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Finding the Therapeutic Window in Patients with Spine Metastasis Treated with Stereotactic Body Radiotherapy: Impact of Dosimetric Factors on Vertebral Compression Fracture and Local Failure

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Abstract
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Abstract

Objectives:

Stereotactic body radiotherapy (SBRT) provides durable local control for patients with spine metastasis. Dose escalation may improve local control but may also increase the risk of normal tissue toxicity including vertebral compression fracture (VCF). Our group recently reported the results of a normal tissue complication probability model which identified that a minimum dose of at least 21 Gy to 80% of the planning target volume (PTV D80%) in 2 fractions was associated with a higher risk of post-SBRT VCF. The purpose of this study is to validate these findings in an international, multi-institutional cohort.

Methods:

Patients with spine metastasis treated with SBRT at 5 international institutions between 2010 - 2020 were retrospectively reviewed. Patients who had prior surgical stabilization or radiation at the same site prior to SBRT were excluded. VCF was defined as new development or worsening of existing vertebral body height not attributable to tumor growth. Local failure (LF) was defined per SPine response assessment in Neuro-Oncology (SPINO) criteria. Variables examined included body mass index, history of osteoporosis, use of bisphosphonate and/or denosumab, spinal instability neoplastic score (SINS), and dosimetric/volumetric characteristics of radiation planning. All fractionation schemes were converted to 2-fraction equivalent doses (2fxED) using the linear quadratic model with an alpha/beta of 3 and used in analyses of PTV D80%. Univariate and multivariate Cox proportional hazard models for VCF and LF and were constructed using the Fine and Gray competing risk method.

Results:

357 vertebral segments from 234 patients were treated with SBRT. Common primary tumor types were prostate (n = 50, 22%), non-small cell lung cancer (n = 42, 18%), and breast (n = 35, 15%). The majority (n = 199, 242 segments) were treated with 2 or 3 fractions with a mean dose of 24 Gy or 27 Gy, respectively. Median followup was 21.1 months (0.6-88.4 mo). VCF incidence was low in this cohort, at 4.2% and 6.7% at 1- and 2-years, respectively. On univariate analysis, total SINS score was associated with increased risk of VCF (HR 1.22, 95% CI 1.10-1.36, p < 0.001), while PTV D80% at 2fxED > 21 Gy showed a trend towards association with VCF (HR 3.30, 95% CI 0.80-13.6, p = 0.10). LF incidence was 12.6% and 18.1% at 1- and 2-years, respectively. On univariate analysis, PTV D80% at 2fxED > 21 Gy was associated with reduced risk of LF (HR 0.36, 95% CI 0.20-0.65, p = 0.001). Additional dosimetric factors associated with increased risk of LF were lower prescription dose BED3 (HR 0.98 as a continuous variable, 95% CI 0.97-0.99, p = 0.04) and higher prescription isodose line (HR 1.04 as a continuous variable, 95% CI 1.01-1.06, p = 0.002). Higher PTV D80% remained predictive of LF on multivariate analysis (HR 0.45, 95% CI 0.23-0.88, p = 0.02).

Conclusion(s):

A PTV D80% at 2fxED > 21 Gy may improve local control but may also increase the risk of VCF. Prospective investigation is needed to explore this complex relationship and better understand the therapeutic window which best balances local control and normal tissue toxicities.