

Stereotactic body radiotherapy for the treatment of spine metastasis

Ehsan H. Balagamwala, MD, Samuel T. Chao, MD, and John H. Suh, MD

CASE SUMMARY

A 56-year-old female with renal cell carcinoma (RCC) diagnosed 7 months prior to presentation was evaluated for severe left-sided back pain originating in the left anterior hip with radiation down the left leg. She reported paresthesias along with the pain, which was present at rest and worsened with movement. She denied any associated bowel or bladder dysfunction, saddle anesthesia, or gait difficulties. At presentation, she was on maintenance Sunitinib and had an increasing narcotic requirement.

IMAGING FINDINGS

Magnetic resonance imaging (MRI) with and without intravenous contrast demonstrated loss of L4 vertebral height and replacement of the L4 vertebral body with a contrast-enhancing heterogenous expansile mass, which extended into the left pedicle. Mild extraosseous epidural soft tissue as well as moderate narrowing of the

Prepared by Dr. Balagamwala while at Cleveland Clinic, Cleveland OH, and by Dr. Chao and Dr. Suh while at Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center, Tassig Cancer Institute, Cleveland Clinic, Cleveland OH.

L4-5 neural foramen was also noted (Figure 1).

DIAGNOSIS

Spine metastasis from renal cell carcinoma

DISCUSSION

Spine is the third most frequent site of metastasis, and approximately 10% of all cancer patients develop symptomatic spinal metastasis. About 10% to 20% of patients with spine metastasis will develop spinal cord compression.¹ The majority (70%) of spinal metastases are located in the thoracic spine and approximately half of all patients have multiple spinal metastases. Patients with spine metastasis can present clinically with pain and/or neurologic dysfunction. In patients with neurologic dysfunction, it is imperative to rule out spinal cord compression. The preferred imaging modality for spine imaging is MRI, however, in patients with contraindications to MRI, a computed tomography (CT) scan or a myelogram would be acceptable. Prompt spine imaging also helps in establishing the stability of the spine.

Initial management of spinal metastasis involves the use of narcotic and non-narcotic pain medications. However,



FIGURE 1. The image shows a sagittal T2-weighted MRI sequence demonstrating a heterogenous expansile mass in the L4 vertebral body with mild epidural extension.

if spine instability or spinal cord compressions are present, surgical decompression and spinal stabilization are mainstays of therapy. Radiotherapy, either conventionally fractionated external beam radiotherapy (CRT) or spine stereotactic body radiotherapy (sSBRT) can also be utilized for the treatment of spinal metastasis.

One of the main goals of palliative radiotherapy to the spine is pain control.² For many decades, CRT has been utilized. Because the treatment field involves the spinal cord, CRT can be delivered safely up to 2 times before the risk of myelopathy outweighs the

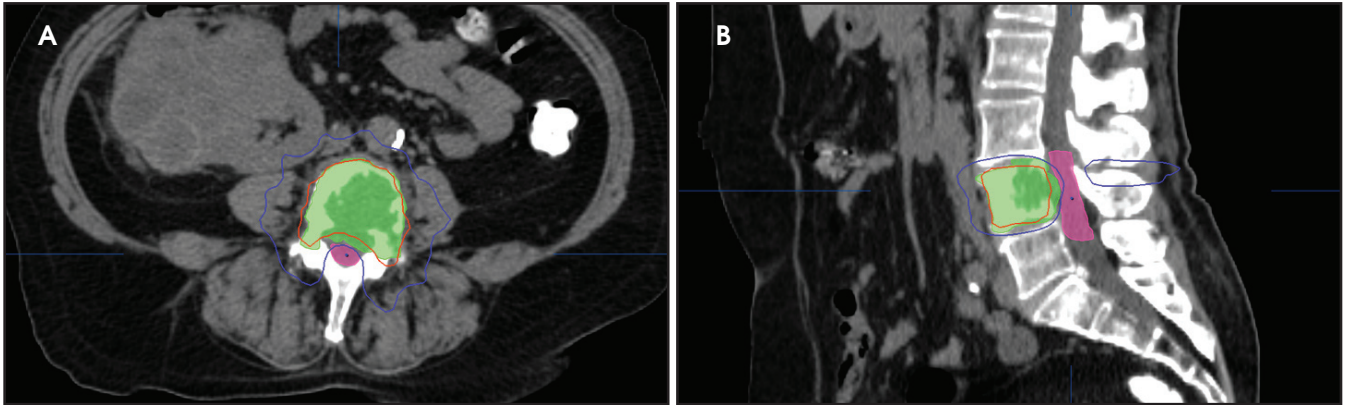


FIGURE 2. Axial (A) and sagittal (B) treatment planning CT images for sSBRT to the L4 vertebral body. The planning treatment volume (PTV) is demonstrated by the green color wash, the cauda equina by the pink color wash, the 16Gy isodose line (IDL) by the red line and the 10Gy IDL by the blue line.

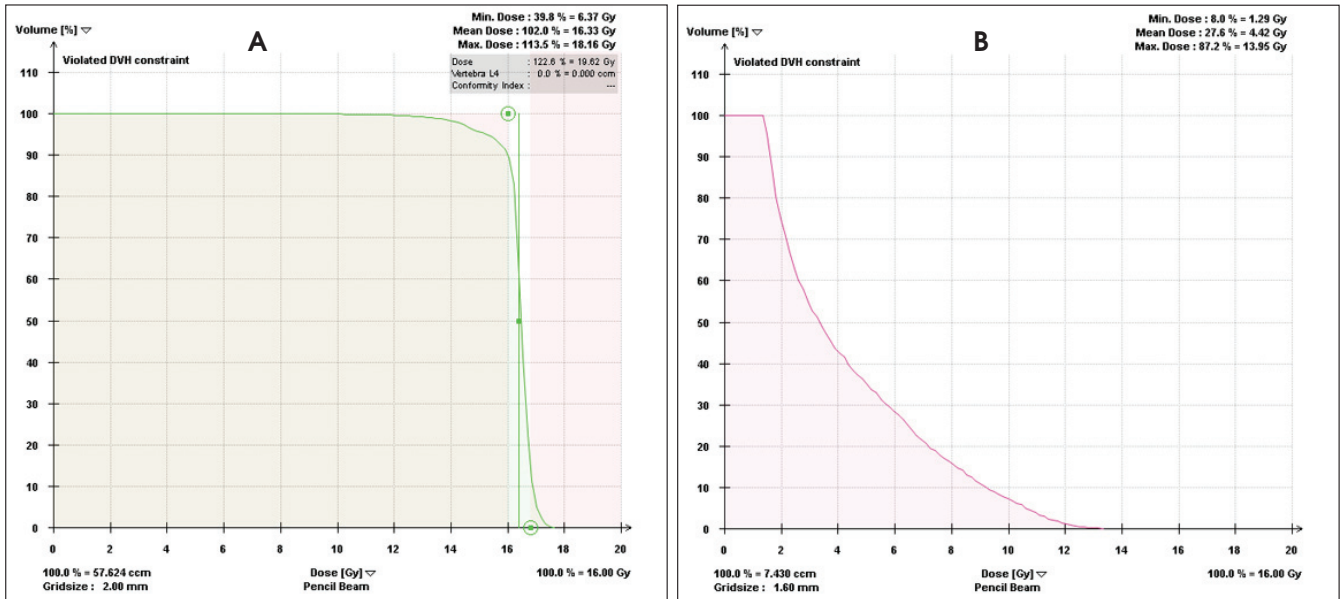


FIGURE 3. PTV (A) and cauda equina (B) dose volume histograms (DVHs) are shown. We aim to achieve $\geq 90\%$ coverage of the PTV by the prescription dose. For the cauda equina we limit the maximum dose to $< 16\text{Gy}$ and 10% of cauda equina receiving $\leq 12\text{Gy}$.

potential benefits.³ With the advancement of chemotherapy regimens and the development of targeted chemotherapeutics, patients with metastatic RCC have longer survival, which necessitates more durable pain control.⁴ Furthermore, patients who have undergone prior CRT without significant pain relief or patients who have received prior incidental spinal radiation secondary to treatment for their primary cancer (such as lung cancer or anal cancer) are poor candidates for CRT for spinal metastasis.

Over the past 2 decades, sSBRT has been developed and refined, allowing for the delivery of high dose conformal radiotherapy to the spine, while adequately sparing the spinal cord. Importantly, sSBRT enables the delivery of a higher biologically effective dose (BED) than CRT does. Although differences in technique exist between institutions, here we will discuss the approach utilized at the Cleveland Clinic, which is congruous with the approach of the ongoing RTOG 0631 trial.⁵ We refer the interested reader to

a recent review for a detailed discussion of institutional differences.⁶

Most centers utilize either a single-fraction or a hypofractionated regimen. At Cleveland Clinic, most patients are treated with either 16Gy or 18Gy in 1 fraction with the higher dose reserved for radioresistant histologies. For treatment planning, we limit the spinal cord to a maximum dose $< 14\text{Gy}$ and 10% of spinal cord receiving $\leq 10\text{Gy}$ and limit the cauda equina to a maximum dose $< 16\text{Gy}$ and 10% of cauda equina receiving $\leq 12\text{Gy}$ (Figures 2 and 3).

CME

With either the single fraction or hypofractionated regimens, most centers have reported local control rates $\geq 80\%$.⁶

Nguyen et al studied sSBRT in 48 patients with 55 RCC spinal metastases treated with either 24Gy in 1 fraction, 27Gy in 3 fractions, or 30Gy in 5 fractions and demonstrated a local control rate of 82.1% and a complete pain response of 44% and 52% at 1 month and 12 months post-sSBRT, respectively.⁷ We recently reported our results for 57 patients with 88 spinal metastases from RCC and demonstrated a complete pain response of 27.1% and 63.6% at 1 month and 12 months post-sSBRT, respectively. Multivariate analysis demonstrated that multilevel disease and neural foramen involvement were associated with radiographic failure and multilevel disease and pre-existing vertebral body fracture were associated with pain failure.⁸ Hunter et al recently compared the efficacy of CRT versus sSBRT for patient RCC spinal metastases. He showed that sSBRT offered more complete pain relief (33% vs 12%, $p=0.01$), whereas CRT offered more partial pain relief (56% vs 29%, $p=0.01$). A trend towards longer duration of pain relief with sSBRT was also demonstrated (4.8m vs 1.7m, $p=0.05$).⁴ These differences may be attributable to the higher BED delivered by sSBRT compared to CRT.

The most common acute toxicities from sSBRT include fatigue (up to 40%) and gastrointestinal effects (10-20%).⁹ Major long-term toxicities include the risk of developing vertebral body fractures as well as the risk of spinal cord myelopathy.

Rose et al evaluated 62 consecutive patients with 71 vertebral bodies

treated with 18Gy to 24Gy in a single fraction and reported a 39% incidence of new or progressive vertebral fractures. Risk factors for fractures were location (T10 to sacrum), lytic metastasis and $> 40\%$ vertebral body involvement.¹⁰ A multi-institutional study by Sahgal et al of 254 patients with 410 vertebral levels found a fracture incidence of 14% and identified dose per fraction ($> 20\text{Gy}$), preexisting vertebral fracture, lytic metastasis presence of paraspinal, and/or epidural disease and spinal deformity as risk factors for developing a vertebral fracture post-sSBRT (Sahgal et al, provisionally accepted to *Journal of Clinical Oncology*).

Risk of spinal cord myelopathy from sSBRT is estimated to be $< 1\%$.³ Sahgal et al performed a multi-institutional study of 5 myelopathy cases comparing it to 19 unaffected patients post-sSBRT. His analysis demonstrated that thecal-sac maximum doses of up to 10Gy in a single fraction were safe. Furthermore, using BED calculations, he demonstrated that 30 to 35 2-Gy equivalent for up to 5 fractions was also safe.¹¹ Aggregating all the available clinical reports of spinal-cord tolerance in the setting of sSBRT, Kirkpatrick et al concluded that 13Gy in 1 fraction or 20Gy in 3 fractions confers a spinal-cord myelopathy risk of $< 1\%$.³

CONCLUSION

Spine SBRT is now a well-established technique for the treating spinal metastasis that has enhanced the treatment of patients with spine metastasis. Many studies have shown that sSBRT provides excellent local control and is safe and effective in the primary as

well as salvage settings. sSBRT provides rapid and durable pain relief and can also be utilized in patients that have significant epidural disease. Currently, sSBRT remains the only effective nonsurgical option in patients previously irradiated for spinal metastases. sSBRT is not only a convenient option for patients as it can be delivered in one setting but it also has a low risk of acute and late toxicities.

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