Intraoperative Margin Sampling in Soft Tissue Sarcoma

Lauren Zeitlinger, R Lor Randall¹, Robert Canter, Morgan Darrow², George Chavez, Steven Thorpe ¹Orthopedic surgery, UCDavis Health, ²Pathology

INTRODUCTION:

Intraoperative surgical margin sampling in soft tissue sarcoma has several classification schemes and many variables factoring into the adequacy of margins¹⁻³. In the setting of bone sarcomas, marrow margin frozen assessment has been scrutinized with little impact on intraoperative decisions, with increased cost and time³. Contrary to this, breast conserving surgery potentially avoids re-excision in 25% of patients with margins sampled ². This practice has not been evaluated in soft tissue sarcomas.

Several recommendations regarding intraoperative margins have been made, including: "6-8 perpendicular sections from all margins < 2cm," 2 samples from the closest margin and 1-2 sections from all other margins, and 6 or more specimens taken from margins <2cm⁴⁻⁶. Ultimately, there are no current evidence-based recommendations for patterns of soft tissue margin sampling.

Questions:

A: What were the patterns of peripheral margin sampling within our institution?

B: Did peripheral margin status correlate with final tumor margin pathology?

C: Did peripheral margin/final specimen margin correlate with local recurrence?

D: What is the cost of peripheral margin sampling based on CPT code?

METHODS:

This study was a retrospective chart review of extremity and truncal soft tissue sarcoma patients treated at a tertiary sarcoma center by three subspeciality trained musculoskeletal oncologists from 2005-2019 with at least 2 year clinical follow up. Patients were excluded if initially treated elsewhere/referred for unplanned excisions. Sarcoma subtype, AJCC 8th ed Stage, final margin status, peripheral margin sampling, 2 year local recurrence were all considered. RESULTS:

A total of 179 patients were identified for inclusion into the study; 119 patients (66%) had peripheral margins sampled, of which 27 (23%) had frozen margins. If peripheral margins were obtained, five or six samples were most common (56%). Positive peripheral margins were identified in 10 patients (5.5% of all patients; 8.4% in those with margins sampled) and R1 margins on the final tumor specimen were identified in 15 patients (8.3%). If a positive peripheral margin was identified, there was a 50% chance that final margins would be positive (R1), vs. if margins were negative only 4.6% had an R1 final margin which was statistically significant (P= 0.003). There was weak to moderate agreement between positive peripheral margins (kappa=0.42). When subdivided between frozen and permanent only, there was moderate agreement between positive final specimen margin and positive frozen margins (kappa=0.74, McNemar's p-value=.31) and weak agreement between positive permanent only peripheral margins (kappa= 0.42, McNemar's Test p= 0.32). There was no statistically significant difference in final margins and AJCC tumor size or stage (p-value = 0.7043, 0.6800 respectively). Overall 2-year local recurrence rate was 8.86%, which was not statistically significant by final margin status (P= 0.9765) or by sarcoma subtype (P= 0.8149) although likely underpowered. Ten of the 14 patients who developed a local recurrence had R0 resections, 3 R+1 and 1 was R1. At this institution, the inpatient charge for frozen margin is \$503.69 and permanent \$500.80 respectively, resulting in an average total cost of \$5,022.45 per patient based on 5 margin samples.

DISCUSSION AND CONCLUSION: While there is moderate agreement between frozen peripheral margin sampling and final R margin classification of the resected tumor specimen, the utility of routine margin sampling at the time of resection is in question. While underpowered to account for subtype and recurrence, it is reasonable to suggest a practice of selective margin sampling when there is concern for focal inadequate margins or in select cases of particular histologies, like myxofibrosarcoma. Further, there may be utility to frozen margin sampling prior to definitive complex soft tissue reconstruction given the moderate agreement between positive frozen margins and final pathology. There does not appear to be utility for intraoperative margins for permanent analysis without frozen due to weak agreement and also does not guide surgical decisions. Lastly, there is an inherent cost to sampling with intraoperative frozen assessment which does not account for operative time. Ultimately, we propose a selective margin sampling practice, with use of frozen decision margins for real time data to drive surgical making.



Table of positive peripheral by final			
Positive peripheral	final		
Frequency Percent Row Pct Col Pct	0	1	Total
0	104 87.39 95.41 95.41	5 4.20 4.59 50.00	109 91.60
1	5 4.20 50.00 4.59	5 4.20 50.00 50.00	10 8.40
Total	109 91.60	10 8.40	119 100.00
Frequency Missing = 60			