Soft Tissue Sarcomas Margin Assessment

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Many classifications to assess margins status for soft tissue sarcomas are reported in the literature. Most of the series are heterogeneous and variable in size, making it difficult to compare results from study to study.

margins soft tissue sarcoma classification infiltrative local recurrence

1. Introduction

Surgical excision with a broad margin of the surrounding normal tissue is the mainstay of treatment for localized soft tissue sarcomas (STS) [1][2], in order to minimize the risk of local recurrence (LR). Current guidelines recommend complete resection of STS with a negative surgical margin, without a specific recommendation for the width of that margin or a standard definition of a negative margin [3]. Due to their rarity and heterogeneity, most studies regarding treatment outcomes in STS included all histologic grades and histologies (infiltrative and non-infiltrative subtypes) [4], leading to general outcomes, which are intricate to use in a clinical setting. An adequate margin must take into consideration both the margin width (quantity) and the type of anatomic barrier (quality) [5]. There are several classification schemes for reporting surgical resection margin status for STS (Table 1).

Table 1. Classifications of margins in soft tissue sarcomas.

Classification	MSTS [6]	AJCC [7]	UICC [8]	Tumor Clearance [2]	TMCC [9]	Margin Quality [6]
Description	Radical: all normal tissue involved anatomic compartment excised en-bloc	R0: tumor does not reach intact barrier or resection margins	R0: resection margin >1 mm	Metric distance from edge of tumor to inked surgical resection margin	Negative margins: tumor does not reach intact barrier or resection margins	Anatomic factors (the tissue composition of the margin)
-	Wide: histologically non-reactive normal tissue at margin	R1: Microscopic tumor contamination of margins or resection	R1: Resection margin < 1 mm	-	Unplanned positive margins	-

Classification	MSTS [6]	AJCC [7]	UICC [8]	Tumor Clearance [2]	TMCC [9]	Margin Quality [6]
		alongside pseudocapsule				
-	Marginal: pseudocapsule present at margin	R2: Macroscopic tumor contamination	R2: Macroscopic tumor contamination	-	Planned close but with an ultimately positive microscopic margin along a critical structure	-
-	Intralesional: Tumor present at margin	-	-	-	Positive margin after a tumor bed re-excision in patients treated initially with inadequate surgery elsewhere (“whoops procedure”)	-

AJCC: American Joint Committee on Cancer (R classification); MSTS: Muscoloskeletal Tumor Society; UICC: Union Against cancer; TMCC: Toronto Margin Context Classification.

If the tumor is resected with a broad margin, a variety of tissues may exist between the resection margin and tumor. Anatomic factors such as the tissue composition of the margin may impact the appropriateness of margin [6][9], with dense regular connective tissue assumed to provide a more robust anatomic barrier to tumor cell infiltration. However, the significance of margin quality has been investigated rarely, so the efficacy of these structures as a barrier is still debated.

2. Margins and Imaging

Modern imaging facilitates successful functional limb salvage, often with margins that would be classified as marginal in the Enneking system [10]. Precisely this distinction is important in the light of sparing as much tissue as possible for preferable functional outcomes [11]. Magnetic resonance imaging (MRI) is the imaging tool most sensitive and accurate to assess margins in STS. On conventional MRI, there are several recognized features related to margins infiltration and subsequent increased risk of LR after surgical excision.

Recent technical development of imaging analyses and the increasing request for evidence-based medicine, led to a greater use of quantitative imaging. One of the most promising tool is radiomics: it is a quantitative tool applicable to imaging, which aims at enhancing the existing data by means of advanced mathematical analysis. Through mathematical extraction of the spatial distribution of signal intensities and pixel interrelationships, this tool quantifies textural data by using analysis methods from the field of artificial intelligence [12].

3. Margins Assessment

A recent consensus practice guideline remarked that “no available evidence-based data addressed how to adequately assess margins” [3]. Pathologists assess surgical resection margins by submitting more sections from margins that are close or concerning on gross inspection. However, careful gross assessment of surgical resection margins can be misleading. Therefore, microscopic examination of six to eight perpendicular sections in total from all margins <2 cm in width is a practical compromise and a reasonable recommendation [13].

4. Comparison between Classifications

Gundle et al. [14] by direct comparison of three schemes (R, R+1 and TMCC classifications) concluded that the traditional R classification best determined the risk of LR, but TMCC provides additional stratification of positive margins that may aid in the surgical planning. Kainhofer et al. [15] compared different classifications of resection margins (R and R+1 classifications) on LR and found out that margin status according to both classifications was a significant prognostic factor for LR. However, they observed that a R0 margin determined by the UICC classification is a better discriminator for LR than R0 resections according to the R classification. A higher percentage of positive resection margins naturally results by applying the stricter definition of the UICC classification [15]. This indicates that R1 resections as defined by the UICC-classification pick out more patients with high risk of LR than R1 resections according to the R-classification would do.

5. Margins Width

Most of the series observed that tumor resection with a gross positive margin are accompanied by unacceptably high rates of LR [16][17][18][19]. However, a solely positive or negative status of a margin, as clear but close margins and broader margins should not be considered equal in their risk to the patient [20]. The real question is what constitutes an “optimal” margin?

Adequate margin has been described in several ways, ranging from adjectives like a radical, wide, or close [6] until negative (>0 mm) margin [52,57], up to 3 cm [53,58], or even 5 cm [53].

Two different series reported that a minimum 5 mm margin is adequate if no adjuvant radiation therapy (RT) is administered, but it can be reduced to 1 mm with post-operative RT [13][21]. Sadoski et al. [22], as well as many other series [9][10][23][24][25][26][22], suggested that patients who have microscopic positive margins have lower rates of LR

as long as the surgical excision is coupled with adjuvant RT. On the other hand, another series [23] observed that positive margins were associated with lower local control despite the utilization of adjuvant RT, suggesting negative margins remains a primary objective for all treatment options.

6. Margins in Specific STS Histotypes

Specific STS subtypes such as myxofibrosarcoma (MFS) and undifferentiated pleomorphic sarcoma (UPS) frequently present with an infiltrative growth pattern [27][28][29][30][31][32]. They have an increased likelihood of LR irrespective of the surgical margins [33]. Therefore, it is crucial to analyze the entities separately and to assess the prognostic significance of treatment-related factors for every histologic subset specifically. A resection margin of 2 cm away from the end of the radiological tumor infiltration would be the ideal margin because the vast majority of cases could achieve broad histological in infiltrative sarcomas resection seems to be overstated. Nevertheless, such a broader resection can increase the demand for plastic reconstruction surgery, risk of wound complication, and functional deterioration.

7. Conclusions

Most of the studies regarding treatment outcomes in STS included all histologic grades and histologies (infiltrative and non-infiltrative subtypes) [4][34][35] and are very heterogeneous in terms of both histologic characteristics and treatment modalities (adjuvant treatments or not). This lack of consistency as well as very variable sample size between studies, makes it difficult to compare study results. Therefore, there is a great need for evidence-based standardization concerning the width of resection margins. None of the reported classifications is completely reliable for predicting the risk of recurrence.

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