Title: Impact of Neoadjuvant Radiation on Pathogen Profiles and Cefazolin Coverage in Soft Tissue Sarcoma Resection

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Significance & Hypothesis/Techniques:
Treatment of soft tissue sarcoma (STS) is associated with high rates of postoperative wound complications, particularly following neoadjuvant radiation therapy (RT). First-generation cephalosporins remain the standard perioperative antibiotics; however, infections after STS resection are frequently polymicrobial, and limited data support current prophylactic regimens. The impact of radiation on pathogen profiles remains unclear. Surgical resection disrupts soft tissue barriers, and radiation may further alter the local environment, resulting in more complex infections. The primary goal of this study is to characterize pathogens in surgical site infections following STS resection and compare irradiated versus non-irradiated wound beds. A secondary goal is to assess cefazolin susceptibility.

Innovation:
Currently, antibiotic prophylaxis for STS resections follows standard orthopedic guidelines. However, extensive soft tissue loss, devascularization, and neoadjuvant radiation may alter tissue susceptibility to infection. This study provides clinically actionable data by characterizing pathogen profiles after STS resection and evaluating cefazolin adequacy to identify gaps in coverage.

Approach (Materials & Methods):
We performed a retrospective review of adult patients with surgical site infections following STS resection with (n=39) or without (n=10) neoadjuvant RT at a single tertiary center (2015–2025). Postoperative infection was defined as culture-proven deep infection within 180 days; later infections were included in time-to-infection analyses. Polymicrobial infections were defined using standard (>1 organism) and class-based (organisms from more than one bacterial or fungal class) approaches. Tumor location was grouped as upper extremity, groin/pelvis, or lower extremity. Cefazolin susceptibility was reviewed by an Infectious Disease physician. Fisher's Exact tests were used to evaluate associations.

Results:
Baseline demographics were similar between cohorts. Overall, 69.2% of infections were polymicrobial, and 59.0% involved multiple bacterial or fungal classes. Coagulase-positive Staphylococci (CoPS) was the most common organism (27.3%).

Polymicrobial infections were common in both groups (69.0% irradiated vs 60.0% non-irradiated, p=0.708). Irradiated tissue demonstrated a significant increase in gram-negative organisms (59.0% vs 20.0%, p=0.0374), with trends toward fewer gram-positive organisms (32.2% vs 45%, p=0.305), including CoPS (25.6% vs 35%, p=0.412). Class-based polymicrobial infections were more frequent in irradiated tissue (59.0% vs 40.0%, p=0.311). Cefazolin susceptibility remained low in both groups (17.9% vs 40%, p=0.201). Infections in irradiated tissue were more likely to occur within 90 days (80% vs 50%, p=0.101). Infections after 90 days were more likely to harbor gram-positive organisms (58% vs 80%, p=0.287) and CoPS (56% vs 80%, p=0.284). Incision location was not associated with pathogen profiles.

Discussion & Impact:
Infections following STS resection were frequently polymicrobial, with irradiated tissue demonstrating more complex pathogen profiles. Cefazolin showed very low susceptibility overall. Although many comparisons did not reach statistical significance, likely due to a small non-irradiated cohort, consistent trends included increased

polymicrobial infections, reduced gram-positive predominance, and poor cefazolin coverage in irradiated wounds. Importantly, most infections in irradiated tissue occurred early postoperatively, suggesting perioperative inoculation and a window where appropriately selected prophylaxis may have the greatest impact. These findings highlight a mismatch between standard prophylaxis and infecting organisms and support consideration of broader, more appropriate perioperative antibiotic strategies, particularly following neoadjuvant RT.

Table 1: Pathogen Profiles in Irradiated versus Non-Irradiated Tissue (Per Patient)

	total	Irradiated tissue	Non-Irradiated tissue	p-value	odds ratio
# of patients	49	39	10		
patients with polymicrobial infection (vs single bug)	33	69.23%	60%	0.708	1.487
patients with infection containing multiple polymicrobial classes	27	58.97%	40%	0.311	2.122
infections containing gram positive organisms	38	74.36%	90%	0.419	0.328
infections containing gram negative organisms	25	58.97%	20%	0.0374	5.551
infections containing anaerobes	9	21.05%	10%	0.663	2.289
infections containing coagulase positive staph (MSSA/MRSA)	30	58.97%	70%	0.719	0.621
infections containing mixed, unspeciated	20	46.15%	20%	0.167	3.35
infections containing yeast	4	10.26%	0%	0.568	Inf
Complete cefazolin susceptibility	11	17.90%	40%	0.201	0.328

Table 2: Time to Infection

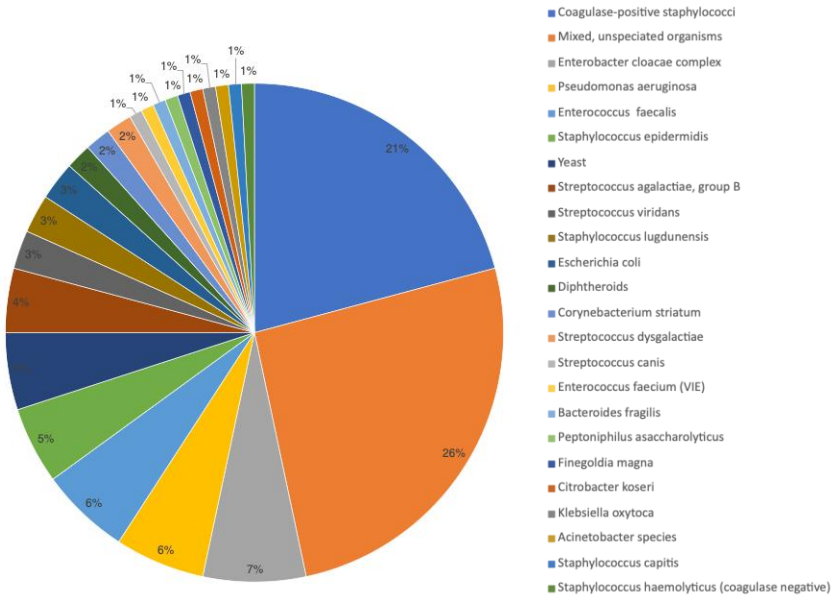
	infection within 90 days	infection after 90 days	p-value	odds ratio
# of patients	45	10		
polymicrobial infection (vs single bug)	62%	70%	0.731	0.7
gram positive	58%	80%	0.287	0.34
gram negative	40%	30%	0.724	1.56
anaerobes	16%	10%	1	1.65
coagulase positive staph (MSSA/MRSA)	56%	80%	0.284	0.3
mixed, unspeciated	31%	50%	0.288	0.44
yeast ("yeast" or "candida")	9%	0%	1	inf
Complete cefazolin susceptibility	24%	10%	0.43	2.9
received pre-op RT	80%	50%	0.101	4

Figure 1: Distribution of Cultured Organisms Across Infections (Pathogens Listed in Descending Order of

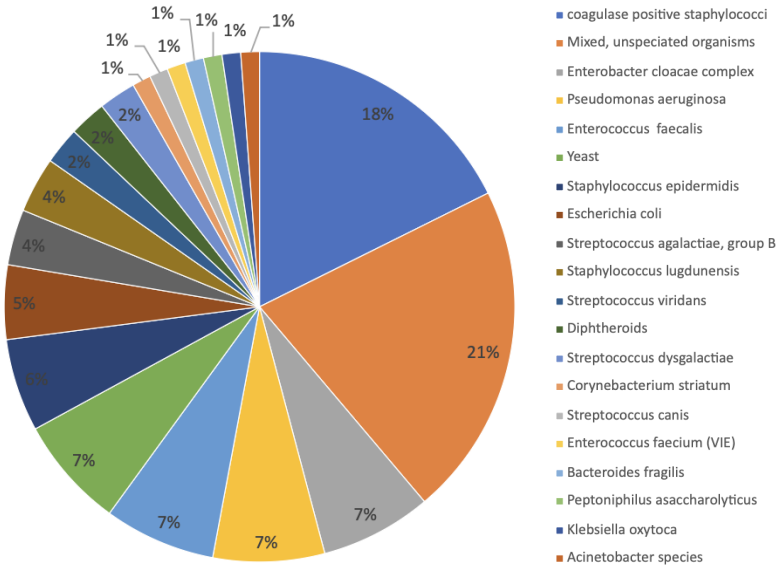
Frequency)

a) overall, b) irradiated tissue, c) non-irradiated tissue

a)



b)



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