

Pre-operative Radiation Therapy Followed by Re-Excision May Improve Local Control and Progression-Free Survival in Unplanned Excisions of STS of the Extremity and Chest-wall

Abstract Number: 11408

Meena Bedi, MD¹; David M. King, MD²; John C. Neilson, MD²; Donald A. Hackbarth, MD²; John A. Charlson, MD³

Departments of Radiation Oncology¹, Orthopaedic Surgery² and Medical Oncology³ at the Medical College of Wisconsin.

Email Addresses:

Meena Bedi: mbedi@mcw.edu

David M. King: dking@mcw.edu

John C. Neilson: jneilson@mcw.edu

Donald A. Hackbarth: hackbarth@mcw.edu

John A. Charlson: jcharlson@mcw.edu

Background: Unplanned excision (UE) of soft tissue sarcomas (STS) is a common occurrence for which the optimal management strategy has not been fully established. Studies have shown that UEs may lead to poorer outcomes compared to planned oncologic resection. In this study we aim compare outcomes of UE vs planned excision (PE), as well as assess various factors that may predict for disease control in this setting.

Methods: A retrospective chart review was performed on all patients treated at our institution for STS from 2000-2014. All patients undergoing oncologic and non-oncologic (unplanned) excision of their STS with greater than 6 month follow-up of the extremity or chest-wall were identified. UE was defined as an excisional biopsy or unplanned resection of a mass without consideration for the need of a negative margins.

Patient, tumor and treatment characteristics were determined and clinical outcomes including local recurrence-free survival (LRFS), progression-free survival (PFS) and overall survival (OS) were evaluated using the Kaplan-Meier estimate of the survival function. The log-rank test was used to compare two survival curves. Univariate (UVA) and multivariate (MVA) analyses were performed to determine prognostic variables in correlation with the above survivals. For MVA, the Cox proportional hazards model was used.

Results: 245 patients with stage I-III STS were identified in our database with greater than 6 month follow-up. Of these, 34 (14%) had undergone UE of their STS. Median follow-up was 2.8 years. Patient and tumor characteristics are located in Table 1.

Median OS and 2-year OS for the entire cohort was 14.8 years and 88%, respectively. Median PFS and 2-year PFS for the entire cohort was 9.3 years and 75%, respectively. The overall local recurrence (LR) rate was 8.6%. The LR

rate for patients undergoing UE was 35% versus 4.2% in those who underwent a PE ($p < 0.0001$) (Figure 1). 2-year PFS for patients undergoing UE was 4.2 years versus 9.3 years in patients undergoing a PE ($p = 0.08$).

Of the patients who had UE, 15 (44%) underwent pre-operative imaging. Table 2 lists the various post-UE interventions. Of note, 11 (32.3%) patients received pre-operative radiation (RT) followed by re-excision. Of the patients that underwent re-excision after UE, 7 (30%) had no residual disease. Of those that had no residual disease, 4 (57%) had pre-operative RT followed by re-excision, 2 (28.7%) had re-excision alone and 1 (14.3%) had re-excision followed by post-operative RT. The LR rate for patients undergoing pre-operative RT followed by re-excision was 9% (1/11), 58% (7/12) in those that received no RT and 45% (5/11) in those that underwent post-operative RT.

Significant variables on UVA for LRFS, PFS, and OS for patients undergoing UEs are listed in Table 3. Pre-operative RT ($p = 0.01$) (Figure 2) and the use of any RT in the management of UE ($p = 0.003$) (Figure 3) both led to improved PFS. Median PFS for patients who underwent pre-operative RT was not met (> 120 months) compared to 11.5 months in patients who did not receive RT and 88.1 months in patients who received post-operative RT.

On MVA for LRFS, decreased performance status ($p = 0.01$) led to decreased LRFS. On MVA for PFS, pre-operative RT ($p = 0.04$) and increased performance status ($p = 0.01$) led to improved PFS. There were no factors that predicted for increased OS on MVA in patients who underwent UE.

Conclusions: UEs led to decreased local control and PFS compared to oncologic/planned excisions in STS of the extremity and chest-wall. However, the use of pre-operative RT followed by re-excision improved local control and PFS in patients who had non-oncologic resections of their primary sarcoma. This study highlights the importance of multimodality therapy in the setting of UEs, particularly with preoperative RT and re-excision. Further studies are warranted to corroborate these findings.

Variable	All patients	Planned Excision	Unplanned Excision
Number	245	211	34
Median Age	57	57	64
Median Tumor Size	7.9 cm	8.5 cm	4 cm
Stage	I: 46 (18.7%) II: 62 (25.3%) III: 137 (56%)	I: 40 (19%) II: 46 (22%) III: 125 (59%)	I: 6 (17.7%) II: 16 (47%) III: 12 (35.3%)
Grade	Low: 47 (19.1%) Intermediate: 20 (8.2%) High: 178 (72.7%)	Low: 45 (18.4%) Intermediate: 15 (6.1%) High: 185 (75.5%)	Low 1 (3%) Intermediate 5 (14.7%) High 28 (82.3%)
Histology	Undifferentiated: 56 (22.9%) Leiomyosarcoma/Liposarcoma: 77 (31.4%) Synovial: 45 (18.4%) Other: 67 (27.3%)	Undifferentiated: 51 (24.1%) Leiomyosarcoma/Liposarcoma: 68 (32.2%) Synovial: 38 (18%) Other: 48 (22.7%)	Undifferentiated: 6 (17.6%) Leiomyosarcoma/Liposarcoma: 9 (26.5%) Synovial: 7 (20.6%) Other: 12 (35.3%)
Tumor Location	Upper Extremity: 64 (26.1%) Lower Extremity: 181 (73.9%)	Upper Extremity: 50 (23.7%) Lower Extremity: 161 (76.3%)	Upper Extremity: 13 (38.2%) Lower Extremity: 21 (61.8%)
Subcutaneous Disease (TXa)	45 (18.4%)	36 (17%)	9 (26.5%)
Timing of RT	No RT: 36 (14.7%) Pre-operative: 174 (71%) Post-operative: 35 (14.3%)	No RT: 24 (11.4%) Pre-operative: 163 (77.2%) Post-operative: 24 (11.4%)	No RT: 12 (35.4%) Pre-operative: 11 (32.3%) Post-operative: 11 (32.3%)
Chemotherapy	68 (28%)	67 (32%)	1 (3%)

Table 1: Patient, Disease and Treatment Characteristics between Patients who Underwent UE and PE

Intervention After UE	Patients (%)
Chemotherapy Alone	1 (2.9)
Re-excision Alone	8 (23.5)
RT alone	5 (14.7)
Re-excision followed by post-operative RT	6 (17.7)
Observation Alone	3 (8.8)
Pre-operative RT followed by Re-excision	11 (32.4)

Table 2: Post-Unplanned Excision Therapies

Variables	LRFS	PFS	OS
Age	NS	NS	NS
Tumor Size	NS	NS	NS
Grade	NS	NS	NS
Stage	NS	NS	NS
Karnofsky Performance Status	P=0.002	P=0.0007	NS
Tumor Location	NS	NS	NS
Chemotherapy	NS	NS	NS
Timing of RT	P=0.06	P=0.01	NS

Table 3: Univariate Analysis for Local Recurrence-Free, Progression-Free and Overall Survival (NS: Not significant)

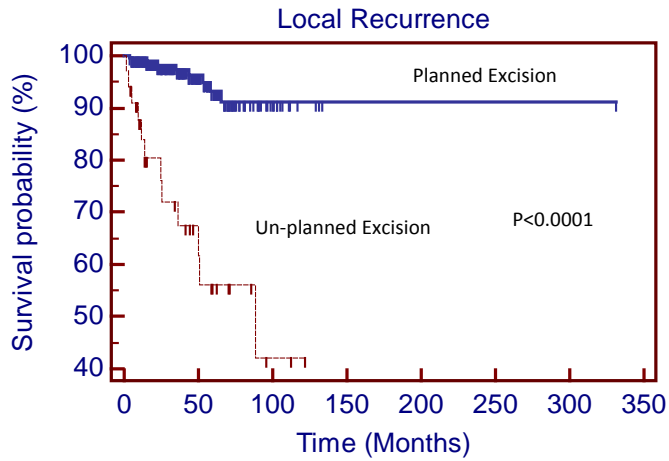


Figure 1: Local Recurrence-Free Survival and Excision Type

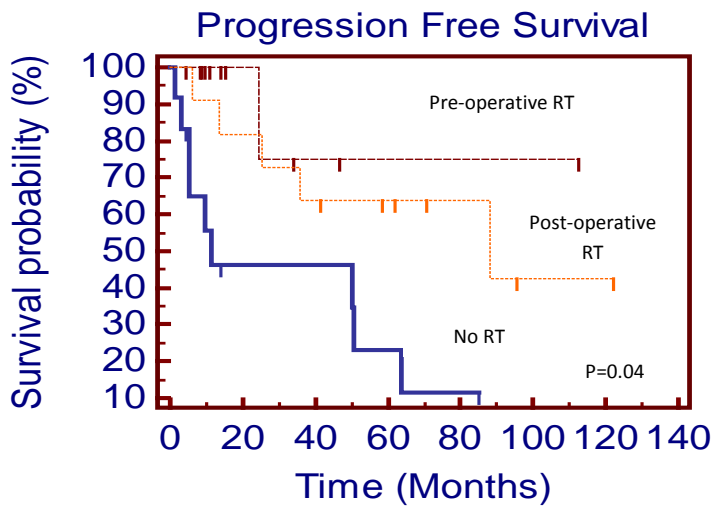


Figure 2: Progression-Free Survival and Timing of Radiation

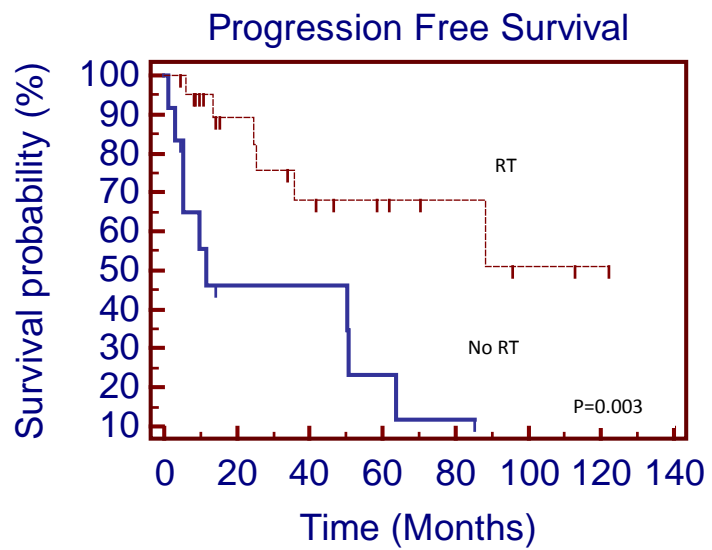


Figure 3: Progression-Free Survival and Timing of Radiation