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A system describing surgical field extension associated with flap reconstruction after resection of a superficial malignant soft tissue tumor.

Thank you very much for your email and the reviewers' comments regarding our manuscript. I have revised our manuscript by incorporating the reviewers' suggestions.

*Reviewer #1's comment*

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** The authors have proposed a very interesting classification system for understanding whether the operative field was extended due to reconstruction as it is necessary to include that area for evaluation during the follow up to look for recurrence. I have following comments regarding the manuscript: 1. In the Discussion section, please compare the proposed classification with the existing classifications reported in the literature. 2. Please mention the study limitations in the Discussion section.

***Response:***

I have added a discussion associated with the classification and limitations.

## **Added manuscript: Introduction**

The current Cancer Staging Manual of the American Joint Committee on Cancer (AJCC) of soft tissue sarcoma is widely used based upon tumor size, histologic grade, and the presence of metastasis<sup>[6]</sup>. The American Joint Committee on Cancer (AJCC) supports the *R classification*, which categorizes surgical margins as negative (R0), microscopically positive (R1), or grossly positive (R2)<sup>[7, 8]</sup>.

## **Added manuscript: Discussion**

The AJCC Staging of Soft Tissue Sarcomas (eighth edition) is based upon the tumor size, histologic grade, and the presence of metastasis. Tumor size is classified into four categories with border values of 5, 10, and 15 cm. The notation regarding tumor depth (superficial or deep from the superficial fascia) has been eliminated from the seventh edition of the AJCC Staging of Soft Tissue Sarcomas<sup>[6]</sup>. The surgical staging of musculoskeletal sarcomas has 4 types of surgical margins (intralesional, marginal, wide, and radical [compartmental]), as proposed by Enneking et al.<sup>[16]</sup>. A 2-3 cm surgical margin provides reasonable local control of soft tissue sarcomas<sup>[17]</sup>. The AJCC supports the R classification, which categorizes margins as negative (R0), microscopically positive (R1), or grossly positive (R2)<sup>[7, 8]</sup>. Furthermore, the Union Against Cancer (UICC) proposed a R + 1 mm classification that requires 1 mm of healthy tissue between the tumor and margin to define a negative margin (R0)<sup>[18, 19]</sup>, thus resulting in more resections being considered microscopically positive (R1). Radiation therapy can be performed as adjuvant therapy, especially if cancer cells remain after the resection. Radiation has a role in reducing the risk of recurrence in soft tissue sarcoma resection<sup>[5]</sup>. The term, tumor bed, refers to the area of tissue remaining after a malignant tumor is removed. The tumor bed may have cancer cells<sup>[5]</sup>. Recognition of tumor bed extension is necessary for postoperative radiation. Without flap reconstruction following soft tissue sarcoma resection, the tumor bed can largely be predicted with the preoperative staging based upon the images and the histologic findings. With flap reconstruction, tumor bed prediction is difficult without the surgical method information. Indeed, the new grading system can give information of surgical field extension associated with flap reconstruction.

There are several limitations in the new grading system. First, this classification is completely new and still theoretical. Clinical use of the assembled clinical data would be necessary, and some modification may be required for improvement. Second, the new

grading system was used for superficial soft tissue sarcomas resected in the extremities and fascio-(musculo)-cutaneous flaps, in which hands and feet were not included. The new grading system might be modified for any part of bones and soft tissue sarcomas. Third, flap type description is not strictly defined in the new grading system, which may result in ambiguity; however, according to the flap technique improvement, description of the flap would be diverse. Therefore, no flap description restrictions were used in the new grading system. Finally, the new grading system cannot describe the length or area required for postoperative radiation. Excessive information in the grading system, however, would make the new grading system difficult for clinical use.

#### ***Science editor's comment***

The manuscript has been peer-reviewed, and it is ready for the first decision.

#### ***Response:***

I have amended the manuscript for improvement.

#### ***Company editor-in-chief's comment***

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, please provide and upload the following important documents: Biostatistics Review Certificate, a statement affirming that the statistical review of the study was performed by a biomedical statistician; Institutional Review Board Approval Form or Document, the primary version (PDF) of the Institutional Review Board's official approval, prepared in the official language of the authors' country; Signed Informed Consent Form(s) or Document(s), the primary version (PDF) of the Informed Consent Form that has been signed by all subjects and investigators of

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***Response:***

We have amended the entire document to answer the queries. Specifically, ARTICLE HIGHLIGHTS were added.

**ARTICLE HIGHLIGHTS**

**Research background**

Flap reconstruction can extend the surgical field or tumor bed because of flap elevation or dissection of recipient vessels during resection of superficial soft tissue sarcomas. There is currently no method describing extension of the surgical field.

**Research motivation**

Extension of the surgical field cannot be predicted based on preoperative images for flap reconstruction after superficial soft tissue sarcoma resection. Knowledge of the surgical field extension is important information for evaluation of recurrence images or possible

postoperative radiation.

### **Research objectives**

A theoretical CD-grading system was developed consisting of C and D values in the surgical field extension. The C-value represents the flap beyond the nearby large joint and the D-value pertains to a deeper extension.

### **Research methods**

C1/D1 and C0/D0 are positive and negative values, respectively. With a known location, C values are "p" (proximal), "d" (distal), and "b" (in the tumor bed). The description method is as follows: flap type, CxDx [x=0, 1, p, d or b].

### **Research results**

Classification and possible values are shown in the tables (transpositional fascial flap/propeller, pedicled, and free flaps). Four representative patients with subcutaneous sarcomas who underwent reconstruction using fasciocutaneous flaps are presented.

### **Research conclusions**

The new grading system can give values for tumor bed extension after flap reconstruction following superficial soft tissue sarcoma resection. The description of whether or not the operative field has been extended due to reconstruction is thought to be important information for evaluation of recurrence images.

### **Research perspectives**

Clinical use of assembled clinical data would be necessary and some modification may be required for improvement, especially if the new grading system is modified for any part of bone and soft tissue sarcomas.