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Technical Report

Assessment of intrafraction motion for spine and non-spine bone metastases treated with image-guided stereotactic body radiotherapy without 6 degrees-of-freedom couch correction

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ABSTRACT

Stereotactic body radiotherapy (SBRT) planning target volume (PTV) margins are influenced by multiple factors. Data is limited on intrafraction motion in bone SBRT, particularly non-spine lesions. We analyzed intrafraction motion in bone SBRT patients treated on a standard treatment couch without 6 degrees-of-freedom (6-DOF) correction.

Extracranial bone SBRT patients were included. Patients were treated using two volumetric-modulated arcs and targets were localized using daily cone-beam computed tomography (CBCT) prior to each arc. Alignments between the first and second CBCT images yielded intrafraction positional shift values used to compute translational 3-dimensional vector shifts.

125 fractions from 43 patients were reviewed. Median vector shift for all SABR fractions was 0.7 mm (range 0-6.6 mm); spine 0.7 mm (range:0-2.3 mm) and non-spine 0.9 mm (range:0-6.6 mm). Of the 125 fractions, 95% had IFM vectors within the prescribed PTV margin.

Intrafraction motion is small for bone SBRT patients treated on a standard couch without 6-DOF correction capabilities. Intrafraction motion was slightly larger for non-spine sites and may require treatment with larger PTV margins than spine cases.

Keywords: SBRT, SABR, spine, non-spine, bone metastasis, stereotactic body radiotherapy, stereotactic ablative radiotherapy, intrafraction motion

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INTRODUCTION

Technological advances have led to stereotactic body radiotherapy (SBRT), which allows the precise delivery of large radiation doses that are more conformal than conventional radiotherapy (1). In the oligometastatic setting, SBRT may offer a survival advantage over the use of standard palliative radiotherapy regimens although risk of acute and late toxicities remains a concern (2). Population-based data on the use of SBRT suggests that toxicities from this technique are low when standardized processes such as peer review and prioritization of organs-at-risk are employed (3). Additionally, SBRT is becoming a standard of care indication for polymetastatic disease, such as spinal metastases, where it can provide better complete pain response compared to conventional external beam radiotherapy (4).

Since SBRT uses large doses of hypofractionated radiotherapy, it is critical to limit the treatment volume with the use of smaller planning target volume (PTV) margins in order to minimize exposure to nearby organs, such as the spinal cord, which is often only millimeters away from spinal targets. PTV margins used in SBRT are often influenced by uncertainties in patient positioning, immobilization, on-board image-guidance, and intrafraction motion, among other factors. These advanced technologies are often associated with increased cost of delivery, however cost-effective and simplified approaches can still lead to the effective and safe delivery of SBRT (5).

Intrafraction motion (IFM) is of high importance in SBRT due to delivery of higher radiation doses and consequently longer treatment times. As such, patients undergo daily image-guidance using on-board imaging features, such as cone beam computed tomography (CBCT) to assess and correct any translational (lateral, longitudinal, vertical) or rotational (pitch, yaw, roll) shifts in patient position at multiple time points during treatment. There is limited published data on the assessment of IFM in bone SBRT, particularly for non-spine lesions. Although robotic treatment couches with automated 6 degrees-of-freedom (6-DOF) correction makes accurate patient positioning significantly easier, this advanced technological feature may not be accessible in resource-limited areas of the world. This study assessed our institutional data on IFM in patients with spine and non-spine bone metastases treated with SBRT using a standard treatment couch.

MATERIALS AND METHODS

All patients who received extracranial bone metastasis-directed SBRT between January 2017 and July 2021 at our institution were included in this study as part of local continuous quality improvement practices. Patients were classified as spine or non-spine depending on target location.

All patients were immobilized with a commercial immobilization system specific to the location being treated. Targets superior to and including the T4 vertebra were immobilized with an Intuition (CDR Systems, Calgary, Canada) thermoplastic mask of the head and shoulders, while targets inferior to T4 were immobilized using the Civco Pro-Lok ONE immobilization system (Civco Radiotherapy, Coralville, USA).

The gross tumor volume (GTV) is defined as tumor visible on CT and/or MRI images, while the clinical target volume (CTV) is an expansion of the GTV to include areas at risk for micrometastasis. The GTV and CTV were contoured as guided by international consensus guidelines (6, 7). The CTV was then expanded to create the planning treatment volume (PTV). Spinal metastases were given a 2 mm PTV margin, while non-spine metastases were given a 5 mm PTV margin per institutional policy (8).

The prescribed dose was either 35 Gy given in 5 fractions or 24 Gy given in 2 fractions, with priority given to meeting organ-at-risk (OAR) constraints (3). All treatment plans were created with volumetric modulated arc therapy (VMAT) using two (2) coplanar arcs in 6MV photons with flattening filter free delivery mode, and were calculated using the Eclipse™ (Varian Medical Systems, Palo Alto, USA) treatment planning system.

Patients were treated on a Varian Exact™ IGRT couch (Varian Medical Systems, Palo Alto, USA) where pitch and roll rotational corrections could not be applied. Daily CBCT was employed prior to each of the two arcs to localize the targets as per institutional policy. CT images were acquired with 1.25 mm axial slice thickness for spine, and 1.25-2.5 mm for non-spine targets. During CBCT, auto-matching was initially done on bone window level using a clip box that included one vertebral body above and below the level of interest for spine target. For non-spine targets, a clip box that included a region of interest approximately 5 cm beyond the PTV in all directions. A radiation oncologist was present at each fraction to verify the auto-match and to correct any intrafractional shift in real-time. To limit inter-observer variability, a medical physicist and two radiation therapists were also present to verify the final match. All patients were treated on a Varian TrueBeam™ (Varian Medical Systems, Palo Alto, USA) linear accelerator equipped with a standard treatment couch that did not have automated 6-DOF correction capability.

Alignments between the first and second CBCT images yielded intrafraction positional shift values in the lateral (X), longitudinal (Y), and vertical (Z) axes.

The absolute values of these shifts were recorded and the translational 3-dimensional vector values were computed.

RESULTS

A total of 125 SBRT fractions from 43 patients were reviewed. This included 57 fractions from 19 patients with spine metastases and 68 fractions from 24 patients with non-spine metastases (Table 1).

Table 2 shows a summary of mean absolute shifts in lateral (X), longitudinal (Y), and vertical (Z) axes, classified according to location of bone metastasis.

Among the spinal metastases, the largest mean X shift was observed from the lumbar lesions (0.6 mm), while the largest mean Y and Z shifts were both observed from the sacral lesions (0.54 mm and 0.57 mm, respectively).

Among the non-spinal metastases, the largest X shift was observed from lesions in the ischium (1.9 mm), the largest Y shift was observed from lesions in the sternum (1.6 mm), and the largest Z shift was observed from lesions in the humerus (1.66 mm). Overall, these non-spinal lesions also represent the largest mean shift values of each axis in this study (Table 2).

The mean and maximum computed 3D vector shifts for each bone metastatic site are shown in Table 3.

Table 1. Intrafraction CBCT investigated per site of bone metastasis

bone metastases sites	No. intrafraction CBCTs investigated
Spine	
Cervical	0
Thoracic	33
Lumbar	9
Sacral	15
TOTAL	**57**
Non-spine	
Humerus	5
Ribs	11
Scapula	2
Sternum	5
Pubis	7
Ischium	7
Ilium	19
Acetabulum	5
Femur	7
TOTAL	**68**

Table 2. Summary of intrafraction shifts in the x-, y-, and z-axes

	Mean absolute shifts (mm; SD)		
Bone metastases sites	**X (medial-lateral)**	**Y (superior-inferior)**	**Z (anterior-posterior)**
Spine			
Thoracic	0.32 (0.38)	0.16 (0.25)	0.44 (0.51)
Lumbar	0.6 (0.67)	0.4 (0.35)	0.56 (0.74)
Sacral	0.25 (0.22)	0.54 (0.5)	0.57 (0.47)
Non-spine			
Humerus	1.42 (1.1)	1.36 (1.6)	1.66 (1.3)
Ribs	0.34 (0.37)	0.41 (0.76)	0.8 (0.93)
Scapula	1.65 (1.35)	1.25 (0.95)	0.7 (0.5)
Sternum	0.7 (0.82)	1.6 (1.67)	1.06 (1.83)
Pubis	0 (0.19)	0.37 (0.38)	0.14 (0.17)
Ischium	1.9 (1.6)	0.49 (0.62)	0.83 (0.59)
Ilium	0.41 (0.37)	0.47 (0.37)	0.33 (0.42)
Acetabulum	1.52 (0.94)	0.56 (0.65)	0.58 (0.5)
Femur	0.36 (0.43)	0.33 (0.57)	0.2 (0.45)

Table 3. Computed 3-dimensional vector displacement

Bone metastases sites	Mean 3D vector shift (mm)	Max 3D vector shift (mm)
Spine		
Thoracic	0.69	2.2
Lumbar	1.03	2.3
Sacral	0.93	2.2
Mean (mm)	**0.8**	
Median (mm)	**0.7**	
Max (mm)	**2.3**	
Non-spine		
Humerus	3.1	4.7
Ribs	1.21	3.6
Scapula	2.2	3.9
Sternum	2.3	6.5
Pubis	0.53	1.2
Ischium	2.5	5.3
Ilium	0.8	1.9
Acetabulum	2.0	3.6
Femur	0.55	2.5
Mean (mm)	**1.4**	
Median (mm)	**0.9**	
Max (mm)	**6.5**	
All bone lesions		
Mean (mm)	**1.1**	
Median (mm)	**0.7**	
Max (mm)	**6.5**	

Among the spinal metastases, the largest mean (1.03 mm) and maximum (2.3 mm) 3D vector shifts were from the lumbar lesions. The mean, median, and maximum 3D vector shifts for all spinal lesions are 0.8 mm, 0.7 mm, and 2.3 mm, respectively (Table 3). Fifty-three (53) of the 57 fractions (93%) had IFM vectors that are within the 2 mm PTV margin for spine SBRT.

Among the non-spinal metastases, the largest mean 3D vector shift (3.1 mm) was from humeral lesions, while the largest maximum 3D vector shift (6.5 mm) was from sternal lesions. The mean, medium, and maximum 3D vector shifts for all non-spinal lesions are 1.4 mm, 0.9 mm, and 6.5 mm, respectively (Table 3). Sixty-six (66) of the 68 fractions (97%) had IFM vectors that are within the 5 mm PTV margin for non-spine SBRT.

For all of the bony lesions, the mean, median, and maximum 3D vector shifts were 1.1 mm, 0.7 mm, and 6.5 mm, respectively. For 95% of fractions (119 out of 125), the IFM vector was within the institutional PTV margin expansions.

These vectors shifts were also plotted against the time between the first CBCT and the mid-treatment CBCT and are shown in Figure 1 for spine lesions and Figure 2 for non-spine lesions.

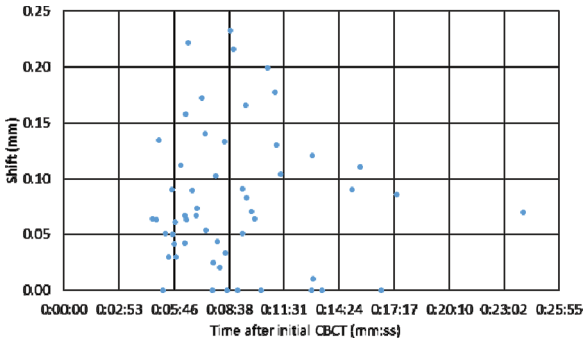

Figure 1. Vector shifts versus time between initial and mid-treatment CBCT in spine SBRT.

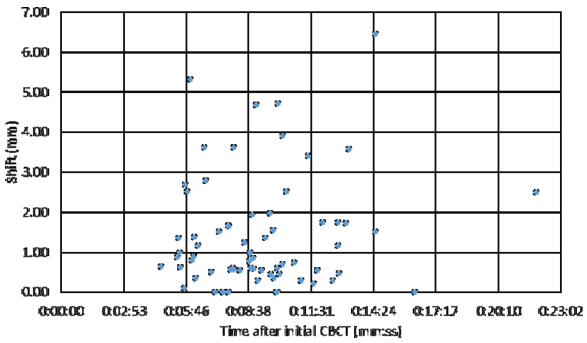

Figure 2. Vector shifts versus time between initial and mid-treatment CBCT in non-spine SBRT.

DISCUSSION

The routine use of daily image-guidance such as CBCT has paved the way for evaluation of IFM during bone metastasis SBRT. Svestad et al. (9) retrospectively evaluated pre-treatment and post-treatment CBCT images in 78 fractions in 54 patients who received spine SBRT. Initial CBCT was performed and translational and rotational errors were corrected. A verification repeat CBCT was performed for a subset of patients and corrections were made prior to treatment. All patients received post-treatment CBCT and positional errors were recorded as well. The study found smaller positional errors for patients who had the verification CBCT, with translational standard deviations (SD) ranging from 0.5 to 0.6 mm compared to the 0.7 to 1.0 mm of the group without verification CBCT. Our institutional policy was to perform a mid-treatment CBCT (prior to the second treatment arc) to allow for potential corrective action which served as our verification CBCT and measure of intrafraction motion. In this study, we observed a lower mean translational SD range of 0.22 to 0.74 mm for the spinal SBRT fractions (Table 3) compared to the study of Svestad et al. (9), although we acknowledge that a post-treatment CBCT might help in getting the whole IFM picture. However, it is also possible for patients to potentially move after treatment but before a post-treatment CBCT thus limiting the accurate measurement of intrafraction motion by relying on positions from CBCT alone. Alternative assessment methods such as the use of surface-guided imaging may better reflect the degree of intrafraction motion although advanced real-time imaging technology may not be readily available in most clinics.

Henni et al. (10) compared setup errors in two immobilization devices for spine SBRT using inter- and intrafraction vector shift values from 20 patients and found a significant difference in shifts between the two devices and a correlation between displacement vector and fraction treatment time. The shift values gathered by Henni et al., however, includes rotational movements (pitch, yaw, roll) in addition to the usual translational (lateral, longitudinal, vertical) movements which were evaluated in our study. In addition, only spinal bone metastases were evaluated in that study, whereas our study includes non-spinal bone metastases since there seems to be a significant practice pattern heterogeneity in this area (11).

Bredfeldt et al.(12) evaluated IFM of non-spine bone SBRT patients and found that the shift standard deviations were 0.6, 0.6, and 0.4 mm in the lateral, longitudinal, and vertical directions for femur lesions, and were 0.4, 0.5, and 0.4 mm in the same directions for iliac lesions. Our study observed lower shift standard devia-

tions in the lateral, longitudinal, and vertical directions, which were 0.43, 0.57, and 0.45 mm for femur lesions and were 0.37, 0.37, 0.42 mm for iliac lesions, respectively. Their study concluded that a 2 mm target margin is enough to achieve 99% target coverage for 99% of all observed shifts for femur cases, while 1.5 mm was required to achieve the same for iliac cases. Our study is similarly helpful in confirming that our institutional PTV margin was able to cover IFM 95% of the time.

All three studies (9, 10, 12) evaluated IFM using both translational (lateral, horizontal, vertical) and rotational (pitch, yaw, roll) errors, whereas our study only accounted for translational errors. We report our IFM data to demonstrate the feasibility of providing bone SBRT without 6-DOF correction, which was not available in our institution during the study period. Although there have been conflicting views on the utility of 6-DOF couches for the stereotactic treatment of extracranial targets (13)–citing the insignificant effect of rotational errors on target coverage especially if rigid immobilization is available, the benefit of using 6-DOF couches has already been demonstrated by multiple studies (14-16). Data on its availability worldwide and in low-resource countries is, however, lacking. In a 2018 survey among institutions included in the National Clinical Trials Network, 7.2% of the respondents would indeed like to add a 6-DOF couch for better patient repositioning during stereotactic radiotherapy (17).

The margins used to expand the clinical target volume (CTV) to planning treatment volume (PTV), to account for setup inaccuracies and patient motion (18), vary from center to center due to differences in treatment equipment, patient immobilization protocols, availability of image guidance for position verification, and level of experience of among staff. In an international consensus guideline for target volume definition in spinal SBRT, a CTV to PTV margin of ≤3 mm was used by the survey participants but they acknowledged that PTV contour recommendations could not be made due to "significant differences in inter- and intrafraction motion management techniques, treatment platforms, immobilization methods, and prescription dose-fractionation schedules" among different institutions (6, 7, 19). A 1-3 mm uniform CTV to PTV expansion was used in the SC24 trial protocol for the spine SBRT arm, which was adopted by the British Columbia provincial guideline on spine SBRT (4), whereas a larger 2-5 mm uniform CTV to PTV expansion was used for non-spine bone SBRT (8). In our institution, a CTV to PTV expansion of 2 mm is used for spine SBRT and an expansion of 5 mm is used for non-spine bone SBRT. Based on the results of this study, the 2-mm expansion margin is adequate to cover 93% of the IFM vectors for spine SBRT, and the 5-mm expansion margin is enough to cover 97% of the IFM vectors for non-spine bone SBRT.

Van Herk et al. (20) and Stroom (21) have proposed algorithms for estimating PTV margins. The recipe proposed by van Herk is based on covering the CTV by 95% for 90% of patients. Meanwhile that proposed by Stroom ensures that 99% of the CTV receives at least 95% of the prescribed dose. To estimate a PTV margin, we followed the procedure outlined by van Herk (22). The standard deviation of the means per patient is used as an estimator for the systematic error. While the root mean square of the SD per patient is used to estimate the random error. Using the formula, for spine targets, a 2.2 mm (van Herk) and 1.9 mm (Stroom) PTV margin is calculated in this study, while for non-spine targets, a 3.8 mm (van Herk) and 3.3 mm (Stroom) margin is calculated for this study. Based on this, we can say that our choice of PTV margin was appropriate given our current techniques and equipment. Finally, Gordan and Siebers (23) noted that for hypofractionated schemes, the popular margin formula proposed by van Herk should be used with caution. Until an accepted margin recipe for SBRT treatments with fractions of 5 or less is available, we report the van Herk and Stroom calculated PTV margin recommendations.

The results should be interpreted in the context of the strengths and limitations of this study, which includes its retrospective nature and its sample size. There is no comparison of our non-6-DOF dataset to a 6-DOF dataset. Our institutional protocol also does not include the performance of a post-treatment CBCT to confirm target alignment after patient repositioning and/or application of shifts. The vector shifts represent IFM from a static point in time between the pre- and mid-treatment CBCT and does not necessarily capture the IFM picture during actual beam delivery. Potential intra- and inter-observer variabilities in target registration are outside the scope of this study as well. We acknowledge that the spine and non-spine lesion categories are heterogeneous since different bones have variable ranges of motion and nearby OAR considerations. However, data on IFM in SBRT for non-spine bone metastasis is sparse, so this study adds to the reported literature on its assessment for this indication. This study also demonstrates that the lack of a 6-DOF couch is not a barrier to providing high quality SBRT for bone metastases. This is particularly important for many resource-limited cancer centers worldwide, who may perceive the lack of certain advanced equipment as reason to not offer SBRT. Despite the challenges of correcting rotational errors without an automated 6-DOF couch, the benefits of SBRT over conventional palliative radiation therapy are becoming more apparent (4) and centers must find ways to adapt in order to provide standard of care SBRT as their resources allow. Potential options include more frequent repositioning and repeat imaging, the use of shims, or the use of couch accessories for

manual correction of rotational shifts. Centers may also limit the complexity of cases treated, such as excluding spine tumors spanning multiple vertebral levels or spine tumors with epidural disease extension, in order to allow patients with simple uncomplicated bone metastases to be treated with SBRT. As long as there is meticulous execution of immobilization and position verification, among other key concepts, bone metastasis SBRT can be done within the limitations of technology that is available.

CONCLUSION

IFM is small for patients with bone metastases treated with SBRT using stereotactic immobilization systems and daily CBCT on a standard couch without automatic 6-DOF correction capabilities. IFM was slightly larger for non-spine sites and may require treatment with larger PTV margins than spine cases. High quality SBRT for bone metastases is feasible in centres with less advanced treatment equipment, provided an appropriate PTV margin is used and CBCT is integrated in routine quality improvement activities.

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Authors' disclosure of potential conflicts of interest

BM declares honoraria from AstraZeneca outside of the submitted work. The remaining authors declare no potential conflicts.

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