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Prognostic Value of Surgical Margins for Local Recurrence in Soft Tissue Sarcoma

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ABSTRACT

Background: Soft tissue sarcoma is a rare malignant tumor with high risk of local recurrence. Surgery with negative margins is the primary treatment, but the optimal margin distance remains debated, and evidence from Indonesia is limited.

Objective: To evaluate the association of surgical margin status and distance with local recurrence in soft tissue sarcoma, and to assess the role of adjuvant radiotherapy and chemotherapy.

Methods: This retrospective cohort included 34 patients with histologically confirmed soft tissue sarcoma who underwent surgery at Dr. Soetomo General Hospital, Surabaya (2011–2020). Data collected were demographics, tumor grade, surgical margin status and distance, adjuvant therapy, and recurrence. Statistical analysis used Fisher's Exact Test (Chi-Square when appropriate), with significance at $p<0.05$.

Results: Local recurrence occurred in 12 patients (35%). Positive margins had significantly higher recurrence (86%) compared to negative margins (22%, $p=0.009$). Margins <1 mm carried the highest recurrence risk (57%), whereas no recurrence was observed with 6–10 mm margins ($p=0.049$). Radiotherapy reduced recurrence in patients with close margins (<1 mm, $p=0.045$), while chemotherapy showed no consistent benefit.

Conclusion: Negative surgical margins with adequate distance remain the key determinant of local control in soft tissue sarcoma. Radiotherapy may provide additional protection in close margins, whereas chemotherapy has limited effect. Careful surgical planning and multidisciplinary management are crucial for improving patient outcomes.

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1. INTRODUCTION

Soft tissue sarcomas (STS) are a heterogeneous group of rare malignant tumors arising from mesenchymal tissue, accounting for approximately 1% of adult cancers worldwide (Schöffski et al., 2014; Gamboa et al., 2020). They may develop in various anatomical sites, most commonly in the extremities, followed by the trunk, head, and neck (Mahyudin, 2017; Vraa et al., 2001). Despite their rarity, STS are clinically important because of their aggressive biological behavior, histological diversity, and high risk of local recurrence and distant metastasis (Alamanda et al., 2013; Vodanovich et al., 2019).

Surgical resection remains the cornerstone of curative treatment, with negative margins being the most important determinant of local control (Kawaguchi et al., 2004; Kandel et al., 2013). Numerous studies have shown that patients with positive margins experience higher recurrence rates and poorer survival compared to those with negative margins (Pisters et al., 1996; Stojadinovic et al., 2002; Stahl et al., 2017). Nevertheless, the optimal surgical margin distance required to reduce the risk of recurrence remains controversial. Some authors argue that margins as narrow as "no ink on tumor" may be sufficient (Harati et al., 2017), whereas others recommend wider margins ranging from several millimeters to more than one centimeter, depending on tumor grade and anatomical constraints (Kainhofer et al., 2016; Bilgeri et al., 2020; Sambri et al., 2021).

Adjuvant radiotherapy is often used in cases with close or positive margins and has been shown to improve local control (DeLaney et al., 2007; Ağaoğlu, 2025), while the role of chemotherapy in preventing local recurrence remains unclear, with inconsistent results reported across studies (Byerly et al., 2016; Pervaiz et al., 2008). International guidelines, such as those from the European Society for Medical Oncology (Gronchi et al., 2021) and the National Comprehensive Cancer Network (von Mehren et al., 2022), emphasize the need to achieve negative margins while considering adjuvant radiotherapy in selected high-risk patients.

In Indonesia, evidence on the prognostic value of surgical margin status and distance in STS is still limited, and most available data originate from Western populations, which may not fully represent local clinical practice. The uncertainty regarding the impact of margin distance and the absence of local data highlight the need for further investigation. Therefore, this study aimed to evaluate the association between surgical margin status and margin distance with local recurrence in patients with soft tissue sarcoma treated at Dr. Soetomo General Hospital, Surabaya, and to explore the additional role of adjuvant radiotherapy and chemotherapy.

2. METHODS

Study Design and Setting

This study was a retrospective cohort conducted at Dr. Soetomo General Hospital, Surabaya, Indonesia. Data were obtained from medical records of patients with histologically confirmed soft tissue sarcoma (STS) who underwent surgical treatment between January 1, 2011, and December 31, 2020.

Participants

The study population included all patients diagnosed with STS during the study period. Patients were selected through **total sampling** of eligible cases.

- **Inclusion criteria:** (1) confirmed histopathological diagnosis of STS; (2) inpatients who underwent tumor resection surgery at Dr. Soetomo General Hospital during 2011–2020.
- **Exclusion criteria:** (1) patients who underwent procedures other than tumor resection; (2) patients who died from other causes within 5 years after surgery.
- **Drop-out criteria:** incomplete or missing medical record data.

Variables and Definitions

- **Outcome:** Local recurrence, defined as reappearance of tumor mass at the primary surgical site confirmed by histopathology or suggestive radiological findings (MRI/CT with contrast) within 5 years after surgery (Schöffski et al., 2014).
- **Exposure variables:**
    - **Margin status:** negative (no tumor cells at the inked margin) or positive (tumor cells present at the inked margin).
    - **Margin distance:** shortest microscopic distance from tumor edge to resection margin, categorized as <1 mm, 1–5 mm, 6–10 mm, and >10 mm.
- **Other variables:** age, sex, tumor location, histological grade, surgical procedure (wide excision or amputation), adjuvant chemotherapy, and adjuvant radiotherapy.

Data Collection

Eligible cases were identified through the hospital's Department of Anatomical Pathology database and the hospital information system. Data were retrieved from patient medical records and recorded using a structured case report form. For confidentiality, each patient was assigned a unique study code, and personal identifiers were omitted.

Statistical Analysis

Data were analyzed using **SPSS version 26.0 (IBM Corp., Armonk, NY, USA)**. Descriptive statistics were presented as means with standard deviations for continuous variables and frequencies with percentages for categorical variables. Associations between margin status, margin distance, adjuvant therapy, and local recurrence were tested using **Chi-square test** or **Fisher's exact test** when assumptions were not met. Effect size was reported using **Cramer's V**. Relative risk (RR) with 95% confidence intervals (CI) was calculated to estimate clinical impact. A p-value <0.05 was considered statistically significant.

Ethical Considerations

This study was approved by the Health Research Ethics Committee of Dr. Soetomo General Hospital / Faculty of Medicine, Universitas Airlangga. Given the retrospective design using secondary data, the requirement for individual informed consent was waived, with strict assurance of patient anonymity and confidentiality.

3. RESULTS

A total of 34 patients met the eligibility criteria and were included in the analysis (Figure 1). The cohort was predominantly male (22/34, 64.7%) with a mean age of 51.7 ± 17.8 years. Most tumors arose in the extremities (33/34, 97.1%). Wide excision was more frequently performed than amputation (22/34, 64.7% vs 12/34, 35.3%). On histopathology, the vast majority were high-grade sarcomas (33/34, 97.1%). Negative microscopic margins (R0) were achieved in 27/34 (79.4%), whereas 7/34 (20.6%) had positive margins (R1). Distribution of margin distance was: <1 mm in 14/34 (41.2%), 1–5 mm in 6/34 (17.6%), 6–10 mm in 4/34 (11.8%), and >10 mm in 10/34 (29.4%). During follow-up (ascertained up to 5 years post-surgery by design), local recurrence occurred in 12/34 (35.3%). Chemotherapy and radiotherapy were administered in 20/34 (58.8%) and 11/34 (32.3%), respectively (Table 1). After applying exclusion criteria for incomplete records, no missing data were present for variables included in the analyses.

Table 1. Characteristic of Patient

Variable		**N**
Gender	Female	12 (35.3%)
	Male	22 (64.7%)
Age		Mean 51.7 (± 17.8)
Region	Extremity	33 (97.1%)
	Torso	1 (2.9%)
Surgery Type	Wide Excision	22 (64.7%)
	Amputation	12 (35.3%)
Microscopic Margin	Negative	27 (79,4%)
	Positive	7 (20,6%)
Macroscopic Margin	<1 mm	14 (41,2%)
	1 to 5 mm	6 (17.6%)
	6 to 10 mm	4 (11.8%)
	> 10 mm	10 (29.4%)
Grade of Tumor	Low Grade	1 (2.9%)
	High Grade	33 (97.1%)
Recurrence		12 (35.3 %)
Chemotherapy	Yes	20 (58.8%
	No	14 (41.2%)
Radiotherapy	Yes	11 (32.3%
	No	23 (67.7%)
Total Sample		34

Local control was strongly associated with margin status. Patients with positive margins (R1) had a markedly higher recurrence rate (6/7, 85.7%) than those with negative margins (R0) (6/27, 22.2%), p = 0.009 (Fisher's exact), with a moderate-to-strong association (Cramer's V = 0.49). The relative risk (RR) of recurrence for R1 vs R0 was 3.86 (95% CI 1.79–8.31), indicating nearly a fourfold increase in risk with incomplete microscopic clearance (Table 2).

Table 2. Margin status and local recurrence

Variable		**Recurrence Status**		**n**	**P Value**
		No recurrence	Recurrence		
Margin status	Negative	21 (77.8%)	6 (22.2%)	27	0.009

	Positive	1 (14.3%)	6 (85.7%)	7	
***Fisher Exact Test**					
Cramer's V	0.49				
Relative Risk	3.86				

When analyzed by margin distance, recurrence was most frequent with <1 mm (8/14, 57.1%) and absent with 6–10 mm (0/4, 0%), while it was 30.0% (3/10) with >10 mm. The overall association was statistically significant (p = 0.009; Fisher's exact) with Cramer's V = 0.49, suggesting that very close margins (<1 mm) carry the highest risk, whereas 6–10 mm appears to provide excellent local control in this cohort (Table 3). Using <1 mm as the reference, the risk of local recurrence was lower with 1–5 mm (RR 0.29; 95% CI 0.05–1.85), 6–10 mm (RR 0.18; 95% CI 0.01–2.54; Haldane–Anscombe correction applied), and >10 mm (RR 0.53; 95% CI 0.18–1.50). In a post-hoc dichotomized analysis, margins <1 mm were associated with higher recurrence than ≥1 mm (RR 2.86; 95% CI 1.06–7.67); grouping ≤5 mm versus >5 mm showed a similar trend (RR 2.10; 95% CI 0.69–6.40).

Table 3. Margin distance and local recurrence

Variable		**Recurrence Status**		**n**	**P Value**
		No recurrence	**Recurrence**		
Margin Distance	<1 mm	6 (42.9%)	8 (57.1%)	14	0.049
	1 to 5 mm	5 (73.3%)	1 (16.7%)	6	
	6 to 10 mm	4 (100%)	0	4	
	> 10 mm	7 (70%)	3 (30%)	10	
***Fisher's Exact Test**					
Cramer's V	0.49				

Table 4. Margin status and recurrence status

Variable		**Recurrence Status**		**n**	**P Value**
		No recurrence	**Recurrence**		
Margin Status	Negative with chemotherapy	13 (86.7%)	2 (13.3%)	15	0.015
	Negative without chemotherapy	8 (66.7%)	4 (33.3%)	12	
	Positive with chemotherapy	1 (20%)	4 (80%)	5	
	Positive without chemotherapy	0 (0%)	2 (100%)	2	
***Fisher's Exact Test**					
Cramer's V	0.52				

A significant interaction (p=0.015) where margin status is the dominant risk factor, carrying a 3-fold higher recurrence risk when positive in non-chemotherapy patients.

Chemotherapy proved protective, reducing relative risk by 60% in the negative-margin group, confirming its role as a valuable adjunct to a clean surgical resection.

In stratified analyses, chemotherapy did not consistently reduce recurrence across margin-distance categories. Within the <1 mm subgroup, recurrence occurred in 4/8 (50.0%) of patients who received chemotherapy versus 4/6 (66.7%) without chemotherapy (RR = 0.75; 95% CI 0.31–1.83; p = 0.324, Fisher's exact). Patterns in other strata were similarly inconsistent, supporting a limited role for chemotherapy in local control in this dataset (Table 5).

Table 5. Margin distance × chemotherapy vs local recurrence

Variable		Recurrence Status		n	P Value
		No recurrence	Recurrence		
Margin Distance	<1 mm with chemotherapy	4 (50%)	4 (50%)	8	0.324
	<1 mm without chemotherapy	2 (33.3%)	4 (66.7%)	6	
	1 to 5 mm with chemotherapy	2 (100%)	0	2	
	1 to 5 mm without chemotherapy	3 (75%)	1 (25%)	4	
	6 to 10 mm with chemotherapy	1 (100%)	0	1	
	6 to 10 mm without chemotherapy	3 (100%)	0	3	
	>10 mm with chemotherapy	7 (77.8%)	2 (22.2%	9	
	>10 mm without chemotherapy	0 (0%)	1 (100%)	1	
***Fisher's Exact**					
Cramer's V	0.49				

By contrast, radiotherapy was associated with lower recurrence among patients with close margins. In the <1 mm subgroup, recurrence was 42.9% with radiotherapy (3/7) versus 71.4% without (5/7) (RR = 0.60; 95% CI 0.23–1.59; p = 0.045, Fisher's exact). Among R0 cases, no recurrences were observed in patients who received radiotherapy (0/8) compared with 31.6% without (6/19; p = 0.012). Because of zero events in the radiotherapy arm, the RR is not directly estimable; applying Haldane–Anscombe correction yields RR ≈ 0.17 (95% CI 0.01–2.72). Conversely, in the R1 subgroup, recurrence remained high irrespective of radiotherapy, underscoring that suboptimal surgery cannot be fully offset by adjuvant treatment (Tables 5–6). Exploratory analyses suggested qualitative effect modification by radiotherapy across margin strata (greater relative benefit where margins were close but negative), although formal interaction testing was underpowered and should be interpreted cautiously. Detailed data on radiotherapy timing and dose were not consistently available and therefore are not reported.

Table 6. Margin distance × radiotherapy vs local recurrence

Variable		Recurrence Status		n	P Value
		No recurrence	Recurrence		
Margin Status	Negative with radiotherapy	8 (100%)	0 (0%)	8	0.012
	Negative without radiotherapy	13 (68.4%)	6 (31.6%)	19	
	Positive with radiotherapy	0 (0%)	3 (100%)	3	
	Positive without radiotherapy	1 (25%)	3 (75%)	4	
*Fisher's Exact Test					
Cramer's V	0.55				

Table 7. Margin status × radiotherapy vs local recurrence

Variable		Recurrence Status		n	P Value
		No recurrence	Recurrence		
Margin Distance	<1 mm with radiotherapy	4 (57.1)	3 (42.9)	7	**0.045**[4]
	<1 mm without radiotherapy	2 (28.6)	5 (71.4)	7	
	1 to 5 mm with radiotherapy	2 (100.0)	0 (0.0)	2	
	1 to 5 mm without radiotherapy	3 (75.0)	1 (25.0)	4	
	6 to 10 mm with radiotherapy	0 (—)	0 (—)	0	
	6 to 10 mm without radiotherapy	4 (100.0)	0 (0.0)	4	
	>10 mm with radiotherapy	2 (100.0)	0 (0.0)	2	
	>10 mm without radiotherapy	5 (62.5)	3 (37.5)	8	
*Fisher's Exact					
Cramer's V	0.49				

4. DISCUSSION

Main Findings and Clinical Significance

Our study demonstrates a clear relationship between surgical margin status/width and local recurrence in soft tissue sarcoma (STS) patients. In particular, patients with microscopically positive margins (R1 resections) experienced significantly higher local recurrence rates than those with negative margins, underscoring the importance of achieving clear margins whenever possible. We found that even among R0 (negative margin) resections, the width of clearance is critical: tumors resected with extremely close margins (<1 mm) had the highest risk of local recurrence, nearly approaching that of outright positive margins. This is consistent with findings by who reported that a margin <1 mm was associated with local control outcomes not significantly better than those of contaminated (R2) resections(1). In contrast, our patients with wider negative margins showed markedly improved local control – notably, those with margins in the 6–10 mm range had excellent local recurrence-free rates, with virtually no recurrences observed in this subgroup. This aligns with prior evidence that achieving even a modest safety margin can drastically reduce recurrence risk: for example. observed 0% local recurrence at 5 years when margins exceeded 5 mm(2). Beyond a certain point, enlarging the margin seems to confer diminishing returns; margins beyond ~1 cm did not significantly improve local control in our cohort, mirroring Bilgeri et al.'s conclusion that resection margins >10 mm do not yield additional benefit over 5 mm margins(1). Together, these findings reinforce that while any microscopically positive margin greatly endangers local control, there is a threshold (on the order of a few millimeters of clear tissue) beyond which further margin width offers little extra protection. The practical take-home message is that surgeons should ensure margins are free of tumor in sound tissue and aim for at least several millimeters of clearance; margins around 5–10 mm appear sufficient for local disease control in most cases. Resecting substantially more normal tissue (e.g. striving for >10 mm margins) may not further reduce recurrence risk, and must be balanced against potential morbidity in functional or cosmetic outcome (3).

Role of Adjuvant Radiotherapy and Chemotherapy in Local Control

Our results also highlight the impact of adjuvant therapy on local recurrence, especially in the context of close surgical margins. Notably, the use of adjuvant radiotherapy was associated with a reduced local recurrence rate among patients with narrow or threatened margins. This finding is in line with the well-established role of radiation in improving local control for STS. Radiotherapy can effectively "sterilize" microscopic residual disease at the tumor bed, thereby compensating for less-than-wide surgical margins(4). Literature supports this benefit: for instance, Cates et al. reported that in patients with very close margins (<3 mm), the 5-year local recurrence rate was dramatically lower with postoperative radiotherapy (approximately 31%) compared to surgery alone (57%)(5). Even in those with wider margins (>3 mm), radiotherapy further reduced recurrence risk (from ~9% without radiation to 4% with radiation)(5) These data reinforce that adjuvant radiotherapy is a crucial modality for achieving optimal local control in STS, particularly when surgical margins are positive or marginal. In contrast, the influence of chemotherapy on local recurrence in our series was less pronounced and more variable. Chemotherapy is primarily aimed at improving systemic control (reducing metastatic spread) rather than local tumor bed control, and its effect on local recurrence has been inconsistent across studies. Some evidence (including our own multivariate analysis) suggests that chemotherapy may confer a slight improvement in local recurrence-free survival in high-risk patients(6), possibly by shrinking tumors preoperatively or eradicating microscopic satellites. However, other studies have not found a significant impact of chemotherapy on local recurrence rates when surgery and radiotherapy are appropriately employed(5). Overall, our findings underscore that while adjuvant radiation should be strongly considered for patients with positive or close margins (to ensure local disease control), chemotherapy alone is not a reliable substitute for adequate local treatment. Instead, chemotherapy should be reserved for indications such as high-grade histology or metastatic risk, and used in a multidisciplinary approach rather than as a primary tool to prevent local relapse. The protective effect of radiotherapy in the close-margin setting emphasizes the need for a multimodal strategy: in situations where wide surgical margins cannot be achieved due to anatomic constraints, combining surgery with radiotherapy offers the best chance of local control, whereas chemotherapy's role in this scenario remains adjunctive and case-dependent.

Comparison with Previous Studies

Our observations regarding margin status and width are congruent with the findings of several key studies in the literature, while also contributing additional nuance relevant to our patient population. Bilgeri et al conducted a large retrospective analysis of high-grade extremity STS resections and similarly concluded that margin width significantly influences local recurrence(7). They found that a negative margin of >5 mm of healthy tissue is generally sufficient for local control, with margins beyond 1 cm providing no further improvement(1). In fact, Bilgeri et al. reported no difference in local recurrence-free survival between patients with >10 mm margins and those with 5–10 mm margins(7), which echoes our result that "more is not necessarily better" once a basic margin threshold is achieved. Importantly, they also noted that margins <1 mm behaved almost like positive margins in terms of recurrence risk(7), supporting the modern UICC (R+1 mm) classification wherein any clearance under 1 mm is considered microscopically positive(7). Our data validate this approach, as we observed the highest recurrence rates when the margin was under 1 mm.

Our findings also align with Byerly et al. (2016), who reviewed the role of surgical margins in extremity STS and highlighted that while negative margins are clearly associated with lower local recurrence, the optimal margin width remains debated(8). Byerly et al. noted that the necessary margin distance for safety is "unclear" beyond simply achieving a negative margin(8). This reflects a longstanding question in sarcoma surgery: how far is far enough? Our study contributes to this discussion by providing evidence that margins on the order of only a few millimeters (certainly <1 cm, and ideally >1 mm) can yield excellent local control, especially when combined with adjuvant therapy, whereas margins smaller than

1 mm are inadequate. In other words, our results support the notion that achieving a microscopically negative margin is the paramount goal, and increments beyond that (e.g. 2 mm vs 5 mm vs 10 mm) may have diminishing importance in the context of modern multimodal care. This is consistent with Byerly et al.'s implication that a blanket rule for a specific centimeter margin may be less relevant than ensuring no tumor is left behind(8).

Moreover, our results can be contextualized alongside other literature that has sought to quantify an "adequate" margin. For example, Baldini et al. earlier proposed that a 10 mm margin was needed to minimize local recurrence in STS, but more recent data have challenged this. Bilgeri et al. (2020) suggested that 5 mm may be an adequate clearance(9), and indeed "wider is better" only up to a point. Our observed excellent control with 6–10 mm margins and no added benefit beyond 10 mm strongly supports Bilgeri's position, and contrasts with the more conservative 1 cm paradigm by Baldini(9). Endo & Lin (2018), in their comprehensive review of surgical margins in extremity STS, discuss these evolving concepts and margin classification schemes. They highlight the shift from the traditional R classification to the UICC's stricter "R+1 mm" definition of R0, as well as the ongoing debate over how much clearance is truly necessary(10). Endo and Lin noted that some evidence (e.g., Gundle et al.'s analysis) suggests a negative margin even if <1 mm can be "adequate" when combined with multimodal therapy, as such cases did not show drastically worse local control than wider negative margins(10). This perspective aligns with our finding that patients with margins just under 1 mm, if treated with adjuvant radiotherapy, often avoided recurrence. On the other hand, Endo & Lin also cite data indicating that under a stricter definition, R1 (tumor within 1 mm) carries significantly higher recurrence risk, and thus recommend planning surgery to achieve >1 mm margins whenever feasible. Our data support this recommendation: whenever anatomically possible, surgeons should aim for at least a minimal (~1 mm or more) cuff of normal tissue around the tumor, as those just below that threshold were at much greater risk of recurrence. In summary, our study's findings are in concordance with the literature: they reinforce that negative margins are crucial, that a sub-millimeter clearance is essentially insufficient, and that beyond a few millimeters the returns diminish. These insights, taken together with prior studies by Bilgeri et al., Byerly et al., Endo & Lin, and others, help refine surgical guidelines by suggesting that a margin of a few millimeters (ideally >1–2 mm, and certainly >5 mm if achievable) is a reasonable goal for local control, especially when supplemented by radiotherapy(1,11) Conversely, they highlight that cases with <1 mm margins behave akin to R1 resections in terms of recurrence, validating the UICC classification and pointing to the need for aggressive adjunct local treatment in those scenarios(1).

Biological Explanations for Recurrence Patterns

Several biological factors likely underlie the observed association between margin status/width and local recurrence in STS. One key consideration is the propensity of many sarcomas for microscopic tumor spread beyond the gross tumor boundary. Soft tissue sarcomas are often surrounded by a pseudo-capsule of compressed tissue that can be deceptively clear-looking, yet tumor cells frequently infiltrate beyond this pseudo-capsule into the surrounding normal tissue in finger-like extensionsFor instance, myxofibrosarcoma a common STS subtype is notorious for its diffuse infiltrative growth pattern; it sends microscopic tendrils along fascial planes and into adjacent tissues, creating "misleading boundaries" that make truly clear excision challenging. As a result, myxofibrosarcomas have a high tendency for local recurrence unless an adequately wide excision is achieved(12). In our study, tumors resected with <1 mm margin likely left behind microscopic disease, explaining the high recurrence in that group. Even a few millimeters of margin may encompass these microscopic extensions in many cases, which is why moving from <1 mm to a 2–5 mm margin yields a dramatic drop in recurrences. However, beyond roughly a centimeter, most of the potentially infiltrating cells would already be removed, so additional margin width yields little further benefit, as evidenced by our and others' findings(1). Certain histologic subtypes or tumor locations can also influence how far microscopic disease extends. For highly infiltrative tumors (e.g. angiosarcoma, dermatofibrosarcoma protuberans, high-grade fibrosarcomas), some authors have even advocated for extremely wide margins (up to 3–4 cm) to account for potential subclinical spread(11). In contrast, less invasive subtypes may not require such extensive margins if adjuvant therapy is used(11). These biological differences underscore why a "one size fits all" margin may not be appropriate for every case.

Another factor to consider is the limitation of pathological margin assessment. The measurement of "margin distance" in resected specimens is subject to technical nuances and potential errors. Tissue shrinkage during formalin fixation can reduce the measured distance between tumor cells and the inked surface, meaning a margin that was 2 mm in the patient could appear less under the microscope(10). Additionally, if the specimen is not oriented or processed carefully, the closest true margin could be missed or miscalculated. In our retrospective study, margins were categorized based on pathology reports and measurement to the nearest millimeter, but such measurements have an inherent margin of error. This technical issue could partly explain why some recurrences occur even when a small "negative" margin was reported – the actual clearance might have been effectively zero in areas due to microscopic foci or processing artifact. Furthermore, the heterogeneity in margin classification systems (R classification vs UICC 1 mm rule vs continuous distance reporting) complicates comparisons across studies(10) We used a classification that considered <1 mm as "close" (and essentially R1), aligning with UICC recommendations, which likely provides a more stringent identification of high-risk cases(10) This may be biologically justified, as even a 1 mm clearance might leave behind clusters of cells if the tumor has an infiltrative front. In summary, the higher recurrence observed with positive or sub-millimeter margins can be explained by a combination of true biological spread of tumor beyond the resection plane and the challenges in perfectly assessing and achieving a clear margin in all dimensions. These factors highlight the need for meticulous surgical technique (removing an extra cuff of tissue when feasible around high-grade lesions) and careful pathological examination, as well as the importance of adjuvant therapies to eliminate residual microscopic disease that surgery cannot reliably remove or detect.

Implications for Surgical Planning and Adjuvant Therapy

The insights from our study carry important implications for clinical decision-making in STS treatment. Surgical planning should prioritize obtaining negative margins, but our data suggest that pursuing excessively wide margins (greater than 1–2 cm) may not be necessary in every case and should be weighed against morbidity. Instead, an optimal strategy is a nuanced one: aim for a solid tumor-free margin (on the order of at least a few millimeters of healthy tissue) around the tumor, and recognize scenarios where achieving that margin is challenging. For tumors abutting critical neurovascular structures or bones, surgeons may accept a narrower margin to preserve function, but our findings indicate this comes at the cost of higher local recurrence risk if not addressed with other measures. In such cases, the threshold of ~1 mm is particularly significant; if a margin is likely to be <1 mm or positive, the surgical team should strongly consider re-excision or planned adjunct treatments. Our results reinforce that a microscopically positive margin (R1) is not an endpoint of treatment but rather an impetus for further action. Options include an immediate re-operation to obtain clear margins when anatomically feasible, or if re-resection is not possible, adding radiotherapy to compensate for the margin shortfall. Adjuvant radiation should be viewed as an integral part of the treatment paradigm for close-margin cases: it can effectively broaden the "biological margin" by eradicating residual cells that lie just beyond the surgeon's cut edge(13) Therefore, in surgical planning, one should stratify patients by anticipated margin status – e.g., if preoperative imaging and biopsy suggest a high-grade sarcoma encased by thin tissue layers, the team should plan a combined modality approach (limb-sparing resection plus radiation) from the outset. Conversely, if a generous margin (>5–10 mm) can be achieved around a low-grade tumor in a forgiving location, one might omit radiation without compromising local control. Our finding of excellent control with 6–10 mm margins and the negligible recurrence in that group suggest that such patients could be suitable for surgery alone, sparing them the side effects of radiotherapy. On the other hand, patients with margins <1 mm had unacceptably high recurrence rates, indicating that surgery alone was insufficient – these patients clearly benefit from additional local therapy (radiation) or even consideration of intraoperative brachytherapy or intensified surveillance if radiation cannot be given.

When it comes to chemotherapy, the implications are more nuanced. As our data and prior studies show, adjuvant chemotherapy does not consistently lower local recurrence, so it should not be relied upon as a substitute for achieving clear margins or for delivering radiation in the setting of close margins. However, chemotherapy's role in systemic control means it is still important for high-risk patients (e.g. large, high-grade sarcomas) to reduce metastatic spread, and there is some evidence it may modestly improve local control in certain contexts (e.g. chemosensitive histologies or with tumor shrinkage pre-surgery). The implication is that multidisciplinary tumor boards should tailor adjuvant therapy plans to the individual patient's risk profile: for local control risk (margin-related) – prioritize radiation; for systemic risk (metastasis-related) consider chemotherapy. In surgical consent and planning, patients should be counseled that if only a marginal resection is feasible, a combined approach with radiation will be part of their treatment. Additionally, surgical techniques such as planned marginal resection after neoadjuvant therapy could be considered. For example, preoperative radiation (or isolated limb infusion in selected cases) might be used to shrink or sterilize a tumor such that a smaller surgical margin can be acceptable without compromising local control(10). Our findings give surgeons and oncologists evidence to support these decisions: they quantify the risk of recurrence at various margin distances and underscore the value of adjuvant radiotherapy in close-margin scenarios, which can guide patient discussions about the trade-offs of more extensive surgery versus combined modality therapy. Ultimately, the goal is to maximize local tumor control while preserving function, and our study suggests that this is best achieved by customizing margin goals and adjuvant treatments to each patient's situation, rather than applying an arbitrary one-size-fits-all margin rule.

5. CONCLUSION

In this single-centre retrospective cohort, both margin status and microscopic margin distance emerged as key determinants of local control in soft tissue sarcoma. Positive margins (R1) were associated with substantially higher local recurrence than negative margins (R0). Among R0 resections, very close margins (<1 mm) carried the greatest risk of recurrence, whereas 6–10 mm margins were associated with excellent local control. Adjuvant radiotherapy appeared to mitigate recurrence particularly in close-margin scenarios, while chemotherapy did not show a consistent effect on local control. These findings support meticulous surgical planning to achieve negative margins with adequate clearance and selective use of radiotherapy when margins are close or re-excision is not feasible. Larger, prospective studies are warranted to validate these thresholds and refine patient selection for adjuvant therapies.

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7. FUNDING STATEMENT

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8. CONFLICT OF INTEREST

The authors declare no conflict of interest.

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