

AO Spine Clinical Practice Recommendations: Reducing the Surgical Footprint of Surgery for Spinal Metastases

Global Spine Journal
2026, Vol. 16(1) 11–18
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DOI: 10.1177/21925682251352442
journals.sagepub.com/home/gsj



Alvaro Silva González, MD¹ , Hanbo Chen, MD, MPH² , Alexander C. Disch, MD, PhD³, Jeremy Kam, MBBS⁴, John E. O'Toole, MD⁵, Nicolas Dea, MD, MSc⁶, Alessandro Gasbarrini, MD^{7,8}, Ilya Laufer, MD⁹, Cordula Netzer, MD, MBA¹⁰ , Jeremy Reynolds, MBChB¹¹, Laurence D. Rhines, MD¹² , Arjun Sahgal, MD², Jorrit-Jan Verlaan, MD, PhD¹³, Charles G. Fisher, MD, MHSc⁶, and Ori Barzilai, MD¹⁴ 

Abstract

Study Design: Literature review with clinical recommendations.

Objective: Spinal metastases represent a late complication of cancer and a major factor in decreased quality of life. The role of surgery for specific indications for spinal metastases is well established. Given the significant morbidity associated with spine surgery in this frail population, efforts are ongoing to decrease the surgical footprint. The objective of this study is to provide the readers with a concise curation of the latest spine literature on reducing the surgical footprint for spine metastases and clinical recommendations for how the practicing clinician should interpret and make use of this evidence.

Methods: The latest spine literature in the topic of reducing the surgical footprint for spine metastases was reviewed and clinical recommendations were formulated. The recommendations are dichotomously graded into strong and conditional based on the integration of scientific methodology and content expert opinion. This opinion considers experience and practical issues such as risks, burdens, costs, patient values, and circumstances.

Results: Four high impact studies were selected for review. The findings suggest that surgery plays a key role in improving patients' quality of life, but incidence of adverse events remains high and hence methods to decrease surgical morbidity are necessary. The integration of radiation into the treatment algorithm allows for less extensive surgical procedures and SBRT

¹ Clínica Alemana - Universidad del Desarrollo, Santiago, Chile

² Sunnybrook Health Sciences Center, Toronto, ON, Canada

³ University Hospital Carl Gustav Carus at the TU Dresden, Dresden, Germany

⁴ Monash Medical Centre, Clayton, VIC, Australia

⁵ Rush University Medical Center, Chicago, IL, USA

⁶ University of British Columbia, Vancouver, BC, Canada

⁷ University of Bologna, Bologna, Italy

⁸ IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy

⁹ New York University Langone Health, New York, NY, USA

¹⁰ Universitätsspital Basel, Basel, Switzerland

¹¹ Oxford University Hospitals, Oxford, England

¹² The University of Texas MD Anderson Cancer Center, Houston, TX, USA

¹³ University Medical Center Utrecht, Utrecht, The Netherlands

¹⁴ Memorial Sloan Kettering Cancer Center, New York, NY, USA

Corresponding Authors:

Ori Barzilai, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10065-6007, USA.

Email: barzilao@mskcc.org

Alvaro Silva, Clínica Alemana - Universidad del Desarrollo, Clínica Alemana, Santiago 7700248, Chile.

Email: alvarosilva@me.com



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should be strongly considered after surgery for spine metastases in appropriate patient populations. Implementation of enhanced recovery after surgery (ERAS) protocols reduce perioperative morbidity for both open and minimally invasive surgeries and should be considered on an institutional level. Utilization of minimally invasive surgical stabilization should be considered as it results in fewer post operative complications, lower infection rates, less blood loss during surgery, and a shorter hospital stay compared to open stabilization of unstable pathology thoracolumbar fractures.

Conclusions: The role and benefits of surgery for metastatic spine disease are well established, yet surgery carries significant risk for adverse events which may negatively affect overall cancer care. Methods for reducing the surgical footprint include incorporation of stereotactic radiation allowing less extensive surgery, implementation of ERAS protocols and utilization of minimally invasive surgical strategies.

Keywords

minimally invasive spine surgery, frail, spinal metases, enhanced recovery after surgery, radiosurgery

Introduction

By 2050, global annual cancer cases are predicted to rise to 35 million, a 77% increase from 2022.¹ Up to 40% of cancer patients may develop spinal metastases (SM), leading to pain from vertebral compression fractures (VCFs), neurological complications, and reduced quality of life. Advances in cancer treatments have improved life expectancy over the past 20 years,¹ especially for renal, lung, colon, and breast cancers, increasing the likelihood of needing medical or surgical treatment for SM.² The role of surgery for patients with SM, as part of a multidisciplinary team, is well established.³ However, these patients are inherently vulnerable,⁴⁻⁸ with a 5 to 7 times higher risk of complications and mortality following elective surgery according to the Metastatic Spine Tumor Frailty Index (MSTFI).⁹ For patients undergoing emergency surgeries² as well as elderly patients with SM the perioperative complication rates are even higher.¹⁰ Thus, efforts must focus on providing optimal cancer care while minimizing complications.

With the increasing occurrence of SM, spine surgeons are likely to encounter and treat these cases more frequently. A recent survey distributed among 312 practicing spine surgeons concluded that additional support is needed in tailoring treatment invasiveness to life expectancy and frailty.¹¹ To this end, the AO Spine Knowledge Forum Tumor, a multidisciplinary international expert group dedicated to research and education in spinal oncology, sought to review the current literature and highlight key articles focused on reducing the surgical footprint in surgery for spinal metastases to inform clinical decision making based on currently available data.¹²⁻¹⁴

Results

Article 1

Patient-Reported and Clinical Outcomes of Surgically Treated Patients with Symptomatic Spinal Metastases: Results from Epidemiology, Process, and Outcomes of Spine Oncology (EPOSO), a Prospective, Multi-Institutional and International

Study. Barzilai et al. Neurosurgery. Nov 12 024;95(5):1148-1157. doi:10.1227/neu.0000000000002989.¹⁵

Clinical Rationale

Patient-reported outcomes (PRO) represent an objective method to study Quality-of-life (QOL) measures and have become a priority in the treatment of patients affected by vertebral metastases. The EPOSO, a prospective, multicenter and international study was unique as it is the first of its kind to utilize a validated spine-cancer-specific PRO tool, the SOS-GOQ2.0. Data from this PRO tool were collected alongside familiar generic QOL measures of SF36v2 and the EQ-5D. Additional descriptive measures on population, treatment approach, pain outcomes and survival were also assessed.

Summary of the Clinical Findings

The EPOSO study presents the largest prospective international multi-institutional cohort of 280 patients with symptomatic spinal metastases surgically treated with stabilization and/or decompression surgery with or without adjuvant radiotherapy, between 2013 to 2018 QOL Outcomes.

Several QOL outcomes tools were used, and results included the SF-36v2 physical component improved from a mean score of 28.9 at baseline to 30.8 6 weeks posts surgery and up to 35.3 at 2 years ($P < .001$, mean change 6.4 [CI 3.1; 9.7]). The SF-36v2 mental component improved from a mean score of 42.5 at baseline to 44.7 6 weeks post-surgery and up to 47.1 at 2 years ($P = .004$ mean change 4.6 [CI 1.2; 8.1]). The EQ-5D (3L) score improved from a mean score of 0.46 at baseline to 0.63 6 weeks post-surgery and up to 0.70 at 2 years ($P < .001$, mean change 0.24 [CI 0.17; 0.30]). Pain NRS index improved from a mean score of 6.4 at baseline to 3.8 six weeks post-surgery and remained stable at 3.8 at 2 years ($P < .001$, mean change 2.6 [CI 3.4; 1.9]). The SOSGOQ2.0 overall score improved from a mean score of 50.0 at baseline to 60.9 6 weeks post-surgery and up to 66.8 at 2 years ($P < .001$, mean change 16.8 [CI 11.2; 22.4]).

Notably, from the 280 patients included in the study, 105 patients (37,5%) had 226 postoperative adverse events, most of which were grade 1 or 2, such as neurological deterioration, urinary tract infection, dysphagia, ileus, delirium, pain, and others. Serious adverse events ($\geq$ grade 3) requiring reoperation or resulting long term disability included: wound complications in 15 patients (5.4%), neurological deterioration in 4 patients (1.4%) and hardware failures in 2 patients (0.8%). This study demonstrated that surgical decompression and / or stabilization for patients with spinal metastases resulted in improved quality of life and pain control. Be that as it may, the incidence of adverse events, mostly low grade, remains high, even in specialized centers.

Methodological Review

The paper directly addresses the impact of surgical intervention on HRQOL in patients with spinal metastases, and is based on a prospective observational cohort study, which is generally considered moderate-quality evidence. The lack of a control group lowers the quality of the analysis. Data collection is prospective, multicenter and therefore generalizability is enhanced. The analysis is robust, the statistical methodology is sound, the assessment tools used are validated and state of the art, the data is mature, with long term follow up and the results are consistent, which strengthens the evidence to moderate/strong.

Recommendation for Integrating into Your Clinical Practice

Based on the GRADE methodology there is a **strong** recommendation for surgical intervention in appropriately selected patients with symptomatic spinal metastases, to improve quality of life, functional status and pain control.

Article 2

Stereotactic Radiosurgery for Postoperative Spine Malignancy: a Systematic Review and International Stereotactic Radiosurgery Society Practice Guidelines. Faruqi et al. *Pract Radiat Oncol.* Mar-Apr 2022;12(2):e65-e78. doi:10.1016/j.prro.2021.10.004.¹⁶

Clinical Rationale

Stereotactic body radiation therapy (SBRT), also known as stereotactic ablative radiotherapy (SABR), aims to deliver high doses of radiation precisely over a small number of treatments, with the intention of long-term ablation of the target lesion.¹⁷ In recent years, SBRT has been successfully applied to both intact spine lesions and post-operative surgical beds in the spine.¹⁸⁻²² SBRT for intact spine lesions demonstrated durable local tumor control, improved pain control

compared to cEBRT, and very low risks of neurological side effects in multiple randomized clinical trials.²¹⁻²³ Guidelines have been generated to improve the quality of post-operative spine SBRT contouring.²⁴

Summary of the Clinical Findings

The study made by Faruqi et al. presents a systematic review and a set of consensus guidelines developed by the International Stereotactic Radiosurgery Society (ISRS) aimed at standardizing the clinical implementation of post-operative spine SBRT.¹⁶

In this systematic review, 12 relevant studies were included, consisting of 461 patients and 499 treated spine segments. Five of the studies included were prospective, while 7 were retrospective. A variety of surgical indications and techniques were included, with some studies reporting a minority of patients treated with a minimally invasive approach. SBRT prescription doses included 15-24 Gy in 1 fraction, 24 Gy in 2 fractions and 24-30 Gy in 3-5 fractions. The overall survival was 57% (46-68%) in 1 year and local control was 70-96% in one year while an analysis showed a summary estimate of 89% (95% confidence interval: 83-94%) for local control at 1 year. The most common area for failure after SBRT was in the epidural space. On regression analyses, potential predictors of local failure included higher grade (Bilsky 2-3) residual epidural disease post-operatively, shorter time to surgery after prior radiation, lower dose per fraction, sarcoma histology, large pre-operative tumor volume, and failure to achieve pain control post-SBRT. Potential predictors of poor OS included lower KPS, lack of systemic therapy post-SBRT, and failure to achieve pain control post-SBRT. In terms of post-SBRT neurological toxicity, only 1 case of myelopathy was reported (0.2%). Twenty-six cases of vertebral compression fracture (VCF) were reported, and the VCF rate on meta-analysis was 2.4% (0.3-6.7%). In terms of other toxicities, one case of grade 4 esophageal fistula was reported, requiring surgical repair.

Based on the systematic review results, Faruqi et al. proposed a number of guidelines regarding post-operative SBRT.¹⁶ The ideal population for post-operative spine SBRT: patients with oligometastatic disease, patients with spine metastases from a radioresistant primary (sarcoma, gastrointestinal primaries, melanoma, renal cell carcinoma, thyroid), patients with spine metastases associated with large soft tissue mass (e.g. paraspinal extension) or patients with prior irradiation to the levels receiving surgery so that a highly accurate and conformal technique such as SBRT can better protect important neural structures. They conclude that all patients should undergo MR-based simulation with or without gadolinium contrast injection, and a planning CT myelogram may be considered if metallic artifacts obscure the spinal canal. A planning organ at-risk volume should be applied around the spinal cord to limit cord dose. Epidural disease should be covered with an appropriate extension based on the

pre-surgery volume using published contouring guidelines. Noteworthy, the most common area for failure after SBRT was in the epidural space, where SBRT dose would have been limited by proximity to the spinal cord or cauda equina. This speaks to the importance of achieving good separation between the gross tumor and spinal cord/cauda equina during surgery.

Methodological Review

This is a systematic review and meta-analysis of all potentially relevant prospective and retrospective studies, although meta-analyses of randomized trials represent the highest level of evidence, the lack of phase III trials, the inclusion of retrospective studies, and the relatively high levels of heterogeneity found in meta-analysis results would somewhat reduce the quality of evidence to moderate/strong. This paper also offers a consensus guideline by a panel of experts in the field that is very valuable but is not a category of medical evidence.

Recommendation for Integrating Into Your Clinical Practice

Based on the GRADE methodology there is a **strong** recommendation for integrating SBRT after surgery for spine metastases in the appropriate patient population as post-operative spine SBRT offers more durable disease control. It is important to consider post-operative spine SBRT, when available, as a treatment option and involve Radiation Oncologists for a multidisciplinary approach to management.

Article 3

Patient outcomes following implementation of an enhanced recovery after surgery (ERAS) pathway for patients with metastatic spine tumors. Chakravarthy et al Cancer. Dec 12 022;128(23):4109-4118. doi:10.1002/cncr.34484.²⁵

Clinical Rationale

Implementation of hospital protocols to enhance recovery after surgery (ERAS) was shown to reduce post operative morbidity in various disciplines^{26,27} including elective spine surgery. ERAS-programs aim to standardize preoperative, intraoperative and postoperative care for various surgical procedures, for elective spine surgery.^{28,29} Limited information is available about the effect of ERAS-programs on the outcome of spinal metastases patients, displaying a need to increase knowledge on this field.

Summary of the Clinical Findings

The study presents findings from a retrospective single institution analysis comparing 177 patients enrolled in an Enhanced

Recovery After Surgery (ERAS) program to 213 pre-ERAS era patients. The authors developed and implemented an ERAS protocol that included preoperative, intraoperative and postoperative measures. Patient education, pain management aiming to reduce opioid use, goal-directed fluid therapy during surgery, early postoperative urinary catheter removal, immediate start of regular diet and early ambulation were part of the program. The findings demonstrated that patients in the ERAS cohort ambulated earlier with a mean of 34 hours (pre-ERAS cohort 57 hours; $P = .0001$); patients in the ERAS cohort had earlier discontinuation of urinary catheters (mean, 36 hours) compared to the pre-ERAS group (56 hours; $P < .001$); the length of hospital stay (LOS) was also shorter in the ERAS cohort (5.4 days) compared to the pre-ERAS group (7.5 days; $P < .0001$); The postoperative day 0-5 cumulative mean opioid use was significantly lower in the ERAS group (178 MME) compared to the pre-ERAS group (396 MME; $P < .0001$).

Implementing a multidisciplinary ERAS program for metastatic spine tumor surgery led to improved clinical outcomes, including earlier mobilization, shorter catheterization duration, reduced hospital stays and decreased opioid consumption.

Methodological Review

This is an observational study that typically provides low-medium quality evidence due to potential biases and confounding factors, such as non-randomization to ERAS or pre-ERAS groups. However, the study demonstrated consistent improvements across multiple outcomes for the ERAS group, suggesting a positive effect of the intervention. The outcomes measured directly relate to the patient population and interventions studied, providing direct evidence of the ERAS program's impact (directness of evidence) and the study reported statistically significant differences with P -values less than 0.05 for key outcomes, indicating even with a limitation of a retrospective design precise estimates (precision). There is no indication of publication bias, but, as a single-center study, the generalizability of the findings may be limited. Taken together, the quality of the data is moderate.

Recommendation for Integrating Into Your Clinical Practice

Based on the GRADE methodology there is a **conditional** recommendation for ERAS protocol implementation to improve postoperative outcomes for patients undergoing metastatic spine tumor surgery irrespective of surgery being performed. The protocol presented in this manuscript can be used as presented or modified according to local preferences in collaboration with anesthesiology and nursing teams.

Article 4

Posterior Percutaneous Pedicle Screws Fixation Versus Open Surgical Instrumented Fusion for Thoraco-Lumbar Spinal

Metastases. Perna et al. *Front Oncol.* 2022;12:884928. doi: 10.3389/fonc.2022.884928.³⁰

Clinical Rationale

Surgical indication for spinal stabilization of unstable pathologic fractures is well established.^{31,32} Open surgical techniques often lead to high perioperative complications in patients with spinal metastases.⁴⁻⁸ Minimally invasive surgery (MIS) techniques for stabilization with percutaneous pedicle screws and rods as well as decompression utilizing MIS access strategies, are known to reduce perioperative complications in degenerative spinal pathologies.³³ Adoption of these techniques to surgical spinal oncology is ongoing as implementation of MIS methods could potentially decrease perioperative complications in this frail patient population.

Summary of the Clinical Findings

Perna et al³⁰ performed a systematic review and meta-analysis comparing traditional open surgery vs MIS techniques for stabilization of pathological fractures in the thoraco-lumbar spine. This review aimed to directly compare two treatment strategies for pathologic fractures in the thoraco-lumbar spine: Posterior Percutaneous Pedicle Screws Fixation (PPSF) (MIS stabilization) and Open Posterior Instrumented Fusion (OPIF) (Open Stabilization). The review includes 8 studies with a total of 448 patients. The authors looked at key results such as complications after surgery, blood loss, infections, death rates, pain levels, and quality of life. The results demonstrated that MIS stabilization has fewer post operative complications after surgery than Open Stabilization. (odds ratio of 0.48, 95% CI 0.27 to 0.83; $P = 0.01$); MIS stabilization reduces blood loss during surgery compared to Open Stabilization (odds ratio of -585.70 , 95% CI -848.28 to -323.13 ; $P < 0.0001$); Patients who had MIS stabilization stayed in the hospital for a shorter time than those who had Open Stabilization. (odds ratio of -3.77 , 95% CI -5.92 to -1.61 ; $P = 0.0006$); The infection rate was lower in the MIS stabilization group. (odds ratio of 0.31, 95% CI 0.12 to 0.81; $P = 0.02$); rates for re-interventions and death are similar for both methods ($P = 0.62$ for reinterventions and $P = 0.51$ for mortality) and both treatments show similar results as far as pain management after surgery.

MIS stabilization results in fewer post operative complications, lower infection rates, less blood loss during surgery, and a shorter hospital stay compared to open stabilization of unstable pathology thoracolumbar fractures.

Methodological Review

This paper is a systematic review and meta-analysis, typically providing robust evidence. Nevertheless, most included studies are observational in nature, which can diminish the quality of evidence due to potential bias. The absence of

randomized controlled trials (RCTs) further contributes to this limitation. Despite these concerns, the results demonstrate consistency across the studies, thereby enhancing their reliability. The research effectively addresses the primary question by directly comparing MIS stabilization and Open Stabilization for patients with spinal tumors. Given these considerations, the evidence quality is rated as moderate (GRADE).

Recommendation for Integrating Into Your Clinical Practice

Based on the GRADE methodology there is a **conditional** recommendation for utilization of MIS stabilization techniques in patients undergoing metastatic spine tumor surgery for pathologic thoracolumbar fractures.

Discussion

Surgery is Essential but Comes with a Price

The role of surgery for treatment of spinal metastases is well established and has demonstrated an effective role in maintaining neurologic function including ambulation,³ improving local control and improvement in their quality of life.³⁴ However, surgery for spinal metastases often occurs in an emergent setting, where there is a high adverse event profile. Dea et al¹⁰ reported in a study of 101 patients that 32% experienced intraoperative complications, including blood loss over 2L (16.8%) and durotomies (9.9%). Postoperative adverse events occurred in 66.3% of cases, such as delirium (20.8%), transient neurological deterioration (5.9%), and superficial or deep wound infections (5.9%). On average, there were 1.8 adverse events per patient, leading to longer hospital stays, increased treatment costs, and reduced quality of life.¹⁰ The EPOSO study¹⁵ highlighted above, demonstrated significant and durable improvement in QOL metrics as evaluated by a spine cancer specific PRO tool, yet adverse events remain high in this contemporary series. The high incidence of surgery-related adverse events highlights the need for preventive strategies to improve outcomes in frail cancer patients.

Integration of Stereotactic Radiation Allows Less Extensive Surgery

Likely the most impactful change to treatment of spinal metastases was the integration of stereotactic radiation. Radiotherapy can be used as primary treatment modality among patients without mechanical instability or high-grade spinal cord compression.³⁵ A randomized control trial by Sahgal et al demonstrated that SBRT results in more significant and durable pain control for painful spinal metastases compared to conventional external beam radiation, further paving the road for routine use of SBRT for spinal metastases.²¹ The utilization of SBRT for local tumor control, negates the need for

extensive surgical procedures for the purpose of surgical cytoreduction. Due to spinal cord constraints, decompressive surgery is necessary prior to SBRT for radioresistant tumors causing high grade spinal cord compression.²⁴ In the post operative setting largest single center study evaluating outcomes of postoperative stereotactic radiotherapy for spinal metastases, Laufer et al³⁶ reported on 186 patients with radioresistant solid tumors and demonstrated a 4.2% rate of local recurrence at one year using high dose hypo-fractionated SBRT and up to 22% local recurrence with lower doses, a remarkable improvement from historic local control data for similar histologies. Since then, robust data have been accumulated and Faruqi et al's meta-analysis¹⁶ found that post-surgery SBRT reliably reduces local recurrence to 89% (70%-96%). This article by Faruqi et al also indicates that the most common site of tumor recurrence after SBRT was in the epidural space, emphasizing the need for adequate separation between the spinal cord and the tumor and suggesting that the quality of epidural decompression impacts the local recurrence rate following SBRT. Therefore, achieving circumferential tumor decompression and separation from the thecal sac, alongside careful planning of SBRT, particularly in the presence of implants, may help reduce the recurrence rates. SBRT availability may remain limited in various regions and a multidisciplinary approach with surgeons, radiation and medical oncologists is key to achieving desired patients' outcomes.

Implementation of Multidisciplinary Protocols - ERAS

ERAS is a multimodal approach to perioperative management, aimed at improving recovery, reducing complications, and shortening hospital stays. ERAS protocols have known benefits in reduction of post operative morbidity in various disciplines.^{26,27} For degenerative spine fusion surgery,^{28,29} prehabilitation, proper nutrition, stopping smoking and alcohol, antibiotic prophylaxis, avoiding urine catheters, optimal analgesia, reducing opioids, and early mobilization are recommended to reduce complications.³⁷ Charkravaty et al²⁵ reported the outcome of implementation of ERAS protocol specifically developed for patients undergoing surgery for spinal metastases. Implementation of this protocol resulted in reduced perioperative complications, regardless of surgical technique. Although more research is needed to determine the true value and reproducibility of this approach, implementation of institutional protocols represents a promising and cost-effective method of reducing surgical morbidity without need to modify routine clinical care.

Utilization of Minimally Invasive Surgery

Minimally invasive surgery (MIS) allows for tumor resection and spinal stabilization with smaller incision size,

less muscle and other soft-tissue dissection and injury compared with traditional open approaches. Percutaneous pedicle screw fixation (PPSF) is a common MIS technique used for stabilization enabling multilevel instrumentation for unstable pathologic fractures and can be coupled with MIS methods of tumor decompression via tubular retractors or a mini-open approaches.³⁸ Pennington et al. conducted a systematic review and meta-analysis of MIS vs open approaches for surgical treatment of spinal metastases, included 9 papers all of which had level 3 data and found that patients treated with MIS approaches tended to have lower intraoperative blood loss, shorter operative times, shorter inpatient stays, and fewer complications relative to patients undergoing surgeries with conventional approaches.³⁹ The study reviewed in our current manuscript by Perna et al³⁰ was included as it targeted a more specific question and evaluated methods of stabilization only for patients with pathologic thoracolumbar fractures. These data demonstrate decreased morbidity with utilization of MIS stabilization techniques for spinal metastases and future, high quality studies are necessary to determine the role of MIS in various surgical scenarios in spinal oncology.

The role and benefits of surgery for metastatic spine disease are well established, yet surgery carries significant risk for adverse events which may negatively affect overall cancer care. This review highlights manuscripts describing methods for reducing the surgical footprint and practice recommendations include incorporation of stereotactic radiation allowing less extensive surgery, implementation of ERAS protocols and utilization of minimally invasive surgical strategies.

Acknowledgements

This work was organized by AO Spine through the AO Spine Knowledge Forum Tumor, a focused group of international spine tumor experts. AO Spine is a clinical division of the AO Foundation, which is an independent medically guided not-for-profit organization. Support was provided directly through AO Network Clinical Research.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Alvaro Silva González  <https://orcid.org/0000-0002-9899-3156>

Hanbo Chen  <https://orcid.org/0000-0002-6447-653X>

Cordula Netzer  <https://orcid.org/0000-0001-7381-373X>

Laurence D. Rhines  <https://orcid.org/0000-0002-8474-1521>
 Ori Barzilai  <https://orcid.org/0000-0002-4037-8716>

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