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SYMPOSIUM: HIGHLIGHTS FROM THE FIRST COMBINED 2011 MEETING OF THE MUSCULOSKELETAL TUMOR SOCIETY AND CONNECTIVE TISSUE ONCOLOGY SOCIETY

Adult Soft Tissue Sarcoma Local Recurrence After Adjuvant Treatment Without Resection of Core Needle Biopsy Tract

Odion Binitie MD, Shawn Tejiram MD, Sheila Conway MD, David Cheong MD, H. Thomas Temple MD, G. Douglas Letson MD

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Abstract

Background Core needle biopsies of sarcomas allow a diagnosis in a high percentage of patients with few complications. However, it is unclear whether the tract needs to be excised to prevent recurrences.

Questions/purposes We therefore determined the rates of recurrence and metastases in patients with Stage III extremity sarcomas, who underwent wide local resection without excision of the needle tract and also received adjuvant treatment.

Methods We retrospectively reviewed 59 adult patients with deep, larger than 5 cm, high-grade soft tissue sarcomas of the upper or lower extremity treated between January 1999 and April 2009. All the patients underwent a core needle biopsy. Resection was performed with wide margins. The biopsy tract was not resected during the definitive surgery. Fifty-seven patients (97%) received preoperative and/or postoperative radiation, whereas 49 patients (83%) received chemotherapy. Local recurrence and distant recurrence rates were determined. The minimum followup was 24 months (median, 56 months; range, 24–122 months).

Results The local recurrence rate was 9%. Fifteen patients (25%) developed metastasis after diagnosis. Seven of the 59 patients (12%) had microscopic positive margins at resection.

Conclusions Our data demonstrate no increase in local recurrence rates or rates of metastatic disease compared with previously published studies when resection of the core biopsy tract was not performed.

Level of Evidence Level IV, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
This work was performed at H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA, and the Department of Orthopaedics and Rehabilitation, University of Miami Miller School of Medicine, Miami, FL, USA.

O. Binitie (✉), S. Tejiram, D. Cheong, G. D. Letson
H. Lee Moffitt Cancer Center & Research Institute,
Sarcoma Program, 12902 Magnolia Drive,
Tampa, FL 33612, USA
e-mail: odionb@gmail.com

S. Conway, H. T. Temple
Department of Orthopaedics and Rehabilitation,
University of Miami Miller School of Medicine,
Miami, FL, USA

Introduction

The staging of musculoskeletal sarcomas includes the evaluation of a tissue biopsy in addition to radiologic imaging of the tumor and imaging for the presence of metastasis [35, 38]. Open biopsy had been the mainstay for obtaining tissue samples; however, the safety and efficacy of percutaneous biopsies have been demonstrated in numerous studies [1, 5, 7, 10, 17, 24, 32, 39–41, 48, 59, 61, 63–65].

Needle tract seeding from percutaneous biopsies has been demonstrated in hepatocellular, breast, thyroid,

non-Hodgkin's lymphoma, vertebral metastasis, and renal and brain tumors among others [11, 21, 26, 29, 31, 46, 54]. However, a study of rates of local recurrence in breast cancer demonstrated no increase among patients who underwent a core needle biopsy [20]. In sarcomas, it has been known that open biopsy incisions and tracts should be resected. A case report documented needle tract seeding in a patient with a distal femoral osteosarcoma [15]; we, however, could not find any reports of needle tract seeding after a closed biopsy in soft tissue sarcomas.

Historically reported rates of local recurrence of soft tissue sarcomas range from 13% to 29% and metastases from 22% to 49% [4, 22, 25, 36, 37, 43, 51, 55, 56, 58, 65]. The addition of radiation to the wide resection of sarcomas improves local recurrence rates from 19% to 30% in certain studies, even in patients with microscopically positive margins [3, 12, 16, 27, 30, 52, 53, 60, 62]. Because patients with Stage III tumors receive adjuvant therapies, in addition to wide resection, to treat microscopically positive margins and/or satellite lesions, it is believed this would also treat any potential tumor cells in the core needle tract. The effect of chemotherapy on outcomes of sarcoma treatment is still debatable; however, a few systematic reviews and meta-analyses have demonstrated improvement in local control rates and, in some cases, overall survival with the use of chemotherapy and radiation [2, 19, 42, 45]. A recent report had no local recurrences from a fine needle aspiration biopsy in 20 patients with high-grade soft tissue sarcomas [28]. The needle tract was excised in two patients who had an amputation. Eighty percent of their patients received adjuvant therapy. However, it is unclear whether the risk of local recurrence or metastases is increased when the core needle biopsy tract is not excised in patients receiving adjuvant therapy.

Our primary focus was to determine whether leaving the core needle biopsy tract unresected in adult patients with Stage III extremity sarcomas who underwent wide resection and received adjuvant treatment would lead to an increase in the local recurrence rate. Our secondary goal was to determine if this affected rates of metastasis.

Patients and Methods

Between January 1999 and April 2009, 288 adult patients (18 years of age and older) underwent core needle biopsies of primary soft tissue sarcomas at two tertiary cancer centers. Tumors were considered primary if the patient had no intervention (including biopsy) before their presentation to either cancer center. We excluded 174 patients with tumors located in the trunk, shoulder, and pelvis; patients with recurrent disease; or those who underwent an amputation as the definitive treatment. This left 114 patients with high-grade tumors, which measured greater than 5 cm in the largest dimension at surgical resection and were located deep to the superficial fascia (American Joint Commission on Cancer Type III [49]). Eighteen patients were lost to followup and 37 did not have up to 24 months of followup or died before that. Most local recurrences occur within 2 to 3 years after resection [18, 36, 51, 56]. Thus, we included 59 patients in the study. Mean age was 56.8 ± 17.1 years. There were 28 male and 31 female patients. Minimum followup was 24 months (median, 56 months; range, 24–122 months). We obtained institutional review board approval and the medical records of these patients were reviewed.

All patients underwent a preoperative workup, which included a history and physical, radiographic imaging of the extremity (radiographs and MRI), CT scans of the lungs to evaluate for metastatic disease, and for patients with leiomyosarcomas, an abdominal and pelvis CT scan was also performed. All patients were reviewed at a multidisciplinary tumor conference where treatment plans were discussed. Tumors were described based on their location. Demographic data including age at presentation, history, sex, and race were also reviewed. Mean measurement of the largest tumor dimension was 12 cm (SD ± 6.4). The most common sarcoma subtype determined by final histopathologic diagnosis was high-grade undifferentiated pleomorphic sarcoma (Table 1).

Core needle biopsy was performed on all the patients in this study. Biopsies were performed in the clinic under

Table 1. Tumor subtype and size.

Tumor characteristic	Number of patients
Subtype	
High-grade pleiomorphic undifferentiated sarcoma	29
Liposarcoma	13
Leiomyosarcoma	5
Synovial sarcoma	4
Malignant peripheral nerve sheath tumor	3
Giant Cell sarcoma	2
Sarcoma NOS	1
Extraskeletal chondrosarcoma	1
Extraskeletal Ewing	1
Size	
5–10 cm	23 (39%)
10–20 cm	29 (49%)
> 20 cm	5 (9%)

NOS = not otherwise specified.

local anesthesia; in the imaging suite, guided by either ultrasound or CT; or in the operating room using a Tru-cut, Temno, or Jamshidi needle (Cardinal Health, McGaw Park, IL, USA; Care Fusion, San Diego, CA, USA). In no case was an incisional biopsy performed. Five patients underwent two biopsies in the clinic as a result of insufficient tissue from the first attempt. One patient had an ultrasound-guided biopsy after an unsuccessful clinic biopsy. Clinic biopsies were performed after informed consent was obtained and the area was prepped and draped in a standard sterile fashion. One percent lidocaine was infiltrated into the area with a 25-gauge needle for local anesthesia. A subcentimeter skin incision, using a Number 11 blade, was made and a 14-gauge core needle was advanced into the mass. Several passes were made and tissue cores were taken directly to the pathology laboratory for histologic analysis. A bandage was placed over the incision. A similar process was performed in the imaging suite by fellowship-trained musculoskeletal radiologists under the guidance of the treating orthopaedic surgeon for the image-guided biopsies after a discussion between both specialists regarding the path for biopsy-sparing neurovascular and other vital structures. Patients who could not tolerate a clinic biopsy were taken to the operating room and under monitored anesthesia care, a small incision after local anesthesia was made over the mass. Through this, a 14-gauge needle was passed into the mass. Samples were taken to the pathology laboratory and the patient awakened from anesthesia. There were no complications from the core needle biopsy procedures. There was a variation between the two institutions where the biopsies were performed. One institution performed all biopsies in the clinic, whereas the other performed 70% in the clinic.

All biopsy material was reviewed by pathologists and the material underwent frozen microscopic analysis. Biopsy samples were deemed diagnostic if there was adequate tissue to make a diagnosis.

All patients were discussed in a multidisciplinary tumor conference at each institution and treatment plans were determined. A total of 57 patients (97%) received radiation therapy (Table 2). Four patients received postoperative interstitial brachytherapy. Interstitial catheters were placed at the time of surgery in single-plane geometry to cover the entire tumor bed. Catheters were loaded with Iridium-192 sources approximately 5 to 6 days after surgery. The median dose was 3500 cGy. Four patients were enrolled in a radiation and dendritic stem cell vaccine trial and received dendritic stem cells in addition to external beam radiation therapy.

Forty-nine patients (83%) received chemotherapy (Table 2). The majority received a doxorubicin and ifosfamide-based chemotherapy regimen. Doses were 75 mg/m^2 Adriamycin, 10 g/m^2 ifosfamide, and 50 mg/m^2 cisplatin per cycle.

Table 2. Treatment characteristics.

Treatment type	Number of patients
Radiation	57 (97%)
Postoperative only	49
Preoperative only	5
Pre- and postoperative	3
Brachytherapy	4
Chemotherapy	49 (83%)
Preoperative only	23
Postoperative only	8
Pre- and postoperative	18
Margin status	
R0	52 (88%)
R1	7 (12%)
R2	0
Local recurrences	5 (8.5%)
Metastatic disease	15 (25%)

All patients underwent wide local resections performed by fellowship-trained orthopaedic and surgical oncologists at the two institutions. Patients who underwent amputations were excluded from this study. Tumor size was determined at the time of resection by the pathologist as the greatest diameter of the gross specimen. Protocols at both institutions were similar in the handling of resected specimens. Tumors were oriented and sent fresh to the pathology department. In the pathology laboratory, tumors were handled according to the College of American Pathologists protocol for soft tissue tumors [47]. The specimen was marked with ink and one section per centimeter of maximum dimension was obtained. These were mostly taken from grossly heterogeneous areas. At the margins, sections were oriented perpendicular to the ink margin. Areas with macroscopic tumor close to the margin were sent for microscopic analysis. During retrospective review, margins that were free from tumor by > 5 mm were defined as R0, R1 margins were equal to or less than 5 mm to the inked surface, whereas R2 margins were macroscopically positive for tumor [43]. There were 52 R0 resection margins, seven R1 margins, and no R2 margins. Of those with R1 margins, two underwent a reresection to R0 margins (Table 2).

Patient followup entailed physical examination and imaging studies on a routine timetable. Patients were seen every 3 months for the first 2 years for a history and physical examination, radiographs and MRI of the limb, chest CT scans, and abdomen and pelvis CT scans in patients with leiomyosarcomas. After 2 years patients were seen every 6 months and after 5 years seen annually. After 5 years either a chest radiograph or a CT scan was obtained. The followup period was measured from the date

of biopsy to last followup or death, whereas time to local recurrence was from the date of biopsy to the date the first local recurrence was diagnosed. Survival data were obtained from the medical records, patient contact, and the Social Security Death Index (http://ssdi.rootsweb.ancestry.com/cgi-bin/ssdi.cgi).

Descriptive statistics were used for overall patient characteristics. Fisher's exact test was used to compare local recurrence and metastatic rates between R1 and R0 margin groups. Statistical analysis was performed using IBM SPSS statistics (Version 19.0; SPSS, Chicago, IL, USA).

Results

There were five local recurrences (9%). Median time to local recurrence was 13 months (range, 6-22 months). All five patients with a local recurrence underwent a repeat resection (Table 3). Fifteen patients developed distant disease (25%). Median time to development of distant disease was 22 months (range, 9–37 months). Seventy-five percent of these patients had metastasis to the lungs.

Two patients with a microscopically positive resection margin (R1) had a local recurrence (Table 4). An R1 margin did not increase the rate of a local recurrence ($p = 0.1$) or metastasis ($p = 0.99$). The results of this study were compared with previously published rates of local recurrence and metastasis (Table 5).

Discussion

There is a concern of needle tract seeding from percutaneous biopsies. Although demonstrated in various other types of cancer, there are no reports of needle tract seeding in closed biopsy of soft tissue sarcoma. The purpose of this study was to determine whether core needle biopsy tracts that were not intentionally resected during wide local resections of large (> 5 cm), deep, high-grade extremity sarcomas in adult patients who also received adjuvant treatment (chemotherapy and/or radiation) had an untoward effect on local recurrence or metastatic rates.

The limitations of our study include a relatively small number of patients. Sarcomas are rare tumors with an estimated 10,520 new cases in the United States in 2010 [6]. The rationale behind selecting patients with high-grade, deep and large tumors was that these have been consistently reported to be factors that increase the risk of local recurrence and/or of metastasis [4, 8, 9, 13, 14, 18, 22–24, 33, 34, 36, 37, 43, 44, 50, 51, 55–57] and these tumors are typically treated with adjuvant treatment, making them a more homogenous group for our research purposes. The inclusion criterion was limited to primary tumors, eliminating those patients with prior treatments or biopsy at outside institutions. Although that limited the number of study patients, we believe this enhanced the study by decreasing confounding variables. Second, we lacked concurrent controls and used historic data for comparison. A cohort of patients who had the needle biopsy tract resected for comparison would have strengthened the study. Third, five patients were lost to followup, two of whom developed metastasis at a median of 3 months after diagnosis. Although none of these patients had a local recurrence at last followup, the total number of local recurrences and metastases may be altered by improved followup. Finally, this was a retrospective study of a specific group of patients with high-grade tumors treated with a multimodality treatment approach (with

Table 4. Margin status as a predictor of local recurrence and metastasis.

Variable	Margins	Total number	Events	Univariate p value
Local recurrence	R0	52	3	0.1
	R1	7	2	
Metastasis	R0	52	13	0.99
	R1	7	2	

Table 3. Local recurrences.

Patient	Sarcoma subtype	CTX	Radiotherapy	Time from diagnosis to local recurrence (months)	Subsequent recurrence	Amputation
1	MPNST	Yes	No	13	No	No
2	Giant cell sarcoma	Yes	Yes	22	Yes	Yes
3	HGPUS	No	Yes	20	No	No
4	MPNST	Yes	Yes	10	Yes	Yes
5	Liposarcoma	Yes	Yes	6	No	No

CTX = chemotherapy; MPNST = malignant peripheral nerve sheath tumor; HGPUS = high-grade pleiomorphic undifferentiated sarcoma.

Table 5. Comparison to the literature evaluating local recurrence and metastasis.

Series	Number of patients	Patient characteristics	Length of followup (months)	Surgical intervention	Adjuvant treatment	Local recurrence	Metastasis
Pisters et al. [43]	1041	Extremity, localized, all grades, > 16 years old	47	LSS 87%	RT 40%, CTX 23%	17%	22%
Trovik et al. [57]	459	Extremity and trunk wall, localized, Stage III, > 16 years old	90	LSS 85%	RT 35%	23%	43%
Heslin et al. [25]	168	Extremity, localized, Stage III	48	LSS 86%	RT 84%, CTX 96%	13%	49%
Stojadinovic et al. [51]	2084	All sites and grades, localized, > 16 years old	50	LSS 92%	RT 34%, CTX 19%	18%	23%
Massi et al. [36]	42	Leiomyosarcoma, localized, extremity, adult	16	LSS 86%	RT 46%, CTX 21%	21%	38%
Weitz et al. [58]	1261	Extremity, localized, > 16 years old, all grades, depths, and sizes	55	LSS 93%	RT 44%, CTX 15%	19%	26%
Alkis et al. [4]	294	Extremity and trunk wall, > 16 years old, low to high grade, all sites	41	NA	RT 43%, CTX 75%	29%	41%
Gronchi et al. [22]	997	Extremity, localized, adult, all grades	85	LSS 96%	RT 45%, CTX 20%	17%	27%
McKee et al. [37]	111	Extremity and trunk, all grades, > 13 years old		LSS 97%	RT 38%, CTX 33%	26%	43%
Tanabe et al. [55]	95	Extremities, > 17 years old, included recurrent tumors, intermediate to high grade	66	LSS 100%	RT 100% (preop only), CTX 27%	15%	NA
Zagars et al. [65]	1225	Localized, all sites, all ages, 16% locally recurrent, all grades	114	NA	RT 100%, CTX 33%	17%	30%
Current study	59	Localized, adult, Stage III	56	LSS 100%	RT 97%, CTX 83%	9%	25%

LSS = limb salvage surgery; NA = not available; CTX = chemotherapy; RT = radiotherapy.

radiation and/or chemotherapy); the study results may not be applicable to patients who do not receive adjuvant treatment.

Our primary aim was to determine if an unresected core needle tract would lead to higher local recurrence rates than that reported in the literature. There were five local recurrences (9%) among our patients, which was lower than numerous studies that evaluated local recurrences in patients with soft tissue sarcomas (13%-39%) [4, 22, 25, 36, 37, 43, 51, 55, 56, 58, 65]. Some of these studies included all tumor grades, superficial and deep tumors as well as trunk wall and retroperitoneal tumors. The median time to local recurrence in this study of 13 months was in line with the majority of the literature that reports local recurrences occurring in the first 2 to 3 years [18, 36, 51, 56]. A positive microscopic surgical resection margin status did not have an adverse effect on local recurrence rates; however, as a result of the small number of local recurrences, a definitive conclusion could not be drawn from this. Five patients had more than one attempt at a core needle biopsy with the first demonstrating nondiagnostic tissue, and one of these patients had a local recurrence. We found no increase in the incidence of a local recurrence from more than one attempt at a biopsy. An important note is that all biopsies were performed either by the orthopaedic oncologist or by a musculoskeletal radiologist after discussion with the treating surgeon. The careful planning of a biopsy path is critical to not contaminate vital structures.

We found metastases in 15 patients (25%). This was equal to or lower compared with previous studies (22%–49%) [4, 22, 25, 36, 37, 43, 51, 55, 56, 58, 65]. Margin status did not have a statistically negative effect on the rate of metastases; however, given the small number of R1 margins, a conclusion cannot be drawn from this either.

This was a retrospective study evaluating the effect of retained core needle biopsy tract in patients with high-grade sarcomas receiving adjuvant treatment. The site of a needle biopsy is very small and unless it is specifically marked afterward, identifying its location becomes a difficult task. Because it is the practice to treat Stage III tumors with adjuvant therapies at these two institutions, it

was believed that any microscopic cells in the tract would be treated with these therapies as would any microscopic positive margins or satellite lesions.

The goals of this study were to determine whether there was an increased rate of local recurrence and metastases in a patient population with unresected core needle biopsy tracts and large (> 5 cm), deep, high-grade extremity sarcomas that underwent wide local resection and adjuvant therapies. Compared with the current sarcoma literature, the local recurrence and metastatic rates in this patient population were similar or lower. These results indicate that retained core needle biopsy tract does not increase the risk of local recurrence or metastatic rates in this specific patient population. However, these results should not be extrapolated to all soft tissue sarcomas or to sarcomas treated without adjuvant therapy. A multidisciplinary management approach, like in the treatment of all sarcomas, is essential.

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