Limb Salvage in Malignant Tumors

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ABSTRACT

Limb-sparing resection and reconstruction has become the treatment of choice in extremity malignancies, as amputation does not provide better long-term survival rates or functional advantages. R0 resection, the removal of the tumor in sano, remains the prerequisite and most important oncologic parameter to avoid local recurrence. Successful treatment requires the combination of surgical eradication and the patient's specific functional and aesthetic rehabilitation. Our clinical rationale resulting from more than 2000 cases will be demonstrated. The problematic aspects of different tumor entities and the locoregional clearance of lymphatic pathways will be discussed. Differential diagnosis and multimodality treatment in high-volume tumor centers is likely to achieve superior oncologic statistics. Long-term survivors after microsurgical reconstructions and possible secondary malignancies will be addressed.

KEYWORDS: Microsurgery in limb oncology, resection and functional reconstruction, tendon transfer in the lower extremity, soft tissue sarcoma, secondary malignancies in long-term survivors

Malignant tumors of the extremities requiring major reconstructive procedures are rare entities usually neglected in official cancer statistics. The overall incidence in Western industrialized countries is estimated between 2 and 6 cases per 100,000 inhabitants. They arise either from mesenchymal cells differentiating into musculoskeletal neoplasms or from epithelial tissues transforming into infiltrating and ulcerating skin cancer (Table 1 depicts the tumor entities). Patients suffering from chronic osteitis fistula or from longstanding unstable scars have considerable risk factors. In addition, irradiated skin, congenital diseases like neurofibromatosis, or exposure to toxic substances like vinyl chloride or anilin are causative conditions. Visceral metastases, malignant melanoma, or lesions from skin adnexa will rarely result in extremity-threatening conditions.¹⁻³

Today, limb-salvage procedures are well accepted as they achieve comparable survival rates and better quality of life.^{2,4-10} Provided the surgical members of the multidisciplinary tumor board offer the reconstructive spectrum, including microsurgical free tissue transfer, these techniques will be integrated as essentials in everyday oncology.^{2,11-15}

Contrary to some statements within the literature, numerous innovative limb-sparing and/or function-preserving methods have been introduced in the past. In 1928, Simon collected more than 670 cases of sarcoma in a foresighted monograph.¹⁶ His meticulous literature survey resulted in surprisingly broad information about international publications that are listed in Table 2: Among these is the replacement of the proximal humerus by transposing the spina scapulae or the clavicle

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Table 1 Microsurgical Procedures in Extremity Malignancies: Entities**Musculoskeletal tumors**

1. Soft tissue sarcoma
2. Osteosarcoma and chondrosarcoma
3. Semimalignant lesions (e.g., Desmoid, giant cell tumor)
4. Secondary malignancies
5. Chronic osteitis; fistula carcinoma
6. Metastases

Superficial lesions

1. Malignant melanoma (acro-lentiginous)
2. Morphea such as BCC, SCC (Marjolin ulcer)
3. Metastases
4. Sweat gland carcinoma
5. Merkel cell tumor

Table 2 Reconstructive Surgery of the Limb: Heritage

Muscle xenotransplant, biceps (Helferich, 1882)
Fibula pro tibia (Tietze, 1895)
Biceps femoris transfer (Lange, 1900)
Clavicula pro humero (Delalange, 1904)
Spina scapulae pro humero (Bardenheuer, 1904)
Salvage replantation, lower leg (Höpfner, 1906)
EHL/TP to anterior tibialis (Lexer, 1912)
Homoplastic femur transfer (Rovsnig, 1913)
Fibula pro humero (Lexer, 1920)
Axial rotationplasty (Sauerbruch, 1924)
Heat sterilization, osteosarcoma (Nussbaum, 1928)

EHL, extensor hallucis; TP, tibialis posterior

Source: From Simon H. Die Sarkome. In: Kuettner H, ed. Neue Deutsche Chirurgie. Stuttgart, Germany: Enke; 1928;43:572–626.

(Delalange and Bardenheuer, 1906), one of the first segmental amputations with salvage replantation of the lower leg (Höpfner, 1903), tendon transfers in the upper and lower extremities (Lange, 1900; Lexer, 1918), and even xenotransplantation of a dog's muscle to replace the biceps humeri of a young lady (Helferich, 1882).¹⁶

Today's oncologic guidelines for the treatment of extremity malignancies should include sophisticated reconstructive options and our surgical heritage. However, no risk of local recurrence and/or adverse effects on survival chances should be tolerated. The primary and main target must be the removal of the tumor in sano (R0 resection).^{2,7,10,17–20} To describe the multimodal oncologic treatment pathways, reconstructive plastic procedures will be addressed and the role of microsurgical techniques will be defined.

PREOPERATIVE TREATMENT RATIONALE

The vast majority of patients suffering from extremity tumors receive the diagnosis after excisional biopsy of a small, slowly growing cutaneous or subcutaneous lesion. No oncologic disadvantage occurs if in these cases with

microscopic tumor cell remnants (R1), a secondary resection including a three-dimensional portion of the surrounding uninvolved tissue is added.^{7,9,17,21}

Deep-seated subfascial lesions or large ulcerating masses, however, infiltrating bone, joints, or neurovascular structures as well as tumor growth within the groin, axilla, or popliteal region are likely to be of malignant origin. Preoperative routine investigations should include analysis of general risk factors to exclude patients not suitable for difficult and long-lasting surgery. Sonography and magnetic resonance imaging (MRI) investigation will clearly define the tumors three-dimensional extent and the relation to neighboring tissues. It will provide information about the optimal area and approach for biopsies. In addition, adequate oncologic tumor removal and potential reconstructive procedures necessary for defect coverage or functional rehabilitation can be discussed. Computed tomography (CT) scans and scintigraphy are helpful to exclude potential metastatic tumor spread. Tumor staging according to the system of the Union Internationale Contre le Cancer (UICC) or the Musculoskeletal Tumor Society (MSTS) should be on the chart throughout the treatment course. It should be updated as necessary during follow-up.^{10,19,22–26}

To avoid the risk of limb ablation and oncologic disadvantages, patients with such extended or complicated lesions should be referred to a tumor board with multidisciplinary, high-volume experience.^{2,7–10,18,27}

The majority of the patients explain that a trauma occurring months ago is the causative factor for tumor development. This phenomenon could be observed as well with extended cutaneous lesions, where bleeding or ulceration of large squamous cell carcinoma (SCC), basal cell carcinoma (BCC), or malignant melanoma occurs after a clearly described trauma. Despite widespread medical information campaigns, patients demonstrate even today large tumors after months of negligent delay.

TUMOR BIOPSY

In extremity malignancies, biopsies should be planned carefully to avoid inadvertent tumor cell contamination with subsequent major soft tissue loss or damage of anatomic structures necessary for reconstructive procedures.^{2,10,23,26}

Small tumors with cutaneous or epifascial location should undergo excisional biopsy, as the vast majority of these outpatient cases are benign lesions.

Open-access incisional biopsies should respect major lymph collectors and main superficial venous systems provided oncologic principles are met.

Neighboring muscle compartments must not be opened. Longitudinal incisions and Redon drainage tracts close to the wound margins are essential. As they are possibly contaminated with tumor cells, they will be removed en bloc during definitive tumor surgery.

Tumor infiltration requiring removal of the deep venous system is likely to cause severe chronic venous obstruction and concomitant lymphedema. Irradiation may potentiate these negative effects. If superficial lymph collectors and veins are left intact during surgery, it will ameliorate conservative physiotherapy and drainage treatment.

Provided the superficial veins could be spared, they will in addition serve as end-to-side recipients in free flap transfer. In complicated cases of local recurrence or irradiation defects, arteriovenous loops of the saphenous or cubitalis system serve as interposition grafts to bridge major distances.²⁸⁻³⁰

Concerning the choice of fine needle, core needle biopsy, or incisional techniques, a final decision is lacking. Whereas some pathologists ask for tumor biopsies of ~2 cm², others are content with needle samples to confirm primary diagnosis.

As musculoskeletal tumors are associated with a high percentage of discordant histopathologic results, a second opinion should be added en principe.^{2,16,19,22,25,26}

LYMPHATIC SYSTEM IN EXTREMITY MALIGNANCIES

Regional tumor spread into lymph nodes is limited to specific species. Whereas malignant melanoma, fistula carcinoma, and some high-risk subtypes like epithelioid cell sarcoma, synovial cell sarcoma, or rhabdomyosarcoma are associated with considerable incidences, the majority of malignant extremity tumors demonstrate lymph node involvement in only ~2 to 6% of the cases.

Of 1546 consecutive soft tissue sarcomas treated at our own institution, 28 cases developed lymph node metastases. Despite radical lymph node dissection and multimodality treatment, only five of these patients experienced no evidence of disease (NED) long-term survival.³¹ Similar results have been reported by other high-volume centers.^{9,10,21,32}

Cutaneous malignancies and high-risk tumors of the limbs should be routinely investigated with the sentinel lymph node technique employing radioactive tracers and/or blue dye injections to identify possible involvement of the lymphatic system. Lymphatic spread is estimated as an oncologic "signum mali ominis." At present, no decisive data are available regarding whether the patient will benefit from primary versus secondary lymph node removal. The treatment rationale, however, should follow curative principles. In addition, palliative resection should be recommended to avoid large fungating ulcerations in the axilla, elbow, knee, or the groin region.

Hyperthermic perfusion of the limb or hyperthermia in connection with chemotherapy have been described as suitable methods for reducing locoregional tumor masses, metastatic spread, cutaneous dissemina-

tion, and/or growth in discontinuity along the main lymphatic pathways. In selected cases, down-staging of the tumor allowing for surgical resection, some months of progress-free survival or in rare cases cure could be observed.³³⁻³⁶ However, in some cases, long-term investigations uncover detrimental effects on the vascular system with secondary amputations.³⁵

TUMOR RESECTION AND MICROSURGICAL RECONSTRUCTIVE OPTIONS

The definitions of safety margins are different within specific subgroups of limb tumors. Cutaneous lesions today require microscopically controlled excisions with some millimeters of cleared zones. Amputation had been recommended in earlier times as the treatment of choice, but oncologic data did not confirm that radical limb ablation is associated with benefits for the patients.

The very same tendency could be observed with musculoskeletal tumors. Originally, amputation or "compartment resection from origin to insertion of the muscle" had been advised. Despite the fact that these definitions have been published as early as 1911 by Küttner,¹⁶ 1928 by Simon, and in 1980 again by Enneking, there are to date no oncologic data presented proving the superiority of these mutilating procedures.^{16,23} Wide local excision leaving a cuff of ~2 to 5 cm of uninvolved tissue is nowadays accepted as the surgical treatment rationale in medium- or high-grade sarcoma (G2/G3) provided preoperative or postoperative irradiation is added.^{2-5,7,12,18,27,37} Even in selected cases of microscopic residual, combined surgery and radiation may result in local control.⁵

Low-grade malignancies (G1) will be sufficiently excised with some millimeters of three-dimensional safety margins. The majority will not require additional treatment.^{8,9,21}

Today, only large fungating anaplastic tumors, infiltration of major nerves, blood vessels, and joints, as well as malignancies developing within the foot or the hand are still likely to be treated with limb ablation. In addition, local recurrence, secondary malignancies, or severe irradiation damage are cited to be a risk factor for amputation.

The indication, however, clearly depends on the abilities of the surgical teams integrated into the tumor board and the interdisciplinary management. Amputation should be the last decision after discussing the whole spectrum of reconstructive options and the patient's demands.^{3,5,11,12,20,29,33,34,38-40}

MICROSURGICAL PROCEDURES

In the past, innovative microsurgical techniques have been involved in complicated cases of extended ulceration,

multiple local recurrences, concomitant irradiation damage, segmental bone defects, or wound-healing disturbances after primary treatment.^{11,13,20,33,41} Today, clinical reports about this special field contain no more singular case descriptions or small series.^{2,10,12,14,32,42-45}

Despite fascinating tools, the indication should follow clear plastic surgical principles: "To choose a simple and effective technique for the patient's needs, not a patient for a new method"!

In planning the reconstruction, the size of the tumor and the location on the limb are both important.^{6,12} Provided that irradiation must not be added, skin grafting is more likely to be possible in the proximal portion of the limbs. Smaller defects may be covered by local transposition flaps or pedicled muscle flaps or musculocutaneous tissues.⁴⁶

At the borderline between conventional techniques and microsurgical tissue transfer, vascular supercharging of large pedicled flaps should be integrated. Additional arterial or venous supply can be achieved with segmental or multiple vascular perforators and septal dominant vessels. In combined superiorly pedicled vertical rectus abdominis myocutaneous flap (VRAM) and transverse rectus abdominis myocutaneous (TRAM) flaps for coverage of large defects in the axilla/shoulder/thoracic wall region, the inferior epigastric vessels are able to reduce the incidence of peripheral flap necrosis if they are anastomosed to axillary partners. The very same procedure can be used vice versa in distally based extended VRAM flaps

Table 3 Treatment Rationale in Limb Oncology

Targets: "R0 resection" and "no evidence of disease"

1. Functional and aesthetic rehabilitation
2. Functional and aesthetic deficiency
3. Basic limb function: sensitive grip tool (U.E.); biological stent (L.E.)
4. Distal amputation levels: spare-part surgery
5. Proximal amputation levels: forequarter, hindquarter

LE, lower extremity; UE, upper extremity.

if the mammarian artery is linked to femoral vessels. In case of segmental resection of tumors infiltrating the axillary vascular bundle and the brachial plexus, thoracic wall coverage and shoulder contour preservation can be obtained by a pedicled filet of arm, whereby the distal part of the radial artery provides additional blood supply via anastomosis, for example, to the inferior thyroid artery (Table 3 illustrates the treatment rationale).

Case no. 1 describes a similar technique after resection of the third local recurrence of a malignant fibrous histiocytoma T1 N0 M0 G2 within the extensors of the left forearm of a 52-year-old woman (Fig. 1). After wide local excision, primary tendon transfer of the flexor carpi ulnaris to the extensor tendons D1 to D5 was performed. A distally based, extended lateral arm flap of 29 cm × 9 cm was harvested. Due to the regional surplus of skin in aged patients, primary tension-free closure of the donor-site defect could be done. After rotating the

Figure 1 (A, B) A 56-year-old woman with the third local recurrence of a malignant fibrous histiocytoma (T1 N0 M0 G2). Wide excision (R0) including the forearm extensors and tendon transfer of the flexor carpi ulnaris to replace the extensors D1 to D5 was performed. Defect coverage could be obtained by a distally based extended lateral arm flap. (B) Vascular supercharging with the circumflex posterior humeral artery linked end to side to the radial artery was performed. (C, D) Nineteen years later, the patient demonstrates no evidence of disease (NED) and nearly normal hand function after primary closure of the donor site.

flap into the defect, auxiliary anastomosis of the preserved branch of the circumflex posterior humeral artery to the radial artery was performed. The postoperative course was uneventful with primary wound healing. After intensive physiotherapy, the patient demonstrates 19 years later no evidence of disease and nearly normal function.

The peripheral areas of limbs, however, require free tissue transfer in cases of exposure of bone, joints, tendons, and neurovascular bundles. Fig. 10 describes the regions likely to require microsurgical procedures.

As a main target, functional reconstructive options should be planned primarily and should be integrated into the tumor board's preoperative recommendations. The principles of, for example, posttraumatic hand reconstruction serve as well in analogous cases of mutilating tumor excisions.

Case no. 2 demonstrates a 42-year-old steel worker suffering from a malignant melanoma (acro-lentiginous) of the left thumb (Fig. 2). Due to the biopsy result of Clark level 4 and Breslow thickness of 1.8 mm, the tumor board recommended amputation at the metacarpo-carpal (MP) joint level.

To achieve professional rehabilitation for the patient's demands, synchronous amputation and replacement with the second toe was performed using the introduced technique of posttraumatic cases. Due to the risk status of the patient, the tumor board deemed it necessary to perform hyperthermic perfusion with the chemotherapeutic agent melphalan 6 weeks postoperatively. The toe-to-hand transfer survived the treatment.

Eighteen years later, the patient shows no evidence of disease and full functional adaptation.

Another major advantage for upper-extremity limb sparing has been introduced with vascularized free bone transfer.^{11,47-50}

Our clinical case no. 3 demonstrates an 18-year-old woman suffering from a parosseous sarcoma pT2 N0 M0 G2 of the proximal humerus infiltrating into the deltoid muscle (Fig. 3). After radical resection (R0), prosthetic supplementation was performed. Two years later, adequate trauma led to the fracture of the shaft. As the patient did not show local recurrence or distant metastasis, the proximal humerus was replaced by a free fibula graft. Revascularization was achieved by end-to-side anastomoses to the brachial vessels. The arm could be suspended by fixing the fibula head with a cuff of nylon mesh to the acromion. As the patient developed severe contour irregularities, a de-epithelialized transverse scapula flap could be harvested and served as soft tissue filler within the subcutaneous shoulder region.

Nineteen years after tumor resection, the patient shows no evidence of disease, a hypertrophied fibula, and an acceptable aesthetic appearance. The functional abilities of the hand and forearm are unimpaired. There is passive pain-free mobility, stability, and some trick movements with the "new" shoulder joint.

Case no. 4 demonstrates a rare long-term survivor problem. Eighteen years after irradiation of an unknown lesion of the posterior shoulder region, a rodent ulcer developed within the former "shrinking field" irradiation

Figure 2 (A, B) Acro-lentiginous malignant melanoma of the thumb: Clark level 4 and Breslow thickness 1.8 mm. Amputation at the MC joint I level and synchronous reconstruction by second toe to thumb transfer was performed. Six weeks postoperatively, hyperthermic perfusion with melphalan was added. (C) Eighteen years later, unimpaired hand function and professional rehabilitation of the patient could be observed.

Figure 3 (A–C) Parosseous sarcoma of the proximal humerus in an 18-year-old woman infiltrating the deltoid muscle (T2 N0 M0 G2). After radical excision, prosthetic replacement was performed. Two years later, she developed a fracture of the shaft. As restaging did not show locoregional or distant metastasis, the fibula could be transferred to replace the humerus. The arm could be suspended by fixing the fibula head with a cuff of Prolene mesh to the acromion. (D, E) The images show stable bony union and some hypertrophy of the fibula.

Figure 3 (Continued) (F, G) Due to radical tumor surgery, the patient developed severe contour irregularities. A de-epithelialized pedicled transverse scapula flap served for subcutaneous defect filling. (H, I) Nineteen years after tumor resection, the patient demonstrates NED. Stable suspension of the arm with full hand and elbow movement and passive trick movements of the shoulder joint could be achieved.

area of this 62-year-old woman (Fig. 4). The long treatment delay was due to the fear of the patient that amputation would be necessary. Microscopically controlled excision was performed, and the defect could be covered by split-thickness skin grafts. A Prolene mesh strip was placed below the remaining musculature to fixate the humerus to the acromion with 0-nonresorbable sutures.

Two years later after careful follow-up investigations and multilocular negative biopsies, a free muscle sparing TRAM flap served as soft tissue replacement. Revascularization could be achieved by end-to-end anastomosis of the epigastric artery to the inferior thyroid artery and end-to-side anastomosis of

the concomitant vein to the superficial jugular vein. Twelve years postoperatively, hand and elbow demonstrate full range of motion, whereas the shoulder joint is restricted to passive mobility.

Similar principles should be considered in the lower extremity. Whereas modern prosthetic supplementation allows for nearly normal gait in transtibial amputation, transfemoral or even more proximal amputation stumps confront the patient with rehabilitation problems. As extremity malignancies achieve an average long-term survival in up to 70 to 80%, the increasing age will add disabilities like arterial occlusive disease, diabetes, arthrosis, cardiorespiratory malfunction, and loss of visual control. It is likely that long-term survivors will

Figure 4 (A) A 62-year-old woman 18 years after irradiation of the posterior shoulder region developing an extensive rodent ulcer. Microscopically controlled excision, scapulectomy, suspension plasty of the humerus to the clavicle, and primary coverage with split-thickness skin grafts was performed. (B, C) Two years later, multilocular negative biopsies allowed for defect coverage with a free muscle sparing TRAM flap anastomosed to the jugular vein and the inferior thyroid artery. Twelve years postoperatively, the patient demonstrates NED. Hand and elbow demonstrate full range of motion, and the shoulder enables passive pain-free motion.

end up as bilateral amputees. The value of a leg, even restricted to biological stilt function, should not be underestimated for independent self-supplementation of our aged patients.⁵¹

This 36-year-old man (case no. 5, Fig. 5) had been referred after removal of a small mass infiltrating

the dorsal cruciate ligament of the ankle joint (synovial cell sarcoma, T1 N0 M0 G3). As the patient refused amputation, the tumor board recommended neoadjuvant irradiation with 16 Gy neutrons. After radical muscle group resection including the ligaments, extensor tendons, and joint capsule with decortication of the tibia,

Figure 5 (A, B) A 36-year-old man suffering from a synovial cell sarcoma of the anterior ankle joint (T1 N0 M0 G3). After neoadjuvant irradiation with 16 Gy neutrons, radical resection including the extensors, the ligaments, and the ventral tibia corticalis was performed. Tendon transfer of the peroneus longus to the midfoot and a latissimus dorsi flap linked to the anterior tibialis artery and the saphenous vein led to functional reconstruction. (C, D) The images show sufficient range of motion of the ankle joint, normal gait, and permanent soft tissue coverage. Twenty-seven years after tumor excision, the patient demonstrates NED.

Figure 6 (A–C) A 41-year-old woman with the fourth local recurrence of a malignant fibrous histiocytoma (T2 N0 M0 G3). As the patient refused amputation, preoperative irradiation with 16 Gy neutrons was done, which resulted in deep ulceration. After careful debridement, the distal toe extensors were fixed to the metatarsal heads, and the defect could be covered with a free latissimus flap. Several biopsies and thinning procedures were performed, and the patient demonstrates NED and normal gait 26 years after the oncologic treatment.

primary tendon transfer of the peroneus longus was performed. Reinsertion through drill holes within the cuneiform bones resulted in sufficient dorsiflexion. The soft tissue defect could be covered by a latissimus dorsi flap with end-to-end anastomoses to the anterior tibial artery and the transposed greater saphenous vein.

Twenty-seven years later, the patient demonstrates no evidence of disease and normal gait. He complains of weakening of the ankle joint extension after 5 miles of jogging.

Preoperative irradiation may sometimes end up with severe soft tissue complications.^{33,37,44,52,53}

Such is the case in this 38-year-old woman (case no. 6, Fig. 6) with a 4-year history of recurrent tumor growth on the dorsum of her right foot. Second opinion uncovered a fourth local recurrence of a malignant fibrous histiocytoma (T2 N0 M0 G3), and amputation was recommended.

The patient refused, and preoperative neutron irradiation (16 Gy) led to a radiogenic ulcer exposing the midfoot bones and destruction of the extensor tendons. After radical debridement, the distal toe extensors D1 to D4 were fixed through drill holes within the metatarsal heads. The defect could be covered by a primarily thinned latissimus dorsi. Revascularization could be obtained by end-to-end anastomoses to the

anterior tibial artery and the saphenous vein. The postoperative course was uneventful. Six months later, a second thinning of the flap was done. Biopsies taken from the former tumor site did not show any evidence for recurrence. Due to difficult and discordant discussions among members of the tumor board, the procedure was repeated 1 year later, again with no signs of local relapse. Twenty-six years postoperatively, the patient demonstrates nearly normal gait and did not experience local or systemic relapse.

Another borderline amputation case (case no. 7, Fig. 7) shows the unexpected functional abilities of a “biological stilt.” In this 17-year-old female, a slowly growing tumor mass infiltrating the fourth compartment of the lower leg was biopsied. After informed consent discussion, she refused amputation, and the tumor board recommended sandwich radiochemotherapy according to the Cooperative Soft Tissue Study (CWS) protocol for rhabdomyosarcoma (T2 N0 M0 G3). Radical resection included the calf muscles and the fourth compartment. The foot received arterial inflow through the anterior tibial artery only. Due to the surplus of soft tissue, primary tension-free closure could be obtained. After completion of adjuvant multimodal therapies, the patient regained nearly normal gait allowing for her daily routine work as a waitress. Two years postoperatively, she received biopsies

Figure 7 (A–D) This 17-year-old female developed a deep-seated rhabdomyosarcoma of the lower leg (T2 N0 M0 G3) infiltrating the fourth compartment. Neoadjuvant radiochemotherapy (CWS) was followed by radical resection of the tumor. Despite severe irradiation skin problems, the postoperative course was uneventful, and the patient was able to work again as a waitress. Two years later, a latissimus dorsi was used to replace the unstable tissue employing venous interposition grafts to the popliteal vessels. (E, F) Twelve years postoperatively, she received a calf implant to improve the aesthetic appearance and to reduce the visible stigma. At present, the patient demonstrates NED.

and a resection of the compromised skin and soft tissue. Using long venous interposition grafts, a 38-cm latissimus flap was connected to the popliteal vessels end to side. Twelve years postoperatively, she received a calf implant as a marriage present, now covered by uninvolved tissues. She has at present no evidence of disease.

In cases of primary bone tumors or osseous infiltration of the tibia or femur, segmental bone resection should be the treatment of choice. Whereas in the

upper extremity, free microsurgical transfer of the fibula has become a routine procedure, corticotomy and bone transport systems should be discussed for the lower weight-bearing areas as alternatives.^{11,43,47,48,54} A series of 134 posttraumatic cases from our own institution demonstrates that Ilizarov's procedure will lead to full weight bearing in cases where sufficient soft tissue coverage is provided. A time range of 38 days per centimeter of defect is required for bony consolidation

without orthotic devices.⁵⁵ Comparable oncologic series using single/double fibula interposition grafts or in combination with allografts required an average period of ~28 months (13 to 45 months) until full use without mechanical support.^{43,56}

Interdisciplinary discussion should lead to choice of a suitable method for a patient's specific demands: Irradiated areas favor replacement by revascularized bone segments; however, complications like refractures or nonunions and the incidence of secondary cancellous bone transplantation should be taken into consideration.⁴⁸

Case no. 8 demonstrates the multidisciplinary procedure (Fig. 8). After neoadjuvant chemotherapy according to the Ewing Sarcoma Study (EICESS) protocol, resection of a Ewing sarcoma (T2 N0 M0 G3) of the distal tibia left a defect of 16 cm in this 28-year-old woman. An unreamed nail fixed with interlocking screws through the proximal tibia and the calcaneus was used to stabilize the osseous gap, and a free latissimus dorsi flap served as soft tissue replacement. After postoperative chemotherapy, corticotomy of the proximal tibia was performed, and transport of the bone segment guided by the nail was initiated using

Figure 8 (A–C) This 28-year-old farmer's wife developed a Ewing sarcoma within a tibial fistula formation. After radio-chemotherapy according to the EICESS protocol, segmental resection was performed including the talus and the distal tibia. The defect was stabilized by an unreamed nail fixed with interlocking screws to the proximal tibia and the calcaneus. The soft tissue loss was replaced by a free latissimus dorsi flap. After postoperative adjuvant therapy, corticotomy of the proximal tibia was performed. The transport of the tibial segment was guided by the nail and forced via a Regazzoni ventral bar system. (D, E) Sixteen years later, she is able to manage the farm without major impairment and demonstrates NED.

a ventral fixator bar with screw device. Full weight bearing could be allowed after 19 months. Sixteen years later, she is managing her farm without major impairments and no evidence of disease.

The borderline between reconstructive options and amputation is met in cases of severe segmental circumferential irradiation damage and/or local recurrences infiltrating into major bones, joints, and neurovascular bundles. A combination of radical surgery and prolongation of the amputation stump should be tried to ameliorate prosthetic supplementation. In the upper extremity, shoulder contour preservation could be achieved by replantation of forearm segments with and without bony support of the angulated radius and ulna.^{11,48,57-63} Concomitant resections of neurovascular structures should not be a contraindication. Vascular repair and neurorrhaphy will successfully lead to limb segments allowing for end bearing with protective sensation, provided careful prosthetic supplementation and continuous follow-ups are integrated.

Different techniques for lower-extremity stumps are demonstrated with our cases (Fig. 9A–C). In a lower leg (Fig. 9A), an osteomyocutaneous partial foot transplant could be used to keep the knee joint in a case of a locally recurrent adamantinoma within a severely irradiated tibial shaft segment. The calcaneus was fixed to

the proximal tibia, and the posterior tibial vessels were anastomosed to the popliteal vessels, while a tibial nerve neurorrhaphy led to protective sensation within the weight-bearing areas.

The very same procedure was performed at the distal femoral level (Fig. 9B). After segmental resection of an extended chondrosarcoma infiltrating the knee joint and the proximal tibia, free transfer of a calcaneus-foot segment changed the transfemoral amputation from a short above-knee to a transgenicular level. The last example (Fig. 9C) demonstrates a transfer of a lower-leg segment to achieve a long “femoral” shaft. This large local recurrence of an irradiated malignant fibrous histiocytoma infiltrating the femur and the neurovascular bundle required segmental amputation. Revascularization, neurorrhaphy, and amputation of the forefoot were performed, and the ankle joint was fused by cannulated screws inserted through the sole of the foot. This procedure left a stable quadrangular stump suitable for rotation-free supplementation with a knee joint disarticulation prosthesis.

DISCUSSION

To define the value of microsurgical procedures within the oncologic treatment rationale is difficult due to the

Figure 9 (A–C) Segmental resection and salvage replantation at different levels. (A) Osteomyocutaneous foot segment transplanted to a short tibial stump after irradiation and recurrence of a recurrent adamantinoma. (B) Analogous distalization of a femoral stump. After radical segment resection of a large chondrosarcoma infiltrating the knee joint, free transfer of a foot segment changed the proximal transfemoral amputation level into a transgenicular plane. (C) Transfer of a lower-leg segment to the subtrochanteric level after radical segmental excision of a malignant fibrous histiocytoma infiltrating the femur and the neurovascular structures. Reattachment of the tibia to the proximal femur, revascularization, and neurorrhaphy of the tibialis nerve to the sciatic nerve stump were performed. After amputation of the forefoot and ankle joint fusion, a quadrangular stump allowed for rotation-free end-bearing transgenicular prosthetic supplementation.

fact that extremity tumors are rare. They include a large variety of entities and subgroups.

Single case solutions are convincing, as they demonstrate safe reconstructive methods for extensive soft tissue and bone defects even in irradiated areas. At present, survival rates of the transplanted tissues vary in larger series between 92% and 97%, provided careful postoperative check-ups are performed.^{12,15,43,47} The indication for revisional surgery is given with the first sign of perfusion disorders. The final results justify secondary interventions, as salvage of up to 90% of the transplants are reported.^{11–13,15,28,44} No anticoagulative treatment, leeches, or infusions may substitute for an early second look. Medications reduce the risk of deep vein thrombosis in tumor patients; however, they should be applied as the very last option in microcirculatory or anastomoses problems.^{64–66} Concerning the multimodal treatment, microsurgical procedures will be used to decrease the rate of accompanying complications.^{12,42,44,52,67} Provided early radical debridement was performed removing the tissue until blood points are visible, microsurgical tissue transfers will solve the problem in the majority of the cases with postoperative wound-healing disturbances. After delayed treatment, however, septic rupture of the exposed artery, chronic radiogenic osteitis, or empyema of joints all are potential risk factors for amputation. After major resections, such conditions should be treated as emergency cases.

In addition, adjuvant chemotherapy should not be underestimated. As patients suffering from the tumor burden are likely to develop major psychological problems, the team should be aware to provide them with interventional care. Before surgery, the somatic side effects should be treated by the oncologist.

Detrimental influence on microsurgical procedures are rarely if ever to be observed. Surprisingly, even isolated limb perfusion employing TNF- α and melphalan, intra-arterial chemotherapy, or intraoperative radiotherapy do not demonstrate a higher complication incidence.^{34,36,38,44,53}

If we consider specific functional reconstructive subgroups, long-term results demonstrate a large scale of useful limb restorations. Our own series of nine malignant tumors of the thumb (seven malignant melanomas and two ulcerated SCCs) required four toe-to-hand transfers, and five patients preferred pollicization of the index finger. The conventional and microsurgical procedures were both successful leading to sufficient hand functions, and overall disease-free survival and functional results appeared comparable with those of internationally published series.

The case collection of our sarcoma reference center clearly demonstrates similar aspects. Despite a series of 2056 soft tissue sarcomas treated between 1990 and 2007, the heterogeneity, specific localization of the tumors, the rate of incomplete resections upon admission, different ages of the patients, and varying multimodal treatment decisions all introduce additional bias conditions (Fig. 10). We included tumors of semimalignant origin like desmoids and dermatofibrosarcoma protuberans, as they require comparable resection and reconstructive procedures.

In addition, the histopathologic status may change considerably after reevaluation or redefinition of tumors. Six hundred three investigations using consecutive second specialist's opinions in soft tissue sarcoma resulted in sufficient primary oncologic data in only ~40% of the cases.²⁵ Reference pathology should be routinely integrated into the treatment rationale.^{1,2,19,22,24}

Figure 10 Distribution of entities and subgroups (N 2056), November 1990 to July 2007. Soft Tissue Sarcoma Reference Center, BG–University Hospital “Bergmannsheil,” Bochum, Germany.

If we analyze specific tumor sites, soft tissue sarcoma of the lower leg and foot may demonstrate the value of microsurgical limb-sparing procedures. Between 1981 and 1995, we treated 102 patients either by wide local excision (among these were 78 patients with safety margins less than 2 cm) or ray amputation and modified foot stumps (17 cases). Only two trans-tibial, one transfemoral ablation, and four segmental resection-replantations were deemed necessary. Upon admission, our patient population had a high incidence of local recurrence after surgery at another institution. Fifty-two presented the first local relapse, and 22 were suffering from more than two local recurrences. Seventy-four patients had to be categorized as oncologic high risk T2 and G2/G3 cases.

Despite negative selection, the patients' 15-year overall disease-free survival rate was 62%. After primary resection with curative intention at our institution, only 6.3% oncologic borderline indications (safety margins of less than 1 cm) experienced local recurrence. Microsurgical free tissue transfer—dominated by the work-horse latissimus dorsi—was performed successfully in 39 cases (three successful vascular revisions), whereby five previously irradiated patients developed minor wound-healing complications. Another 19 problematic defect conditions could be solved by conventional local fasciocutaneous or muscle flaps.

Again, microsurgery is only one possibility from the reconstructive ladder. Thirty-one patients received synchronous primary tendon transfers to correct severe functional disabilities.

If we analyze the value of free tissue transfer, the incidence of partial or even proximal amputation would have been raised in our lower-leg cases to more than 45%. In addition, the combination of free tissue transplantation and primary tendon transfer led to nearly normal ambulation without orthotic supplementation in 17 cases. Such "historic" procedures may provide the patient with a short functional restoration period of ~8 to 10 weeks, whereas microvascular free muscle transfers require longer time spans supported by orthoses.^{16,68}

Our experiences are comparable with those of international high-volume centers, where the indication for free tissue transfer varies between 18% and 40% and is mainly used for peripheral tumor defects, irradiated local recurrences, exposed allografts and joints, and sophisticated restoration of hand function.^{12,14,33,56,69,70}

A similar trend could be observed with specific tumor subtypes. The whole spectrum of reconstructive plastic procedures and multimodal concepts dropped our amputation rate to 3% in cases of extremity liposarcoma. Of 167 patients treated between 1991 and 2002, 33 were admitted to our sarcoma center with the first local recurrence, 30 with the second or third, and 25 with more than three local relapses. Despite negative selection, an overall 5-year disease-

Table 4 Microsurgical Procedures in Limb Oncology: Goals

1. Preventive surgery to avoid malignant tissue transformation
2. Extended defect coverage to obtain grossly negative margins (R0)
3. Extension of primary functional reconstruction and limb sparing
4. Save coverage of implants
5. Salvage or distalization of amputation stumps
6. Reduction of local recurrences
7. Reconstructive surgery in postoperative complications after multimodality treatment
8. Palliative surgery
9. Treatment of late sequelae and secondary malignancies
10. Aesthetic appearance
11. Reduction of health care expenses

free survival rate of 79% and a local recurrence rate of 12.5% in patients treated primarily in domo was achieved.⁸ Similar results could be achieved in a series of 140 malignant fibrous histiocytomas localized in the extremities.⁷¹ The tumor boards results of our interdisciplinary management including routine microsurgical reconstructive options are comparable with those of international publications.

CONCLUSION

Plastic surgical techniques are nowadays essential methods in limb-sparing tumor surgery. Patients suffering from deep-seated primary lesions, postoperative wound-healing disturbances, or local recurrences should be referred to high-volume tumor centers providing the whole spectrum of reconstructive options. Table 4 describes the microsurgical treatment goals. Long-term results demonstrate that introduction of microsurgical tissue transplantation reduces amputation rates in cases of extended, oncologically necessary defects and in complications after multimodal treatment. In addition, functional restoration, salvage replantation, and aesthetic corrections frequently require microsurgical techniques to remove the stigma and burden of a tumor-bearing limb.

Analyzing the international literature, the success rate of microsurgical tissue transfer averages 95%, and limb sparing could be achieved in more than 90% of the oncologic patients. As long-term survival and locoregional relapse rates are comparable with those for limb ablation, an experienced reconstructive team should be integrated into the decision making of tumor boards.

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