recommended.

On univariate analysis, only higher SINS (SINS  $\geq 7$  vs. < 7, Chi-squared 5.80,  $p = 0.027$ ) and presence of paraspinal tumour (Chi-squared 4.19,  $p = 0.041$ ) were associated with statistically higher rates of surgical referral pre-RT. There was no statistically significant association with patient age, gender, ECOG  $\geq 2$  (vs. < 2), primary tumour type, metastatic disease limited to bone (vs. visceral involvement), control of primary tumour, use of bisphosphonate, use of hormone therapy, use of chemotherapy, use of targeted therapy, epidural tumour component, and estimated prognosis based on the TEACHH score.

We performed an external validation of the TEACHH score, which will be reported elsewhere (submitted). Patients with predicted long (> 1 year), intermediate (3 months to 1 year) and short (< 3 months) life expectancies according to the TEACHH model had median (95% confidence interval) survivals of 22.3 (15.7 to 36.1) months, 4.9 (3.8 to 6.6) months, and 1.5 (0.8 to 5.4) months, respectively.

## Secondary Outcomes

Sixteen percent of patients experienced a SAE. The most common SAEs were hospitalization for site-related pain and symptomatic vertebral body fracture (Table II).

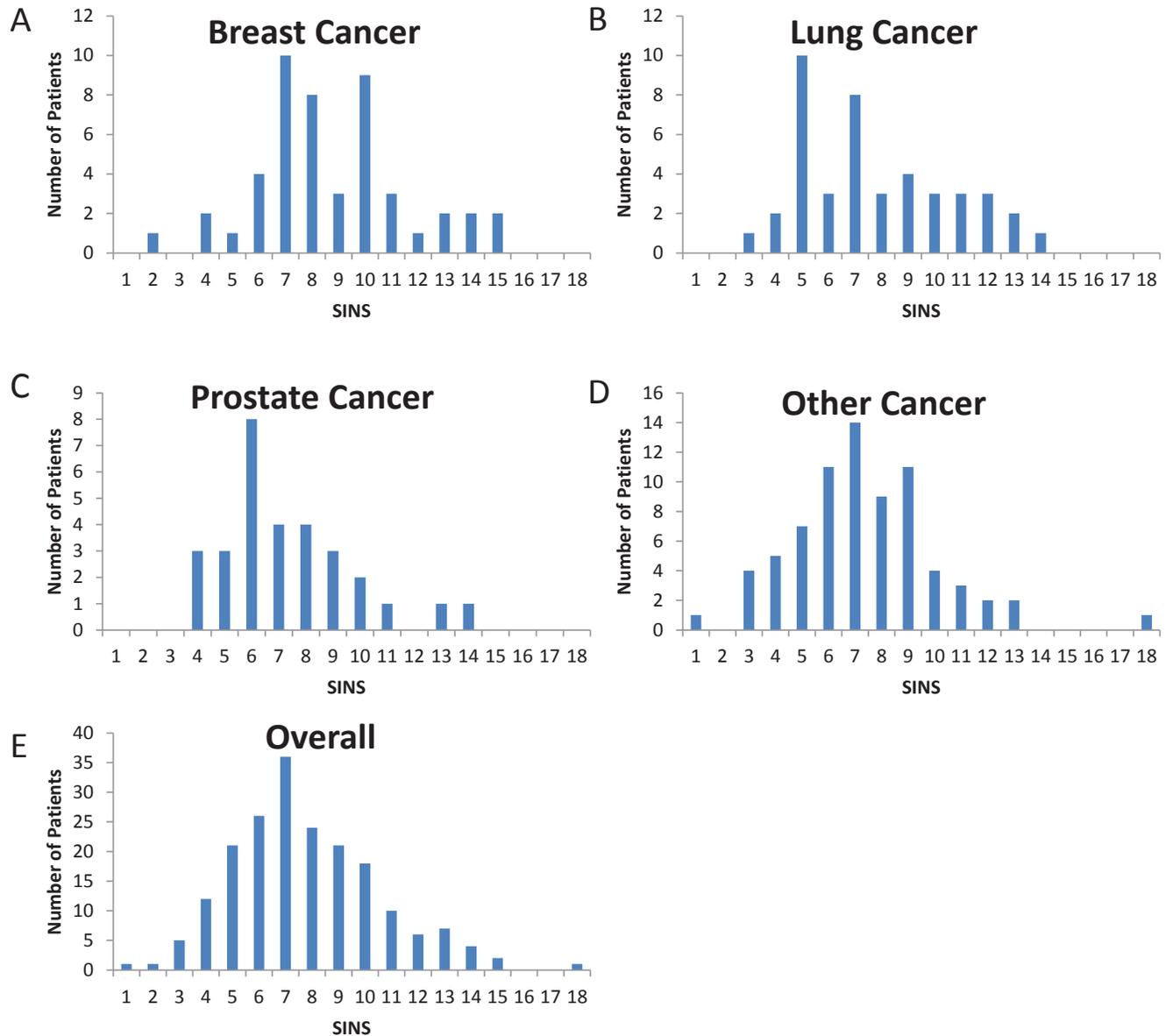
On actuarial analysis, there was no statistically significant difference in outcomes of overall survival, freedom from salvage RT, freedom from SAE, or maintenance of ambulatory ability at six months between patients with low (SINS < 7) vs. high (SINS  $\geq 7$ ) scores (Table III). Using alternate thresholds of SINS < 11 vs. SINS  $\geq 11$ , or SINS < 13 vs.  $\geq 13$ , we did not find a significant difference in any outcomes, including SAE. The use of single fraction RT was not associated with a significantly higher rate of SAE.

**TABLE I** Patient, tumour, and treatment characteristics

Age (years) at time of treatment, median (range)	66 (34–95)
Gender, <i>n</i> (%)	
Female	98 (50.3)
Male	97 (49.7)
ECOG performance status, <i>n</i> (%)	
0	6 (3.1)
1	53 (27.2)
2	35 (17.9)
3	33 (16.9)
4	3 (1.5)
Unable to determine	65 (33.3)
Primary tumour, <i>n</i> (%)	
Breast	117 (60.0)
Lung	29 (14.9)
Prostate	15 (7.7)
Other	34 (17.4)
Use of bisphosphonate, <i>n</i> (%)	49 (25.1)
Use of hormone therapy, <i>n</i> (%)	68 (34.9)
Use of chemotherapy, <i>n</i> (%)	94 (48.2)
Use of targeted therapy, <i>n</i> (%)	34 (17.4)
Epidural involvement by tumour, <i>n</i> (%)	34 (17.4)
Paraspinal involvement by tumour, <i>n</i> (%)	41 (21.0)
RT dose fractionation	
Single	64 (32.8)
Fractionated	131 (67.2)
Spinal Instability Neoplastic Score (SINS)	
Median, range	7 (1–18)
SINS 1–6, stable, <i>n</i> (%)	66 (33.8)
SINS 7–12, potentially unstable, <i>n</i> (%)	115 (59.0)
SINS 13–18, unstable, <i>n</i> (%)	14 (7.2)
Charlson Comorbidity score, median (range)	0 (0–4)
Prognosis based on TEACHH score, <i>n</i> (%)	
>1 year	29 (14.9)
3 months–1 year	89 (45.6)
<3 months	13 (6.7)
Insufficient information	64 (32.8)

ECOG = Eastern Cooperative Oncology Group ; RT = radiotherapy; SINS = Spinal Instability Neoplastic Score; TEACHH = type of cancer, Eastern Cooperative Oncology Group performance status, age, prior palliative chemotherapy, prior hospitalizations, and hepatic metastases.

Seven patients were referred for surgical consultation for the previously radiated area post-RT. The median (range) pre-RT SINS of patients referred post-RT was 7 (6 to 10). Salvage surgery was performed in two of these patients. Pre-RT SINS in these patients were 7 and 9. The median (range) time to referral from the date of radiation was 4.0 (0.1 to 6.8) months.



**FIGURE 1** Distribution of Spinal Instability Neoplastic Scores in patients with A) breast, B) lung, C) prostate, and D) other cancer. The overall distribution of SINS is shown in E. SINS = Spinal Instability Neoplastic Scores.

**TABLE II** Incidence of spinal adverse events

Spinal adverse event (SAE)	n (%)
Hospitalization due to uncontrolled pain at RT site	10 (5.1)
Symptomatic vertebral fracture	10 (5.1)
Interventional procedure	7 (3.6)
Salvage surgery	2 (1.0)
New or deteriorated neurologic symptoms	7 (3.6)
Cord/cauda equina compression	7 (3.6)
Number of patients affected by SAE	32 (16.4)

RT = radiotherapy.

## DISCUSSION

This study investigated the distribution of SINS in a population-based cohort of patients treated with radiotherapy for vertebral body metastases, the factors associated with referral pre-RT, and outcomes of patients with low vs. high SINS. We found that 7% of patients had an unstable spine based on the SINS, and an additional 59% of patients had potentially unstable spines. This distribution of SINS is similar to that reported in the literature from non population-based studies<sup>10,11,12</sup>. Different primary cancers demonstrate a different propensity for lytic or blastic metastases with differing survival and lines of available systemic

**TABLE III** Actuarial outcomes of patients with low (<7) vs. high (≥7) SINS

	Low-SINS (n=102)	High-SINS (n=93)	p
Overall survival (months), median (95% CI)	7.9 (4.5–11.3)	7.8 (3.1–12.5)	0.396
Freedom from salvage RT or surgery to same vertebral level at 6 months, % (95% CI)	91.1 (84.2–98.0)	83.2 (74.0–92.4)	0.239
Freedom from spinal adverse event at 6 months, % (95% CI)	90.5 (83.6–98.7)	85.2 (77.4–93.0)	0.282
Maintenance of ambulatory status at 6 months, % (95% CI)	58.7 (45.7–68.9)	57.1 (45.5–68.7)	0.349

SINS = Spinal Instability Neoplastic Score; RT = radiotherapy.

therapy. We showed that the distribution of SINS did not differ statistically significantly between tumour types.

Patients with potentially unstable or unstable spines based on the SINS were more likely to be referred for surgical assessment pre-RT. However the vast majority of these patients was not referred, either prior to radiotherapy or subsequent to it. This is particularly the case for the potentially unstable (SINS 7 to 12) group, in which only 6.1% were referred pre-RT and another 6.1% were referred post-RT. We did not find a relationship between pre-RT SINS and patient outcomes of referral to a spine surgeon post-RT, overall survival, maintenance of ambulation, need for re-intervention, or presence of SAE. While the paper describing SINS scores was published at the time of this study, the penetrance of the scoring system into routine clinical practice was limited.

If all patients with potentially unstable or unstable spines were referred for surgical consultation, the number of urgent spinal assessments required pre-RT would have increased in our cohort from 6% of patients to 66% of patients, representing an 11-fold increase in urgent surgical assessments for the management of spinal instability caused by metastatic disease. This may have necessitated increased funding, space, or surgical personnel, and would have required additional medical visits for patients. These urgent assessments would have been required within days to avoid RT delays in patients who were not treated surgically. The standard of care for timely palliative RT at our institution is to deliver RT for palliation of pain within a week of referral.

The threshold SINS at which surgical referral has been recommended is variable. The Surgical Oncology working group has recommended consideration of surgical referral for patients with SINS ≥ 7 and referral for patients with SINS ≥ 13. It has been suggested that an alternate threshold for referral may be considered<sup>10</sup>. In their study of outcomes of patients treated with single vs. fractionated radiotherapy, Lam *et al.*<sup>12</sup> identified higher rates of SAEs in patients with SINS ≥ 11, particularly in those treated with single fraction radiotherapy. With this threshold, 15.4% of cases in our cohort would need to be seen urgently by a spinal surgeon pre-RT.

There is some preliminary evidence that patients with spinal instability may have worse outcomes after radiation. Higher SINS has been associated with higher rates of treatment failure following palliative RT, defined by need for re-irradiation<sup>11</sup>, and higher rates of SAEs, particularly following single fraction radiation<sup>12</sup>. Components of the SINS are associated with higher rates of vertebral compression fractures after stereotactic radiotherapy<sup>14</sup>. A recent

prospective study noted an association with low SINS and complete (but not overall) pain response to palliative spine RT<sup>15</sup>. The number of patients with a complete pain response in that study was low ( $n = 16$ ), which may limit the generalizability of that finding. These studies do not yet address whether surgical intervention would improve outcomes in patients with high SINS.

There are limited data to inform clinicians on the association between spinal instability and adverse outcomes. In one retrospective review, there was no difference in pain response after RT in patients with CT evidence of increased osseous or soft tissue extent of metastasis, kyphosis, pathologic fracture, or severity of vertebral height loss<sup>16</sup>. Although this study did not look at SINS specifically, it did examine many features that are components of SINS.

Our study has a number of strengths. We examined a consecutive population-based cohort of patients and captured clinically meaningful outcomes not yet examined in the context of SINS. Unfortunately, because of the retrospective nature of this work, we were not able to capture patients referred upfront for surgery without a prior RT planning scan. Based on a different publication in a larger catchment area (which includes our own), the number of patients referred directly to surgery at this time is likely low<sup>10</sup>. The overall survival of patients included in this study was low, which has implications for surgical decision-making. It is possible that SINS may have had a larger impact on outcomes if it was selectively applied to patients with longer life expectancy or higher baseline performance status. Finally, there was significant deterioration in ambulatory function in our population. This may be related to deconditioning and decline in ECOG performance status as patients approached end of life, as opposed to neurological decline caused by uncontrolled spinal metastasis. However, there was insufficient information in our retrospective chart review to determine this conclusively.

## CONCLUSIONS

In conclusion, we found that most patients who underwent palliative radiotherapy for spinal metastases had a potentially unstable spine based on SINS groupings, regardless of primary tumour site, and that the majority of such patients were not referred to spinal surgery either at the time of their radiotherapy, or subsequent to it. Patients with higher SINS and paraspinal tumour were more likely to be referred for surgical assessment pre-RT. In this retrospective review, there was no difference in survival, retention of ambulatory ability, SAEs, or freedom from salvage treatment in patients

with low vs. high SINS. Further studies, and particularly prospective studies, of SINS using clinically meaningful endpoints<sup>17</sup> are needed.

#### CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest and declare the following interests: CF has received fees from Medtronic and Nuvasive, outside the submitted work. ST has received speaker fees from Bayer, outside the submitted work. This research did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

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