Complications of Radiation Therapy to the Hand After Soft Tissue Sarcoma Surgery

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Purpose Radiation has been shown to improve local control after resection of soft tissue sarcomas. However, it may also result in major complications in the hand, given the compact nature of functional tissues and limited tissue volumes in the hand. The purpose of this investigation was to describe the hand-specific complications of radiation therapy for patients with soft tissue sarcoma of the hand (STSH).

Methods We performed a retrospective chart review of 55 consecutive patients with STSH treated by a single surgeon between 1993 and 2006. We identified 26 patients who were treated with external beam radiation, brachytherapy, or both, either preoperatively or postoperatively, and reviewed their clinical course.

Results After a median follow-up of 7 years, 29 treatment-related complications occurred in 19 patients who had received radiation, whereas 3 of the 29 patients treated with surgery alone developed complications. All patients who received brachytherapy and 14 of the 21 treated with external beam radiation alone developed complications. There were 5 early minor, 2 early major, 3 late minor, and 19 late major complications.

Conclusions Patients with STSH who underwent radiation therapy had a high rate of complications. The complication rate in our series was higher in patients who had brachytherapy catheters placed adjacent to finger joints. A better understanding of predictors of complications will help to determine the optimal timing and type of radiation therapy to treat patients with STSH. *(J Hand Surg 2010;35A:1858–1863. Copyright © 2010 by the American Society for Surgery of the Hand. All rights reserved.)*

Type of study/level of evidence Therapeutic IV.

Key words Complications, hand tumor, radiation, soft tissue sarcoma.

Radiation is commonly used in the treatment of soft tissue sarcomas of the extremities to maximize local control after wide excision, or to facilitate limb-sparing surgery. In randomized trials, external beam radiation, administered preoperatively or postoperatively, and brachytherapy reduce the risk of local tumor recurrence in patients with an extremity soft tissue sarcoma.[1,2]

Preoperative external beam radiation offers the advantage of potential downstaging or shrinking of extremity lesions that might improve the ability to preserve major functional tissues and improve

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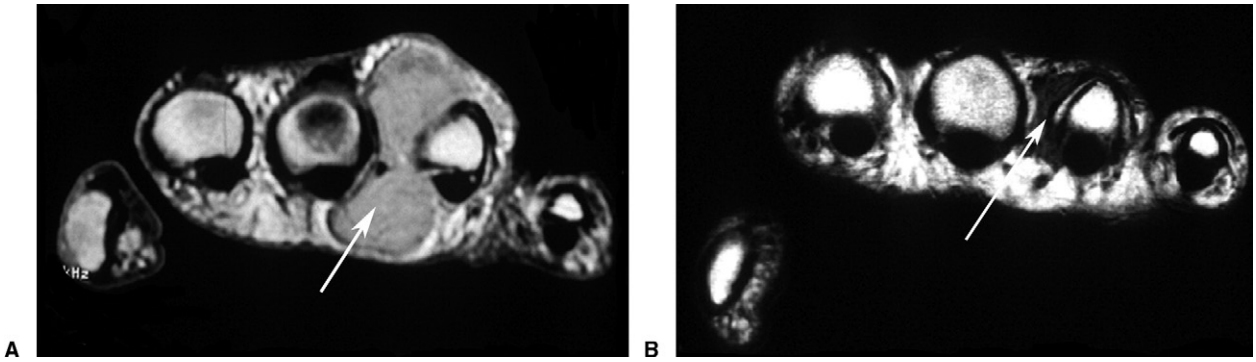

FIGURE 1: A Magnetic resonance imaging of a 51-year-old man with malignant fibrous histiocytoma who underwent preoperative radiation therapy. **B** Diminished size of the lesion after radiation allowed a more limited resection.

hand-sparing options (Fig. 1).[3] Low total doses and decreased field size are additional advantages of preoperative treatment with few late complications.[4] However, these come at the price of a higher risk of surgical wound complications.[3]

Postoperatively, either external beam radiation or brachytherapy can be used. External beam radiation has been associated with improved local control of upper and lower extremity lesions[5,6] even in the presence of positive surgical margins.[7,8] Alternately, brachytherapy catheters can be placed after wide excision of high-grade soft tissue sarcomas. Brachytherapy has the advantages of shortening the time required for treatment and reducing the dose of radiation in addition to reducing the risk of local recurrence.[2,7,9–11]

Unfortunately, the use of radiation has been associated with marked early and late complications.[3,4,7,12–15] In particular, preoperative radiation has been associated with an increased risk of early wound complications in treatment of sarcomas of the extremities.[3,12,15] The effects of radiation on the hand in this setting have not been well characterized. We hypothesize that radiation therapy could be associated with a risk of severe complications in the hand. The purposes of our study were to quantify and describe the complications associated with radiation for patients with soft tissue sarcoma of the hand and to define patient, tumor, and treatment factors that are associated with these complications.

MATERIALS AND METHODS

The institutional review board of the institution at which this study was conducted approved a waiver of authorization. We retrospectively reviewed the records of 55 consecutive patients evaluated for either primary or recurrent soft tissue sarcoma of the hand at our center by a single surgeon between 1995 and 2006. Among them, 26 patients underwent perioperative radiotherapy. Indications for radiation therapy included tumor size greater than 5 cm, high grade, need for improved local control to decrease recurrence, and situations in which decreasing the tumor size would allow a hand-sparing surgical option to be performed (Fig. 1). Decisions on the timing and modality of radiotherapy were made during a combined tumor board that included the radiologist, pathologist, radiation oncologist, medical oncologist, and surgeon.

The mean age of patients at the time of surgery was 40 years (range, 8–80 y). Histological diagnoses included 7 synovial sarcoma, 7 pleomorphic soft tissue sarcomas, 4 epithelioid sarcomas, 2 malignant peripheral nerve sheath tumors, and one each of acral myxoinflammatory fibroblastic sarcoma, alveolar rhabdomyosarcoma, atypical fibroblastic neoplasm, clear cell sarcoma, fibrosarcoma, and liposarcoma. Twelve patients were treated with wide excision, and 13 underwent combined wide excision with partial hand amputation. One patient who had undergone marginal excision for an unsuspected synovial sarcoma at another center was referred to us for further treatment. She refused definitive wide resection and was treated with external beam radiotherapy alone. A total of 18 patients had a tumor maximum dimension of less than 5 cm, whereas 8 had tumors with a maximum dimension of at least 5 cm (Table 1). Flap procedures were done in 17 patients (5 fillet flaps, 3 free gracilis flaps, 2 free parascapular flaps, 6 pedicled radial forearm flaps, and 1 free rectus flap) for wound coverage.

Radiation therapy was administered to 8 patients preoperatively and 18 patients postoperatively. A total of 21 patients received external beam radiation only, 2 received brachytherapy only, and 3 underwent both external beam radiation and brachytherapy. For the purpose of this analysis, we included in the brachyther-

TABLE 1. Patient Demographics

	Surgery and Radiotherapy	Surgery Alone	Total
Number of patients	26	29	55
Mean age (y)	40 ± 22	39 ± 18	40 ± 20
Female/male	14/12	15/14	29/26
Primary tumors	20 (77%)	27 (93%)	47 (85%)
Recurrent tumors	6 (23%)	2 (7%)	8 (15%)
Tumor grade			
Low	5 (19%)	13 (45%)	18 (33%)
High	21 (81%)	16 (55%)	37 (67%)
Size (cm)	4.2 ± 2.1	3.0 ± 2.3	3.6 ± 2.3
Tumor depth			
Deep	26 (100%)	23 (79%)	49 (89%)
Superficial	0	6 (21%)	6 (11%)
American Joint Committee on Cancer stage			
I	5 (19%)	13 (45%)	18 (33%)
II	18 (69%)	15 (52%)	33 (60%)
III	3 (12%)	1 (3%)	4 (7%)
IV	0	0	0

apy group patients given brachytherapy as part of their treatment. The mean radiation dose for external beam radiation was 60.7 Gy (range, 45.0–131.4 Gy). Five brachytherapy patients received a mean dose of 53.2 Gy (range, 45.0–70.4 Gy).

We classified the complications based on timing relative to surgery and severity. Minor complications were those that produced minor functional impairment (skin or wound problems or tendon adhesions causing minor limitation in range of motion but not requiring tenolysis). Major complications were those that resulted in major functional impairment (full-thickness flap loss, contracture, fracture, osteitis, or tendon adhesions requiring tenolysis). Early complications were designated arbitrarily as those occurring within 6 weeks of surgery. Late complications were those that developed after 6 weeks.

RESULTS

After a median follow-up of 7 years, 32 treatment-related complications were observed in 22 patients out of the entire group of 55 patients. A total of 29 of these complications occurred in 19 of the 26 patients who received perioperative radiotherapy. These included 5 early minor, 2 early major, 3 late minor, and 19 late major complications. Of the 29 patients who did not receive radiotherapy, 3 developed complications; all were neuromas that were managed surgically.

FIGURE 2: A 41-year-old woman with pleomorphic soft tissue sarcoma underwent a double ray amputation followed by postoperative radiation therapy. She developed radiation osteitis and sustained a third metacarpal stress fracture 7 years postoperatively that was treated with splinting owing to the poor condition of the overlying skin.

The 5 minor early wound complications included delayed wound healing (1), epidermolysis (2), and wound dehiscence (2), whereas the 2 major early complications were wound necrosis requiring surgical revision. The 3 minor late complications were tendon adhesions not requiring surgical tenolysis, whereas the 19 major late complications included adduction contracture (5), ankylosis (3), joint contracture (2), osteitis (3), tendon adhesions requiring surgical tenolysis (4), and nonunion of a pathologic fracture of the third metacarpal resulting from radiation osteitis (1). This developed in a 41-year-old woman with pleomorphic soft tissue sarcoma who underwent a double ray amputation and wound coverage with a pedicled radial forearm flap followed by postoperative radiation therapy. She devel-

oped radiation osteitis and sustained a third metacarpal stress fracture 7 years after radiation therapy that was treated conservatively because of the poor quality of the overlying skin. The fracture failed to unite and stability was achieved after a prolonged period of splinting but resulted in notable hand stiffness (Fig. 2).

All 5 patients who received brachytherapy (2 received brachytherapy alone and 3 received a combination of brachytherapy and external beam radiation) experienced a complication, even though all patients had catheter loading delayed until the fifth postoperative day. On the other hand, only 14 of 21 patients treated with external beam radiation alone had complications. Two patients of the 3 patients who received a combination of brachytherapy and external beam radiation each had 4 major complications. We observed that brachytherapy near the metacarpophalangeal joints can result in severe functional disability and likely is best avoided in this location. In 3 patients, brachytherapy was used for web space lesions in an effort to facilitate single ray amputation rather than double ray amputation, which otherwise would have been required without radiation. These patients all developed complications, including metacarpophalangeal joint ankylosis, and resulted in notable functional impairment (Fig. 3). Patients who developed complications had received a higher median total radiation dose than those who did not (54.9 vs 50.4 Gy). Six of 8 patients treated with preoperative radiation and 13 of 18 patients treated with postoperative radiation developed complications. Of the 8 patients with tumors 5 cm or larger, 7 developed complications, whereas 12 of the 18 patients with tumors less than 5 cm did so. Of the 17 who had flap coverage performed to the surgical site, 14 had complications, whereas 5 of the 9 who did not have flap coverage had complications.

DISCUSSION

Schoenfeld et al. previously described the effect of radiation therapy on the local control of distal upper and lower extremity soft tissue sarcomas.[16] Of the 23 patients in that series evaluated over a period of 26 years, 12 had lesions of the hand and wrist, whereas the other 11 had lesions of the foot. The late effects of radiation in their patients included edema (14%), fibrosis (24%), telangiectasias (24%), hyperpigmentation (19%), impaired range of motion (33%), and impaired functional use of the extremity (14%); the authors did not identify which complications affected patients with hand or foot lesions and whether certain patients had multiple complications. The combined (major and minor) complication rate of 73% that we observed in the hand is much greater than the rates previously reported in other upper and lower extremity sites, which range from 26% to 44%.[7,12,17–20] However, not all complications seen may have been directly related to radiation and could have been related to surgical treatment. The risk of complications in our series might be attributed to the limited tissue volumes, complex geometry, soft tissue gliding requirement, and joint motion required for proper hand function. We observed no nerve-related complications even when brachytherapy was used in the carpal tunnel.

Arbeit et al. reported a 22% complication rate using brachytherapy, compared with 3% of patients not treated with brachytherapy in those with extremity and superficial truncal soft tissue sarcomas.[21] Shiu et al. described a 44% complication rate in their brachytherapy-treated group in patients with upper and lower extremity soft tissue sarcomas, compared with 14% for patients treated with surgery alone.[11] Decreased complication rates were seen when brachytherapy catheter loading was delayed until 5 days postoperatively.[9,11,22]

FIGURE 3: Radiographs of a 27-year-old woman with synovial sarcoma of the right hand show a normal fourth metacarpal and metacarpophalangeal joint preoperatively **A** and during brachytherapy treatment **B**. **C** Five years after treatment, the patient developed radiation osteitis of the fourth metacarpal and metacarpophalangeal joint changes.

All patients in our study had delayed loading of the brachytherapy catheters; despite this, complications were universal in all patients who received brachytherapy. These complications were both early, such as wound or flap necrosis, and late, such as contractures, osteitis, which can result in secondary pathologic fractures that are difficult to treat owing to poor bone healing and joint ankylosis.[23] All 3 patients for whom brachytherapy was used in the web space to avoid a double ray amputation developed complications, including metacarpophalangeal joint ankylosis, and the complications resulted in marked functional impairment. In retrospect, a primary double ray amputation might have been a better option than a single ray amputation.

We expected to find complications—particularly involving wound healing—in the early (6-wk) postoperative period. These would have been expected to result in minimal functional impairment. However, most of the complications we encountered in our patients occurred beyond 6 weeks postoperatively and resulted in notable functional impairment. Issues such as joint ankylosis, radiation osteitis, and pathological fracture caused severe disability within 5 years of radiation therapy. We have not identified postirradiation sarcomas in our patients.

There are several limitations to this study. The first is the small sample size. The rarity of upper extremity sarcomas of the hand limits the data available for analysis,[24] and we did not have the power to evaluate statistically the effect of each variable on complication occurrence. Another limitation is that this is a retrospective chart review that originated from our observations, which suggested increased complications of radiation therapy in the hand. In addition, patient and tumor variables necessitate treatment individually tailored to each patient and do not allow randomization.

Our study revealed a high rate of complications (73%) in patients with soft tissue sarcomas of the hand who underwent perioperative radiotherapy. These findings require the treating surgeon to justify the use of radiation in the treatment of soft tissue sarcomas of the hand. Surgical alternatives that achieve a wider margin should be considered carefully, including additional digit or partial hand amputation, which might obviate the need for adjuvant radiation. Despite the complication rate identified in our study, we believe that there are important roles for radiation in the management of patients with soft tissue sarcoma of the hand, both to reduce the risk of local recurrence, especially in high-risk tumors, and to reduce the size of tumors preoperatively and improve hand-sparing, function-preserving surgical options.

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