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Abstract

Normal Tissue Complication Probability of Vertebral Compression Fracture after Stereotactic Body Radiotherapy for Spine Metastasis

Xuguang Chen [1] , Chengcheng Gui [2] , Jimm Grimm [3] , Lawrence R. Kleinberg [4] , Kristin J. Redmond [2]

1. Radiation Oncology and Molecular Radiation Science, Johns Hopkins School of Medicine, Baltimore, USA 2. Radiation Oncology and Molecular Radiation Sciences, The Johns Hopkins University School of Medicine, Baltimore, USA 3. Department of Radiation Oncology, Johns Hopkins University, Baltimore, USA 4. Radiation Oncology, The Johns Hopkins University School of Medicine, Baltimore, USA

Corresponding author: Xuguang Chen, xchen140@jhmi.edu

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Objectives: Stereotactic body radiotherapy (SBRT) is increasingly used in the treatment of metastases to the spine, but is associated with post-treatment vertebral compression fracture (VCF). The purpose of this study was to identify clinical and radiation planning characteristics that predict post-SBRT VCF through a novel normal tissue complication probability (NTCP) analysis.

Methods: Patients with de novo spine metastases treated with SBRT between 2009 and 2018 at a single institution were included. Those who had surgical stabilization or radiation to the same spine level prior to SBRT were excluded. VCF was defined as new development or progression of existing vertebral body height loss not attributable to tumor growth. Probit NTCP models were constructed using doses to the maximum point, 1cc, 5cc, 10%, 50% and 80% of the planning target volume (PTV Dmax, D1cc, D5cc, D10%, D50%, D80%), and fitted using a maximum likelihood approach. A multivariate proportional hazard model was used to estimate time to VCF using the Fine and Gray method with tumor progression and death as competing risks.

Results: Three hundred and two vertebral segments from 193 patients were treated with a median dose of 24Gy in 3 fractions (range 15-30Gy in 1-5 fractions). The majority (63.7%) of treated lesions were of radioresistant histologies. The median spinal instability neoplastic score (SINS) was 6, and 41.7% of treated spinal segments had SINS of 7 or greater. With a median follow up of 13.9 months, local control was 89.3% at 1 year. A total of 26 SBRT-induced VCFs were observed with a median time to VCF of 4.2 months. The 1 and 2-year cumulative incidences of VCF were 4.6% and 6.7%. Eleven of the 26 VCFs were managed conservatively, while 15 required vertebroplasty (13 patients) or surgery (2 patients). NTCP modeling demonstrated a steep response of VCF risk to D80% and D50%, but not Dmax, D1cc, D5cc or D10%. D80% of 17Gy and D50% of 20Gy in 3 fractions had a predicted VCF risk of 5%, while D80% of 25Gy and D50% of 28Gy corresponded to 10% risk. Multivariate analysis demonstrated an association between VCF risk and lower body mass index (HR 0.89 per unit increase, p=0.04), SINS (HR 2.66 unstable vs stable, P=0.02), dose per fraction greater than 12Gy (HR 6.21, p=0.001) and lower prescription isodose line (HR 3.92 for <=70% vs >70%, p=0.006).

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Interestingly, lower BMI (<=25) and higher SINS (>=7) were also more prevalent among patients who had early VCF (below median time of 4.2 months) compared to those who had late VCF (p= 0.05 and 0.02 respectively), which may indicate a difference in the pathophysiology of early vs late VCF. These results support the use of BMI <=25, SINS >=7, PTV D80% >25Gy in 3 fractions and D50% >28Gy in 3 fractions, and prescription isodose line <=70% for selecting patients who may benefit most from prophylactic treatment to prevent VCF.

Conclusions: NTCP modeling suggests that the volume of spine receiving intermediate to lower radiation doses are more correlated with post-SBRT VCF than high dose regions. Common SBRT regimens such as 27Gy in 3 fractions that covers at least 90% of PTV may be inherently associated with VCF risk of 10% or greater. Further reduction of VCF risk may require reduction in the treatment volume, but has to be balanced with maintaining the rate of local control. Future studies exploring optimal target delineation to minimize fracture risk while preserving tumor control will be essential.