Indications of Microsurgery in Soft Tissue Sarcomas

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Abstract

Sarcomas are uncommon tumors and free-margin surgical resection remains the single most important treatment in the curative therapy of soft tissue sarcomas. Refinements in surgical techniques have led to increased function preservation and limb salvage.

Patients and Methods The records of patients ($n = 41$) who underwent microsurgical soft tissue reconstruction subsequent to resection of soft tissue sarcoma during the period 1998 to 2010 were reviewed and compared with a general nonmicrosurgery group ($n = 188$) in relation to clinicopathological characteristics, surgical procedures, postoperative complications, time until start of adjuvant radiation, functional outcome (Toronto Extremity Salvage Score, TESS), local recurrence, free survival, and disease-specific survival.

Results Forty-one patients (age range: 23 to 95 years) received a total of 42 free flaps. When compared with the general nonmicrosurgery group, these patients presented significant differences with regard to location, histological grade, and neoadjuvant treatments. Complications were encountered in 10 cases, including 3 patients with complete flap loss and 1 patient with partial flap loss; other complications were cervical fistulae, knee arthritis, nonconsolidation, and wound infection. Extremity salvage was achieved in 90% (19/21) of limb sarcomas, with these patients showing adequate postoperative ambulation (TESS 77 $\pm$ 16) and adequate use of the upper extremity (TESS 66 $\pm$ 26). Two patients underwent amputation after recurrence. Disease-specific survival rates at 5 and 10 years were 79.49% and 76.93%, respectively.

Conclusion The microsurgical repair of sarcoma defects is a reliable option that, though not free of complications, is necessary in selected cases such as patients receiving neoadjuvant treatments and those with head and neck location and high-grade tumors. The procedure enables both adequate oncosurgical resection and function preservation. Our microsurgical sarcoma reconstruction data, based on an observation period of 12 years and presenting the results of 42 free tissue transfers in 41 patients, adds further evidence to the previously published smaller series.

Keywords
- sarcoma surgery
- free tissue repair
- microsurgery sarcoma

Sarcomas are uncommon tumors (1% of all malignancies), of which 80% originate in soft tissue and the other 20% in bone. The current management of sarcomas is multidisciplinary and includes surgery, radiation, and chemotherapy. However, surgery remains the key component of therapy.[1–3]

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With the development of microsurgery, modern surgical approaches to soft tissue sarcoma resection have moved away from amputation and compartmental excisions toward both radical and function-maintaining resection. This surgical evolution has been followed by the use of free tissue transfer providing stable soft tissue coverage, vascularized bone, and functioning muscle replacement.[1,4,5] Limb salvage has thus become the standard treatment for extremity sarcomas, as it has been shown to achieve survival rates equivalent to those associated with amputation.

Free tissue transfer has numerous advantages over primary wound closure.[6] It allows radical oncosurgical resections and provides adequate defect coverage, together with preservation of function and aesthetics. The use of free tissue transfer also reduces wound complications and enables fast reconstruction of function and form without delaying adjuvant therapy and rehabilitation.[4,5]

This study analyzes our results with respect to free flap coverage.

Patients and Methods

The records of 229 patients who had undergone surgical therapy for soft tissue sarcoma with curative intent in the Department of Plastic Surgery (Bellvitge University Hospital) were reviewed. Patients who underwent a microsurgical reconstructive procedure were analyzed in detail (for the period 1998 to 2010).

The inclusion criterion was soft tissue free flap coverage after sarcoma resection. Primary reconstruction was performed in all patients, with the oncological procedure being followed by free flap coverage during the same surgical event. All surgical procedures were performed and/or supervised by the same senior oncological and reconstructive surgeon (J. M. V. V) from the Department of Plastic and Reconstructive Surgery of the Bellvitge University Hospital. All patients were treated by the multidisciplinary medical team within the Sarcoma Unit.

The methodology involved analyzing the clinicopathological characteristics, free flap type, surgical complications, and functional outcomes of all patients. The oncological features analyzed were oncosurgical procedure, adjuvant therapy, time to the start of adjuvant radiotherapy, and disease-specific survival.

Complications were defined as flap loss (partial/total), dehiscence, wound infection, arthritis, late bone consolidation, and cervical fistulae.

Functional outcome was evaluated by the Toronto Extremity Salvage Score (TESS), but only in patients with extremity sarcoma.[7]

A descriptive analysis of the series was conducted according to central trend measurements (mean, median) or dispersion (standard deviation [SD], interquartile range), in accordance with the normal distribution of quantitative variables (Kolmogorov-Smirnov test). Qualitative and quantitative variables were compared by means of the Chi-square test or Student's *t*-test, with statistical significance being set at $p < 0.05$.

Disease-specific survival was analyzed using the Kaplan-Meier method.

Clinical Handling

In the majority of cases, diagnosis was based on histological findings, ultrasound, or computed tomography (CT)–guided core-needle biopsy. Our pathologists reviewed the histology of patients sent from and diagnosed in other centres.[8]

The surgical strategy followed was based on local radical surgery in conjunction with adjuvant radiotherapy and chemotherapy, avoiding amputations and compartmental resections of the extremities whenever possible.[8] Exeresis with minimum margins of 2 cm was always performed when localization and size permitted.[9] Important aspects of the sarcoma surgery, which are generally accepted, involved avoiding tumor expression, making early proximal venous ligatures, performing the acute dissection with an electrical scalpel, planning the incisions by following the axes of the limbs, and eliminating the biopsy routes and tissues that were possibly contaminated by previous surgery.

As regards reconstructive surgery, the basic principles were to undertake primary reconstruction so as to ensure maximum radicality, avoiding limb amputations, and to give adequate coverage to structures such as bone, joints, nerves, vessels, and tendons, avoiding dead spaces, poorly vascularized tissues, and closures under pressure. In cases requiring complex reconstructions, the approach involved working in two teams simultaneously. Special care was always taken to avoid mixing anything in the fields of tumor resection and flap preparation.

The criteria for adjuvant treatment were decided by consensus of the Sarcoma Committee and based on the unit's specific protocol.

Results

Patients and Tumors

Nineteen female and 22 male patients ranging in age from 23 to 95 years (mean: 57 years) were included in the study. The most common histological diagnoses were pleomorphic sarcoma and fibrosarcoma (►**Table 1**). All patients underwent primary reconstruction with free tissue transfers at the time

Table 1 Pathologic Diagnosis

Histological Classification	Cases (N)
Pleomorphic sarcoma	7
Fibrosarcoma	7
Leiomyosarcoma	5
Malignant peripheral nerve shealt tumor	5
Angiosarcoma	4
Extraesqueletal osteosarcoma	3
Others	10

Table 2 Clinicopathological Characteristics

Anatomical location	Microsurgical Group		Non-Microsurgical Group		*p* Value 0.0003694
	N	%	N	%	
Pelvis-lower limb	13	31,7	92	48.4	
Shoulder-upper limb	8	19.5	46	24.5	
Trunk	6	14.6	33	17.6	
Head and neck	14	34.1	17	9	
Tumor size					**0.1329**
Over 5 cm	31	75.6	119	63.3	
Less than or equal to 5 cm	10	24.4	69	36.7	
Depth					**0.1139**
Superficial (skin/subcutaneous)	10	24.4	27	14.4	
Deep	31	75.6	161	85.6	
Histological grade					**0.0002150**
G1	5	12.2	81	43.1	
G2–3	36	87.8	107	56.9	0.09063
Recurrent tumors	8	19.5	19	10.1	0.06377
Previous rt treatment	9	22	21	11.2	0.7577
Previous inappropriate surgery	14	34.1	69	36.7	0.01555
neoadjuvant qt +/− rt treatment	7	17.1	11	5.9	
Total	41		188		

qt, chemotherapy; rt, radiotherapy.

of tumor resection. We compared the clinicopathological features of the microsurgical reconstruction group with those of all the sarcoma patients operated on with curative intent in our department (►**Table 2**).

Oncosurgical Procedure and Reconstructions

Local radical surgery was the oncosurgical procedure in all but three patients, who underwent compartmental resection. No primary amputations were performed. Radical surgery with good margins was not possible in seven cases, five of which were located in the head and neck region.

Several free flaps were used, the main ones being the anterolateral thigh (ALT) flap and the latissimus dorsi flap (see ►**Table 3**). Mean operating time was 5.2 hours (range: 4 to 7.5 hours).

Any main vessels or nerves that were affected were resected, and vascular and neural reconstruction was performed if possible. Twelve vessel and/or nervous reconstructions (29%) were performed. Five patients required vascular reconstruction, and bypass procedures were performed in four femoral arteries, two humeral arteries, one radial artery, and two ulnar arteries. In our department, autologous venous grafts are preferred to synthetic materials. A further five patients underwent nervous reconstruction, involving three sural grafts for ulnar and median nerve repair, two motor muscle flaps inset at the thigh and anastomosed to the crural nerve, and one gracilis flap anastomosed to the anterior interosseous nerve.

Hip prosthesis was needed in one case and a mesh was inserted in two cases.

Table 3 Microsurgical Flaps used for Reconstruction

Free Flaps	Cases Number
Anterolateral thigh flap fasciocutaneous	13
Latissimus dorsi	7
Deep inferior epigastric perforator	6
Rectus abdominis muscle	5
Radial forearm fasciocutaneous	3
Thoracodorsal artery perforator fasciocutaneous	3
Cubital forearm fasciocutaneous	1
Gracilis myocutaneous	1
Fibular osteocutaneous	2
Iliac osteocutaneous	1

Adjuvant Therapy

Histological analysis revealed tumor stage T1 in 10 patients and T2 in 31 patients. Differentiation grade G1 was found in 5 (12%) patients and G2–3 in 36 (88%) patients. Deep involvement was observed in 31 patients (76%) (►**Table 2**) Follow-up ranged from 13 to 83 months, with a mean of 30 months.

In total, 21 patients (54%) received adjuvant treatments, specifically radiotherapy in 13 (32%); radiotherapy + brachytherapy in 3 (7%); radiotherapy + chemotherapy in 3 (7%); and chemotherapy in 2 (5%). Median time to the start of adjuvant radiotherapy was 60 days (interquartile range 52.5 to 85.5 days).

Flap Survival and Complications

Comparison of the microsurgical group with the general one revealed, in the former, a higher rate of head and neck locations, larger tumors, more recidivated cases, more cases that had received previous radiotherapy, and more cases that needed neoadjuvant chemotherapy and/or radiotherapy for tumors that could not initially be resected.

The large majority of our patients ($n = 31$, 76%) had an uneventful postoperative course. Complications were encountered in 10 patients (►**Table 4**). Of these, three incurred total flap loss. Total flap necrosis was resolved with a pectoralis flap, and a free radial flap that suffered complete necrosis was successfully rescued with an omental pedicle flap.

The overall success rate for the 42 flaps was 93%. Perioperative mortality was nil. Although other risk factors were involved, we also observed that all flap failure developed in patients who had previously received radiotherapy plus chemotherapy (despite no significant differences being observed).

Follow-Up

Follow-up in the Sarcoma Unit included clinical assessment every 3 to 4 months for up to 3 years, every 6 months from 3 to 5 years, and every year from 5 to 10 or more years (with chest x-ray in high-grade sarcomas). Magnetic resonance imaging was performed 6 months after the end of the treatment and then every year for 5 years.

Follow-up ranged from 13 to 83 months, with a mean of 30 months. Of the 39 patients undergoing free tissue transfer, one was lost to follow-up (a case of dermatofibrosarcoma protuberans who returned to his native country).

Table 4 Flap Complications

Complications	Cases Number
Total necrosis	3
Partial necrosis	1
Dehiscence	3
Wound infection	3
Bone late consolidation	1
Cervical fistulae	1
Arthritis	1

Thirty-two patients (78,5%) showed no evidence of disease. Eight patients had local recurrence (19.5%): two were treated by amputation, two by local surgical excision, and the remainder with radiotherapy/chemotherapy sessions (metastatic or impossible-to-resect cases). The limb salvage rate was 90.5% (19/21). Nine patients (22%) died as a result of disease.

Analyzing the whole series ($n = 229$), disease-specific survival was 81.58% at 5 years and 78.5% at 10 years. In the microsurgical reconstruction group, disease-specific survival at 5 and 10 years was 79.49% and 76.93%, respectively. The 5-year survival rate by sarcoma location was as follows: limb, 82.17%; head and neck, 67.71%; and trunk, 85.25%.

Functional Outcome

Nineteen patients receiving free tissue transfer for tumor resection in extremities had successful limb salvage and showed both good ambulation after postoperative physiotherapy (TESS 77 ± 16) and adequate use of the upper extremity (TESS 66 ± 26). A further two limb sarcoma patients developed local recurrence and underwent amputations.

Two representative cases are shown in ►**Figs. 1**, **2**.

Discussion

Radical resection and limb salvage surgery is nowadays recommended as the treatment of choice for sarcomas in resectable soft tissue and bone sarcomas of the extremities.[10] However, limb salvage and safe resections cannot be achieved without an adequate reconstructive procedure, including pedicled or free tissue transfer.[11,12] It is also suggested that the use of tissue transfer to rectify defects has influenced the outcome of the management of these tumors, since the approach allows adequate resection of tumors, and tumor recurrence may be reduced with good reconstructive recovery.[13]

Recent advances in microsurgical techniques and the associated technologies, coupled with a better understanding of microvascular anatomy, have enabled us to carry out single-stage reconstruction covering wide and composite tissue losses in any anatomical location.

Our series is the largest reported to date for sarcoma patients undergoing microsurgical repair in the same unit. Comparison of clinicopathological aspects revealed significant differences between the microsurgery and nonmicrosurgery groups in terms of location, histological grade, and neoadjuvant treatments. These differences were also observed for tumor size, depth, and recurrence, but in this case they were not statistically significant.

Selection of the type of free flap is primarily dictated by the needs of the recipient defect. As do many other centers, we have certain flap preferences. In the case of bone tissue defects we tend to use the fibular flap (2), with the iliac flap as the second option. When the defect is suitable for a muscular or myocutaneous flap, we use the latissimus dorsi flap (7) or the rectus abdominis flap (5). When fasciocutaneous coverage is required, our preference is for the ALT (12) and deep inferior epigastric perforator (DIEP)(6) flaps.

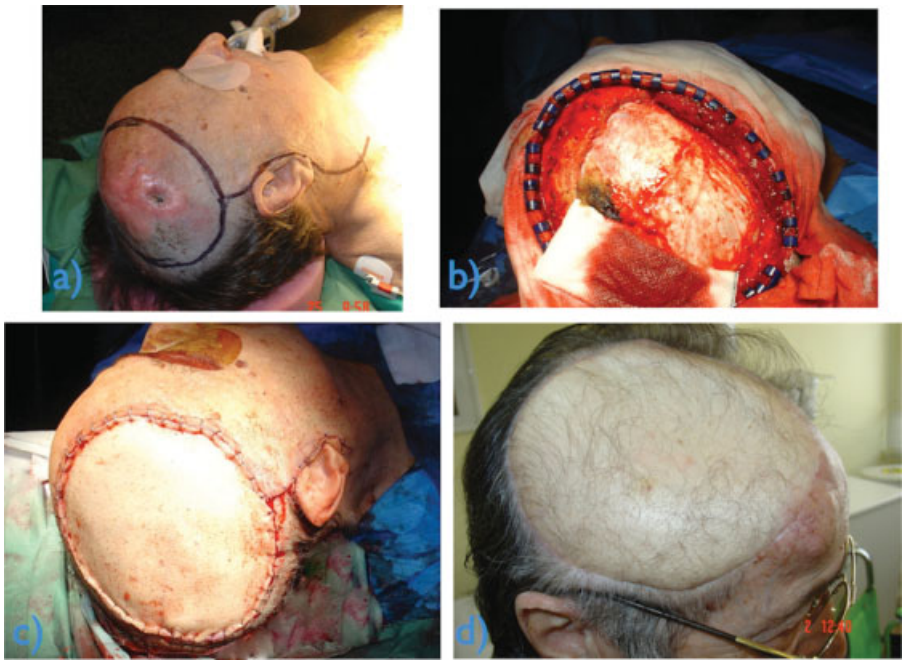

Figure 1 Case 1. (a) 71-year-old man with ulcerated tumor of the scalp. Biopsy suspects malignant peripheral nerve sheath tumor. (b) Radical resection was performed, including external skull table. (c) Microsurgical repair has consisted in anterolateral thigh flap coverage and patient has been suitable to adjuvant radiotherapy (RT). (d) Result after surgery and RT.

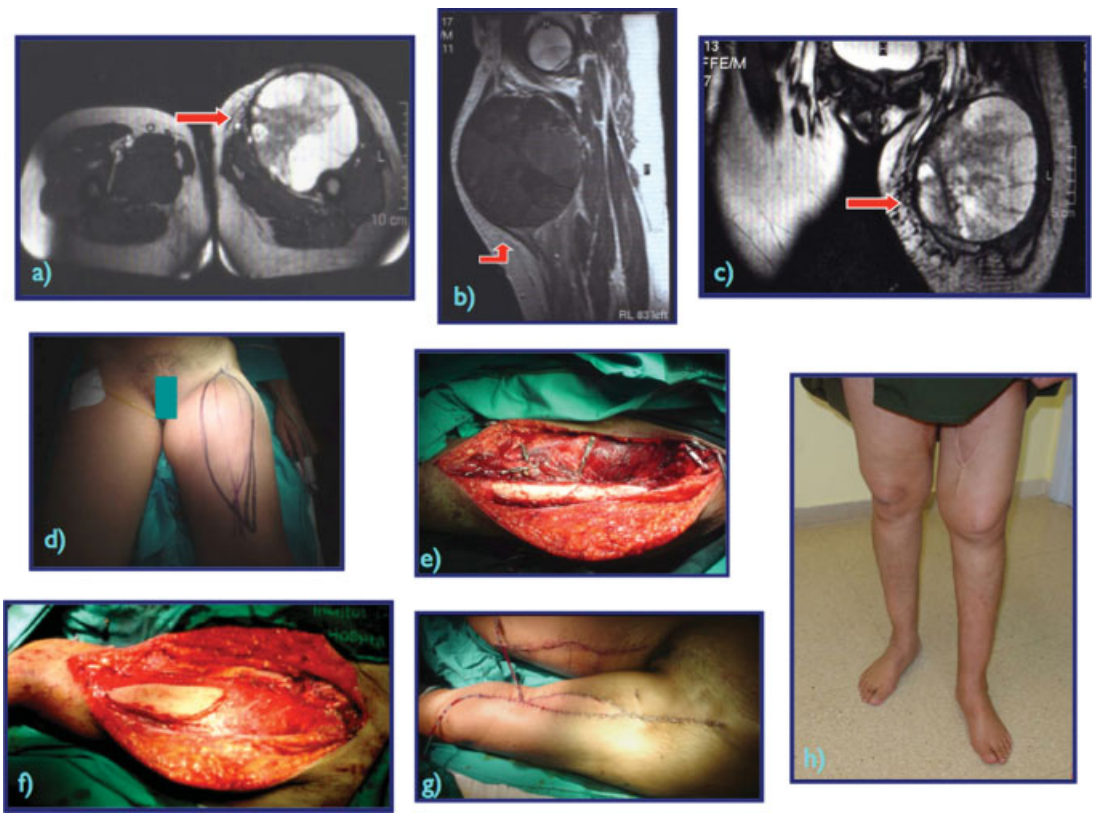

Figure 2 Case 2. 47-year-old woman with fast-growing thigh tumor. (a–c) Imaging showed a 10 × 13 cm anteromedial neoformation in thigh, and biopsy suspects pleomorphic sarcoma. Neoadjuvant treatment with chemoradiotherapy shows no effect. (d,e) Compartmental resection was performed involving femoral bundle and with preservation of the great saphenous vein. (f,g) Microsurgical repair consisted of myocutaneous latissimus dorsi transfer, neurotized to crural nerve and inserted between quadriceps and sartorius remaining tendons. (h) Free from disease 5 years later, with positive electromyography signal at the latissimus dorsi muscle.

Suitable preoperative planning is crucial to the success of single-step operations involving radical tumor excision and simultaneous reconstruction. We consider the single-step approach to be the gold standard in these patients. In our center, plastic surgery is the responsibility of the multidisciplinary Sarcoma Unit, which performs both oncological and reconstructive surgery. With two teams working simultaneously, one resecting the tumor and the other performing the flap, the entire operation can be performed effectively but with a shorter operating time and duration of general anesthesia.[14] Special care is always taken to avoid mixing anything in the fields of the tumor resection and flap preparation.

Prospective randomized trials have shown that adjuvant radiation improves local control in patients with high-grade soft tissue sarcoma of the extremity that is treated with limb-sparing surgery.[15,16] The advantage of using free flaps over local and regional flaps is that a stable wound platform can be established for initiating adjuvant radiotherapy.[17,18] Good soft tissue coverage is very important with sarcomas in difficult locations, such as the head and neck, as well as for large or recurrent tumors or zones affected by radiotherapy or previous surgery, and the use of a free flap may be the only way of achieving good coverage in these cases.

In limb sarcoma records, local recurrence rates are ~10%, with fewer than 5% of patients requiring amputation.[16,19] The most important predictive factor for local recurrence is a positive surgical margin at the time of resection.[20,21]

Studies of sarcoma resection and free tissue reconstruction in extremities have reported overall complication rates of 2 to 22%,[4,22–25] limb salvage rates of 61 to 100%, and a 5-year survival rate of 61 to 90%.[3,6,17,22,25]

Reports on free tissue transfer for upper and lower reconstruction after sarcoma resection observation periods of between 5 and 25 years and free tissue transfers ranging from 7 to 34.[4,6,21–23,26–28]

Studies of head and neck sarcomas have reported a disease-free survival rate of 41 to 54% and a specific disease-death rate at 5 years of between 18% and 34.5%.[29–33] The head and neck location represents a factor of poor prognosis in all series.[34,35]

Our series presents similar clinical, pathological, and prognostic factors to those described in the literature. It should be noted that limb salvage surgery was possible in 90% of cases, and good functional outcomes were achieved in both lower (TESS 77 ± 16) and upper extremities (TESS 66 ± 26). Our microsurgical group had a higher rate of head and neck locations, larger tumors, more cases of recidivism, more cases who had received previous radiotherapy, and more cases that needed neoadjuvant chemotherapy and/or radiotherapy for tumors that could not initially be resected. These are known factors of poor prognosis and are associated with a higher risk of surgical complications. The microsurgical group also required the exposure of large neurovascular structures and/or a large osteotendinous surface. All this justifies the need for complex reconstructive techniques.

Conclusion

The microsurgical repair of sarcoma defects is a reliable option that, while not free from complications, is often necessary in cases involving a head and neck location, high-grade tumors, and neoadjuvant treatments. The procedure allows both adequate oncosurgical resection and function preservation.

Our microsurgical sarcoma reconstruction data, based on an observation period of 12 years and presenting the results of 42 free tissue transfers in 41 patients, adds further evidence to the previously published smaller series.

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