Skeletal Radiology (2023) 52:1747–1754
https://doi.org/10.1007/s00256-023-04338-z

SCIENTIFIC ARTICLE

Radiation osteitis: incidence and clinical impact in the setting of radiation treatment for soft tissue sarcoma

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Received: 24 February 2023 / Revised: 1 April 2023 / Accepted: 2 April 2023 / Published online: 13 April 2023

Abstract

Objective Radiotherapy is an important component of soft tissue sarcoma management. Radiation osteitis is a common radiographic finding identified in the setting of radiotherapy on magnetic resonance imaging (MRI). This study aims to identify the incidence of radiation osteitis in patients who received radiotherapy for soft tissue sarcoma and if a further workup, including a biopsy, was performed for concerning MRI findings.

Materials and Methods Medical records of patients with soft tissue sarcoma who received radiotherapy from 2008 to 2020 were retrospectively reviewed. Patients with at least one MRI of the sarcoma site following radiotherapy and information regarding radiotherapy treatments were included. MRIs of these patients were reviewed for the presence of radiation osteitis by two musculoskeletal radiologists. The clinical course of these patients including biopsy for concerning MRI findings, local recurrence, and metastasis was recorded.

Results Thirty soft tissue sarcoma patients who received radiation for soft tissue sarcoma were included. Radiation osteitis was present in 18 patients. The time to osteitis present on MRI following radiotherapy completion was a median of 4.5 months. Biopsy for concerning MRI findings was performed in eight patients, five for local recurrence, and three for regional osseous metastasis. Three patients had confirmed osseous metastases.

Conclusion Although radiation osteitis is often a benign imaging finding, it can be difficult to discern these lesions from potentially malignant sites of disease. We recommend multidisciplinary management of soft tissue sarcoma at sarcoma centers to appropriately identify benign from malignant lesions and decide the necessity of a biopsy.

Keywords Soft tissue sarcoma · Radiation osteitis · Biopsy

Introduction

Soft tissue sarcomas (STS) encompass a rare and heterogeneous group of malignant tumors that account for roughly 1% of all adult malignancies [1, 2]. In 2019, an estimated 12,750 patients were diagnosed with STS in the USA [3]. STS can involve the head and neck, trunk, and retroperitoneum, but the majority of cases arise in the extremities [2, 4, 5]. Multidisciplinary management of STS is crucial given the rarity and complexity of the disease, and primary treatment modalities include surgery, radiation, and at times, chemotherapy [1, 2]. Radiotherapy is often used in addition to surgical management to prevent local recurrence and is well established in STS care [2, 6].

Although radiotherapy is commonly utilized in STS treatment, it is not without complications. Common adverse outcomes following radiotherapy include delayed wound healing, fibrosis, edema, nerve damage, and bony changes [6–9]. These bony changes include radiation osteitis (RO), which is the result of the damage to osteoblasts and vascular insult from radiotherapy and is often identified by magnetic resonance imaging (MRI) [7, 10–12]. On MRI, RO is typically described as areas of variable signal intensity on T1-weighted imaging and hyperintensity on T2 [13, 14]. The incidence of RO following radiotherapy for STS is highly

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variable with previous studies reporting cases ranging from 5 to 40% at different intervals following radiotherapy [11, 15, 16]. Although RO is a benign imaging finding, it can be concerning for tumor recurrence, metastasis of the primary tumor to the bone, or radiation-induced sarcoma [7, 9, 15].

For the oncology team, RO on surveillance imaging can be a clinically complex scenario. As RO includes a broad spectrum of imaging findings on MRI, it can be difficult to discern which lesions are truly benign and which may have malignant potential. A biopsy is required to determine if the lesion is malignant; however, biopsies are invasive and predispose patients to infection or damage to vasculature. Furthermore, each sarcoma center may have different thresholds for biopsy based on imaging findings. One study reported on 12 patients who received pelvic radiotherapy, and five of these patients received biopsies for radiation-induced changes; however, all biopsies were negative for metastasis [17].

The purpose of this study is to identify the incidence of RO in patients who received radiotherapy for STS and if further management including a biopsy was performed concerning MRI findings at our institution. The study also aims to document the clinical course of these patients including local recurrence and metastasis.

Materials and methods

Patient cohort

Following Institutional Review Board approval, our institutional sarcoma database was retrospectively reviewed to identify all patients with biopsy-proven, soft tissue sarcoma from 2008 to 2020. As this was a retrospective review, informed consent was not required. Our initial search included 100 patients; however, due to a number of these patients receiving imaging at outside centers, we were unable to review MRIs for 70 patients. Inclusion criteria were those who received radiotherapy for soft tissue sarcoma and had at least one MRI examination of the sarcoma site following radiotherapy. Patients with no accessible MRI examination of the sarcoma site following radiotherapy and no information regarding radiotherapy treatments were excluded. The records of 30 patients were then reviewed retrospectively.

Basic patient, tumor, and treatment variables were collected, including age, sex, primary tumor location, tumor type, tumor grade, chemotherapy, and radiotherapy treatment. For tumor grade, intermediate- and high-grade tumors were grouped together as high-grade, while low-grade tumors remained in a low-grade group. Information regarding radiotherapy including completion date of radiotherapy to primary tumor location, modality of radiotherapy, and amount of radiotherapy in gray (Gy) to sarcoma site were recorded. The patient's clinical course including biopsy for concerning findings present on surveillance imaging and date of local recurrence were recorded.

Imaging

Every T1, T2-FS, or STIR sequence in all available imaging planes was analyzed for each MR in the cohort. The bone marrow was evaluated utilizing T1 non-fat saturated sequences and T2-fat saturated sequences. Short tau inversion recovery (STIR) sequences were used as a substitute for T2-FS given its significant overlap with T2-FS signal characteristics. A total of 158 MRI examinations were reviewed by our senior authors, who specialize in musculoskeletal tumor imaging. J.M. is a fellowship-trained musculoskeletal radiologist who has been in practice for over 15 years, and S.S is a current musculoskeletal radiology fellow. A median of 5 MRIs (IQR 2–8) were reviewed in this study per patient. The median interval from completion of radiotherapy to the first follow-up MRI reviewed was 1 month (IQR 0.89–4.5 months). The median interval from completion of radiotherapy to the last follow-up MRI reviewed was 22.5 months (IQR 14–44 months).

Image analysis

RO was defined on MRI as focal or diffuse hyperintense T2-FS/STIR bone marrow signal alteration within the radiation field (Fig. 1). The signal alteration could be normal or hypointense on T1-weighted sequences (Fig. 2). Post contrast bone marrow appearance was not considered, as some MRIs were performed without contrast. Osteitis present on imaging was confirmed by our senior authors, and the date of initial osteitis present on imaging was recorded. Time to osteitis present on MRI was reported as months and calculated as the difference between the date of osteitis present on MRI and the date of radiotherapy completion.

Statistical analysis

Categorical variables were described using frequencies and percentages and compared using the χ^2 test. Continuous data were reported as median with interquartile range (IQR) and compared using the Mann-Whitney U test. All statistical analysis was performed using SPSS statistical software (version 26.0 IBM, Armonk, NY, USA). A p value < 0.05 was considered significant.

Results

Demographics and clinical characteristics of this population are illustrated in Table 1. This cohort consisted of fifteen (50%) males and fifteen females with a median age

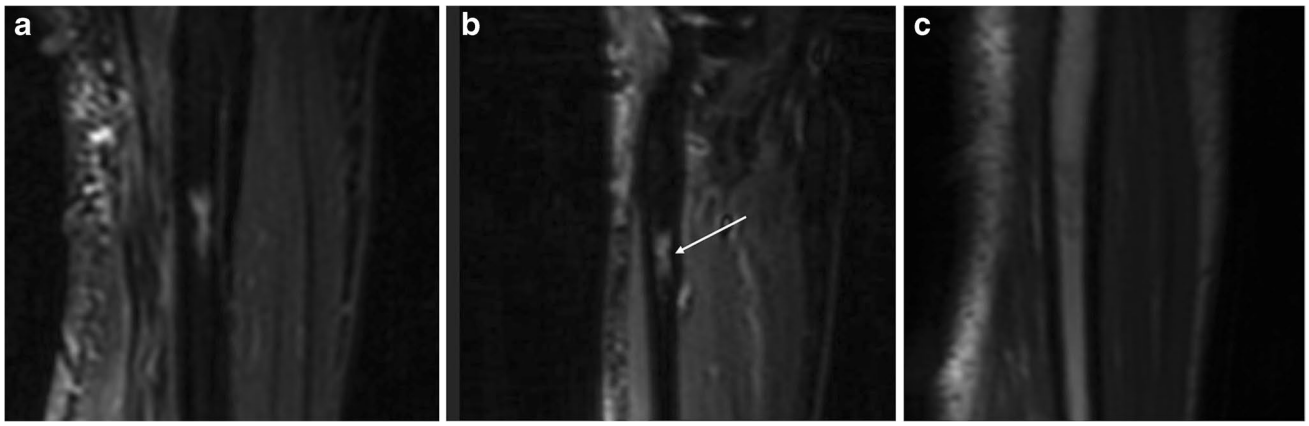

Fig. 1 **a** Coronal STIR image of the proximal ulna. There is a new, focal T2 hyperintense bone marrow signal alteration with ill-defined edges compared to pre-treatment marrow. **b** Sagittal STIR image of the proximal ulna further demonstrates the focal hyperintense bone marrow signal alteration with ill-defined and convex edges. **c** Coronal T1 image of the proximal ulna demonstrates a corresponding focal marrow signal alteration which is slightly less intense compared to the background marrow but remains brighter than the adjacent skeletal muscle

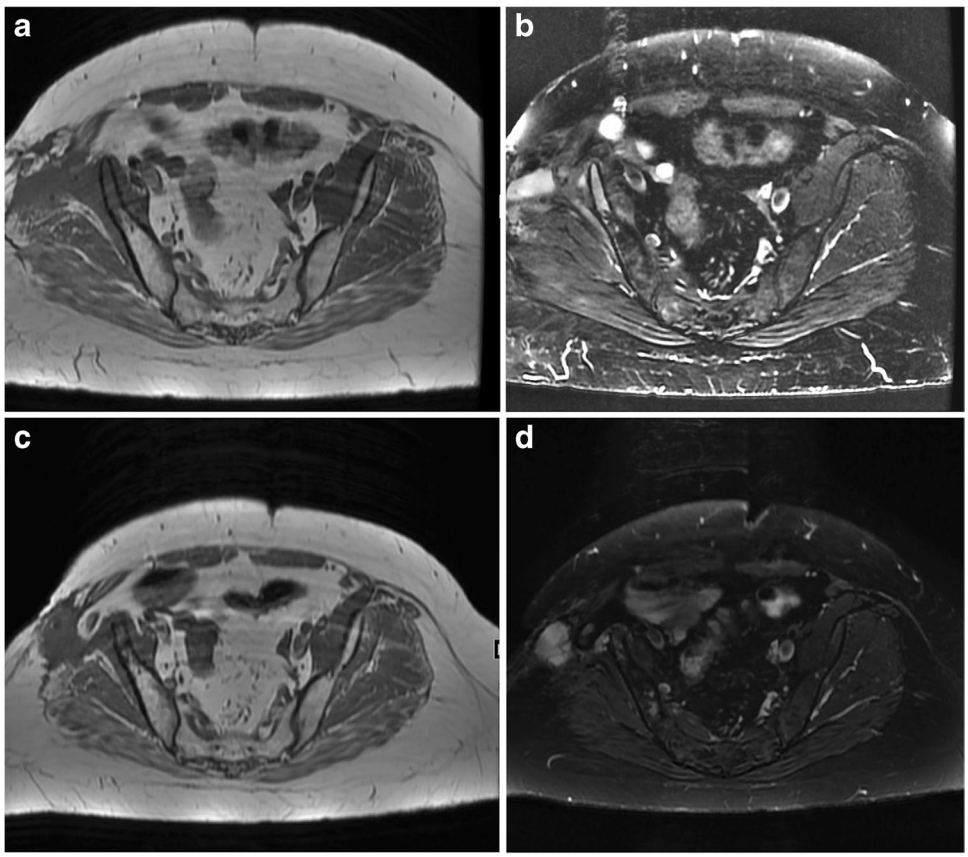

Fig. 2 **a** Axial T1 MRI image of the pelvis. There is a new, focal T1 hypointense signal abnormality in the right iliac bone compared to pre-treatment marrow. **b** Axial T2 fat suppressed MRI image of the pelvis. Corresponding T2 hyperintense bone marrow signal in the anterior right iliac bone. This lesion was indeterminate for osseous metastasis versus radiation osteitis by imaging. **c** Axial T1 and **d** axial T2 images of the pelvis 18 months later demonstrating a persistent, but improved signal abnormality on both T2- and T1-weighted sequences in the right iliac bone. Although this lesion was not biopsied, metastasis is extremely unlikely given the improvement in the signal alteration

of 66.5. The most frequent subtype of STS in this cohort was undifferentiated pleomorphic sarcoma (UPS) (86.6%). Seventeen (56.7%) patients received chemotherapy during their sarcoma management. The modality of radiotherapy is also recorded in Table 1. The most common radiotherapy modality in this cohort was intensity-modulated radiation therapy (IMRT) followed by volumetric modulated arc therapy (VMAT) (13.3%) and three-dimensional conformal radiotherapy (3DCRT) (13.3%). Patients received a median of 50 Gy (range 44 Gy to 66 Gy) at their sarcoma site. Median Gy was 50 Gy in RO patients and 50 Gy in patients without MRI evidence of RO (Table 2).

Table 1 Demographics

Age median (range)	66.5 (16–77)
Sex	
Male	15 (50%)
Female	15 (50%)
Primary tumor type	
Undifferentiated pleomorphic sarcoma	26 (86.6%)
Myxofibrosarcoma	2 (6.7%)
Ewing's like sarcoma	2 (6.7%)
Tumor Grade	
Low grade	1 (3.3%)
High grade	29 (96.7%)
Tumor location	
Proximal lower extremity	11 (36.7%)
Distal lower extremity	8 (26.7%)
Proximal upper extremity	3 (10%)
Distal upper extremity	2 (6.7%)
Pelvis/gluteus	3 (10%)
Head and neck	2 (6.7%)
Flank	1 (3.3%)
Modality of radiotherapy	
Intensity-modulated radiation therapy (IMRT)	9 (30%)
Volumetric modulated arc therapy (VMAT)	4 (13.3%)
Three-dimensional conformal radiotherapy (3DCRT)	4 (13.3%)
External beam radiation therapy (EBRT)	3 (10%)
Proton	1 (3.4%)
Unknown	9 (30%)
Total Gy to sarcoma site (median, IQR)	50 Gy (50–60 Gy)
Chemotherapy for sarcoma	17 (56.7%)
Local recurrence	6 (20%)
Metastatic disease	14 (46.7%)

IQR, interquartile range; *Gy*, gray

We found no significant difference between radiotherapy modalities between patients with RO compared to those without RO ($p = 0.537$) (Table 2).

Radiation osteitis was present on MRIs for 18 (60%) patients (Figs. 3 and 4). The time to RO present on MRI was 4.5 months (IQR 1.50–11.60 months). Of these 18 patients, three (16.7%) had a biopsy for potential osseous malignancy. An additional five had soft tissue biopsies to rule out soft tissue recurrence (Table 2 and Table 3). Although four of the 18 patients with osteitis present on imaging following radiotherapy had MRI findings concerning osseous metastasis, only three patients received biopsies of these lesions. One of those biopsies was for a patient who was diagnosed with UPS of the gluteal/iliac crest, received 50 Gy through VMAT radiotherapy, and developed MRI findings concerning RO on MRI 4 months following radiotherapy completion. Three months later, the patient developed T2 hyperintense lesions in the right femoral neck which were biopsied and returned as negative for potential osseous metastasis. Another patient was diagnosed with UPS of the left thigh, received 50 Gy through IMRT, and developed MRI findings concerning RO in the left femur, 7 months later. Nine months after initial osteitis on MRI, a T2 bright signal in the mid diaphysis of the left medial femur and a T2 hyperintense T1 hypointense lesion in the left intertrochanteric proximal femur presented on MRI (Fig. 5). Both lesions were biopsied, and only the diaphyseal lesion was positive for metastatic sarcoma. The third patient was diagnosed with Ewing's like sarcoma of the right sacrum, received 55.8 Gy through proton radiotherapy, and developed MRI findings concerning RO on MRI, 31 months later. Four months after initial osteitis on MRI, the patient developed a T2 hyperintense T1 hypointense lesion in the right ilium confirmed as a metastatic lesion on positron emission tomography-computed tomography scan (PET-CT), but unfortunately, the

Table 2 Comparison of patients with and without radiation osteitis present on MRI

	Radiation osteitis present on MRI	No radiation osteitis on MRI	
Total	18	12	
Tumor type	16 UPS 1 myxofibrosarcoma 1 Ewing's like sarcoma	10 UPS 1 myxofibrosarcoma 1 Ewing's like sarcoma	$p = 0.685$
Chemotherapy received	10	7	$p = 0.880$
Radiotherapy modality	7 IMRT 3 3DCRT 2 VMAT 1 EBRT 1 proton therapy 4 unknown	2 IMRT 1 3DCRT 2 VMAT 2 EBRT 5 unknown	$p = 0.537$
Total Gy received	50 Gy (IQR 47–58.7)	50 Gy (IQR 50–63)	$p = 0.231$

MRI, magnetic resonance imaging; *IQR*, interquartile range; *UPS*, undifferentiated pleomorphic sarcoma; *IMRT*, intensity-modulated radiation therapy; *3DCRT*, three-dimensional conformal radiotherapy; *VMAT*, volumetric modulated arc therapy; *EBRT*, external beam radiation therapy; *Gy*, gray

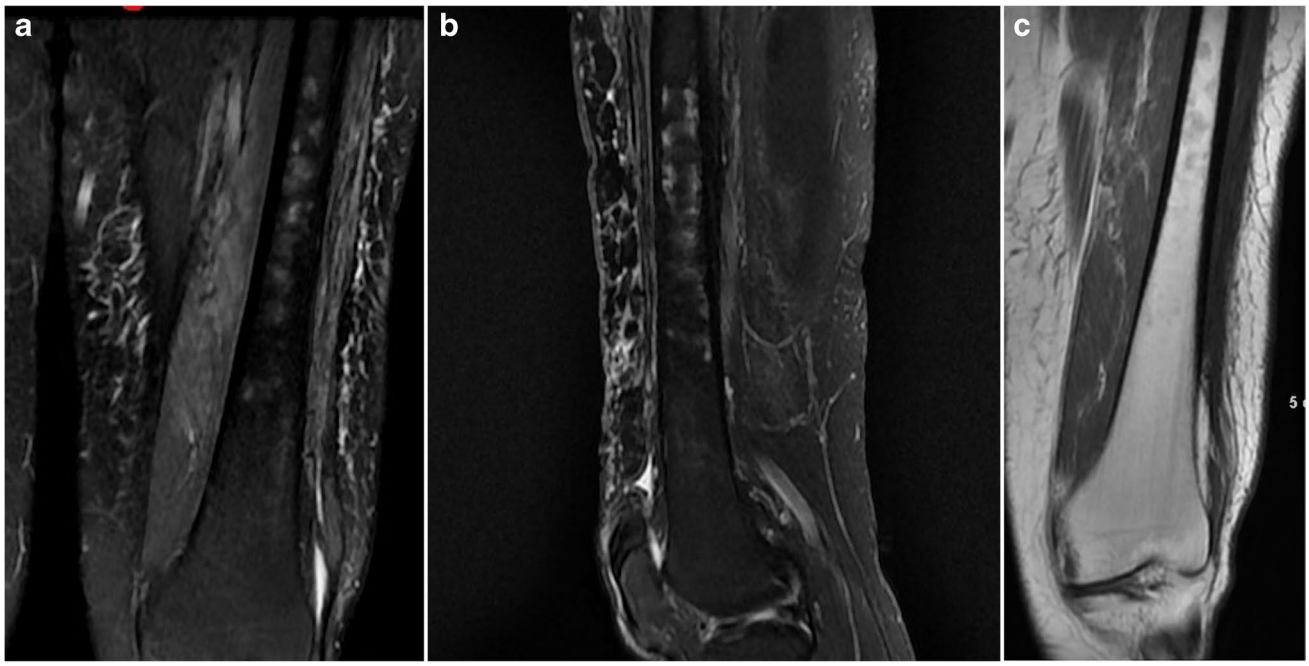

Fig. 3 **a** Coronal STIR image of the left femur following radiation to the left thigh. Patchy non-focal hyperintense bone marrow signal alteration in the mid to distal diaphysis with ill-defined borders most suggestive of radiation osteitis. **b** Sagittal STIR image of the left femur following radiation to the left thigh which further demonstrates the lack of focality to the bone marrow signal alteration and is new compared to pre-treatment marrow. **c** Coronal T1 image of the distal femur in the same patient demonstrates a corresponding signal alteration that is lower than the background marrow signal, but still brighter than the adjacent skeletal muscle

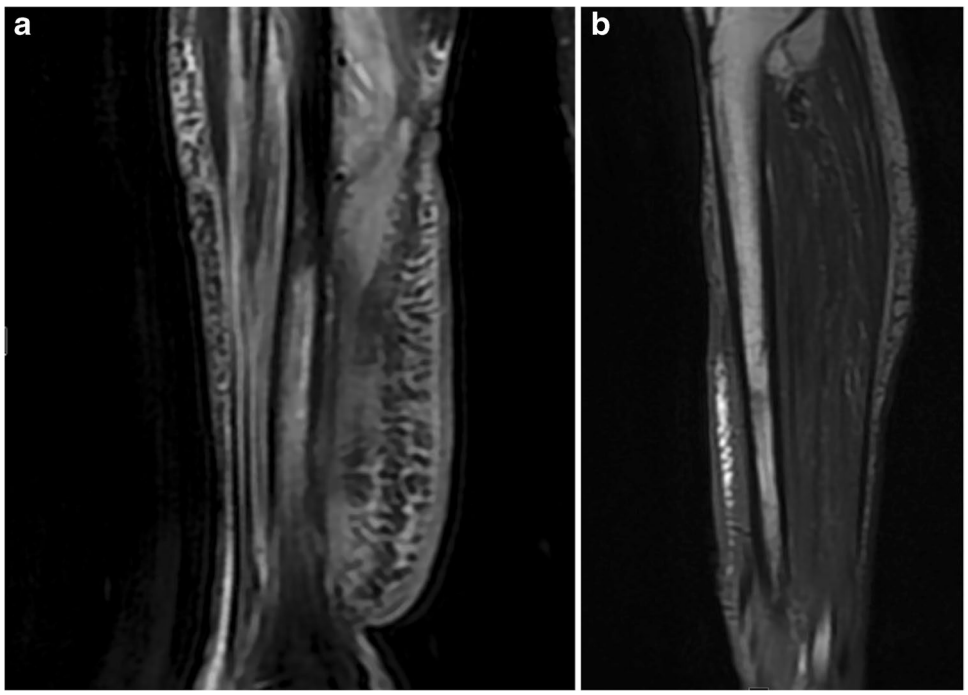

Fig. 4 **a** Sagittal STIR image of the left tibial diaphysis. Diffuse hyperintense bone marrow signal alteration in the distal tibial diaphysis is most compatible with radiation osteitis and is new compared to pre-treatment marrow. Additional diffuse hyperintense STIR signal is seen in the leg musculature also compatible with post treatment changes. **b** Sagittal T1 image demonstrates diffuse patchy signal alteration. The signal intensity is normal or lower than the background marrow, but still brighter than the adjacent skeletal muscle. Overall, the signal characteristics are more suggestive of RO

patient shortly expired after the discovery of this lesion. The fourth patient was diagnosed with UPS of the right thigh, received 50 Gy through IMRT, and developed MRI findings concerning RO within 1 month of radiotherapy completion. Four months later, the patient developed a lesion in the proximal left femur and left iliac bone. The left iliac bone

Table 3 Osteitis present on MRI and biopsy for MRI findings

Osteitis present on MRI	18
Time to osteitis	4.5 months (IQR 1.50–11.60 months)
Biopsy performed based on MRI findings	
Potential soft tissue recurrence	5
Potential osseous metastases	3

IQR, interquartile range

was biopsied and was negative for metastatic disease. The proximal left femur lesion was not biopsied per the patient's request; however, metastatic disease was confirmed on PET-CT in the left femur and distant osseous metastases including the left humerus, sternum, right scapula, and vertebral lesions. Unfortunately, the patient shortly expired after the discovery of these lesions.

In our cohort, six patients (20%) experienced a local recurrence of their STS, and fourteen patients (46.7%) developed metastatic disease. Five patients who experienced a local recurrence of their STS received biopsies for MRI findings concerning sarcoma recurrence. All five patients incidentally also had RO present on MRI. Two patients had distal lower extremity UPS that both locally recurred at 10 months following radiotherapy, while the other three patients had proximal lower extremity UPS that locally recurred at 13, 16, and 47 months. The sixth patient experienced a pathologic fracture 27 months following their surgical resection for UPS in their proximal lower extremity which was diagnosed at the time as recurrence. Excluding the patients with osseous metastases, eleven other patients developed metastatic disease. The other patient in our cohort with Ewing's like sarcoma of the proximal upper extremity had metastatic disease to their lung at initial presentation. Nine other patients with UPS developed metastatic disease to the lung while one patient with UPS developed metastatic disease to adjacent lymph nodes.

Discussion

Soft tissue sarcomas (STS) are rare, malignant tumors that encompass several histologic subtypes and account for 1% of adult malignancies [1, 2]. Treatment of these tumors includes a multidisciplinary approach involving radiation therapy which is utilized to prevent local recurrence [2, 6]. Although radiation therapy is instrumental in STS management, potential complications from radiation include impaired wound healing, fibrosis, nerve damage, and skeletal changes such as RO [6–9]. RO is often an incidental imaging finding; however, certain characteristics of RO on imaging can overlap with findings of osseous metastasis or radiation-induced sarcoma creating a diagnostic dilemma. In our cohort, the signal characteristics on MRI were not a reliable predictor of osseous metastasis vs RO. RO and osseous metastases both demonstrated hyperintense signals on T2 or STIR-weighted sequences. The T1-weighted signal intensity was variable for RO in our cohort. Some patients with RO demonstrated iso to hyperintense T1 bone marrow signal, while others demonstrated a hypointense T1 signal. For example, one patient's imaging demonstrated a low signal on T1 in the iliac bone. This lesion remained stable over subsequent MRIs and demonstrated signal improvement making metastasis extremely unlikely. In contrast, another patient had a biopsy-proven osseous metastasis in

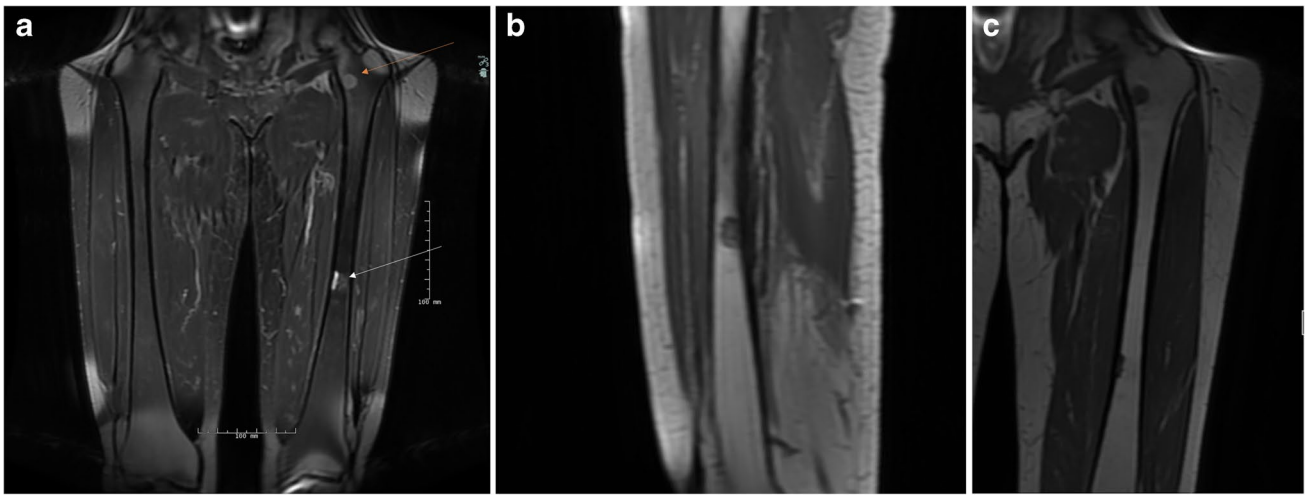

Fig. 5 **a** Coronal T2 fat-suppressed MRI demonstrating metastatic sarcoma in mid diaphysis (white arrow) and proximal femur (orange arrow). **b** Sagittal T1 MRI demonstrating ovoid hypointense lesion within the mid femoral diaphysis. **c** Coronal T1 MRI demonstrating ovoid focal T1 hypointense lesion in the intertrochanteric region of the proximal femur

the femoral diaphysis which also showed a low T1 signal. Although biopsies can readily distinguish RO from malignancy, biopsies are invasive and may predispose the patient to other complications. In this study, we sought to evaluate the incidence of RO following radiotherapy for STS, and the additional workup osteitis may present to the sarcoma management team.

Microscopic changes to the bone have been documented at doses as low as 3 Gy with increasing cellular damage at 12 Gy [18]. Damage to osteoblasts and the bone remodeling system creates the characteristic appearance of RO on imaging: mottled areas of bone with osteopenia and focal areas of increased bone density [7, 9]. The extent of structural and cellular damage is dependent upon radiotherapy-related factors including the modality, total dose, duration, and fractionation [9]. The true incidence of radiation osteitis has been quite variable in the literature [10, 11, 13, 14, 16, 19]. Ugurluer et al. [13] reported a 4.1% incidence of radiation osteitis in 122 gynecological, colorectal, and bladder cancer patients receiving 45 to 60 Gy through EBRT. Meixel et al. [10] reported an 83.3% incidence of radiation osteitis in 410 gynecological and anal cancer patients receiving a median of 45 Gy through IMRT or 3DCRT. In patients with STS, Hwang et al. [11] reported MRI signal changes in the bone marrow of 87% of patients who received radiotherapy and chemotherapy compared to 45% of patients who only received radiotherapy. All patients in this cohort received external beam radiation therapy (EBRT) with a mean dose of 58 Gy. Carvajal et al. [19] reported a 14.2% incidence of radiation osteitis in 21 extremity STS patients. All patients with RO in this cohort received EBRT and mean 55 Gy of radiation. Rohde et al. [16] reported an 11.5% incidence of radiation osteitis in 26 hand STS patients who received either mean 60.7 Gy through EBRT or mean 53.2 Gy through brachytherapy. In our cohort, the incidence of radiation osteitis was 60%. The differences in RO incidence may be a result of the differences in radiotherapy modality between our cohort and the other STS studies. Given the variability in the literature regarding radiation osteitis in STS patients, studies with larger STS cohorts are necessary to evaluate the true incidence of radiation osteitis.

Several studies have also reported variability with RO presentation on imaging following radiotherapy completion. Ugurluer et al. [13] reported pelvic bone changes on MRI at a median of 25 months following radiotherapy for gynecological, colorectal, and bladder cancer; however, this was not specific to radiation osteitis and included insufficiency fractures as well as avascular necrosis. Meixel et al. [10] reported a median latency of 4 months from completion of radiotherapy for gynecological and anal cancer to the first onset of radiation-induced changes on MRI such as radiation osteitis and osteoradionecrosis. Yoshioka et al. [14] reported a mean of 3.8 years from completion of 50 Gy of radiotherapy to radiation osteitis on MRI; however, this cohort was limited to seven patients with gynecological malignancy. In STS patients, Hwang et al. [11] reported bone marrow changes at a median of 9.5 months following radiotherapy. In our cohort, we report a median of 4.5 months from the completion of radiotherapy to MRI evidence of RO. The different time points in each study in which MRIs were performed for each patient may account for this discrepancy in the median onset of bone marrow changes following radiotherapy.

Skeletal metastasis from STS is dependent on the histologic subtype of the primary sarcoma, and under 10% of all STS, patients may develop skeletal metastasis in their clinical course [20–22]. Yoshikawa et al. [22] reported an 8.1% incidence of skeletal metastasis in 64 UPS patients with roughly one-third of these skeletal metastases occurring in regional bone 4 to 66 months after initial presentation. Unfortunately, this study did not report if patients received radiotherapy. In a cohort of 43 STS patients who received radiation, Hwang et al. [11] reported no cases of bone metastasis in the region of STS in 70 STS patients at a median follow up of 24.4 months. In our cohort, 10% of patients developed skeletal metastases which are consistent with the literature [20, 21]. Two patients with UPS and one patient with Ewing's like sarcoma developed skeletal metastasis to the regional bone between 4 months and 35 months following radiotherapy. Of these three patients, we appreciated MRI findings potentially consistent with RO; however, only two patients were biopsied for concerning MRI findings which confirmed metastatic disease. On the other hand, another UPS patient had received a biopsy for potential bony metastasis, and this returned as negative. If MRI signal characteristics are equivocal, PET-CT may be a reasonable alternative to detect osseous metastases [23, 24]. However, obtaining PET-CT scans may be difficult for patients, and at our institution, we typically proceed with a biopsy to investigate the lesion. Given the difficulty in discerning RO from bony metastasis on MRI, we continue to encourage multidisciplinary management of STS at sarcoma centers to appropriately delineate benign from malignant lesions as well as decide when a biopsy is necessary to differentiate the lesion.

This study has several limitations. This was a retrospective study and is subject to the biases inherent in retrospective analysis. Additionally, the selection bias present in this cohort may limit the generalizability of its findings as several eligible patients had to be excluded due to a lack of surveillance MRI in our imaging system of the sarcoma site following radiotherapy. Another limitation is the minimal information regarding radiotherapy modality for nine patients and for the total Gy received in three patients. Furthermore, six patients only had one post radiotherapy MRI available for review. The timing of follow-up MRIs was variable for

some patients affecting the analysis of the time course for the development of radiation osteitis. The lack of heterogeneity in the STS histologic subtype may also be a limitation. Limited follow up was another issue as some patients passed away within 6 months of radiotherapy completion.

In summary, this study is the first to document the incidence and clinical impact of RO in patients with STS. Although RO is often a benign imaging finding, it exists on a spectrum on MRI which can make it difficult to discern which lesions may represent metastatic disease. In our study, three of 18 patients with imaging findings concerning RO present were eventually diagnosed with metastasis to the bone. Although regional metastasis to the bone from STS is rare, the incidence seen in this cohort is likely attributed to the selection bias from this high-grade, high-risk cohort. We believe multidisciplinary care of STS is crucial to evaluate concerning imaging findings. Future multi-institutional studies should evaluate the need for biopsy based on characteristic findings on MRI in this setting.

Availability of data The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the Rush University Medical Center Institutional Review Board and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Competing interests The authors declare that they have no conflict of interest.

References

1. Gilbert NF, Cannon CP, Lin PP, Lewis VO. Soft-tissue sarcoma: J Am Acad Orthop Surg. 2009;17(1):40–7.
2. Gamboa AC, Gronchi A, Cardona K. Soft-tissue sarcoma in adults: an update on the current state of histiotype-specific management in an era of personalized medicine. CA Cancer J Clin. 2020;70(3):200–29.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019;69(1):7–34.
4. Blay JY, Honoré C, Stoeckle E, Meeus P, Jafari M, Gouin F, et al. Surgery in reference centers improves survival of sarcoma patients: a nationwide study. Ann Oncol Off J Eur Soc Med Oncol. 2019;30(7):1143–53.
5. Brennan MF, Antonescu CR, Moraco N, Singer S. Lessons learned from the study of 10,000 patients with soft tissue sarcoma. Ann Surg. 2014;260(3):416–21 discussion 421-422.
6. Salerno KE. Radiation therapy for soft tissue sarcoma. Surg Clin North Am. 2022;102(4):567–82.
7. Bluemke DA, Fishman EK, Scott WW. Skeletal complications of radiation therapy. Radiogr Rev Publ Radiol Soc N Am Inc. 1994 Jan;14(1):111–21.
8. El-Bared N, Wong P, Wang D. Soft tissue sarcoma and radiation therapy advances, impact on toxicity. Curr Treat Options Oncol. 2015;16(5):19.
9. Mitchell MJ, Logan PM. Radiation-induced changes in bone. Radiogr Rev Publ Radiol Soc N Am Inc. 1998;18(5):1125–36 quiz 1242–3.
10. Meixel AJ, Hauswald H, Delorme S, Jobke B. From radiation osteitis to osteoradionecrosis: incidence and MR morphology of radiation-induced sacral pathologies following pelvic radiotherapy. Eur Radiol. 2018;28(8):3550–9.
11. Hwang S, Lefkowitz R, Landa J, Akin O, Schwartz LH, Cassie C, et al. Local changes in bone marrow at MRI after treatment of extremity soft tissue sarcoma. Skeletal Radiol. 2009 Jan;38(1):11–9.
12. Eiving J. Radiation osteitis. Acta Radiol. 1926;6(1–6):399–412.
13. Ugurluer G, Akbas T, Arpaci T, Ozcan N, Serin M. Bone complications after pelvic radiation therapy: evaluation with MRI. J Med Imaging Radiat Oncol. 2014;58(3):334–40.
14. Yoshioka H, Nakano T, Kandatsu S, Koga M, Itai Y, Tsujii H. MR imaging of radiation osteitis in the sacroiliac joints. Magn Reson Imaging. 2000;18(2):125–8.
15. Garner HW, Kransdorf MJ, Bancroft LW, Peterson JJ, Berquist TH, Murphey MD. Benign and malignant soft-tissue tumors: post-treatment MR imaging. RadioGraphics. 2009;29(1):119–34.
16. Rohde RS, Puhaindran ME, Morris CD, Alektiar KM, Schupak KD, Healey JH, et al. Complications of radiation therapy to the hand after soft tissue sarcoma surgery. J Hand Surg. 2010;35:1858–63.
17. Kanberoglu K, Mihmanli I, Kurugoglu S, Ogut G, Kantarci F. Bone marrow changes adjacent to the sacroiliac joints after pelvic radiotherapy mimicking metastases on MRI. Eur Radiol. 2001;11(9):1748–52.
18. Dalinka MK, Mazzeo VP. Complications of radiation therapy. Crit Rev Diagn Imaging. 1985;23(3):235–67.
19. Carvajal C, Casquero F, Hortelano E, Gomez-iturriaga A, Cacicedo J, Muruzabal I, et al. Radiation osteitis after radiotherapy of soft tissue sarcomas. Rep Pract Oncol Radiother. 2013;18:S300–1.
20. Yoshikawa H, Myoui A, Ochi T, Araki N, Ueda T, Kudawara I, et al. Bone metastases from soft tissue sarcomas. Semin Musculoskelet Radiol. 1999;3(2):183–90.
21. Pretell-Mazzini J, Seldon CS, D'Amato G, Subhawong TK. Musculoskeletal metastasis from soft-tissue sarcomas: A Review of the Literature. J Am Acad Orthop Surg. 2022;30(11):493–503.
22. Yoshikawa H, Ueda T, Mori S, Araki N, Kuratsu S, Uchida A, et al. Skeletal metastases from soft-tissue sarcomas. Incidence, patterns, and radiological features. J Bone Joint Surg Br. 1997;79(4):548–52.
23. Caglar M, Kupik O, Karabulut E, Høilund-Carlsen PF. Detection of bone metastases in breast cancer patients in the PET/CT era: do we still need the bone scan? Rev Espanola Med Nucl E Imagen Mol. 2016;35(1):3–11.
24. Rodrigues M, Stark H, Rendl G, Rettenbacher L, Datz L, Studnicka M, et al. Diagnostic performance of [18F] FDG PET-CT compared to bone scintigraphy for the detection of bone metastases in lung cancer patients. Q J Nucl Med Mol Imaging Off Publ Ital Assoc Nucl Med AIMN Int Assoc Radiopharmacol IAR Sect Soc Of. 2016;60(1):62–8.