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Outcome analysis in stereotactic body radiation therapy for spine metastases: dose-response for toxicity and pain relief analysis

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INTRODUCTION

Metastases to the spinal column are a relatively common manifestation of cancer accounting for approximately 70% of bone-related metastases and can lead to significant morbidity and mortality. Spinal column disease presentation can cause severe pain, lead to fracture and drastically reduce patients' quality of life and functional ability.

Studies have shown stereotactic body radiotherapy (SBRT) shows high levels of local control[1] and is increasingly used as an effective treatment method.

MOTIVATION / PURPOSE

Current studies of spine SBRT suffer from low statistics, lack of quantitative dosimetric data and no patient reported outcomes. This study includes a relatively large patient cohort, detailed dosimetric data and patient-reported pain relief from the treatment.

The purpose of this investigation aimed to evaluate and understand any dosimetric factors associated with local control, toxicity and pain relief. A fracture risk parametrization was formulated based on the data.

METHODS

A single institution, retrospective analysis of 124 spine metastases from 89 patients treated with SBRT between 2010 and 2017 were identified. Patient characteristics, follow-up data and current treatment parameters - including target and spinal cord dosimetric data - were collected. Treatment related outcomes including freedom from fracture rate, myelitis, and freedom from local recurrence were assessed radiographically.

Fracture risk and patient-reported pain relief were fit using multivariate linear regression analysis. The dependent variables were similar to previous studies[2]. In addition, presence of epidural extension, target maximum dose, number of vertebral levels treated and circular involvement (angular extent around spinal cord) were included. Statistical significance was defined by a p-value < 0.05.

The dose-response of fracture risk was obtained by dividing the dose data into five bins with equal entries, averaging fracture risk in these dose bins and fitting a logit function.

A previously published model of SBRT myelitis probablity[4] using dose-volume histogram (DVH) data was also used to assess an individuals theoretical risk versus realized myelitis.

RESULTS

Patient characteristics are shown in Table 1: 17 out of the 124 patients had prior treatment and 74% had pain at presentation with an average pain level of 3 (range 1-10) on a scale of 1 to 10. Eighty three patients had pain relief after treatment with an average reduction of pain by 2.4 ± 3.1. There were 71 patients treated with a single fraction, 20 treated with 3 fractions and 32 treated with 5 fractions.

Figure 1: Freedom from local recurrence rate

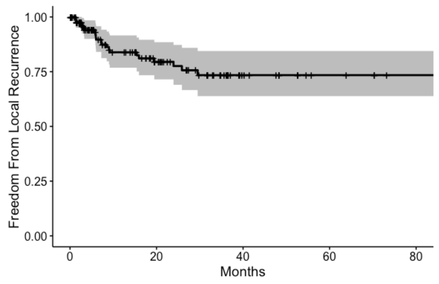


Figure 2: Freedom from fracture rate

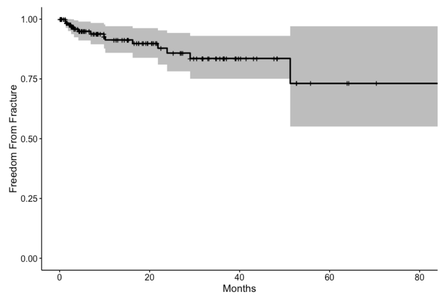


Table 1: Patient characteristics

age	57.1 ± 11.9 yrs
KPS	81 ± 10
prior treatment	13.7%
epidural extension	39.5%
pain at presentation	74.2%
pain scale	3 (1,10)
pain relief?	66.9%
change in pain	2.4 ± 3.1
vertebrae levels treated	1 (1,6)
target volume	53.7 ± 59.0 cc
Fraction / Dose data	
single fraction	71 patients
single fx dose	17 (14,20)
three fractions	20 patients
three fx dose	25 (24,27)
five fractions	32 patients
five fx dose	32 (30,40)

The median clinical follow up time was 19.6 months (range: 4.8-73.2) with 78 patients (63%) receiving follow up imaging at 17.4 months (range: 1.1-70.0); all outcomes were assessed radiographically.

Freedom from local recurrence at 12 and 24 months were 84% (CI: 77-92) and 78% (CI: 69-87), respectively, shown in Figure 1. No significant association was found with freedom from local recurrence and histology, dose, or fractionation. Shown in Figure 2, the freedom from fracture at 12 and 24 months was 91% (CI: 86-97) and 86% (CI: 78-94) respectively.

A total of 16 (12.9%) patients had ≥2 grade toxicity and 13 (10.5%) experienced fracture after treatment.

The variables used in the analysis and their corresponding significance for vertebral fracture and pain relief are shown in Table 2.

Fracture and biological effective dose (BED3) was *not* associated with fracture as has been reported in other references. But, BED3 was a significant predictor of pain relief.

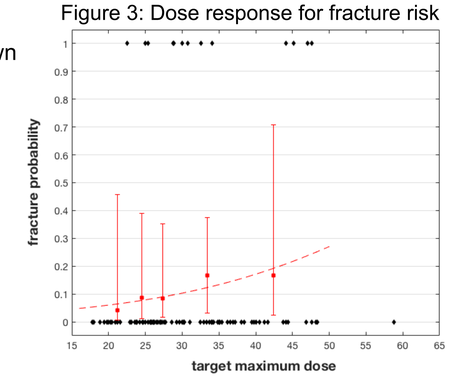
The significant predictor of fracture was the maximum dose to the target. Out of the 13 fracture cases, 9 were CyberKnife and 4 were LINAC treatments.

The fracture risk dose response is shown in Figure 3 and shows similar rates compared to other studies.

Table 2: Multivariate analysis variables

	Fracture	Pain Relief
age	p = 0.073	p = 0.137
retreatment	p = 0.108	p = 0.671
KPS	p = 0.188	p = 0.107
vertebrae involved	p = 0.397	p = 0.113
epidural extension	p = 0.395	p = 0.686
prior compression fracture	p = 0.359	p = 0.645
fractions	p = 0.294	p = 0.825
target max dose	**p = 0.042***	p = 0.137
target volume	p = 0.422	p = 0.786
BED3 dose	p = 0.093	**p = 0.047***
circular involvement	p = 0.239	p = 0.824

Figure 3: Dose response for fracture risk



Only one case of myelitis was observed in this cohort. Applying the model from the literature[4], a total of 55 cases had >5% risk of myelitis. Also, TG101 threshold doses , but NOT point doses, were exceed in some cases without any observed myelitis; this warrants further study.

CONCLUSIONS / FUTURE WORK

SBRT treatment for spine metastases was associated with acceptable toxicity profile and vertebral compression fracture while achieving high local control. Greater BED and maximum point target dose were associated with patient-reported pain relief and fracture. The extracted dose-dependent fracture risk shows agreement with other studies present in the literature. The data set will be used to test existing and further develop models to ensure safe SBRT practice.

Applying previously reported knowledge-based planning methods (Ziemer, AAPM2018) to this data set could reduce multiple dosimetric variables yielding lower fracture risk and rates of treatment related toxicity by reducing both the target maximum dose and the dose to the spinal cord. This is being studied currently with hopes to report this at a later date.

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