Quantitative Evaluation of Local Control and Wound Healing Following Surgery and Stereotactic Spine Radiosurgery for Spine Tumors

Ran Harel[1,2], Todd Emch[3], Samuel Chao[4-6], Paul Elson[6], Ajit Krishnaney[1], Toufik Djemil[5,6], John Suh[4,5], Lilyana Angelov[1,4,6]

■ OBJECTIVE: **The present study evaluated the optimal measuring criteria to assess spinal tumor response to surgery followed by stereotactic spine radiosurgery (SRS) and reports the local control and wound complication rates following combined multimodality treatment.**

■ METHODS AND MATERIALS: **Prospectively collected patient information was retrospectively reviewed to identify patients treated with spine surgery followed by SRS. Tumor sizes and volumetric assessment were formally measured. Local control status was defined according to World Health Organization (WHO, bidimensional), RECIST (unidimensional), or volumetric size change. Statistical comparative assessments of tumor measurements were performed.**

■ RESULTS: **Twenty-two patients were eligible for evaluation after having undergone surgery followed by single-fraction SRS within a 2-month period. Seventeen had follow-up magnetic resonance imaging (MRI) with a mean patient follow-up of 12.59 months (range 3–36 months). None developed wound complication after radiation therapy (95% lower confidence bound 13%). Two patients had clinical recurrence while 15 of 17 achieved local control (88.3%). A test of marginal homogeneity for RECIST versus WHO was not statistically significant, $P = 1.0$ suggesting similar response classifications with both systems. Spearman correlations among 1) volumetric assessment, 2) bidimensional size, and 3) unidimensional size were significant for all groups ($P < 0.05$).**

■ CONCLUSION: **High local control rates can be achieved with surgery followed by SRS. Further, adjuvant SRS following spine tumor surgery delivers less radiation to the wound than conventional radiation and thus potentially reduces wound complications. Unidimensional, bidimensional, and volumetric tumor assessments demonstrate similar results. Hence the use of the simpler RECIST criteria is suitable and appropriate for evaluating the response to treatment after spine radiosurgery.**

INTRODUCTION

The management of metastatic spine tumors has extensively changed in the recent decades. Previously, the lack of spinal instrumentation and inability to approach the spine by ventral or lateral approaches yielded poor surgical results and showed no benefit over conventional radiation.[1-6] However, advances in operative skill sets and instrumentation have allowed surgeons to directly decompress the spinal cord, swinging the pendulum back to operative management of spine tumors. This paradigm shift became widely recognized as an appropriate standard of care for patients with metastatic epidural spinal cord

Key words
- Local control
- Spine radiosurgery
- Spine surgery
- Tumor
- Wound infection

Abbreviations and Acronyms
CT: Computed tomography
CTV: Clinical target volume
DRR: Digitally reconstructed radiograph
ESCC: Epidural spinal cord compression
IM: Infrared markers
MESCC: Metastatic epidural spinal cord compression
MRI: Magnetic resonance imaging
PD: Progressive disease
PR: Partial response
RECIST: Response Evaluation Criteria In Solid Tumors
SD: Disease is considered stable
SRS: Stereotactic spine radiosurgery
TPS: Treatment planning system

From the [1]Center for Spine Health, Neurological Institute, [3]Imaging Institute, Section of Neuroradiology, [4]Rose Ella Burkhart Brain Tumor and Neuro-Oncology Center, Neurological Institute, [5]Radiation Oncology, Taussig Cancer Institute, and [6]Taussig Cancer Institute, Cleveland Clinic, Cleveland, Ohio; and [2]Spine Unit, Neurosurgery Department, Talpiot Medical Leadership Program, Sheba Medical Center, Israel

To whom correspondence should be addressed: Lilyana Angelov, M.D. [E-mail: angelol@ccf.org]

Citation: World Neurosurg. (2016) 87:48-54.
http://dx.doi.org/10.1016/j.wneu.2015.10.075

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

compression (MESCC) after the randomized study by Patchell et al.[7] They demonstrated superior results in terms of ambulation and pain control with surgery followed by fractionated radiation when compared with radiation alone in patients with single-site MESCC with nonradiosensitive pathologies. However, in the postoperative setting, it is well known that radiation treatment can impede the wound healing process and may cause elevated rates of wound complications.[8-11]

Similar to the changes seen in the surgical management of patients with spine tumors, there are novel radiation targeting and delivery methods that offer significant advantages.[3,12-15] One such method is stereotactic spine radiosurgery (SRS) that delivers a highly conformal, high dose of ionizing radiation with a steep dose fall-off in 1–5 sessions for the treatment of spine tumors. This modality has been shown in several studies to be safe and effective, and many patients are now experiencing greater and more rapid relief of pain with SRS, as well as higher local control rates when compared with conventional radiation treatments.[12-14,16] Another advantage of SRS over conventional radiation in the postoperative setting is the potential sparing of regions at risk, such as the fusion or instrumentation site and the operative wound.[17]

In 2006, Rock et al.[18] described their series of 18 patients with metastatic spine tumors treated with surgery followed by SRS. At 7 months' mean follow-up, 92% of these patients remained neurologically stable or improved. This series, however, did not formally evaluate the radiographic impact of treatment with SRS. Laufer et al.[19] reported the results of 186 patients operated and treated with SRS. The local control rate reported was 83.6% at 1 year post SRS on the basis of a blinded neuroradiologist evaluation using computed tomography (CT) and magnetic resonance imaging (MRI) scans for tumor measurement and incorporating a 6-point epidural spinal cord compression (ESCC) scale[20] to determine the response to treatment or recurrence. The radiosurgery literature lacks reports of formal radiologic evaluation of tumor response and determining the most reliable response criteria for the evaluation of these lesions.

The World Health Organization (WHO) criteria to evaluate local control, recurrence, and progression in solid tumor, first published by Miller et al.,[21] measures the largest tumor diameter multiplied by its largest perpendicular dimension. A 50% tumor size reduction was defined as partial response (PR), and a 25% increase was defined as progressive disease (PD). Otherwise, the disease is considered stable disease (SD). In 2000 the Response Evaluation Criteria In Solid Tumors (RECIST) criteria were introduced and tumor response was evaluated, using the largest tumor measurable in a unidimensional manner.[22,23] A 30% tumor diameter reduction was defined as partial response (PR), and a 20% increase was defined as PD. Otherwise, the disease is SD. In recent years, the improved imaging technology, combined with advanced computational abilities, allow for volumetric measurements of tumor load.[23,24] These measurement criteria, however, have never been applied or directly compared to evaluate and quantify the effect of treatment in spine metastases.

This paper addresses the benefits of SRS following spine surgery in terms of wound complications and radiographic local control and evaluates optimal local control assessment methods.

METHODS AND MATERIALS

A retrospective review of patient records prospectively collected through the Cleveland Clinic Spine Tumor Board database was performed. After the study was approved by the Cleveland Clinic Institutional Review Board, the authors reviewed the records of 925 spine tumor patients added to the database from 2006–2009. These patients had undergone various treatment regimens including surgery, chemotherapy, radiotherapy, radiosurgery, or various combinations. Patients included in this series had been managed with planned staged treatment for either metastatic spine tumors or primary spine tumors comprising spine surgery followed by adjuvant SRS to the surgical bed within 2 months of initial surgery.

For the actual SRS treatment, the patients were immobilized supine in either the Efficast (Orfit Industries) 5-point mask for tumors involving occiput to T5 or the BodyFix Immobilization System (Elekta) for lesions involving T6 to sacrum. At the time of simulation, 6–7 infrared markers (IMs) were placed above the treatment region asymmetrically to avoid ambiguities during patient setup. All patients were then scanned using 2-mm thick contiguous CT slices using a large-bore CT simulator. Additionally, all patients underwent spine MRI with axial turbo spin echo T1-weighted images and axial STIR images to optimize tumor delineation unless there was a contraindication to MR imaging.[25,26] CT myelograms were performed in patients who could not undergo MRI scans or those with incomplete visualization of the neural structures or thecal sac related to instrument artifact.

MRI and CT image datasets were then imported into the iPlan RT 4.1or BrainScan 5.31 treatment planning system (TPS) (Brainlab, Feldkirchen, Germany) and rigorously fused. All infrared markers (IMs) were identified during localization. The clinical target volume (CTV) and critical structures (cord or thecal sac in the area of the cauda; kidneys, bowel, and esophagus) were contoured. Spinal cord contouring was extended 4 mm rostrally and caudally beyond the CTV in all cases. No margins were added (PTV = CTV). A plan involving 7–9 mostly posterior coplanar beams using step-and-shoot intensity-modulated radiation therapy technique was generated. The prescription dose was typically 14–16 Gy (to cover $\geq$90% of the identified CTV). Cord constraint was set at no more than 10% of the volume to receive 10 Gy or more, maximum cord point dose limited to 14 Gy. The inverse planning algorithms used robust planning software, which accounted for instrument-related scatter and allowed for more accurate tumor and spinal cord dosing. On the day of treatment, the patient was positioned automatically so that the IM matched a predetermined position found during the localization. Two orthogonal stereo x-ray images were obtained and fused to 2 digitally reconstructed radiographs (DRRs) generated in the same orientation from the simulation CT. Shifts were made in x, y, and z directions as needed. Two orthogonal port films were taken to confirm final patient positioning. Treatment was delivered using the 6-MV linear accelerator with micromultileaf collimator for beam shaping (Novalis, Brainlab). The patients were monitored during treatment using Exactrac (Brainlab).

For local control evaluation, the patients considered for this study had to have had at least 1 follow-up magnetic resonance