CT-guided Interstitial Brachytherapy Followed by External Bean Radiotherapy for a Patient With Relapsed Extremity Soft Tissue Sarcoma

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Case report

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Abstract

Purpose: Locally recurrent extremity soft tissue sarcoma remains a therapeutic challenge; conservative surgery alone results in an inferior local control rate. This study demonstrates a new interstitial (IS) brachytherapy (BT) technique in a patient with recurrent extremity soft tissue sarcoma.

Patients and methods: A 53-year-old man with recurrent left thigh malignant fibrous histiocytoma underwent conservative surgery and adjuvant intensity-modulated radiotherapy (IMRT) after two surgical excisions. A magnetic resonance imaging (MRI) of the lower extremity after the conservative surgery and IMRT revealed a left thigh mass measuring 12 cm × 8 cm × 7 cm. An IS BT with 3 fractions of 8 Gy each and guided with three-dimensional (3D) computed tomography (CT) was administered. For this procedure, IS metal needles were inserted at a depth of 1 cm into the tumor as a preliminary implantation, and their direction and depth were adjusted repeatedly until a satisfactory distribution was achieved through multiple CT scans.

Results: The course of the IS BT procedure was uneventful. No severe bleeding, infection, or other complications were observed. At 3, 12, and 24 months after the IS BT, lower extremity MRI scans showed a left thigh mass measuring 10 cm × 5 cm × 4, 8 cm × 3 cm × 2 cm, and 6 cm × 2 cm × 2 cm, respectively. Minimal fibrosis, local numbness, and edema in the treatment area were noted. The patient had an excellent quality of life.

Conclusion: Favorable oncologic outcomes for locally recurrent extremity soft tissue sarcoma were achieved using 3D CT-guided IS BT. This BT technique may contribute to an excellent local control rate and offer an effective and safe therapeutic option in selected cases.

Introduction

Sarcomas are rare solid tumors of mesenchymal cell origin, each with a different clinical and pathologic characteristics, 80% of which originate from soft tissues including the muscle, nerve, fat, blood vessels, and connective tissues[1]. The most common anatomic sites of soft tissue sarcoma are the extremities, which account for approximately 43% of all the cases.[2] Surgical resection is the standard treatment modality for patients with extremity soft tissue sarcoma. Preoperative radiotherapy is often used for extremity tumors that are close to the neurovascular structures for a complete and effective radical resection[2]. Some other advantages using Preoperative radiotherapy include: low toxicity profile and shorter course. Postoperative radiotherapy is also considered for macroscopically or microscopically positive margins after surgical resection when a re-resection strategy cannot be implemented for critical structure saving and limb-sparing[3–5].

Postoperative radiotherapy mainly includes external beam radiotherapy (EBRT) and brachytherapy (BT). Much more advanced technique, particular in interstitial (IS) BT with inserted catheters into the tumor, was encouraged for better tumor coverage and easier normal tissue sparing. This report describes a new BT technique, three-dimensional (3D) computed tomography (CT)-guided IS BT, for a patient with recurrent extremity sarcoma after conservative surgery and adjuvant intensity-modulated radiotherapy (IMRT). The BT implementation of the cancer treatment of this particular patient mentioned above may be summarized as follows: (1) simulation position: the position with pathological is determined by T2-weighted MRI scan so that predetermined position of needle-insertion can be confirmed before operation; (2) insert needles on the basis of images from the previous step; (3) confirm and adjust the depth and angle of insertion through CT scan once again; (4) delineate target region on images transmitted from the last CT scan after the placement of needles-insertion; (5) IS BT implementation.

Patient And Methods

In October 2016, a 53-year-old man with a one-month history of a progressive left thigh mass underwent a wide local excision. The results of the postoperative pathology revealed a malignant fibrous histiocytoma. Five months later, a second radical resection of the tumor was performed because of a relapsed tumor at the same site, which was confirmed using a postoperative pathology. In September 2017, another relapsed tumor was observed in the original site, and the patient underwent a third surgical resection. However, only partial tumor resection could be performed because severe neuromuscular involvement was observed during the surgery. From October 2017, the patient was treated with IMRT at a total dose of 50 Gy in 25 fractions. Besides, one cycle of concurrent doxorubicin (50 mg/m^2) chemotherapy was given because of the critical consequence that the overall survival (OS) has achieved to 71% when patients treated with chemotherapeutics after operation[6]. The therapeutic evaluation of the EBRT indicated stable disease (SD). Magnetic resonance imaging (MRI) of the lower extremity after EBRT revealed a left thigh mass measuring 12 cm × 8 cm × 7 cm (Figure 1). The timeline of anti-cancer treatments the patient underwent has displayed concretely in table1.

Following the EBRT, IS BT was administered to the patient in the supine position under local anesthesia in the CT simulator room. As a preliminary implantation according to T2-weighted MRI and clinical physical examination results, metal needles (length: 16 cm, diameter: 1.3 mm, Elekta) were inserted perpendicular to the tumor at a depth of approximately 10 mm. Additionally, the usage of metal needles has drawn lots of interests recently, because it has advantages of being reusable, easy to adjust and low cost. Thus, it might have gained widespread acceptance for patients on low incomes. Multiple CT scans were performed at 3-mm slice intervals, and the direction and depth of the metal needles were repeatedly adjusted until a satisfactory distribution was achieved (Figure 2). During the insertion procedure, several critical attentions should be paid to evaluate the exactitude distribution of needles and final dose: (1) accurate needle insertion into the tumor; (2) symmetrical distribution in the tumor at a 1-cm distance; (3) and parallel arrangement of all needles. In addition, images from CT scan provide very clear views on current work in process and consequently make it a perfect visualization for doctors and medical physicist to design an eligible dose-volume histogram of target volume in treatment plan.

The high-risk clinical target volume (HR-CTV) that represented the remaining tumor volume was contoured in the CT image. T2-weighted MRI was also used as a reference for tumor delineation. The needles were reconstructed and registered on the CT images (Oncentra Brachytherapy Treatment

Planning System, Elekta). Thereafter, inverse-planning simulated annealing (IPSA) was performed with an 8 Gy prescription dose for the HR-CTV. The dwell time and the position of the radioactive source were manually adjusted to acquire adequate dose coverage if the initial IPSA did not meet the dose requirement (Figure 3). Naghavi et al.[7]suggest that the constraint dose of BT may limit from 30 Gy to 50 Gy when prior EBRT was treated with conventional fractionation (2 Gy/d) for patients with soft tissue sarcoma. In addition, Petera et al. recommend that it is appropriate to use 45–50 Gy conventional EBRT dose and 8 Gy × 3 fractions for patients undergo a combination of EBRT and BT. Furthermore, the toxicity and adverse reactions of brachytherapy should be taken into account when it comes to affirmation of individualized treatment regimen. Hypofractionated radiotherapy may improve the patient's survival quality and shorten the patient's treated time. Moreover, for radiotherapy, fractionation of the dose delivered to a tumor is able to improve the differential effect of killing tumor cells relative to normal cells, as splitting the dose allows time for normal cells to repair damage between fractions[8]. The total dose of HR-CTV D90 (the minimum dose delivered to 90% of the target volume) which combined the previous EBRT and the present BT was converted to an equivalent dose of 2 Gy (EQD2) by applying the linear-quadratic model (α/β = 10). It's worth noting that minimizing radiation dose to organs at risks (OARS) is vital and necessary, and the dose constraints are displayed in table 2[7]. In this sense, the patient was administered a total of 24 Gy of IS BT with 8 Gy each on days 1, 4, and 8, which means three separate insertion have been implemented.

Results

A total of 180 metal needles (60 for each insertion) were used for the three fractions of IS BT and the magnitude of dose equivalent of exposure dose is 90.7 Gy EQD2 during the period of prior EBRT and IS BT. The number of CT scans was 4, 4, and 3 for the first, second, and third IS implantations, respectively. The HR-CTV D90 for the target volume combining the previous EBRT and the present IS BT was 90.7 Gy EQD2. The radiation dose to OARS were controlled within the constrains as mentioned in table 2. The patient had an uneventful course during the CT-guided interstitial needle implantation. No infection or other complications occurred during this procedure. Further, severe bleeding was not observed when removing the needles, and gauge padding was sufficient for hemostasis. The patient was discharged on day 9. Three months after the IS BT, a repeat lower extremity MRI scan showed a left thigh mass measuring 10 cm × 5 cm × 4 cm with a 70% reduction in the tumor volume. A Positron Emission Tomography-Computed Tomography (PET-CT) image revealed a left thigh low-density mass (8 cm × 4 cm × 3 cm) with increased glycometabolism, which was considered to be the remaining tumor. The high glycometabolism in the muscle and subcutaneous tissue edema surrounding the tumor was considered as inflammatory or physiological uptake (Figure 4). No metastatic diseases were observed. At 12 and 24 months after the IS BT, lower extremity MRI scans revealed a left thigh mass measuring 8 cm × 3 cm × 2 cm and 6 cm × 2 cm × 2 cm, respectively. Minimal fibrosis, local numbness, and edema in the treatment area were observed, and no tumor relapse or any other serious complications were noted (Figure 5).

Discussion

Historically, amputation, which is associated with a severely impaired quality of life, was the main treatment option for limb soft tissue sarcoma. However, amputation does not seem to contribute to survival benefits, and limb-sparing surgery with adjuvant RT may offer comparable local control rates and disease-specific survival as amputation [5, 9, 10]. At present, limb-sparing surgery is a standard treatment option. Adjuvant RT can be divided into three types: EBRT alone, BT alone, or a combination of EBRT and BT.

In this study, we presented the case of a 53-year-old man with relapsed extremity soft tissue sarcoma in which a third-time conservative surgery was performed after two radical resections for structural and functional reservation. Further treatments were required for this case since R2 surgical resection (visible positive margins) and common therapeutic options, such as chemotherapy and EBRT, were limited. Consequently, the patient received adjuvant EBRT and concurrent chemotherapy and refused adjuvant chemotherapy because of severe side effects.

After the EBRT with a total dose of 50 Gy in 25 fractions and one cycle of concurrent chemotherapy, an MRI scan revealed an SD with a 12 cm × 8 cm × 7 cm sized-mass. An EBRT boost with a reduced irradiation field did not seem eligible for a large tumor because of severe complications to the surrounding normal tissue. However, because a BT boost assures a relatively higher dose to the tumor with a rapid dose drop in the surrounding normal tissue than an EBRT boost, it seemed to be reasonable for the present case. Therefore, we chose a novel IS BT technique, namely 3D CT-guided IS BT. During the preliminary implantation, the metal needles were inserted at a depth of 1 cm into the tumor. Thereafter, the direction and depth of the metal needles were repeatedly adjusted using multiple CT scans to assure a satisfactory needle distribution for better dose coverage of the tumor during the treatment.

A combination of EBRT and BT is recommended for relapsed sarcoma or tumor resection with positive surgical margins[11]. Previous studies have demonstrated an improved local control rate with this combination mode[12, 13]. EBRT can deliver a homogeneous dose to a large volume at risk as well as the surrounding normal tissue, while BT allows a high radiation dose to the tumor bed but spares the surrounding normal tissue to avoid severe side effects. Thus, the combination mode has the advantage of providing a sufficient dose to a microscopic disease with EBRT as well as boosting the dose to a macroscopic bulk with BT. For a combination of EBRT and BT, a 45–50 Gy conventional EBRT dose and 8 Gy × 3 fractions[12] or 4–6 Gy × 4 fractions[14] are acceptable. We chose an EBRT with 50 Gy in 25 fractions followed by 8 Gy in 3 fractions of IS BT.

Traditionally, IS BT catheters have been implanted during surgery, and IS BT doses have been delivered intraoperatively or postoperatively. However, both these treatment methods need to be performed in a well-experienced cancer center. In particular, intraoperative facilities, which are usually absent from departments with limited resources, are necessary for intraoperative BT. Further, when performing postoperative IS BT, some issues, including catheter entry point (at least 1 cm away from wound incision), catheter stabilization, and catheter displacement due to seroma, should be carefully considered[7]. It is difficult to handle these issues at less experienced cancer centers. In our hospital, the traditional postoperative IS BT with catheter implantation at the time of surgery, could not be performed because of limited medical resources and absent experience. Therefore, we performed a new 3D CT-guided IS BT technique. To our knowledge, this is the first report of the use of an IS BT with multiple CT scans to guide the implantation needles for macroscopic limb soft tissue sarcoma. Our IS BT technique achieved an excellent therapeutic outcome with no obvious side effects for two years. Further, the long-term clinical results should be observed in future follow-ups.

Conclusion

In this case, an effective attempt has been implemented and the significant favorable prognostic of the patient with soft tissue sarcoma also impressed us. Thus, we may suggest that the 3D CT-guided IS BT technique used in macroscopic limb soft tissue sarcoma treatment has its unique priority over other type of BT owing to its maneuverable, accurate, economical and effective characteristics. These features and advantages indicate fully the important place and role of such technique in the similar situation and may offer an alternative treatment option for selected cases, both in departments with limited resources and high volume centers.

Abbreviations

Interstitial: IS

Brachytherapy: BT

Intensity-modulated radiotherapy: IMRT

Magnetic resonance imaging: MRI

Computed tomography: CT

External beam radiotherapy: EBRT

Overall survival: OS

Stable disease: SD

High-risk clinical target volume: HR-CTV

Inverse-planning simulated annealing: IPSA

Organs at risks: OARS

Positron Emission Tomography-Computed Tomography: PET-CT

Declarations

Ethical Approval and Consent to participate

This study was approved by the ethics committee of our institution, and this patient signed informed consents.

Consent for publication

All authors of this study have read and approved this manuscript for publication

Availability of supporting data

All the data involved this study were included in patient and methods, and results.

Competing interests

The author reports no conflicts of interest in this work.

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Authors' contributions

Zhongshan Liu: Patient treating and paper writing.

Yangzhi Zhao: Literature searching, and grammar review.

Yunfeng Li: Patient treating.

Xia Lin: Patient treating.

Dongzhou Wang: Case following up.

Tian Tian: Tables making.

Tiejun Wang: Idea presenting.

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and outcome among adult patients with soft tissue sarcomas of the extremity and superficial trunk treated with greater than conventional doses of perioperative high-dose-rate brachytherapy and external beam radiotherapy. Int J Radiat Oncol Biol Phys 2011; 81: e529-539.

Tables

Table 1.

treatment experience of the patient

time	stage	pretherapy MRI(length of tumor)	Antineoplastic Protocols	posttherapy inspection
10/2016	1st surgery	5cm	wide local excision: tumor and surrounding areas of normal tissue	postoperative pathology: malignant fibrous histiocytoma, clear margin
03/2017	2nd surgery	4cm	radical compartmental resection: integrated muscle involved in pathological tissue	postoperative pathology: malignant fibrous histiocytoma, clear margin
09/2017	3rd surgery	14cm	partial tumor resection	postoperative pathology: malignant fibrous histiocytoma
10/2017	EBRT & chemotherapy	12cm	EBRT: 50Gy/25f chemotherapy: one cycle of doxorubicin (50 mg/m2)	12cm(length of tumor checked by MRI right after therapy)
11/2017	3D CT-guided IS BT	12cm(length of tumor checked by MRI right after EBRT)	3D CT-guided IS BT: 24Gy/3f	10cm(length of tumor checked by MRI 3 months later) or 8cm (length of tumor checked by PET-CT at the same time)
				8cm(length of tumor checked by MRI 12 months later)
				6cm(length of tumor checked by MRI 24 months later)

* **EBRT**: external beam radiotherapy; **MRI**: magnetic resonance imaging; **IS BT**: interstitial brachytherapy; **PET-CT**: Positron Emission Tomography-Computed Tomography

Table 2.

Recommended dose constrains of OARS

OAR	Constraints	Postoperative BT (Gy)	Comments
Skin	$D_{0.1cc}$	40	≤2/3 the prescribed dose
	D_{2cc}	37	
Nerve	$D_{0.1cc}$	32	Full dose if involved
	D_{2cc}	30	(30 ~50 Gy)
Vascular	$D_{0.1cc}$	53	Full dose if involved
	D_{2cc}	47	
Bone	$D_{0.1cc}$	43	avoiding periosteal stripping,
	D_{1cc}	35	avoid limb bone BT
* BT brachytherapy; OAR organ at risk			

Figures

Figure 1

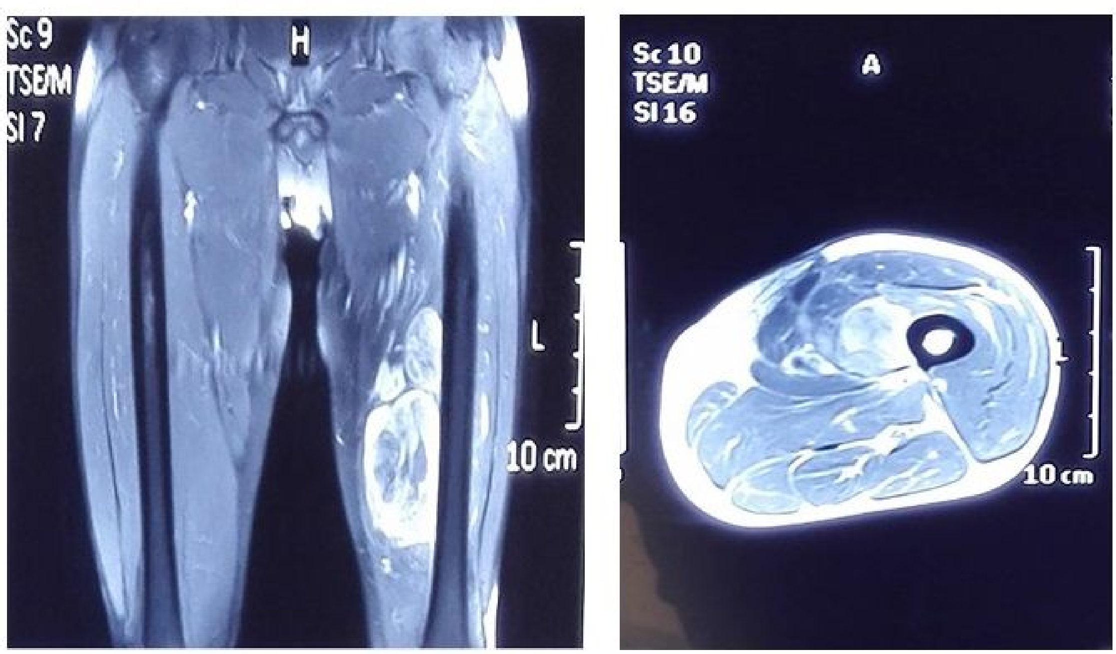

Figure 1

Magnetic resonance image (MRI) scan of the lower extremity after conservative surgery and external beam radiotherapy (EBRT).

Figure 2

Figure 2

Process of three-dimensional (3D) computed tomography (CT) guided metal needles implantation.

Figure 3

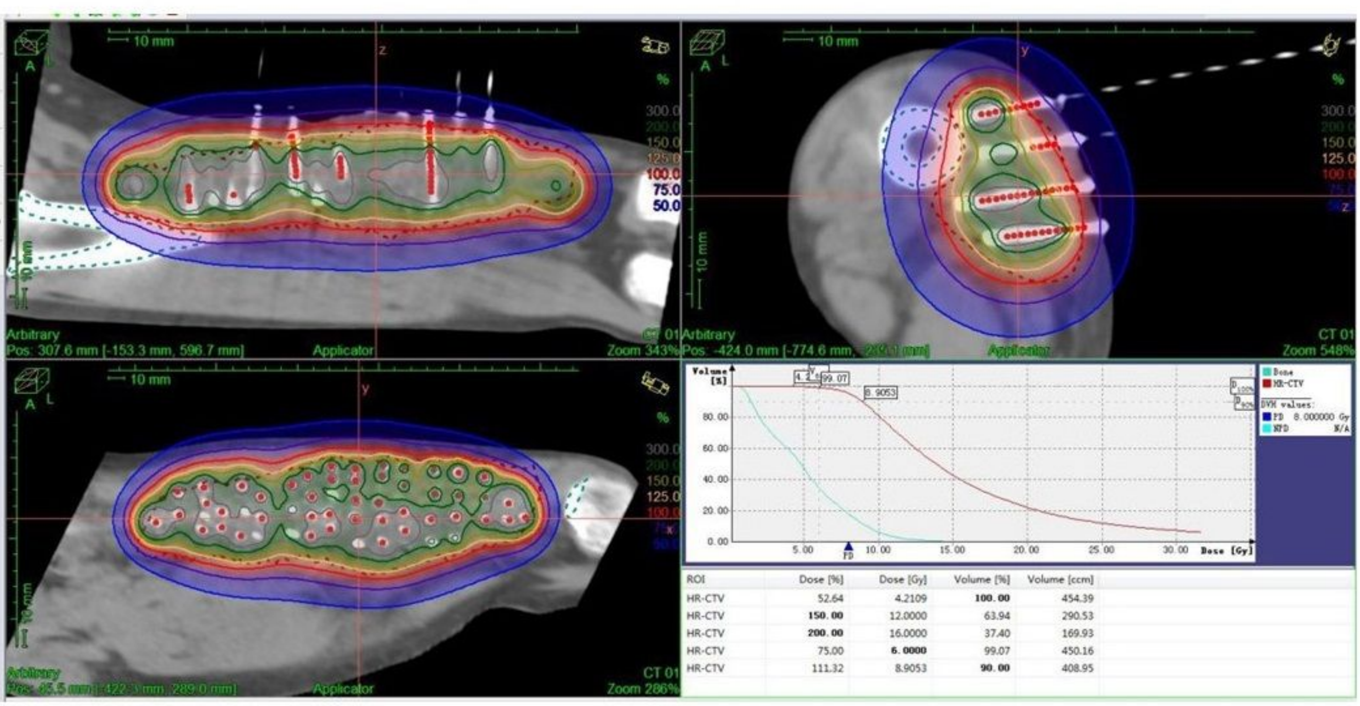

Figure 3

Representative treatment plan of three-dimensional (3D) computed tomography (CT) guided interstitial (IS) brachytherapy (BT).

Figure 4

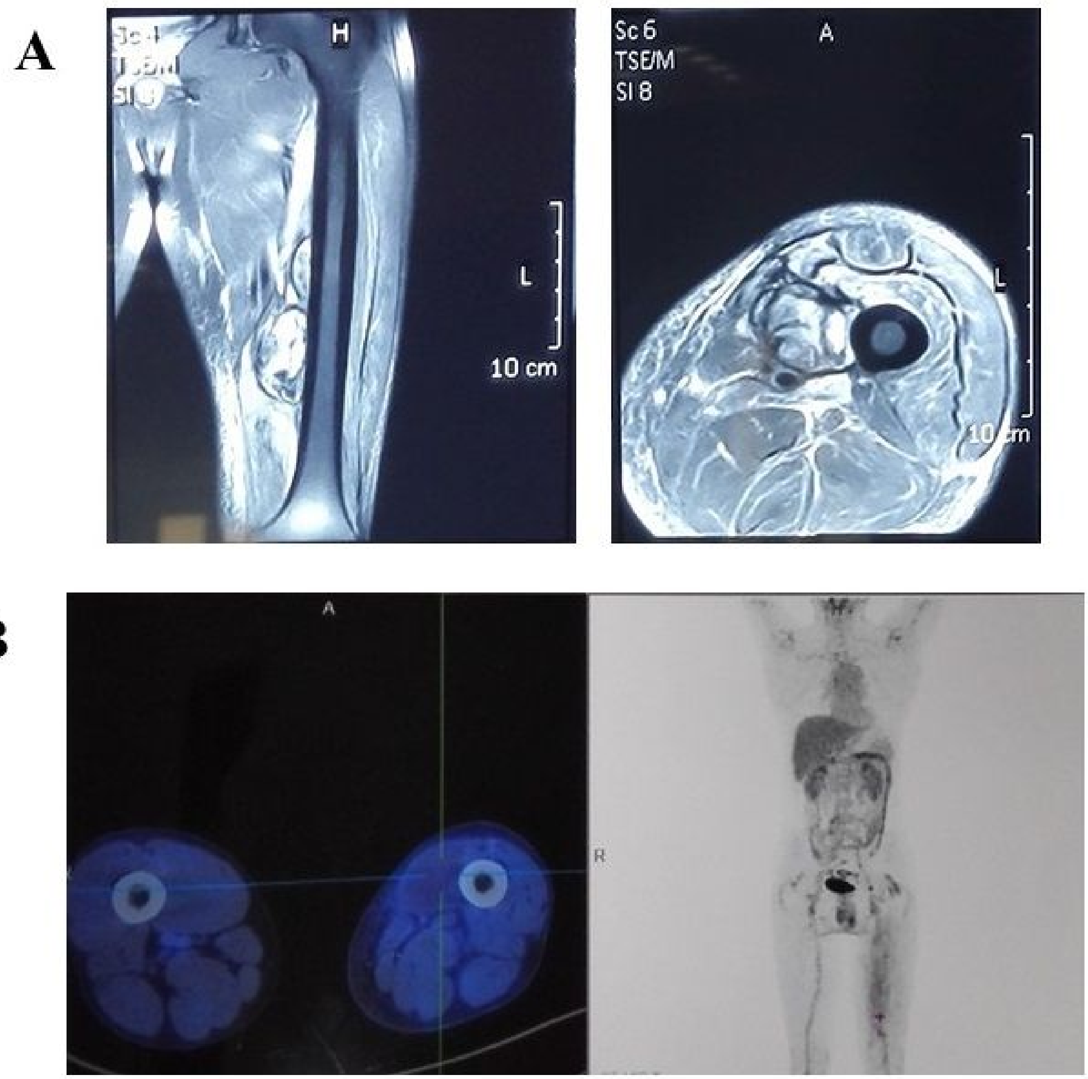

Figure 4

Lower extremity magnetic resonance image (MRI) scan (A) and Positron Emission Tomography-Computed Tomography (PET-CT) image (B) three months later after interstitial (IS) brachytherapy (BT).

Figure 5

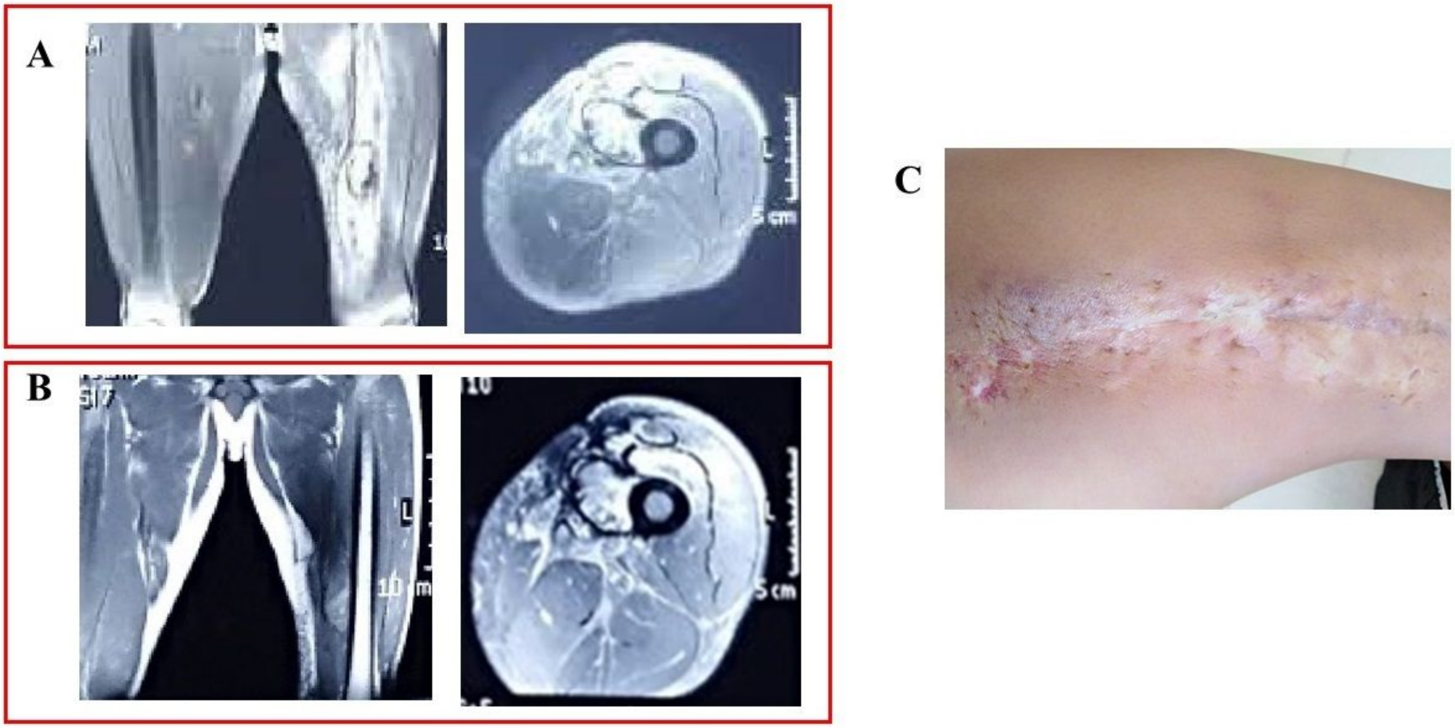

Figure 5

Lower extremity magnetic resonance image (MRI) scan 12 months (A) and 24 months (B) after interstitial (IS) brachytherapy (BT). The patient experienced minimal fibrosis, local numbness, and edema in treatment area (C).