Optimized workflow to minimise intra-fractional motion during stereotactic body radiotherapy of spinal metastases

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ABSTRACT

Background and purpose: This study evaluated translational and rotational intra-fractional patient movement during spinal stereotactic body radiotherapy (SBRT) using 6D positioning based on 3D cone beam computerized tomography (CBCT) and stereoscopic kilovoltage imaging (ExacTrac). The aim was to determine whether additional intra-fractional image verification reduced intra-fractional motion without significantly prolonging treatment time, whilst maintaining acceptable imaging related dose.

Materials and methods: A retrospective analysis of 38 patients with 41 primary tumour volumes treated with SBRT between September 2018 and May 2021 was performed. Three different image-guided radiotherapy (IGRT) workflows were assessed. The translational and rotational positioning errors for the different imaging workflows, 3D translational vectors and estimates of imaging dose delivered for the different imaging workflows were evaluated.

Results: As the frequency of intra-fractional imaging increased from workflow 1 to 3, the mean intra-fraction 3D translational vector improved from 0.91 mm (±0.52 mm) to 0.64 (±0.34 mm). 85 %, 83 % and 97 % of images were within a tolerance of 1 mm/1 ◦ for workflows 1, 2 and 3 respectively, based on post treatment CBCT images. The average treatment time for workflow 3 was 13 min, as compared to 12 min for workflows 1 and 2. The effective dose per treatment for IGRT workflows 1, 2 and 3 measured 0.6 mSv, 0.95 mSv and 1.8 mSv respectively.

Conclusion: The study demonstrated that the use of additional intra-fractional stereoscopic kilovoltage image-guidance during spinal SBRT, reduced the number of measurements deemed “out of tolerance” and treatment delivery could be optimized within a standard treatment timeslot without applying substantial additional radiation dose.

Introduction

Stereotactic body radiotherapy (SBRT) also referred to as Stereotactic body radiosurgery (SBRs) is a non-invasive radiotherapy technique used to deliver high doses of radiation to a tumour in a single or limited number of fractions [1–4]. SBRT for spinal metastases is established as an effective treatment modality with proven clinical efficacy [1,3,4,5]. A high degree of spatial accuracy is achieved by using image-guided radiotherapy (IGRT) to accurately irradiate the target, whilst minimizing the dose delivered to the healthy neighbouring tissues, thus avoiding potential toxicities, particularly to the spinal cord [2,6,13]. For high precision treatments techniques such as spinal SBRT, it is crucial to minimize positional errors in order to ensure a high dose gradient at the spinal cord and tumour interface [1–4,13]. Patient positioning in six degrees of freedom (6 DoF) with stereoscopic kilovoltage imaging (ExacTrac, BrainLab, Germany) and 3D kV cone beam computerized tomography (CBCT) image guidance systems can be used in combination, to achieve the required high precision and is highly beneficial for spinal SBRT [5,3].

Over a period of two years after the introduction of our spine SBRT programme, our image guidance procedure was reviewed several times and changed with the intention of improving the accuracy of treatment...
delivery. This was prompted on noting that occasional fractions showed larger than desirable patient movement. The assumption is that patients may move over time during treatment and thus more frequent checking of the patient setup and correction should improve overall accuracy. Stereoscopic kilovoltage imaging offers a fast, low dose image guidance method suited to more frequent intra-fraction position verification and correction.

The aim of this retrospective, single institution study was to evaluate whether additional intra-fractional imaging and correction of any patient movement, which may occur during the treatment delivery procedure, could be shown to improve positional accuracy and reduce total intra-fraction motion, without significantly prolonging treatment times. A further aim was to maintain radiation dose incurred through additional imaging within acceptable limits.

Materials and methods

Patient selection

38 patients with 41 primary tumour volumes who received spinal SBRT from September 2018 until May 2021 were identified in the institutional database. Data were extracted from the hospital information system by the study team. Ethics approval for the retrospective analysis was obtained (EKNZ 2019-01705). The dataset for workflow 1 consisted of 13 spinal SBRT treatments performed from September 2018 to December 2019, while the dataset for workflow 2 also with 13 volumes, included spinal SBRT treatments from January 2020 to October 2020. The dataset for workflow 3 consisted of 15 volumes treated between November 2020 and May 2021. In total, 283 fractions were included in the complete data set. Various fractionation schemes in accordance with international spinal SBRT standards were considered during the course of our study [7,2], from which 5 × 8 Gy and 10 × 4.85 Gy were most commonly prescribed. A dosis study by Guckenberger et al. (2012) regarding fractioned radiosurgery for painful spinal metastases, was used as a reference for our spinal SBRT dosis protocol. The planning target volume (PTV), was created by expanding the gross tumor volume (GTV) as determined on planning computer tomography (CT) and planning magnetic resonance imaging (MRI) isotropically by a margin of 2 mm. A 1 mm margin is added to the spinal cord resulting in the planning organ-at-risk volume (PRV). The treatment sites for spinal SBRT included 2 cervical spine, 27 thoracic spine, and 12 lumbar spine cases. Patient and treatment characteristics for all three IGRT workflows are described in Table 1.

Table 1

| Characteristics of patients and treatment | IGRT workflow 1 | IGRT workflow 2 | IGRT workflow 3 | Total |
|------------------------------------------|----------------|----------------|----------------|-------|
| Patient characteristics                  |                |                |                |       |
| Number of patients                       | 12             | 12             | 14             | 38    |
| Number of volumes                        | 13             | 13             | 15             | 41    |
| Cervical spine                           | 2              | 0              | 0              | 2     |
| Thoracic spine                           | 8              | 8              | 11             | 27    |
| Lumbar spine                             | 3              | 5              | 4              | 12    |
| Treatment characteristics                |                |                |                |       |
| Number of fractions                      | 105            | 85             | 93             | 283   |
| 5 × 7 Gy                                 | 1              | 0              | 0              | 1     |
| 5 × 8 Gy                                 | 5              | 9              | 10             | 24    |
| 10 × 3 Gy                                | 0              | 0              | 1              | 1     |
| 3 × 4.85 Gy                              | 0              | 0              | 1              | 1     |
| 10 × 4.85 Gy                             | 6              | 4              | 3              | 13    |
| 15 × 2.6 Gy                              | 1              | 0              | 0              | 1     |
| 2 Arcs                                   | 13             | 11             | 8              | 32    |
| 3 Arcs                                   | 0              | 1              | 7              | 8     |
| 4 Arcs                                   | 0              | 1              | 0              | 1     |
| Wingboard                                | 11             | 13             | 12             | 36    |
| Treatment mask                           | 2              | 0              | 3              | 5     |

Patient immobilization and planning CT/MRI

Non-rigid immobilization using supportive devices according to the treatment region and with an emphasis on patient comfort, were used to minimize patient movement and ensure inter-fractional set-up reproducibility. Standard immobilization for thoracic and lumbar spine SBRT include a wingboard, radiosurgical blue mat, knee- and footrest. For cervical spine SBRT, a thermoplastic 5-point mask with cast, radiosurgical blue mat and knee rest were used. Fig. 1 demonstrates the standard positioning utilized during patient setup for thoracic and lumbar spine SBRT using BrainLab Infrared (IR) Reflective Reference Star (BrainLab AG, Feldkirchen, Germany).

Planning CT and MRI were performed for all patients in the treatment position. CT slice spacing was 1 mm and the pixel resolution 1 mm.

Treatment delivery

All spinal SBRT treatments were performed on a Varian TrueBeam STx with incorporated BrainLab couch, Novalis Radiosurgery platform (BrainLab/Varian) with high-definition MLC leaves (2.5 mm). Stereoscopic kilovoltage imaging were performed with BrainLab ExacTrac version 6.2 system. SBRT was delivered with 2–4 VMAT coplanar arcs per fraction using 6 MV flattening filter free (FFF) beams for higher dose rates thus reducing treatment times. IGRT verification with correction of patient positioning in six degrees of freedom (6 DoF) was performed before each fraction using CBCT and stereoscopic kilovoltage imaging, referred to from now on as ExacTrac (EXT). This was then followed by another ExacTrac verification to verify the couch shifts applied and to verify any patient motion during the treatment according to the IGRT workflow used.

The following three IGRT workflows were used, and their effectiveness compared:

IGRT workflow 1 – kV-CBCT and ExacTrac imaging with 6 DoF patient positioning correction prior to radiation, 2–4 treatment arcs delivered, kV-CBCT immediately following the patient treatment to determine the intra-fraction motion.

IGRT workflow 2 – as for IGRT workflow 1, but with additional ExacTrac image verification and positioning correction before each arc is treated.

IGRT workflow 3 – as for IGRT workflow 2, but with additional ExacTrac image verification and positioning correction in the middle of
Image guidance treatment procedure details

The general IGRT workflow procedure is illustrated in Fig. 2.

Fig. 3, Fig. 4 and Fig. 5 illustrate IGRT workflow 1, 2 and 3 respectively.

The match area was set to include a vertebral body above and below the target vertebrae. For the initial set up, if rotation adjustments exceed 3° for yaw and 2° for pitch and roll, the patient was re-positioned on the couch, before restarting the IGRT procedure. Thereafter our departmental SBRT spine protocol tolerances of 1 mm for translational errors (lateral, longitudinal and vertical) and 1° for rotational errors (pitch, roll and yaw) were followed. If the ExacTrac verification is within 1 mm/1° the irradiation may start. Any verification showing that positioning is out of this tolerance will force the required corrections to be applied with the 6 DoF couch. After any couch movement a further ExacTrac verification x-ray is performed to verify and correct any misalignment.

![General IGRT workflow procedure diagram]

Fig. 2. General IGRT workflow procedure.
verification is necessary and this procedure is repeated until the ExacTrac verification is within tolerance, (see dashed section in flowchart in Fig. 2). Only after an “in tolerance” ExacTrac verification, can the irradiation proceed.

Quality assurance of the image guidance methods

It is essential to ensure that both the CBCT imaging isocenter and the ExacTrac imaging isocenter are accurately matched to the linac radiation isocenter. Daily checks of the CBCT versus the radiation isocenter are carried out as part of the Machine Performance Check (MPC) of the TrueBeam. For the ExacTrac system, a daily modified Winston Lutz test (WLT) is done, whereby the ball bearing is positioned at the ExacTrac isocenter by using ExacTrac images. In both cases, results exceeding the in-house tolerance of 0.5 mm require new calibration of the corresponding imaging system.

Evaluation of imaging dose

To evaluate and compare the imaging dose for the different IGRT workflows described, measurements were made of the entrance dose for ExacTrac image pairs (120 kV, 25 mAs) using RaySafe X2 Solo R/F system. For the CBCT (Varian TrueBeam spotlight protocol 125 kV, 750 mAs) the Computed Tomography Dose Index (CTDI) was measured in the 32 cm PMMA CTDI phantom using a 10 cm cylindrical ionisation chamber.

Results

Intra-fractional motion evaluation

A total of 1280 images out of 1291 verifications were included in our study. Eleven images were not included due to suboptimal image quality. For details see Table 2.

Two senior radiation therapists evaluated positional errors offline by comparing the three translational and three rotational deviations when matching each CBCT or ExacTrac image pair to the planning CT (defining the planned treatment position). The percentage of images found to be within the defined 1 mm/1° tolerance at various stages of each IGRT workflow was calculated. In addition, the 3D vectors of the translational shifts were calculated for all mid- treatment images.

| Total images | Workflow 1 | Workflow 2 | Workflow 3 | Total |
|--------------|------------|------------|------------|-------|
| Varian CBCTs | 210        | 169        | 185        | 564   |
| ExacTrac images | 103      | 170        | 454        | 727   |
| Total CBCTs & ExacTrac | 313 | 339 | 639 | 1291 |
| CBCTs suitable | 204 | 165 | 184 | 553 |
| ExacTrac suitable | 103 | 170 | 454 | 727 |
| Total CBCT & ExacTrac | 307 | 335 | 638 | 1280 |
(ExacTrac) and post-treatment images (CBCT) by a senior medical physicist.

IGRT workflow 3 recorded 97% of images within the 1 mm/1° tolerance limit, compared to 85% and 83% in workflows 1 and 2 respectively, as measured on post-treatment CBCT. Fig. 6 represents the percentage of “in tolerance” verifications at various stages during the treatment procedure. Workflow 3 achieved a marked reduction in the intra-fraction motion compared to workflows 1 and 2.

The mid-treatment verification in workflow 2 resulted in 28% of fractions being corrected (due to having a positional error >1 mm/1°), and between 5 and 13% needed to be corrected mid-treatment (including mid-arc) in workflow 3. The 3D translation vectors for intra-fraction motion evaluated at mid-treatment (where available) from ExacTrac and post-treatment CBCT were reduced from a mean (standard deviation) of 0.91 mm (±0.52 mm) for IGRT workflow 1, to 0.84 mm (±0.44 mm) for IGRT workflow 2 and further reduced to 0.64 mm (±0.34 mm) for IGRT workflow 3, demonstrating a reduction in motion error with increased frequency of mid-treatment position verification and correction. Across all workflows, the maximum deviations as measured on post-treatment CBCT are 2.2 mm (lateral), 3.3 mm (longitudinal), 1.7 mm (vertical), 1.1° (pitch), 1.6° (roll), and 1.4° (rotation), see Table 3.

It is worth noting that it was evident from data retrieved from workflow 3 that spinal level and amount of vertebrae included in PTV may also influence “out of tolerance” incidence. However, because of limited sample size, the author proposed further studies to confirm this statement. It was also noted that most of the intra-fraction motion occur at the ExacTrac pre RT Arc 1 stage, suggesting that some patients may move, or make a counter movement in response to applying the initial shifts.

For all three workflows based on the final CBCT, the mean translational shifts are less than 0.2 mm and mean rotational values around 0.1° in all directions, indicating no systematic error in patient motion and no shifts between ExacTrac and CBCT positioning systems as demonstrated in Fig. 7. The standard deviation of the position errors is seen to be reduced from the initial to the final verifications (for workflows 2 and 3). The spread of the intra-fraction motion measured post-treatment is reduced between IGRT workflows 1 and 2 and is smallest for workflow 3. There are notably more outlying values for IGRT workflow 1, with intra-fraction motions above 2 mm for a few individual fractions and up to a maximum of 3.3 mm. Through repeated imaging, intra-fraction motion is detected and corrected during the treatment, reducing the maximum intra-fraction motion to 1.4 mm for IGRT workflow 3. The mean translational shifts at the initial ExacTrac after the couch corrections based on the CBCT have been applied and are all within 0.5 mm, indicating a minimal systematic shift. (This could be explained by patients making counter movements in response to the applied 6 DoF couch movements).

**Treatment time**

The standard treatment timeslot for a typical spinal SBRT patient at our institution is 30 min. The time taken per arc treatment with VMAT technique and FFF-beams is on average 1 min, 13 s and per CBCT with spotlight protocol 37 s, for the patients included in this study. The complete spinal SBRT treatment time per fraction (including pre- and post-treatment CBCT, ExacTrac verifications and the VMAT arc delivery time, but not the initial patient positioning) for IGRT workflow 3 recorded a mean of 13 min compared with 12 min for IGRT workflow 1 and 2. The dose fractionation and the number of arcs will also impact the treatment time, perhaps more than the additional imaging.

**Dose from image guidance procedures**

The entrance dose for the ExacTrac image pairs was measured as 186 μGy. This is comparable with the Swiss Federal Office of Public Health.
diagnostic reference level (DRL) for thorax radiographic images (150 μGy) [8]. The corresponding whole-body dose in terms of effective dose for an ExacTrac image pair is thus estimated at 0.05 mSv [8]. Table 4 shows the effective whole-body dose for each IGRT workflow based on the respective average number of images taken. The actual number of images taken will depend on the number of total fractions, the number of arcs in the plan, and the number of corrections required due to patient movement, so is to be understood as a representative number. The CBCT CDTI for the spotlight protocol using an 18.5 cm scan length was measured as 14.5 mGy, the DLP 270 mGycm. Based on these measurements and using the software CT-Expo v2.7 (Medizinische Hochschule Hannover, Dept. of Experimental Radiology), the effective dose is estimated at 5.9 mSv for a female and 3.8 mSv for a male.

### Discussion

Fig. 6 shows an improvement in the number of treatment fractions with positional error less than 1 mm/1° from 85 % to 97 % for workflow 1 to workflow 3. From this it appears evident that increased intra-fractional imaging resulted in a clear reduction in intra-fraction motion. These findings are consistent with other studies of intra-fractional motion during spinal SBRT which report an improvement from 77 % to 95 % of the treatment fractions having a positional error within 1 mm/1°, by adding a second CBCT verification prior to treatment start [4].

Some studies have questioned whether ExacTrac imaging can provide the same degree of precision as CBCT [3,5]. The low percentage of ExacTrac verification images within tolerance (1 mm/1°) in the ExacTrac pre-RT Arc 1 (Fig. 6), which is taken after the correction based on CBCT, also caused matching in spinal regions with ExacTrac to be questioned. Discrepancies between ExacTrac and CBCT matching could be both equipment-related (accuracy of the ExacTrac and CBCT isocenter calibrations, different matching algorithms, image parameter settings prior to matching), and patient-related (patient movement between the two images, which may be motion over time, or in response to applying couch translational and rotational shifts).

Equipment related differences between ExacTrac and CBCT are thought to be minimal, as the daily in-house adapted Winston Lutz Test confirms the congruence of the ExacTrac and TrueBeam radiation isocenters, so we exclude this as a cause in our centre. Similarly the results of the final CBCT in IGRT workflow 3, which follows shortly after the final mid arc ExacTrac, shows 97 % of verifications within tolerance and so confirms the agreement between the ExacTrac- and CBCT systems as used in this study. In terms of patient-related motion, CBCT imaging, image reconstruction and matching takes minutes, it is suggested that some patients may move, or make a counter movement in response to applying the shifts. This could explain the high proportion of positioning errors >1 mm/1° seen in the first ExacTrac image, which is around 50 % in all workflows and demonstrates the importance of verification imaging after the initial setup corrections, as also reinforced by others [9,10,11]. In contrast the ExacTrac imaging and matching procedure takes in the order of seconds, reducing the time during which the patient may move prior to the start or continuation of the dose delivery. Koo et al. use triggered kV imaging during SBRT treatment and highlight the need to promptly detect and correct any movements that occur during spinal SBRT [6]. It is also plausible that the patient might move more at the beginning of the treatment, before “settling” into the treatment position. This could explain the form of the graphic for IGRT workflow 3 in Fig. 6, whereby the percent of “in tolerance” images increases as the treatment progresses (with mid-treatment motion corrections).

Svestad et al. reported a 10–20 min spine SBRT treatment time, depending on the patient’s general condition and the time needed for positioning [4]. Our treatment times are 12–13 min from initial CBCT imaging through to the end of the post treatment CBCT. Our analysis of the motion errors indicate that despite relatively short treatment times, patient movement can occur and that these errors are reduced by further intra-fractional imaging. Based on the correlation between treatment time and intra-fraction motion observed in spinal SBRT, the use of faster imaging modalities to reduce the treatment time could minimise the positioning uncertainty [12].

The standard deviation (or spread) of the shifts as illustrated in the box plots of Fig. 7, are seen to reduce from workflow 1 to 3 as imaging, and so the potential for motion correction, is more frequent. In workflow 1, 15 % of the fractions were shown to have a motion error of >1 mm/1° (Fig. 6). For cases with high dose target volumes in close proximity to the spine, this could cause dose in the spinal cord to be above the tolerance dose and so was the motivation for further improvement to the image guidance procedure. Only in workflow 3 are the shifts measured in all fractions always below 2 mm, suggesting that a 2 mm PTV margin is reasonable when this workflow is used. Further, the mean 3D translational vector of 0.64 mm (±0.34 mm) for workflow 3, would suggest 1 mm to be a safe margin for the spinal cord planning organ at risk volume (PRV).

The total effective dose acquired over the whole course of the treatment due to ExacTrac imaging (estimated at 1.8 mSv for IGRT

| Workflow 1 | lateral | 2.9 mm | N/A | N/A | N/A | N/A | 1.8 mm |
|------------|---------|--------|-----|-----|-----|-----|--------|
|            | longitudinal | 2.2 mm | N/A | N/A | N/A | N/A | 3.3 mm |
|            | vertical | 1.9 mm | N/A | N/A | N/A | N/A | 1.7 mm |
|            | roll | 1.4° | N/A | N/A | N/A | N/A | – |
|            | rotation | 1.5° | N/A | N/A | N/A | N/A | – |

| Workflow 2 | lateral | 2.9 mm | N/A | 1.9 mm | N/A | N/A | 2.2 mm |
|------------|---------|--------|-----|--------|-----|-----|--------|
|            | longitudinal | 2.6 mm | N/A | 1.3 mm | N/A | N/A | 1.3 mm |
|            | vertical | 2.6 mm | N/A | 1.7 mm | N/A | N/A | 1.3 mm |
|            | pitch | 2.3° | N/A | 1.2° | N/A | N/A | 1.1° |
|            | roll | 1.3° | N/A | 1.3° | N/A | N/A | 1.6° |
|            | rotation | 1.2° | N/A | 1.3° | N/A | N/A | – |

| Workflow 3 | lateral | 2.1 mm | 1.2 mm | 1.9 mm | 1.2 mm | 1.2 mm | 1.0 mm | 1.3 mm |
|------------|---------|--------|-----|--------|-----|-----|--------|--------|
|            | longitudinal | 1.6 mm | 1.5 mm | 1.0 mm | – | – | – | 1.3 mm |
|            | vertical | 2.5 mm | 1.4 mm | – | 1.3 mm | 1.4 mm | 1.1 mm | 1.4 mm |
|            | pitch | 1.1° | – | 1.1° | 1.0 mm | 1.8° | – | – |
|            | roll | 1.9° | 1.7° | 1.3° | – | – | – | – |
|            | rotation | 1.4° | 1.1° | – | – | – | – | – |

Table 3

Maximum “out of tolerance” values in mm/° for all three IGRT workflows.

*ExacTrac (EXT), Radiation Treatment (RT).*
workflow 3 (Table 4) with the greatest amount of image verification), is considerably less than that from a single CBCT (estimated at 5.9 mSv for a female, 3.8 mSv for a male). Therefore, the use of low dose ExacTrac portal verifications during and between arcs to monitor patient position, limits additional radiation dose to the patient and organs at risk while giving clear benefits in terms of accuracy of the treatment.

**Conclusion**

This study demonstrated that additional intra-fractional stereoscopic kilovoltage imaging to correct any intra-fraction patient motion when using a non-rigid immobilisation system could improve the precision of
Without additional imaging, an intra-fraction motion of >1 mm or >1° could be seen in 15 % of the fractions, whereas the percentage of patients with “out of tolerance” images was reduced to below 5 % by using additional mid-arc verifications with positional correction if required. The intra-fraction motion was reduced without any significant increase in average treatment times or in radiation dose.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: S. J. Rogers has received speaker’s honoraria from BrainLab.

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