Title

**A service evaluation of on-line image-guided radiotherapy to lower extremity sarcoma: investigating the workload implications of a 3mm action level for image assessment and correction prior to delivery.**

**Key words:**

**Radiotherapy setup errors, sarcoma, extremities, IGRT, Imaging protocol**

**Abstract**

**Purpose**

Although all systematic and random positional setup errors can be corrected for in entirety during on-line image- guided radiotherapy, the use of a specified action level, below which no correction occurs, is also an option. The following service evaluation aimed to investigate the use of this 3mm action level for on-line image assessment and correction (online, systematic set-up error and weekly evaluation) for lower extremity sarcoma, and understand the impact on imaging frequency and patient positioning error within one cancer centre.

**Methods**

All patients were immobilised using a thermoplastic shell attached to a plastic base and an individual moulded footrest. A retrospective analysis of 30 patients was performed. Patient set up and correctional data derived from cone beam CT analysis was retrieved. The timing, frequency and magnitude of corrections were evaluated. The population systematic and random error was derived.

**Results**

20% of patients had no systematic corrections over the duration of treatment, and 47% had one. The maximum number of systematic corrections per course of radiotherapy was 4, which occurred for 2 patients. 34% of episodes occurred within the first 5 fractions. All patients had at least one observed translational error during their treatment greater than 0.3cm, and 80% of patients had at least one observed translational error during their treatment greater than 0.5cm. The population systematic error was 0.14cm, 0.10cm, 0.14cm and random error was 0.27cm, 0.22cm, 0.23cm in the lateral, caudocranial and anteroposterial directions. The required Planning Target Volume margin for the study population was 0.55cm, 0.41cm and 0.50cm in the lateral, caudocranial and anteroposterial directions.

**Conclusion**

The 3mm action level for image assessment and correction prior to delivery reduced the imaging burden and focussed intervention on patients that exhibited greater positional variability. This strategy could be an efficient deployment of departmental resources if full daily correction of positional setup error is not possible.

**Introduction and Background**

Sarcoma is a relatively rare diagnosis, accounting for 1% of cancer diagnoses; with around 25% of cases occurring in the limbs1,2. Surgery is the primary treatment used in the management of sarcoma3 and whilst conservative surgery is the major goal, amputation is indicated in some cases4. In cases where limb preservation is possible, lower limb sarcomas are typically treated with conservative surgery and adjuvant or neo-adjuvant radiotherapy and this combination achieves high rates of local control whilst preserving the limb’s function5. Post-operative radiotherapy is considered the standard treatment for intermediate and high grade disease6; however, both types of radiotherapy have been reported to have similar local control rates and similar long-term survival7.

When patients are managed with radiotherapy, patient immobilisation is a vital part of minimising patient positioning uncertainties. Due to the freedom of rotation and movement in the lower limb, immobilisation is often bespoke8 with a combination of thermoplastic moulds, vacuum pillows and polystyrene cradles used depending on local departmental practice9, 10. Improper immobilisation could result in the reduction of dose to target volumes and an increase in dose to healthy tissue in the limb with resultant toxicity such as fibrosis, joint stiffness, lymphoedema or pathological fracture11.

Imaging Guided Radiotherapy (IGRT) allows the treating radiographers to assess and correct for some of the remaining patient positioning uncertainties during treatment. Furthermore, the retrospective collection of imaging data is recommended to inform local decisions on planning margin, and any change in imaging strategy or Planning Target Volume (PTV) margin should be carefully audited and assessed. For the lower limb, previous UK guidance for IGRT using Megavoltage portal images recommended large planning margins of 2-5cm12. Recently, small magnitude (~0.5cm) setup margins have been investigated using daily on-line cone beam Computed Tomography (CBCT), surface marker localisation and surface imaging10, 13, 14. However, daily on-line imaging is resource intensive and other less intensive strategies are little explored for this patient group.

The purpose of on-line CBCT imaging is to control both systematic and random errors in patient positioning reproducibility, and it is usual for the measured error to be corrected in entirety each time a match is performed. Nevertheless, the use of a specified action level for correction (a level below which no correction is made) is supported by recent UK national guidance15 if it is carefully evaluated for a given treatment site.

In May 2015, an online imaging protocol with a 3mm action level for image assessment and correction was introduced at the authors’ institution. During the first three fractions, all displacement was corrected provided that the 3mm action threshold was reached. Correction of systematic error was made after the first three fractions and evaluated online weekly thereafter. The following service evaluation aimed to investigate the impact of this imaging strategy. The objectives of the evaluation were to quantify the imaging workload and positioning reproducibility errors by assessing: timing, frequency and magnitude of correctional episodes, quantification of population systematic and random error and CTV-PTV margins.

**Methods**

Approval was gained from the institution’s clinical governance committee and XXXXXXX to conduct a retrospective imaging evaluation. All patients treated with radiotherapy for sarcoma of the lower limb between 25th May 2015 and 25th May 2016 were initially identified by treatment site in the MOSAIQ (Version 2.5 Elekta, Sweden) electronic booking system and the Webpublisher (V2.3.25 Phillips, The Netherlands) electronic prescription software at YYYYYYY. Patients were then screened to assess their suitability for the evaluation using criteria in Table 1. Clinical notes were used to record patient characteristics.

***Immobilisation and treatment planning***

All patients included in this evaluation were immobilised using a thermoplastic shell attached to a plastic base and an individual moulded footrest to help keep the foot and ankle stable (see image 1). CT scans were performed during the pre-treatment process, using 0.5 cm slices and the images transferred to Pinnacle software (Version 9.8, Phillips, The Netherlands) for clinical target volume (CTV) delineation to be completed. Treatment planning was performed using 3D conformal radiotherapy or IMRT dependant on the clinicians’ preference.

***Image verification***

Matching and assessment was performed by therapy radiographers that had passed an in-house IGRT training programme. Patients were imaged immediately before treatment on days 1-3 and automatically matched to bony anatomy using the CBCT automatic Bone T+R, Grey T+R or Grey T algorithms (Elekta, Sweden), followed by a visual assessment of target coverage and organs at risk. If errors were greater than 0.3cm in any axes (anteroposterior, caudocranial and mediolateral) then patient position was corrected on-line for that fraction. Mean errors (fractions 1-3) were calculated after fraction 3 and a systematic correction applied if an action threshold of 0.3cm was reached. If no correction was necessary, on treatment verification occurred weekly. If corrective moves were necessary, the patient would be imaged for a further 2 fractions in the manner described above (see supplementary flowchart).

***Data analysis***

Cone beam imaging data was collected (fraction number, magnitude of setup error in 3 translational axes, action taken by treatment team) from a summary sheet generated in MOSAIQ at the end of the patient’s treatment. Timing and magnitude of systematic corrections, and frequency of online corrections were tabulated. Translational setup uncertainty was used to calculate the population systematic and random setup error. The contribution of interfractional setup error to the PTV margin for the sample population was calculated using:

PTV Margin setup= Σsetup 2.5 + 0.7σsetup

Where Σ setup is the standard deviation of the corrected interfractional systematic error and σsetup is the standard deviation of the interfractional random error 16.

**Results**

30 consecutive patients with complete CBCT data sets were evaluated. Treatment subsite for the 30 evaluated patients are recorded in table 2. 18 received postoperative radiotherapy, 11 received preoperative radiotherapy and 1 patient received radiotherapy alone. 826 fractions were delivered, the mean number of fractions per patient was 27.5 (range 20-30) and dose ranged between 45-60Gy.

436 CBCT images were delivered (per patient: range 8-22, median 13.5, mean of 14.5; per fraction: mean 0.52). 29 (97%) of patients had at least one on-line CBCT correction during their treatment. Of all CBCT images taken, 45% were corrected on-line, with a mean of 6.6 images corrected per patient. 8 (27%) patients had more than 50% of imaged fractions corrected on-line; these patients accounted for 48% of all on-line corrections. Figure 1 demonstrates that 27% of all on-line corrections were made in the first 3 fractions, and 40% in the first 6.

Table 3 shows the number of systematic error corrections over the evaluated population. 20% of patients had no systematic correctional episodes over the duration of treatment, and 47% had one. The maximum number of systematic corrections per course of radiotherapy was 4, which occurred for 2 patients. 34% of episodes occurred within the first 5 fractions. Figure 2 shows the timing of systematic error corrections.

Table 4 shows the magnitude of errors (without on-line corrections) and their direction. All patients had at least one observed error during their treatment greater than 0.3cm, with 46% occurring in the left/right direction. 80% of patients had at least one observed error during their treatment greater than 0.5cm, with 53% occurring in the left/right direction.

Table 5 shows the mean population systematic and random errors for the evaluation dataset without taking into account on-line corrections. The population systematic error was 0.14cm, 0.10cm, 0.14cm and random error was 0.27cm, 0.22cm, 0.23cm in the lateral, caudocranial and anteroposterial directions. If other errors are assumed to be minimal, the required PTV margin would be 0.55cm, 0.41cm and 0.50cm in the lateral, caudocranial and anteroposterial directions.

**9. Discussion**

Although daily on-line image analysis and correction with no specified action level will achieve the largest reduction of systematic and random error, it is believed to be time consuming and labour intensive17-18, and there is a duty to keep concomitant exposure as low as reasonably possible19. For sarcoma of the limb, patient specific factors such as: pre/postoperative status; tumour location in the limb; and limb swelling could potentially affect the magnitude and fluctuation of translational error. Given the rarity of cases in even large treatment centres, the prospective selection of patients that require less intensive imaging is problematic. This retrospective analysis included 30 lower extremity sarcoma patients all immobilised in a consistent manner. The composition of subsites within the group is comparable to other published data on lower extremity treatment position setup error13. As UK guidelines suggest an evaluation population of over 20 patients12, a sub analysis of the above patient factors is beyond the scope of this paper.

The purpose of using an action level of 3mm for correction after online imaging is to focus resource on patients with poorer positional reproducibility, thereby reducing concomitant exposure of the extremity sarcoma population. This evaluation shows a reduction in exposures compared to daily online imaging, with a mean of 0.52 images captured per fraction. 27% patients accounted for 48% of all on-line corrections, suggesting that resources (and exposures) were concentrated on patients where intensive monitoring and intervention are of most benefit. Furthermore, as the IGRT protocol enabled the radiographers to make on-line corrections for error greater than 0.3cm, large random errors were managed when observed across the entire population and were corrected in 45% of images taken.

Systematic reproducibility was good for most patients, with 67% of patients requiring 0 or only 1 systematic error corrections. We found the effect of time trend errors (e.g. swelling in the treatment site and relaxation) to be small, with the majority of on-line and systematic corrections occurring at the beginning of treatment. However, daily monitoring for all patients would have enabled true quantification of this effect.

Increasing error correction frequency from weekly to daily yields large reductions in planning margins17. For lower extremity sarcoma, such careful control of patient positioning errors is increasingly topical as the use of IMRT is subject to a UK-wide trial20. Previous reports suggest population inter-fractional systematic error for this treatment site is between 0.06-0.29cm, and the population inter-fractional random error is between 0.18-0.46cm10,13. The data presented here shows a comparable population systematic error of 0.10-0.14cm and a population random error of 0.22-0.27 cm. However, our reported data does not take any into account corrections on-line. As 45% of images required correction on-line, the true inter-fractional setup error for this cohort is lower than reported here. This suggests that a 3mm action level can be utilised and still keep population systematic and random error low.

It should be noted that this was a retrospective evaluation, and post correctional CBCT were not are not routinely taken as part of our imaging strategy. This is an important limitation in interpreting this data. However, the literature reports that intra-fractional error for lower extremity sarcoma is low (0.06-0.07mm) 10 and will therefore have only a small effect on overall margins13, 14. Additionally, our calculated PTV margin of 0.55cm, 0.41cm and 0.50cm in the lateral, caudocranial and anteroposterial directions does not incorporate other systematic errors such as delineation. Therefore, although margin reduction in our evaluation population looks promising, other components of potential error need to be quantified to enable a true evaluation of margin adequacy.

**Conclusion**

This evaluation aimed to investigate the impact of a 3mm action level for online assessment and correction in our departmental IGRT practice for lower extremity sarcoma. This strategy reduced the imaging burden and focussed intervention on patients that exhibited greater positional variability. The evaluation suggests that the impact of image matching and positional correction was greatest at the beginning of treatment, time trend errors were small, despite common site-specific problems such as lympheodema and joint stiffness. Although use of an action level for online assessment and correction is infrequently reported in the literature, this evaluation suggests it can be an efficient deployment of departmental resources, whilst still keeping population systematic and random error low.

Table 1. Evaluation criteria

* Patients immobilised with a thermoplastic shell, plastic base and individual moulded footrest
* 3-dimensional conformal or IMRT planned
* Patients imaged with CBCT
* Patients where online images were assessed and corrected using 3mm action level (see supplementary information)

Table 2. Treatment sub-site of evaluated patients

|  |  |
| --- | --- |
| **Treatment sub-site** | **Number of patients** |
| **Thigh** | 16 |
| **Knee** | 8 |
| **Calf/shin** | 4 |
| **Foot** | 2 |

Table 3. Systematic Error Corrections per patient

|  |  |  |
| --- | --- | --- |
| **Correction Episodes** | **Number of patients** | **Percentage of patients (%)** |
| **0** | 6 | 20.00 |
| **1** | 14 | 46.67 |
| **2** | 5 | 16.67 |
| **3** | 3 | 10.00 |
| **4** | 2 | 6.67 |

Figure 2. Timing of systematic error corrections

Figure 1. Timing of on-line corrections

Table 4. Magnitude of errors and frequency

|  |  |
| --- | --- |
| % patients with >0.3cm errors | 100% |
| no. of errors >0.3cm per patient | 11.6 |
| % all errors >0.3cm in l/r direction | 46% |
| % all errors >0.3cm in s/i direction | 24% |
| % all errors >0.3cm in a/p direction | 30% |
| % patients with >0.5cm displacements | 80% |
| no. of errors >0.5cm per patient | 4.0 |
| % all errors >0.5cm in l/r direction | 53% |
| % all errors >0.5cm in s/I direction | 15% |
| % all errors >0.5cm in a/p direction | 32% |

Table 5. Systematic and Random Error, PTV margin using the vanHerk Recipe

|  |  |  |  |
| --- | --- | --- | --- |
|  | Lateral (cm) | Craniocaudal | Anteroposterior |
| Systematic Error ΣAll fractions | 0.14 | 0.10 | 0.14 |
| Random Error σ | 0.27 | 0.22 | 0.23 |
| PTV margin | 0.55 | 0.41 | 0.50 |

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