Editorial Commentary

Minimal late effects of stereotactic body radiation therapy for spine metastases years post treatment

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Introduction

Stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) delivers high doses of radiation in 5 or fewer sessions or fractions. To do this safely, inherently it has to minimize dose to the surrounding normal tissue through very conformal and accurate delivery which have been developed and refined over the last decade. For spine metastases, there is increasing evidence that supports its efficacy, as well as safety. Ling *et al.* published in their manuscript, "Long-term outcomes after stereotactic radiosurgery for spine metastases: radiation dose-response for late toxicity", their findings in regards to late toxicities and dosimetric factors that contribute to these toxicities in 43 patients who had follow-up of at least 5 years (1). This level of long-term follow-up makes this series unique.

Methods

The authors analyzed 562 patients with a minimum of 5 years of survival to look at the toxicities developed in patients after 5 to 10 years after SRS. All treatments were delivered in a single fraction to a dose ranging from 12 to 24 Gy. There was some variability with how the cord was contoured. In 62% of the patients, the entire spinal canal was contoured, but in the remaining 38%, the spinal cord was contoured. Toxicity was coded according to the CTCAE version 4.

The authors chose to calculate cumulative biological equivalent dose based on the linear quadratic model. While this is the most used model to compare dose, there is debate whether the linear quadratic model is accurate for SRS.

The authors looked at vertebral compression fractures (VCFs) as either *de novo* compression fracture or progression of pre-existing compression fracture.

Results

While excellent local control is seen at 1 year at 82.7%, it declines to 58% and 54% at 5 and 10 years respectively. This is consistent with data from other institutions. Nine patients out of 43 developed Grade 2 or more late toxicity in this series. Five patients had Grade 3 or more toxicity, 3 of which had painful sensory neuropathy, one had esophageal stricture, and one had urethral stricture requiring a stent. The patient with the urethral stricture also had a Grade 4 non-healing wound requiring hyperbaric oxygen. Both of the side effects are unusual, but need to be reported to fully understand potential issues that can develop post SRS depending on the treatment volume is contoured and the doses used. Three patients who developed sensory neuropathy post SRS also had prior external beam radiation therapy, which suggests cumulative dose does increase the

Table 1 Predicted Pmax (thecal sac point maximum) volume absolute doses in Gy for 1 to 5 SBRT that results in 1–5% probability of radiation myelopathy

Radiation myelopathy	1 fraction Pmax limit (Gy)	2 fraction Pmax limit (Gy)	3 fraction Pmax limit (Gy)	4 fraction Pmax limit (Gy)	5 fraction Pmax limit (Gy)
1% probability	9.2	12.5	14.6	16.7	18.2
2% probability	10.7	14.6	17.4	19.6	21.5
3% probability	11.5	15.7	18.8	21.2	23.1
4% probability	12.0	16.4	19.6	22.2	24.4
5% probability	12.4	17.0	20.3	23.0	25.3

SBRT, stereotactic body radiation therapy.

risk for late effects. Cumulative BED3 >200 Gy appears to increase this risk, for both the sacral nerve roots and spinal cord.

VCFs occurred at a median of 10 months in 16.7% of the patients, consistent what is seen with other series. Unlike other studies however (2-5), they did not find factors that contributed to VCF, including age, gender, presence of pre-existing compression fracture, SRS dose, cumulative BED, and gross tumor volume.

Discussion

The strengths of this series are the number of patients with long term follow up as systemic therapies have improved survival in patients with metastatic disease. It is reassuring to see that there does not appear to be a dramatic increase in late effects many years out from SBRT. This knowledge is critical as SBRT is increasingly being utilized for benign tumors where long term late effects may be of even greater concern (6-8). Also of note, the modest dose used in spine SBRT comparative to lung SBRT may result in recurrence even after 5 to 10 years as has been reported in patients with lung malignancies (9). Ongoing follow up is necessary for this patients treated with spine SBRT as late recurrences can develop.

In regards to radiation myelopathy, one of the best data looking at the rate of complications and dose is provided from multi-institutional data comparing 9 patients with myelopathy against a large cohort from multiple academic institutions (10). This analysis used a logistic regression model yielding estimates of radiation myelopathy specific to SBRT. Thecal sac contours was used as a correlate for spinal cord contours and recommendations were given to limit the maximum point volume doses to what is summarized in *Table 1* to reduce risk of radiation myelopathy to less than 5% (10). Other multi-institutional analysis have shown that re-irradiation with spine SBRT is safe and have reported no cases of radiation myelopathy, but have had limited patient follow up of a median 8.1 months (11).

VCF is another late complication seen with spine SRS. The risk of VCF range from 10% to up to 40%. This risk appears to be correlated to the dose per fraction. The rate of VCF is 10% at 1 year for fractional doses 19 Gy or less, but it is 39% for 24 Gy or more with the vast majority of VCFs occur within the first few months (2). This risk of fracture does need to be balanced with the potential for better control with higher doses. For those patients with a more limited life expectancy one may look to minimize risk of VCF which may lead to intervention at the end of life versus those patients with a longer life expectancy and excellent performance status who may be more willing to have an intervention for VCF and where disease control becomes more important. Potentially hypofractionated SRS can provide that higher ate of control without increasing the risk of radiation necrosis and studies have suggested low rates of VCF (12,13).

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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