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Clinical Study

Early magnetic resonance imaging biomarkers to predict local control after high dose stereotactic body radiotherapy for patients with sarcoma spine metastases

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Abstract

BACKGROUND CONTEXT: Recent advances in image guidance and stereotactic body radiotherapy (SBRT) have resulted in unprecedented local control for spinal metastases of all histologies. However, little is known about early imaging biomarkers of local control.

PURPOSE: This study aimed to identify early magnetic resonance imaging (MRI) biomarkers to predict local control after SBRT for patients with sarcoma spine metastases.

STUDY DESIGN/SETTING: This study used a retrospective case series at a large tertiary cancer center.

PATIENT SAMPLE: From 2011 to 2014, 9 consecutive patients with 12 metastatic sarcoma lesions to the spine were treated with SBRT and underwent evaluation with dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) both pre- and post-SBRT.

OUTCOME MEASURE: Changes in perfusion metrics, including the wash-in rate constant (Ktrans), plasma volume (Vp), composite multiparametric magnetic resonance imaging (mpMRI) score, bi-dimensional tumor size, and a graded response assessment were performed and correlated to local control.

METHODS: All measurements were independent and blinded by two neuroradiologists. R^2 statistics were performed to document correlation, and two-tailed *t* tests were used to compare groups. $p<.05$ was deemed statistically significant.

RESULTS: The median time from SBRT until posttreatment MRI was 57 days. Local failure developed in one lesion (8.3%) 10 months after SBRT. The Vp mean, Ktrans mean, Vp max, and Ktrans max were significantly decreased post-SBRT as compared with pre-SBRT (58.7%, 63.2%, 59.0%, and 55.2%; all p-values <.05). Bi-dimensional tumor measurements demonstrated an average increase in size across the cohort, and 50%, 25%, and 25% of the treated lesions demonstrated features of "worsening," "no change," or "improvement," respectively, by both radiologists' graded impressions. There was good inter-reader reliability for both size and subjective disease response scores

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(R^2=0.84). The mpMRI score had 100% accuracy in predicting local control at time of last follow-up. There was no apparent correlation with size changes compared with the mpMRI score change post-SBRT (R^2=0.026).

CONCLUSIONS: We report the first analysis on the utility of DCE-MRI for metastatic sarcoma spine metastases treated with SBRT. We demonstrate that early assessment at 2 months post-SBRT using size and subjective neuroradiology impressions is insufficient to judge ultimate disease progression, and that a combination of perfusion parameters provides excellent correlation to local control.

Keywords: Imaging; Metastases; MRI; Radiotherapy; Sarcoma; Spine; Stereotactic radiotherapy

Introduction

Sarcomas are an uncommon form of cancer representing only 0.7% (n=15,040) of all newly diagnosed cancer cases in the United States each year [1]. Development of metastatic disease is dependent on histology, and long-term incidence of metastatic disease for soft-tissue sarcomas of the extremity is approximately 20% [2]. Metastatic sarcoma to the spine is extremely rare and portends a dire prognosis. It is therefore difficult to study this cohort of patients, and novel therapeutic options are needed.

Metastatic disease to vertebral bodies can result in pain and deterioration in quality of life [3]. The involvement of adjacent nerve roots or the spinal cord itself can lead to life-threatening neurologic symptoms [4]. Palliative therapies such as radiotherapy have historically had limited success in controlling sarcomas near the spine because of their radioresistant phenotype and nearby essential normal structures [5]. In the past decade, there has been a surge of advances in image-guided and stereotactic body radiotherapy (SBRT) that have allowed for high single and hypofractionated courses of radiotherapy [5,6]. This technological advance has resulted in unprecedented rates of 1-year local tumor control upward of 85% [6]. Effective measures are needed to assess those patients who will experience local failure after SBRT, particularly given the improved prognosis of many of these patients with advances in systemic therapy.

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a potential predictor of treatment response that uses quantitative metrics [7,8]. This is in stark contrast to traditional subjective reads that rely on reader expertise and demonstrate greater inter-reader variability. In addition, when monitoring response to SBRT to vertebral bodies, significant posttreatment effects and changes to the bone make common response criteria such as Response Evaluation Criteria in Solid Tumors difficult to implement [9].

Given the poor prognosis of patients with metastatic sarcoma to the spine and the difficulty in assessing early response, we herein report the results of 12 consecutively treated lesions from patients with metastatic sarcoma to the spine who underwent pre- and post-SBRT DCE-MRI and correlate various radiologic metrics to long-term outcome.

Methods

Patient details

After institutional review board approval, our center's sarcoma spine database of 240 patients was queried to identify eligible patients. Criteria for inclusion were patients who were treated with SBRT and were imaged pre- and posttreatment with DCE-MRI. We excluded patients who underwent surgical resection before radiotherapy. Nine patients who were treated with SBRT to 12 independent spinal lesions were identified.

All patients had histologic confirmation and pathology review at our institution. Pre- and posttreatment imaging were performed at our institution and read by a board-certified neuroradiologist. A multidisciplinary team of experts in spinal malignancy comprising a neurosurgeon, radiation and medical oncologists, interventional radiologists, and neuroradiologists reviewed each case before administration of SBRT and used the Neurologic Oncologic Mechanical Instability Systemic Disease (NOMS) framework for clinical decision making [10].

Simulation, treatment planning, and radiotherapy details

Hypofractionated and single-fraction SBRT techniques were performed as previously described [11]. In brief, patients were immobilized in our institutionally custom-made cradle. Patients underwent a myelogram before computed tomography (CT) simulation for improved visualization of the spinal canal. The CT simulation used 2-mm slice thickness. The Spratt Six Segmentation System was used for target delineation as per the International Spine Radiosurgery Consortium consensus guidelines [12]. Dose constraints have been previously reported [11]. Treatments were delivered with 7–11 coplanar fields with dynamic multi-leaf collimation. The dose was prescribed to the 100% isodose line in all cases. A mix of 6- and 15-MV beam energies was most commonly used. A cone beam CT was used for image guidance, and orthogonal kV imaging was obtained for each fraction to verify the patient position.