ISSN 2689-8268 | Volume 6

American Journal of Surgery and Clinical Case Reports

Case Series Open Access

Neoadjuvant Lattice Radiotherapy for Bulky Soft Tissue Sarcoma: Single Institution Case Series

Lutsyk M[1]*, Bar-Deroma R[2] and Borzov E[3]

[1]Senior Radiation Omcologist, Radiation Treatment Unit, Oncology Institute, Emek Medical Center, Afula, Israel

[2]Chief Medical Physicist, Radiation Treatment Unit, Oncology Institute, Rambam Health Care Campus, Haifa, Israel

[3]Medical Physicist, Radiation Treatment Unit, Oncology Institute, Rambam Health Care Campus, Haifa, Israel

***Corresponding author:**

Lutsyk Myroslav,
Senior Radiation Omcologist, Radiation Treatment Unit, Oncology Institute, Emek Medical Center, Afula, Israel

Received: 20 May 2023
Accepted: 29 June 2023
Published: 07 July 2023
J Short Name: AJSCCR

Citation:

Lutsyk M. Neoadjuvant Lattice Radiotherapy for Bulky Soft Tissue Sarcoma: Single Institution Case Series. Ame J Surg Clin Case Rep. 2023; 6(13): 1-6

Keywords:

Lattice Radiotherapy, Bulky Sarcoma, Neoadjuvant Radiotherapy, Free margins

1. Abstract

1.1. Introduction: Large and bulky disease cannot be effectively treated with conventional radiotherapy approach. Megavoltage linear accelerators with multileaf collimators (MLC) allow to adapt the dose to the target volume, although leaving unmet the needs of safe and effectiveness while treating large tumor masses.

1.2. Methods: Neoadjuvant Lattice radiotherapy Bulky soft tissue sarcoma

A possible solution for large and bulky tumor masses treatment is the delivery of spatially distributed very high radiation doses within the tumor volume.

We present a series of 5 cases of bulky sarcoma treated with Lattice Radiotherapy technique in neoadjuvant settings for achievement free resectional margins. In Israel we used the technique for the first time.

2. Introduction

Radiotherapy is used for better local control by sterilizing tumor viable and stem cells. Large tumor volumes contain increased clonogenic cell numbers [1, 2] Different tumor volumes demand different doses, the concept postulates adaptive radiotherapy [3]. Therefore, large and bulky disease cannot be effectively treated with conventional radiotherapy approach. Doses required for tumor local control, may cause unacceptable skin toxicity or vice versa: skin sparing doses are inadequate for sterilizing tumor volumes. For example, there is a well-known correlation between volume and local recurrence in head and neck tumors [4]. One of the possible solutions for large and bulky tumor masses treatment is the delivery of spatially distributed very high radiation doses within the tumor volume. The rest of tumor volume is covered or not by lesser radiation doses depending on the clinical situation – the concept known as spatially fractionation radiotherapy technique (SFRT). In the orthovoltage machine era, SFRT was applied using physical grid collimators allowing the delivery of higher doses through the open areas of the grid while sparing skin and beneath lying tissue under the grid wires [5]. The spared, or unirradiated with high dose areas helped rapid regenerating processes and reducing toxicity. SFRT is currently delivered by the use of several techniques and devices applied accordingly to the clinical situation and setting [6,7,8]. Megavoltage linear accelerators equipped with multileaf collimators (MLC) allow delivering MLC-based GRID or MLC-based LATTICE (LRT) with sharp dose gradients giving the opportunity to adapt the dose to the target volume and shape. In a neoadjuvant approach, the SFRT followed by a conventional radiotherapy regimen was applied for the treatment of soft tissue and osteosarcomas showing high pathological tumor response rate in large tumor cases.(9) For instance, LRT delivered in a single fraction of 10-20 Gy followed by a conventional radiotherapy dose (45-50.4 Gy, 1.8-2.25 Gy/fx) was used for the treatment of radioresistant bulky sarcoma masses like liposarcoma, leiomyosarcoma, chondrosarcoma, pleomorphic sarcoma in a neoadjuvant setting with a 39% complete pathological response [6, 10].

The aim of this manuscript is to present the results of our short series of patients treated with the LRT technique in a neoadjuvant setting for soft tissue sarcomas.

3. Materials and Methods

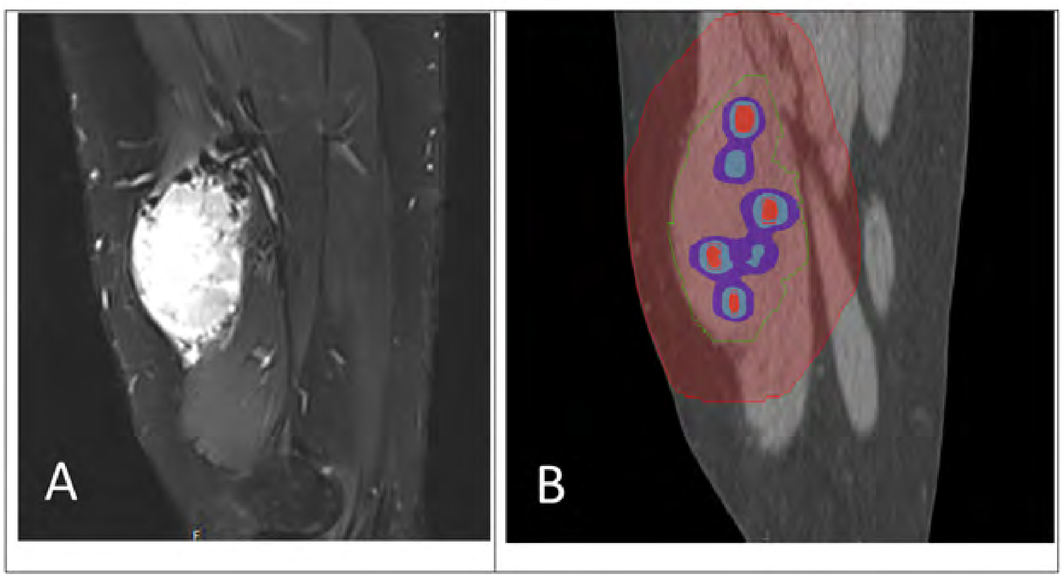
In the series are the presented cases have histologically proven soft tissue sarcomas. MRI-based radiological examination revealed tumor mass of at least 10 cm in the largest dimension [7]. Systemic evaluation didn't show metastatic dissemination of the disease. All patients have been discussed in a multidisciplinary tumor board and referred to a radiation therapy unit for neoadjuvant radiotherapy. The following two-step radiation therapy regimen was used: LRT was applied as a first step on day zero and from day one conventional radiotherapy was administrated as a second step. For the LRT step several high dose regions or nuclei (HDNs) within the tumor mass were planned, their number and location conditioned by the given clinical situation. Each of the HDNs were designed to receive 20 Gy in one treating fraction. The treatment delivery was the same standard approach used for stereotactic radiotherapy that includes vacuum cradle immobilization, treatment planning strategy and IGRT. For step two, an additional 50 Gy in 25 fractions were delivered in 5 weeks with 5 days-a-week treating sessions. Treatment was delivered by Elekta Versa HD linear accelerator using a volumetric modulated arch therapy (VMAT) technique with a 6MV FFF beam. Physical aspects of the technique were fully disclosed [8].

All patients were studied on US and MRI a month after completion of the whole course of radiotherapy, LRT and conventional. Following assessment of the results with a senior radiologist and further surgery planning, patients underwent surgery. In the period after RT and before surgery, both the radiation oncologist and the surgeon continued patient follow-up, registering toxicity and adverse events. Toxicity evaluation was based on CTCAE v4, Classificatory [11].

4. Case Description

4.1. Case 1

A 24-year-old female, healthy otherwise, 4 months after her first delivery, no personal or family history of malignancy, was admitted to the outpatient orthopedic department due to an increasing painful lump on her right thigh. Physical examination revealed a hard consistency deep seated round mass with a size of 10*5*6 cm on the lower third of the right thigh highly suspicious for soft tissue sarcoma. One of the tumor mass boundaries was long 4 cm long adherent to the sciatic nerve (Figure 1). Biopsy and histological examination showed alveolar soft part sarcoma; tumor cells were positive for TFE3. Further work-up did not reveal secondary tumor dissemination. The onco-orthopedic surgeon expert concluded that above knee amputation is a very high possible surgical option in this case. The case was discussed in the multidisciplinary tumor board and referred the patient to neoadjuvant LRT.



Case 1: Round mass with size of 10*5*6 cm^3 on the lower third of the right thigh. LRT delivered with 8 vertices

A. Tumor mass in the MRI sagittal view

B. Radiation treatment plan showing high dose Vertices ("Peaks") placed within the gross tumor volume (GTV). GTV – green line; "The Valley" 50 Gy PTV – red line; 20 Gy Vertices ("the Peak") – dark red solid; 15 Gy isodose – solid light blue; 10 Gy isodose – solid dark blue

LRT was applied using 8 HDNs within the tumor mass and along the sciatic nerve and vessels. The treatment was delivered without discontinuation. The patient the skin toxicity was 'Faint erythema or dry desquamation', Grade 1, as defined by CTCEA v4. In the postoperative period wound healing was compromised by wound infection and plastic surgery intervention was needed with eventual full recovering and preservation of extremity functionality. Topic treatment was applied. Signs of radiation dermatitis resolved 10 days after end of treatment. One month after completion of radiotherapy the patient underwent the planned orthopedic surgery. The postoperative period was complicated by slow wound healing that demanded additional surgical interventions.

The pathology report showed about 20% of tumor necrosis. At least a 3 mm free surgical margin at the sciatic nerve region and more than 10 mm free surgical margins elsewhere where observed.

After 10 months of follow-up the patient remains with no evidence of disease. The ECOG performance status is 1. The patient is under orthopedic follow-up.

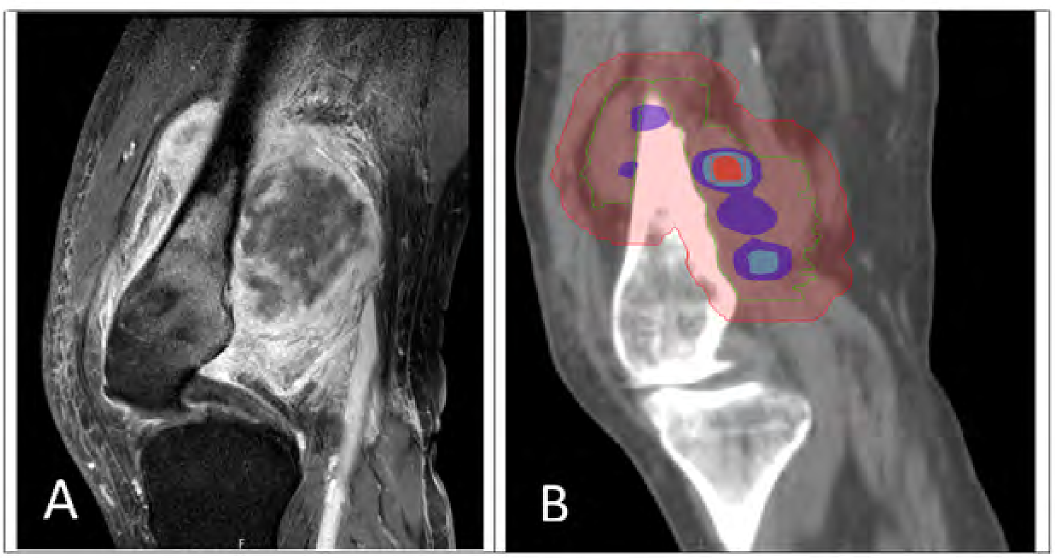
4.2. Case 2

A 66-year-old male, suffering from essential hypertension and diabetes mellitus type 2 well compensated. During the last 6 months before visiting his general practitioner doctor, the patient felt an unusual sensation in the distal part of his left thigh. Later on, the palpable mass started to grow along with increasing painfulness of the region. The patient was referred to an US study that revealed a solid lesion behind the distal epiphysis of the left femur. A further MRI study confirmed the presence of a solid lesion 15*8*7 cm in size, involving the distal part of the femur, entrapping sciatic nerve and femoral vessels. Biopsy and histologic examination reported a high grade pleomorphic rhabdomyosarcoma. Further work-up did not reveal secondary tumor dissemination. The patient was initially treated with 4 courses of Adriamycin- based chemotherapy. The tumor response was minimal, the largest tumor size decreased by only 4 cm. The patient was referred to an onco-orthopedic surgeon whose conclusion was to perform a large surgical intervention which didn't exclude an option of above knee amputation. The case was discussed in a multidisciplinary tumor board and the patient was referred to neoadjuvant LRT (Figure 2).

LRT was applied using 7 HDNs within the tumor mass and along the sciatic nerve and vessels. The treatment was delivered without discontinuation. The patient suffered from Grade 1 radiation dermatitis and some feeling of stiffness of left hip muscles. Topic treatment was applied for a short period (about one week). One month after completion of radiotherapy the patient underwent the planned osteotomy with distal femur resection. The postoperative period was uncomplicated with satisfying wound healing.

The pathology report revealed complete pathological response.

At the last visit after 6 months of follow-up the patient showed no in-field recurrence. The ECOG performance status is 1 with slight limping. The patient was under close orthopedic follow-up for 2 months when on MRI an additional tumoral mass was determined in the upper third of the ipsilateral tibia. Biopsy revealed high grade soft tissue sarcoma. After discussing treatment options, the patient chose above knee amputation. Currently, the patient is free of local and distant recurrences.



Case 2: Bulky sarcoma with size 15*8*7 cm^3 on the lower third of the left thigh. LRT delivered with 7 HDNs

A. Tumor mass in the MRI sagittal view

B. Radiation treatment plan showing dose Vertices ("Peaks") placed within the gross tumor volume (GTV). GTV – green line; "The Valley" 50 Gy PTV – red line; 20 Gy Vertices ("the Peak") – dark red solid; 15 Gy isodose – solid light blue; 10 Gy isodose – solid dark blue

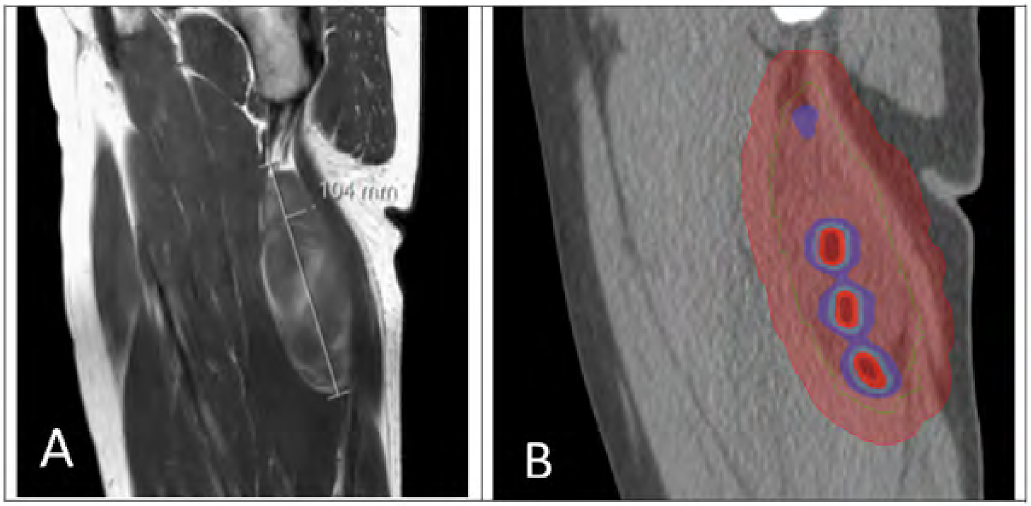
4.3. Case 3

A 42-year-old male, with gout, personal history of renal cell carcinoma treated with partial nephrectomy about 5 years before current admission. During follow-up examination, the patient complained on a painful mass in the upper third of the right thigh which precluded him to drive a car. The patient was referred to a MRI study confirming the presence of a solid lesion of 10*6*4 cm in size, closely adhering the sciatic nerve and femoral vessels. Biopsy and histologic examination reported a myxoid liposarcoma with 10% of atypical cells. Further work-up didn't reveal secondary tumor dissemination. The patient was referred to the onco-orthopedic surgeon for consultation who was concerned about clean resectional margins near the sciatic nerve. After wide staff discussions, it was decided to refer the patient to neoadjuvant LRT (Figure 3).

LRT was applied using 5 HDNs within the tumor mass and along the sciatic nerve and vessels. The treatment was delivered without any discontinuation. The patient had sings of radiation dermatitis (Grade 2) and it is defined as 'Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema'. The signs were observed after RT completion, after one week of topical treatment there were completely resolved long before surgery.

The pathology report revealed complete pathological response.

Patient is being followed up for 3 months after the surgery. ECOG performance status was 0. The further orthopedic follow-up is continuing.



Case 3: Tumor mass with size 10*6*4 cm^3 on the upper third of the right thigh. LRT delivered with 5 HDNs

A. Tumor mass in the MRI sagittal view

B. Radiation treatment plan showing high dose Vertices ("Peaks") placed within the gross tumor volume (GTV). GTV – green line; "The Valley" 50 Gy PTV – red line; 20 Gy Vertices ("the Peak") – dark red solid; 15 Gy isodose – solid light blue; 10 Gy isodose – solid dark blue.

4.4. Case 4

A 46-year-old male, healthy otherwise, was referred to the orthopedic department due to increasing painful lump in the mid third of left forearm. The patient complained on sleep disturbances because of pain. Physical examination revealed a hard consistency elongated lesion of size 13 cm long and about 5 cm in diameter in the mid part of the radial aspect of left forearm. On MRI the lesion entrapped the superficial branch of the radial nerve, close to the radial bone. Biopsy and histological examination showed low grade myxofibrosarcoma, tumor cells being negative for actin, desmin, SOX10, CD34. As further work-up did not reveal secondary tumor dissemination, patient was referred to neoadjuvant LRT.

LRT was applied using 3 HDNs within the tumor mass and along the radial nerve branch and radial bone. The left forearm lesion that prevented the patient from normal night sleep turned into a painless mass after first week of RT, but, more correctly speaking, in two days following LRT delivery the pain was mostly gone and completely disappeared passing the first week. During the last week of treatment and for the coming 3 weeks the dermatitis radiation signs reached a Grade 2 level and resolved fully 2 weeks before the planned surgery without needing to postponed it.

The pathology report showed about focal tumor necrosis. Along 12.5 cm of the lesion boundary a free surgical margin of at least 2mm was observed. The superficial branch of the radial nerve was resected. No functional defect was registered during follow up time (for 7 months passed after surgery).

4.5. Case 5

A 81-year-old male, suffering from diabetes mellitus type 2, essential hypertension, was referred to the orthopedic department due to an increasing painful mass in the upper third of the right thigh which precluded him to sit, lie down, or drive a car. Physical examination revealed a hard consistency elongated lesion with of size 17*10*6 cm in the upper mid third of the posterior region of the thigh. On MRI the lesion showed closely adhered femoral vessels. Biopsy and histological examination showed high grade fibromyxosarcoma. As further work-up of the patient did not reveal secondary tumor dissemination, the multidisciplinary team decision was a neoadjuvant LRT.

LRT was applied using 15 HDNs within the tumor mass near the tumor boundaries and along the large femoral vessels. Radiotherapy was delivered without interruption due to skin toxicity within the irradiated area. In 2 weeks after completion of the RT course skin toxicity signs defined as 'Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion', or Grade 3 toxicity. The dermatitis was resolved at least a week before the surgery. At the surgery time there were no skin toxicity signs.

The pathology report showed hyalinosis, fibrosis, vascularization and an area of tumor necrosis within high grade fibromyxosarcoma. At least a 5 mm free surgical margin along 16 cm of the lesion boundary was resected. No functional defect was registered on follow up visiting. Six months after surgery, the patient was referred to emergency room due to wound dehiscence that treated surgically.

5. Results

All MRI reports showed tumor downsizing and changing in the lesion density but not isotropically, mainly shortening in longest dimension with more overt and dense pseudo capsule around it. In all cases a mosaic heterogeneity within the tumor mass was seen but assertively state that there were high dose regions would be too brave. The pathology reports were performed deliberately assuming that necrosis areas were those where LRT was delivered, but without placing some sort of fiducial markers which may alleviate the search for LRT regions during pathological examination it is hard to clarify the real effect on the tumor of the delivered high doses. The absolute downsizing was significant in all but one case. The forearm lesion case showed a minimal shortening with simultaneously increase in pseudo capsular density. The surgeons stated that the main characteristics of the RT effect was clear demarcation of the tumor mass which allowed more assured resection within obviously healthy tissues.

6. Discussion

For the past 3 decades, the LRT therapy was used mainly to achieve good palliative results in cases of large or previously irradiated areas with high rate response, including 27% rate of complete response [12-14]. Applying this technique to treat bulky tumors in neoadjuvant settings has yielded 86% complete pathologic response [15]. Definitive chemoradiation using LRT techniques treating head-and-neck cancer has brought 79% of tumor control rate while there was no case of Grade 4 toxicity [16].

Nowadays techniques allow delivering large radiation doses to small volumes with very sharp dose gradients in extremely hypofractionated schemes, known as stereotactic body radiotherapy technique (SBRT). Another wide spread RT practice is brachytherapy which exploits the same concept [17]. LRT may be described as a synthesis of these two methods [9]. The advantage of LRT is the combination of well tolerable conventional RT doses and micro-volumes of very high doses within the tumor volume.

The emerged efficiency of spatially fractionated high dose volumes in term of elimination of tumor cells finds its explanation in the modulation of host immune response to irradiated tumor volume [18]. The spatially delivered high doses, present a new pathway of influence on tumor environment eliminating its mitigating or even protective properties against the host immune response [19]. LRT may involve or enhance the host immune response in case of radioresistant tumors [17]. The combination of immune active agents with radiotherapy is a field of intensive studies [20].

Given the available published data, our initial goal of the LRT application was to facilitate obtaining free resectional margins. This radiation treatment technique was never used in our country and we have got the Ethical committee permission from the Israeli Ministry of Health. All five cases were treated within an on-going prospective trial. Only in two cases (Cases 2 and 3) there was complete response to treatment delivered. In the rest of cases (Cases 1, 4, and 5) there was only downsizing with different extent of necrosis within the irradiated volumes. In one case of complete pathological response, the patient presented as Case 2 underwent initial chemotherapy treatment, but the second case (Case 3) was naïve to chemotherapy. The importance of induction courses of chemotherapy prior to LRT was reported but its place in the large soft tissue sarcomas has yet to be established [9].

During the last four decades several approaches were proposed for the classification of surgical margins. Well known from 1980 is the classification of Enneking et al. based on the relationship of the surgical margin to the pseudocapsule and tumor itself and comprising 4 types of margins, which were good theoretically defined with poor reproducibility in practice [21,22]. The introduction in common use of the R classification helped to unify and easily understand the evaluation of resected material. Further evolving the R classification gained in UICC classification providing three types of resection outcomes. Grossly positive margins are classified as R2- margins. If there is 1 mm or more of healthy tissue between tumor and the inked resection margin, it is defined as R0. Margins are considered to be R1 microscopically positive, if tumor is present within 1 mm from the inked border. The classification is widely utilized for pathological assessment of resected specimens [23]. There is still no consensus about the best way of soft tissue sarcoma resection margins evaluation in terms of accurate prediction of local recurrence [24, 25], Gundle et al. reported an analysis of margins status accordingly to “R” and “R+1 mm” classification and showed that R1 positive resection margin may be adequate only in cases of multimodality treatment. From his work 1 mm of normal tissue should be enough for good local control for a 5-year time frame. The situation where a tumor may be resected with high probability of involved, although microscopically, resection margins resembled our patients’ situation in the presented series. For all the 5 cases, margins of 3-5-10 mm from the tumor mass to resection is a good result for those who otherwise doomed to positive margins near critical structures [25].

This very short follow-up period does not enable us to discuss the impact of the proposed radiotherapy technique on local and/or distant relapse. The data we provide may prove a good functionality of the extremities after surgical excision with adequate free margins. The late wound dehiscence in 6 months after surgery is not clear, but may be related to the delivered radiation dose.

Regarding the longest follow-up after the young woman described as Case 1, we may say that there were no registered signs of recurrent disease and she decided to enter her second pregnancy.

7. Conclusion

We presented five cases showing that practical application of LRT can be efficiently used for neoadjuvant treatment of large volume tumor masses. The treatment improves surgical outcomes and preserves extremities functionality.

8. Conflict of Interest

All authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

9. Funding

The study was performed without additional funding.

References

1. Brenner DJ. Dose, volume, and tumor-control predictions in radiotherapy. Int J Radiat Oncol Biol Phys. 1993; 26(1): 171-9.
2. Johnson CR, Thames HD, Huang DT, Schmidt-Ullrich RK. The tumor volume and clonogen number relationship: tumor control predictions based upon tumor volume estimates derived from computed tomography. Int J Radiat Oncol Biol Phys. 1995; 33(2): 281-7.
3. Rutkowski T. The role of tumor volume in radiotherapy of patients with head and neck cancer. Radiat Oncol. 2014; 9(1): 23.
4. Kraas JR, Underhill TE, D'Agostino RB, Williams DW, Cox JA, Greven KM. Quantitative analysis from CT is prognostic for local control of supraglottic carcinoma. Head Neck. 2001; 23(12): 1031-6.
5. Marks H. Clinical experience with irradiation through a grid. Radiology. 1952; 58(3): 338-42.
6. Wu X, Ahmed MM, Wright J, Gupta S, Pollack A. On Modern Technical Approaches of Three-Dimensional High-Dose Lattice Radiotherapy (LRT). Cureus. 2010; 2(3).
7. Grimer RJ. Size Matters for Sarcomas! Ann R Coll Surg Engl. 2006; 88(6): 519.
8. Borzov E, Bar-Deroma R, Lutsyk M. Physical aspects of a spatially fractionated radiotherapy technique for large soft tissue sarcomas. Phys Imaging Radiat Oncol. 2022; 22: 63-6.
9. Snider JW, Molitoris JK, Shyu S, Rice SR, Kowalski ES, DeCesaris C, et al. Spatially Fractionated GRID Radiotherapy (SFGRT) in Conjunction with Standard Neoadjuvant Radiotherapy for Very High-Risk Soft Tissue and Osteo- Sarcomas: Promising Pathologic Response with Safe Dose-Escalation. Int J Radiat Oncol. 2019; 105(1): S238-9.
10. Billena C, Khan AJ. A Current Review of Spatial Fractionation: Back to the Future? Int J Radiat Oncol Biol Phys. 2019; 104(1): 177-87.
11. Cancer Institute N. Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. 2009.
12. Mohiuddin M, Curtis DL, Grizos WT, Komarnicky L. Palliative treatment of advanced cancer using multiple nonconfluent pencil beam radiation. A pilot study. Cancer. 1990; 66(1): 114-8.
13. Mohiuddin M, Stevens JH, Reiff JE, Huq MS, Suntharalingam N. Spatially fractionated (GRID) radiation for palliative treatment of advanced cancer. Radiat Oncol Investig. 1996; 4(1): 41-7.
14. Mohiuddin M, Fujita M, Regine WF, Megooni AS, Ibbott GS, Ahmed MM. High-dose spatially-fractionated radiation (GRID): a new paradigm in the management of advanced cancers. Int J Radiat Oncol. 1999; 45(3): 721-7.
15. Huhn JL, Regine WF, Valentino JP, Meigooni AS, Kudrimoti M, Mohiuddin M. Spatially Fractionated GRID Radiation Treatment of Advanced Neck Disease Associated with Head and Neck Cancer. Technol Cancer Res Treat. 2006; 5(6): 607-12.
16. Peñagarícano JA, Moros EG, Ratanatharathorn V, Yan Y, Corry P. Evaluation of Spatially Fractionated Radiotherapy (GRID) and Definitive Chemoradiotherapy With Curative Intent for Locally Advanced Squamous Cell Carcinoma of the Head and Neck: Initial Response Rates and Toxicity. Int J Radiat Oncol. 2010; 76(5): 1369-75.
17. Griffin RJ, Ahmed MM, Amendola B, Belyakov O, Bentzen SM, Butterworth KT, et al. Understanding High-Dose, Ultra-High Dose Rate, and Spatially Fractionated Radiation Therapy. Int J Radiat Oncol Biol Phys. 2020; 107(4): 766-78.
18. Asperud J, Arous D, Edin NFJ, Malinen E. Spatially fractionated radiotherapy: tumor response modelling including immunomodulation. Phys Med Biol. 2021; 66(17): 175012.
19. Poh SS, Chua MLK, Wee JTS. Why we should give spatially fractionated radiation therapy (GRID) a second look—especially in nasopharyngeal carcinoma. Ann Nasopharynx Cancer. 2018; 1: 1.
20. Sugiyama T, Fujiwara K, Ohashi Y, Yokota H, Hatae M, Ohno T, et al. Phase III placebo-controlled double-blind randomized trial of radiotherapy for stage IIB–IVA cervical cancer with or without immunomodulator Z-100: a JGOG study. Ann Oncol. 2014; 25(5): 1011-7.
21. Enneking WF, Spanier SS, Goodman MA. The surgical staging of musculoskeletal sarcoma. J Bone Jt Surg - Ser A. 1980; 62(6): 1027-30.
22. Trovik CS, Skjeldal S, Bauer H, Rydholm A, Jebsen N. Reliability of Margin Assessment after Surgery for Extremity Soft Tissue Sarcoma: The SSG Experience. Sarcoma. 2012.
23. Wittekind C, Compton CC, Greene FL, Sobin LH. TNM residual tumor classification revisited. Cancer. 2002; 94(9): 2511-6.
24. Kainhofer V, Smolle MA, Szkandera J, Liegl-Atzwanger B, Maurer-Ertl W, Gerger A, et al. The width of resection margins influences local recurrence in soft tissue sarcoma patients. Eur J Surg Oncol. 2016; 42(6): 899-906.
25. Gundle KR, Kafchinski L, Gupta S, Griffin AM, Dickson BC, Chung PW, et al. Analysis of Margin Classification Systems for Assessing the Risk of Local Recurrence After Soft Tissue Sarcoma Resection. J Clin Oncol. 2018; 36(7): 704-9.