

Fracture after radiation therapy for femoral metastasis: incidence, timing and clinical features

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ABSTRACT

We analyzed 428 femoral metastases initially treated with radiotherapy between 2002 and 2011 to clarify the clinical details of post-irradiation fractures of femoral metastasis. Patients included 161 men and 167 women, with a mean age of 62 years. Fracture incidence, fracture site, fracture risk based on X-ray images before radiotherapy, and interval from completion of radiotherapy to fracture occurrence were assessed. In addition, 24 pathological specimens obtained during 27 surgeries for these fractures were examined. Fractures occurred in 7.7% of 428 femoral metastases (total 33: 28 actual fractures and five virtual fractures with progressive pain and bone destruction). The fracture rate was 7.8% in the proximal femur and 1.5% in the shaft ($P = 0.001$). Fractures occurred a median of 4.4 months after radiotherapy, with 39.4% occurring within 3 months and 63.6% within 6 months. Among femurs with high fracture risk according to Harrington's criteria or Mirels' score, the fracture rate was 13.9% and 11.8%, respectively. Viable tumor cells were detected in all five patients with painful virtual fracture, in 85.7% of femurs with actual fractures that occurred within 3 months, and in only 25.0% of actual fractures occurring after 3 months. Post-irradiation fractures of femoral metastasis most frequently occurred within 3 months after radiotherapy, and were more common in the peritrochanteric area than in the shaft. Radiological evidence of impending fracture did not correlate with a high fracture rate. Actual fractures occurring after more than 3 months were likely caused by post-irradiation fragility of the femur, without viable tumor cells.

KEYWORDS: bone metastasis, femur, fracture, radiation therapy

INTRODUCTION

The femur is the third most common site for bone metastasis requiring treatment, after the spine and the pelvis [1, 2]. When metastasis develops in the femur, the initial symptom is pain, with pathological fracture possible with disease progression. Palliative radiotherapy for painful bone metastasis is well established and frequently performed, with a total dose of 30 Gy delivered in 10 fractions considered a standard schedule [3, 4]. It has been reported that pain relief is experienced by ~47% of patients who undergo radiation therapy for femoral metastasis, and that fractures are avoided in >80% of cases, even in those with signs of impending fracture [5, 6].

Unfortunately, some patients sustain pathologic fracture even after radiation therapy; various rates of pathologic fracture have been reported. Keene *et al.* reported in 1984 that post-irradiation fracture of femoral metastasis (PIFF) occurred in 5 of 56 patients (8.9%) [7]. In 2004 Linden *et al.* reported that PIFF developed in 12.7% of 110 femurs [6, 8]. Harada *et al.* reported that 13% of 84 lesions eventually required surgery [5]. Even with the availability of bone-modifying agents in the last 10 years, a fracture rate of 25% has been reported [9]. However, these reports did not include large numbers of patients, and none of the reports described the histology of the fracture sites. The purpose of this study was to analyze

a large patient series to clarify the incidence and detailed clinical characteristics of PIFF, including the histology of the fracture site, as well as the relationship between PIFF and radiological criteria of impending fracture.

MATERIALS AND METHODS

We treated 501 femoral metastases at our hospital between 2002 and 2011. Among these, 73 femurs (28 impending and 45 actual fractures) were initially treated with surgery. This investigation was carried out in the remaining 428 femurs in 328 patients initially treated with radiation therapy. There were 203 affected femurs in 161 male patients and 225 affected femurs in 167 female patients, with an average patient age of 62 years (range, 30–92 years). The common primary lesions included breast cancer: 125 femurs (29.2%); lung cancer: 101 femurs (23.6%); prostate cancer: 46 femurs (10.7%); gastrointestinal tract cancer: 38 femurs (8.8%); hepatocellular carcinoma (HCC): 14 femurs (3.2%); and other cancer: 104 femurs (24.3%). The average irradiation dose was 30.8 Gy (range, 8 Gy in a single fraction to 50.4 Gy in 28 fractions) (Table 1).

The treatment of femoral metastasis, including radiation planning and surgical indication, was determined at bone metastasis board meetings at our hospital. At our institution, apparent impending fractures with pain were treated surgically unless the patient's general condition was poor. In patients in whom surgery was not possible because of poor general condition, in those with little bone destruction and a primary aim of pain relief, and for metastasis with apparent bone destruction from cancers sensitive to radiation therapy, radiation therapy was performed. Harrington's criteria of impending fracture (cortical bone destruction $\geq 50\%$, lesion ≥ 2.5 cm, avulsion fracture of the lesser trochanter) were used to determine the risk of impending fracture [10]. In patients with apparent bone destruction, 3 months of partial weight-bearing with single or double crutches was prescribed. All patients provided informed consent for each treatment.

We retrospectively reviewed patient background, total radiation dose, irradiated area, fracture site, Mirels' score, and survival period for all patients [11]. From these data, the incidence of PIFF, the relationship between the irradiated area and the PIFF site, the interval from the completion of radiotherapy to PIFF occurrence, the relationship between radiological fracture risk and PIFF event, and the relationship between patient background and PIFF were investigated. To evaluate the relationship between the irradiated area and the fracture site, the femur was divided into two regions: proximal (femoral head, neck and peritrochanteric area) and distal (diaphysis and distal condylar segment). This simple division was chosen because radiation therapy for the femur usually does not target a narrow field such as the femoral head alone, but normally targets a wide field such as the proximal third of the affected femur, including the femoral head and subtrochanteric area. Radiographic imaging before treatment was reviewed and scored separately by two experienced orthopedic surgeons. If there was discrepancy in scoring, the observers re-examined the imaging and discussed their observations to reach a consensus. Background factors, including age (≥ 62 years or < 62 years), irradiation dose (≥ 30 Gy or < 30 Gy) and zoledronic acid administration (regular 4-week interval administration or not)

Table 1. Baseline characteristics of all patients

Characteristic	Value (range)	Femurs (number of patients)	%
Age (mean, years)	62 (30–92)		
Gender			
Male		203 (161)	47.4
Female		225 (167)	52.6
Radiation dose (Gy)			
8–27		90	21
30–39		325	75.9
40–50.4		13	3
Mean	30.8 (8–50.4)		
Radiation field			
Proximal only		230	53.7
Proximal and distal		153	35.7
Distal only		45	10.5
Primary site			
Breast		125 (82)	29.2
Lung		101 (89)	23.6
Prostate		46 (34)	10.7
Esophagus, stomach, intestine, colon, rectum		38 (29)	8.9
Unknown primary origin		28 (24)	6.5
Kidney		14 (12)	3.3
Liver		14 (10)	3.3
Myeloma		10 (6)	2.3
Thyroid		7 (6)	1.6
Others		45 (36)	10.5

were investigated with a χ^2 test to determine their association with fracture occurrence. We divided the study population into groups according to irradiation dose (≥ 30 Gy or < 30 Gy) for two reasons. First, a total dose of ≥ 30 Gy delivered in 10–20 fractions was shown to achieve better local control in the spine than short-course radiotherapy, and we wanted to determine whether this difference could be applied to femoral metastasis [12]. In addition, a total dose of 30 Gy delivered in 10 fractions was the most commonly used schedule for painful bone metastasis, and many radiation oncologists remained reluctant to use short-course radiation therapy [4]. Values of $P < 0.05$ were considered significant. Survival analysis was performed with Kaplan–Meier methods. Furthermore, histopathology

of the fracture site was performed for those patients who underwent surgery for PIFF.

This study was carried out with the approval of the Institutional Review Board at our institution. The treatment policy for each patient was discussed in a multidisciplinary bone metastasis board meeting (including radiation oncologists and orthopedic surgeons) to determine the appropriate therapeutic approach. All data were obtained in routine clinics, and all patients gave their informed consent for each treatment.

RESULTS

Incidence of post-irradiation fractures of femoral metastasis

PIFF occurred in 33 (7.7%) of 428 femurs. Among these, 28 (6.5%) were actual fractures and five (1.2%) were virtual fractures with progressive pain and bone destruction requiring surgery. The average irradiation dose of patients with PIFF was 34.0 Gy (range, 20 Gy in five fractions to 39 Gy in 13 fractions). Among the 395 femurs without PIFF, the average dose was 30.7 Gy (range, 8 Gy in a single fraction to 50.4 Gy in 28 fractions). The common primary cancers in patients with fracture were breast cancer (30.3%), lung cancer (27.3%) and prostate cancer (6.1%). These three cancers accounted for ~70% of fractures, which was not substantially different from the general population of this study (Tables 2, 3).

Location of post-irradiation fractures of femoral metastasis

PIFF occurred in the femoral head and neck region in nine femurs, in the peritrochanteric region in 20, in the shaft in three, and in another location in 1. As for the relationship between the irradiated area and the incidence of fractures, fractures in the proximal femur occurred in 30 (7.8%) of 383 femurs in which radiation therapy included the proximal femur. In contrast, shaft fracture occurred in 3 (1.5%) of 198 femurs in which radiation therapy included the distal femur (diaphysis to condylar segment) (Table 2). PIFF occurred significantly more frequently in the proximal than the distal femur (χ^2 test, $P = 0.001$) (Table 4).

Interval from radiation to post-irradiation fractures of femoral metastasis

The median interval from the completion of radiotherapy to PIFF was 4.4 months. PIFF occurred most frequently within 3 months after radiotherapy (13 femurs; 39.4%), followed by 4–6 months (eight femurs; 24.2%), 7–9 months (six femurs; 18.2%) and 10–12 months after radiotherapy (two femurs; 6.1%). Twenty-nine (87.8%) of 33 PIFF occurred within 1 year (Fig. 1). However, four (12.1%) fractures (three actual fractures and one virtual fracture) occurred after 1 year, one each at 14, 15, 16 and 21 months (Fig. 1). All three actual fractures occurred without traumatic event. These patients complained of no pain or only slight pain, and follow-up X-ray images showed no progressive bone destruction. In the fourth patient, osteolytic change and pain progressed, even after 39 Gy of radiotherapy, and was attributed to a virtual fracture after 14 months.

Thyroid cancer, HCC, cholangiocellular carcinoma, and renal cell carcinoma are characterized by soft-tissue expansion, hypervascularity, and low sensitivity to irradiation [13–19]. It is reportedly

Table 2. Characteristics of the 33 patients with fractures

Characteristic	Value (range)	In fractured femurs (%)
Age (mean, years)	64 (37–87)	
Gender		
Male	18	54.5
Female	15	45.5
Radiation dose (Gy)		
20	3	9.1
30–39	30	90.1
mean	34 (20–39)	
Radiation field		
Proximal only	21	63.6
Proximal and distal	9	27.3
Distal only	3	9.1
Primary tumor		
Breast	10	30.3
Lung	9	27.3
Esophagus, colon	3	9.1
Prostate	2	6.1
Unknown origin	2	6.1
Liver	2	6.1
Others	5	15.2

difficult to achieve local control with radiation therapy for these mass-type bone metastases [20]. There were five cases of these cancers with low radiation sensitivity among the patients with PIFFs. Three of these five fractured within 3 months, and the remaining two fractured within 4 months (Fig. 1, Table 3).

Radiographic impending fracture and post-irradiation fractures of femoral metastasis

For nine femurs, radiation therapy was performed without X-ray images; in the remaining 419 femurs, fracture risk was evaluable on plain X-ray images. According to Harrington's criteria, 137 femurs were evaluated as likely to be subject to impending fracture and the remaining 282 femurs as not likely to be subject to impending fracture. Nineteen fractures (13.9%) occurred in the former group and 14 (5%) in the latter; this difference was significant ($P = 0.002$). As for the Mirels' score, 191 femurs were considered as not likely to be subject to impending fracture. Among these, 51 femurs had bone destruction that was not visible on X-ray images, but that was detectable with CT, MRI or PET. The remaining 140 femurs had Mirels' scores ≤ 8 . Six fractures

Table 3. Details of the 33 patients who sustained a post-irradiation fracture of femoral metastasis (PIFF)

Case	Gender	Primary site	Bone destruction	Dose, (Gy)	Time to fracture after RT (months)	Actual fracture or virtual fracture	Pathological examination
1	M	Lung	Lytic	20	0.0	A	TC+
2	F	Liver ^a	Lytic	39	0.1	A	NP
3	M	Bladder	Lytic	30	0.1	A	TC-
4	M	Esophagus	Lytic	39	0.2	V	TC+
5	M	Liver ^b	Lytic	20	0.3	A	NP
6	M	Esophagus	Lytic	39	0.4	A	TC+
7	F	Breast	Lytic	30	0.6	A	TC+
8	F	Breast	Mixed	39	0.9	A	NP
9	M	Lung	Lytic	30	0.9	A	NP
10	M	Lung	Lytic	20	1.1	A	NP
11	F	Breast	Mixed	30	1.3	A	TC+
12	F	Breast	Mixed	30	1.4	A	TC+
13	M	Liver ^a	Lytic	39	2.7	A	TC+
14	M	Thyroid	Lytic	39	3.1	V	TC+
15	M	Liver ^b	Lytic	39	3.4	A	TC+
16	F	Myeloma	Lytic	39	4.0	V	TC-
17	M	Prostate	Mixed	30	4.4	A	TC-
18	M	Lung	Mixed	39	4.7	A	NP
19	M	Lung	Lytic	39	5.7	A	NP
20	F	Breast	Lytic	39	5.7	A	TC-
21	F	Lung	Lytic	39	5.8	A	TC-
22	F	Colon	Lytic	30	7.2	A	TC-
23	M	Lung	Lytic	30	7.5	A	TC-
24	M	Lung	Lytic	30	7.6	A	NP
25	M	Rectum	Lytic	30	7.7	V	TC+
26	F	Breast	Lytic	39	8.2	A	NP
27	F	Breast	Lytic	36	9.4	A	TC-
28	M	Prostate	Lytic	30	10.4	A	TC+
29	M	Prostate	Lytic	39	10.5	A	TC-
30	F	Lung	Lytic	39	14.4	V	TC+
31	F	Breast	Mixed	39	15.4	A	TC+
32	F	Breast	Lytic	30	16.2	A	TC-
33	F	Breast	Lytic	39	21.0	A	TC+

M = male, F = female. TC+ = tumor cells present, TC- = tumor cells not present, NP = histopathology not performed, A = actual fracture, V = virtual fracture.

^aHepatocellular carcinoma.

^bCholangiocellular carcinoma.

occurred in these 191 patients (3.1% of patients). In contrast, 27 fractures occurred among 228 femurs that had Mirels' scores ≥ 9 (11.8%). This difference was also significant ($P = 0.001$). Details of the Mirels' scores and fracture rate are shown in Fig. 2.

Pathological findings of post-irradiation fractures of femoral metastasis

Surgery was performed on 27 of 33 fractures; the remaining six fractures were treated conservatively because the patient's general condition was poor or the patient refused surgery. The surgeries included endoprosthesis replacement in 12 femurs and

osteosynthesis in 15. Pathological sampling of the fracture site was obtained in 24 patients (19 actual fractures and five painful virtual fractures) during surgery. Cancer cells persisted in 14 of 24 sampled femurs, while no remaining tumor cells were found in 10 (Table 3).

Among seven actual fractures that occurred within 3 months and from which pathological specimens were obtained, six (85.7%) showed remaining tumor cells microscopically. Among fractures that occurred after 3 months, only three of 12 femurs (25%) had tumor cells present; this difference was significant ($P = 0.002$). All painful virtual fractures showed viable tumor cells.

Patient background and post-radiation fracture

We did not find any significant differences between fracture and non-fracture groups with respect to background factors, including patient age, irradiation dose, or regular zoledronic acid administration (χ^2 test) (Table 4).

Table 4. Relationship between the occurrence of femoral fractures after radiotherapy and background characteristics (χ^2 test)

	With fracture	No fracture	<i>P</i> value
Radiation field			0.001
Proximal	30 ^a	353 ^b	
Shaft	3 ^a	195 ^b	
Age			0.28
<62	13 ^a	194 ^b	
≥ 62	20 ^a	201 ^b	
Radiation dose			0.08
<30 Gy	3 ^a	87 ^b	
≥ 30 Gy	30 ^a	308 ^b	
Zoledronic acid administration			0.40
Regular	11 ^a	105 ^b	
Irregular or none	22 ^a	290 ^b	

^aNumber of femurs with fractures.

^bNumber of femurs without fractures

Survival rate for all patients

The median survival period for all patients was 5.5 months. The survival rates at 1, 2 and 3 years were 0.27, 0.12 and 0.08, respectively (Fig. 3).

DISCUSSION

Radiotherapy is currently a mainstream treatment for metastatic bone tumors. Katagiri *et al.* [21] reported that among 808 patients with skeletal metastasis, 749 (93%) were treated non-surgically, and that 623 (77%) of these received radiotherapy. Even in cases in which osteosynthesis or spinal decompression procedures are required, surgery is sometimes impossible, and radiation therapy is indicated because of the patient's poor general condition or patient refusal. Radiation therapy is a mainstream treatment in cases of femoral metastasis as well; however, physicians occasionally encounter PIFF.

The incidence of PIFF varies among previous reports, from 8.9% in the study by Keene *et al.* to 35% in that by Mirels [5–9, 11]. The incidence of PIFF in the present study was 7.7%, which is slightly lower than that of other studies. In the studies by Keene *et al.*, the primary cancer was restricted to breast cancer. However, the primary cancers in the present study were not substantially

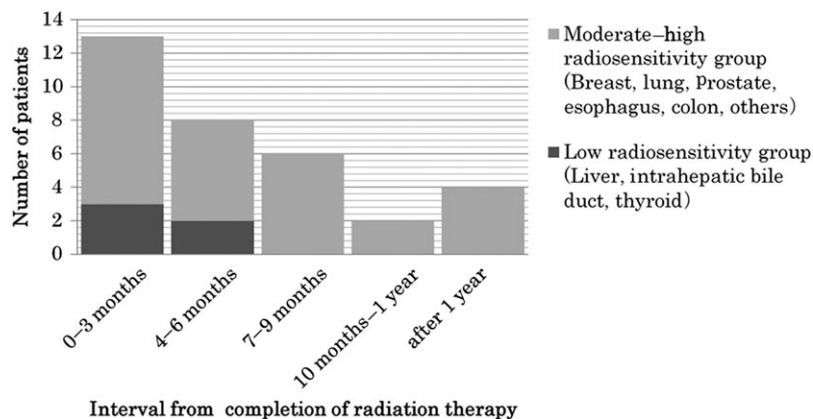


Fig. 1. Time to fracture after radiotherapy for femoral metastasis. Post-irradiation fractures occurred most frequently within the first 3 months (39.4%) after irradiation, and became less frequent over time.

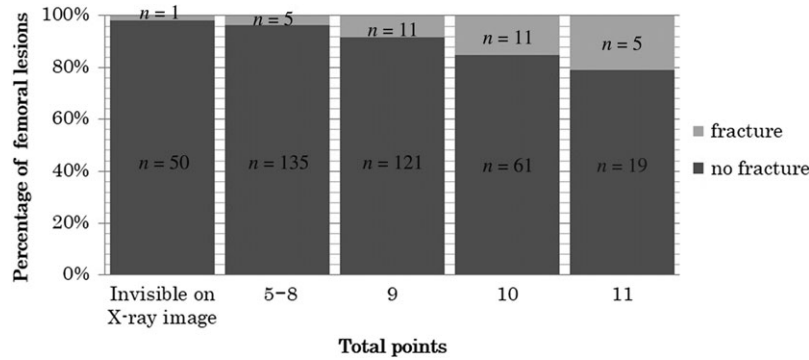


Fig. 2. Likelihood of fracture based on the scoring system of Mirels in 428 femoral metastases.

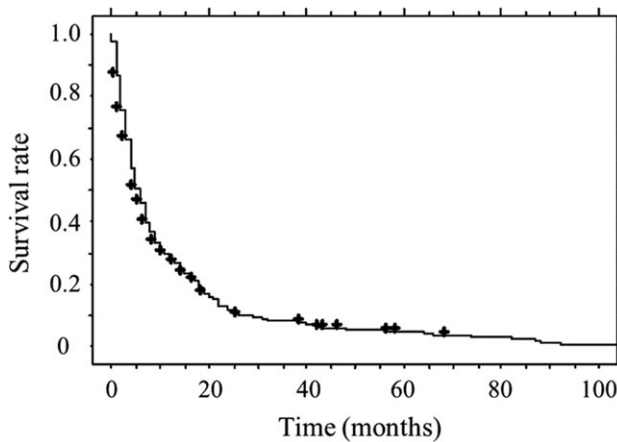


Fig. 3. Survival rates for all patients. Survival rates at 1, 2 and 3 years were 0.27, 0.12 and 0.08, respectively.

different from those in the other reports (Table 5). This lower rate in our study might have resulted from our protocol instructing all patients with painful bone destruction to use crutches for 3 months after radiation therapy, which is the period required for bone regeneration [5]. Other reasons for our lower rate of PIFF could be that many of the patients in these three earlier studies were treated before the use of zoledronic acid became popular, or that the degree of bone destruction and the risk of fracture among our patients might have differed from those of other study populations.

The Mirels' score system [11] includes four factors for evaluating the risk of pathological fracture: the site of metastasis, pain, size of lesion, and X-ray findings. Each factor is scored from 1 to 3 points; combined scores of 9 points or more indicate impending fracture. According to this system, peritrochanteric lesions are scored as 3 points, while the lower limb is scored as 2 points, suggesting that peritrochanteric lesions have the highest risk of fracture. Keene *et al.* reported a fracture rate of 14% in the proximal femur and 0.7% in shaft lesions [7]. Linden *et al.* reported that 86% of fractures occurred in the proximal femur [6]. The current study also revealed that the proximal femur had a higher PIFF rate than the femoral shaft.

In this study, 5 of 33 femurs with post-irradiation fractures were affected by tumors with low sensitivity to radiation; all of these

fractured early (three fractures within 3 months, two fractures within 4 months). These results indicate a tendency for early fracture following radiation therapy in metastases with low sensitivity to radiation therapy. In this study, there were no cases of renal cell carcinoma and only one case of thyroid cancer among PIFF patients. Femoral metastases with evident bone destruction from these two types of cancer are usually treated surgically, because they tend to present as impending fracture in a patient with good general condition and long life expectancy.

The interval from the completion of radiation therapy to PIFF has been briefly reported in the literature. Keene *et al.* reported that PIFF occurred at an average of 10 months, whereas Mirels *et al.* reported that all PIFFs occurred within 6 months. Linden *et al.* found that fracture occurred within a median of 8.5 weeks (2–36) and that 90% of fractures occurred within 6 months [6, 7, 11]. In the recent study by Tatar, all fractures occurred within 6.6 months [9]. In the present study, 39.3% of PIFFs occurred within 3 months, and 63.6% occurred within 6 months. PIFF in the current study developed later compared with the studies by Linden *et al.* and Mirels *et al.*, but a similar tendency of early fracture development and a decrease over time was observed. This finding may be explained by the fact that femurs weakened by metastasis require several months to regain their strength after radiation therapy. Harada *et al.* [5] reported that radiological regeneration of bone was observed on plain X-ray images an average of 3 months after the completion of radiation therapy. Another reason for this finding may be the decreasing number of surviving patients over time. The number of surviving patients generally decreases over time among those with bone metastasis. Consequently, the number of fractures might decrease over time.

Only 13.9% of the impending fractures according to Harrington's criteria eventually developed PIFF. Similarly, the fracture rate of femurs with Mirels' score ≥ 9 was only 11.8%. Even among femurs with a score of 11, the fracture rate was only 20.8%. These results agree with those of Linden *et al.*, who reported a fracture rate of 16.7% for femurs with a Mirels' score ≥ 9 and 23.8% for those with a score of 11 [6]. Therefore, as suggested by Linden *et al.*, deciding on the surgical indication based only on the Mirels' score or Harrington's criteria might lead to unnecessary surgery.

Persistent tumor cells were found more frequently in actual fractures that occurred within 3 months after radiation therapy (85.7%)

Table 5. Comparison with past reports regarding femoral fractures after radiation therapy

	Primary tumor site	Fracture rate (%)	Proximal fracture (%)	Time to fractures after RT (months) Median (months)	Dose (Gy)
Keene <i>et al.</i> [7]	Breast	8.9	N/A	2–18 N/A	20–55
Linden <i>et al.</i> [6, 8]	Breast, lung, prostate, other	12.7	86	0–9 8.5	8–24
Harada <i>et al.</i> [5]	Breast, lung, prostate, liver Thyroid, kidney, other	9.5	N/A	N/A N/A	30–40
Tatar <i>et al.</i> [9]	Breast, lung, prostate, other	25.0	N/A	0–6.6 N/A	7–30
Current study	Breast, lung, prostate, liver Esophagus, colon, other	7.7	91	0–21 4.4	20–39

N/A = Not applicable.

than in those that occurred after 3 months (25.0%). Two reasons are presumed for this difference. First, >3 months may be necessary before the appearance of tumor cell necrosis after radiotherapy. Second, metastasis of tumors that are resistant to radiation therapy might result in early fractures because such metastases (including HCC, cholangiocellular carcinoma, and thyroid cancer) cause fractures early in this series. Approximately 70% of actual fractures occurring after 3 months did not show any remaining tumor cells. Therefore, we surmise that PIFF occurring after 3 months resulted primarily from bone fragility following radiation therapy. Hatano *et al.* [22] reported a case in which a femoral fracture occurred 10 years after radiation therapy. In that case, there were no remaining tumor cells and the fracture was caused by bone fragility resulting from radiation therapy.

Many studies have found that skeletal-related events are prevented or delayed by the administration of zoledronic acid [23, 24]. It has also been reported that performance status and quality of life improve in patients receiving radiotherapy combined with bisphosphonates [25]. An animal model study found a greater increase in bone density in those treated with combined bisphosphonates and radiotherapy than in those receiving radiation therapy alone [26]. However, in the current study, the fracture rate was not lower in the regular zoledronic acid administration group (9.5%) than among other patients (7.1%). Therefore, the usefulness of regular zoledronic acid administration in preventing PIFF could not be confirmed. This finding might have been caused by bias, because only 27.0% of the patients in this study were administered zoledronic acid regularly, and those patients with a higher risk of fracture might have been more likely to receive zoledronic acid treatment. Long-course radiotherapy was reportedly associated with better local control compared with short-course radiotherapy (8 Gy in a single fraction, 20 Gy in five fractions) in the treatment of spinal metastasis [12]. In contrast, Tatar *et al.* reported that procedures and fractionation did not affect fracture incidence [9]. Similarly, we did not find differences in the incidence of PIFF between long-course radiotherapy and short-course radiotherapy.

There were some limitations in this study. First, this was a retrospective study, and the number of fractures was small. Therefore, results concerning fracture timing and the fracture-preventing effect of bisphosphonates are not conclusive. A prospective study comprising a larger number of cases would be required for drawing more definitive conclusions. Second, because tissues were sampled from 24 of 33 fractures, research including more samples is necessary to validate the relationship between tumor remnants and fracture timing. Third, 28 femurs that initially underwent prophylactic surgery were not included in this study. Generally speaking, these lesions were deemed to be clearly subject to impending fracture and were considered appropriate for surgery. Therefore, the PIFF incidence might have been lowered by the exclusion of these 28 femurs.

The current study demonstrated that PIFF occurred most often within the first 3 months after radiotherapy and occurred more frequently in the proximal femur than in the shaft. Therefore, it is recommended that patients undergoing radiotherapy for proximal femoral metastasis be informed of the risk of fracture and that a few months of partial weight-bearing with a crutch be prescribed. The occurrence of actual fracture within 3 months after radiotherapy or painful virtual fracture after radiotherapy may indicate a high likelihood of remaining viable tumor cells. Therefore, when performing surgery under these situations, orthopedic surgeons must take care not to contaminate the surgical field with tumor cells, especially in patients undergoing excision followed by prosthetic replacement.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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