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Original article

Application of IMRT in adjuvant treatment of soft tissue sarcomas of the thigh—Preliminary results

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ARTICLE INFO

Article history:
Received 29 December 2010
Accepted 22 February 2011

Keywords:
IMRT
3D-CRT
Soft tissue sarcoma

ABSTRACT

Background: Fracture of the femur is the most frequent late complication in patients with soft tissue sarcomas (STS) who receive external beam radiotherapy after limb-sparing surgery.
Aim: To reduce the risk of bone fracture following radiotherapy of STS of the thigh, we minimized the dose to the femur and to surrounding normal tissues by applying intensity modulated radiation therapy (IMRT). We report preliminary results of post-surgery IMRT of the thigh in patients with STS in this extremity.
Materials and methods: 10 adult patients undergoing post-operative radiotherapy of STS of the thigh were treated using IMRT. Clinical IMRT plans with simultaneous integrated boost (SIB) and 3-phase three-dimensional conformal radiotherapy (3D-CRT) were designed to adequately treat the planning target volume and to spare the femur to the largest extent possible. Dose distributions and dose-volume histograms were compared.
Results: For either technique, a comparable target coverage was achieved; however, target volume was better covered and critical structures were better spared in IMRT plans. Mean and maximum doses to OAR structures were also significantly reduced in the IMRT plans. On average, the mean dose to the femur in 3D-CRT plans was about two times higher than that in IMRT plans.
Conclusion: Compared with 3D-CRT, the application of IMRT improves the dose distribution within the concave target volumes and reduces dose to the OAR structures without compromising target coverage.

1. Background

Soft tissue sarcomas (STS) are rare neoplasms originating from mesenchymal tissue. Histologically, they form a heterogeneous group. STS occur in about 1% and 10% of all neoplasms in adults or children, respectively. The incidence of STS in Poland (population of ca. 40 million) is about 800–1000 new cases and is increasing.[1] STS occur most frequently in the extremities (60%). Surgery (limb sparing surgery) is

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1507-1367/$ – see front matter
doi:10.1016/j.rpor.2011.02.006

the treatment of choice; nevertheless, radiotherapy is important in adjuvant and neoadjuvant approaches.[2] A combined surgery and radiotherapy improve the patient's quality of life and achieve local control rates equivalent to those after amputation.[2–5]

Irradiation of STS may significantly elevate the risk of morbidity, including wound and skin complications, contractures, oedema, or bone fracture and may introduce region-specific complications (genital in the case of thigh, or spinal cord and salivary gland in the case of head and neck sarcomas).[6] Wound complications may be related to the sequence and timing of surgery and irradiation.[3]

The risk due to radiotherapy may be further reduced by using appropriate radiotherapy techniques. It is essential to spare the circumference of the irradiated extremity and to avoid irradiating adjacent areas, such as the contralateral thigh or the genital region. The relative risk of bone fracture after radiotherapy (5%) is lower than that of other complications, but it can exceed 25% if periosteal stripping is performed.[7] Because treatment of such fractures is difficult and prolonged, and causes a decrease in the patient's quality of life, dose to the bone should be minimized.[8]

Because the target volume is large and irregular and lies close to bone structures, 3D-CRT treatment plans become quite complicated and are not always satisfactory. The shape of the lesion around the surrounding bone after complete surgical excision is usually quite irregular. It is therefore technically difficult to treat such a volume homogeneously, while sparing the bone cortex of the adjacent bone. A conventional 3D treatment plan employs fields covering the entire target with large margins and minimal sparing of normal tissue. The application of the IMRT technique permits high doses of radiation to be delivered much more precisely than in the case of conventional radiotherapy.[9]

2. Aim

We explored the possibility of clinically applying IMRT to treat soft tissue sarcoma of the thigh to demonstrate its advantage versus conventional 3D-CRT treatment of this site, in terms of dose distribution, target coverage and normal tissue sparing.

3. Materials and methods

Radiotherapy plans for 10 patients with STS of the thigh were examined and compared. All patients underwent limb-sparing surgery. The patients were immobilized as close as possible to their neutral anatomic position. To minimize patient movement, customized foam moulded under their leg and a thermoplastic mask fixed onto the baseboard were used. The surgical scar was marked using CT-compatible wire to delineate the anatomic boundaries of the tumour or scar and a bolus was placed to move the build-up zone closer to the skin surface. 2.5-mm slice CT scans were acquired and transferred to a Varian-Eclipse planning system (Varian Medical Systems, Inc.). Appropriate planning target volumes (PTVs) based on CT, as well as normal tissue and organs at risk structures, were delineated. The tumour bed was defined using pre-operative imaging and surgical clips. The surgical scar was marked over the skin surface. PTV1 consisted of the tumour bed with a 2 cm margin in all directions. PTV2 was formed by adding a 3 cm margin axially to the tumour bed and 5–7 cm superior/inferior margins. PTV3 included PTV1, PTV2 and the whole muscular compartment. PTV was modified to exclude the bone and a 0.5 cm layer beneath the skin surface. In all patients, the entire femur was contoured as a critical structure and normal tissue was defined as the limb, excluding the PTV1 and the femur. The same target volumes of OAR and of normal tissues were used to prepare 3D-CRT and IMRT plans.

For every patient, 3D-CRT plans were developed using 3–4 beams. Targets were treated sequentially and required separate dose plans with different dose prescriptions. The three-phase technique using shrinking fields was employed. The prescribed doses were first to deliver 50 Gy in 25 fractions to PTV3, next 10 Gy in 5 fractions to PTV2, and finally 10 Gy in 5 fractions to PTV1.

IMRT plans employing 7–8 fields were generated using the simultaneous integrated boost (SIB) technique where all targets are treated within a single treatment plan over the entire treatment course.[10] The linear quadratic concept was applied and doses were re-calculated in terms of biologically equivalent dose (BED) in order to provide equivalent doses in the comparison.[11,12]

Patients were treated with 6 MV photons generated by a Varian 2300 C/D accelerator equipped with a Millennium 120-leaf MLC (both from Varian Medical Systems, Inc.). IMRT plans were generated using ECLIPSE/HELIOS software (Varian Medical Systems, Inc.) which includes an inverse planning algorithm. The sliding windows technique[13] was used for delivery. In both techniques, the gantry angles were chosen in such a way as to avoid irradiation of the contralateral leg.

In two of the ten patients treated, fields of lengths exceeding 40 cm were required, thus two separate isocenters had to be introduced. For these two patients, we developed a two-isocenter system, for IMRT and for the initial phases of the 3D-CRT technique.

The 3D and the IMRT plans were generated and dose distributions were first compared visually over axial, sagital and coronal slices with respect to the degree of target conformity within the prescribed dose to the PTVS. Plans were evaluated by comparing dose volume histograms (DVHs) for planning target volumes and organ-at-risk structures.

The minimum dose (D_{min}) and the maximum dose (D_{max}) to the PTVs were evaluated. The optimization goal was to achieve 95–105% of the prescribed dose to PTV1, PTV2 and PTV3. Target coverage was estimated by comparing the percentage of PTV3 receiving at least 95% of dose (V95%). The mean and the maximum dose (D_{mean} and D_{max}, respectively) and the volume of the femur receiving 45 Gy (V_{45}) or more were studied. This dose-volume constraint was chosen because fracture of the femur is more frequent in patients receiving high-dose radiotherapy (60–66 Gy) than in those receiving 50 Gy or less (10% vs. 2%).[14]

A dose to the femur was assessed high if encompassing 5% of the volume (D_5). The dose parameters concerning PTVs and the femur were summarized in the form of mean (including $\pm$ SD errors) and median values calculated over all patient treatment plans.