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Surgery in Soft Tissue Sarcomas

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The surgical treatment of soft tissue sarcomas improved in the last decade, with better regional control and an increased number of limb sparing operations, but procedures and criteria of indication are not unified. Moreover, a great discrepancy exists in the incidence rate of local recurrence reported in literature, and also major centres denounce a high rate of local failures. The major predictive parameters of adequate regional control are the size and location of primary lesion, the pathological grading, previous treatments and the quality of surgical margins. Results in terms of regional control of 417 cases treated at our institute in the period 1974–1984 are analysed and discussed. Local failure occurred in 113 cases (27% crude, 31% actuarial risk at 5 years) and has been analysed according to factors which had impact on local failures: pathological grading (low grade 24% local recurrence vs. high grade 35% recurrence, $P=0.05$), site (extremity and girdle 26% vs. trunk and head and neck 47%, $P=0.001$), previous surgical treatment (32% for lesions recurrent at entry vs. 43% for virgin tumours, $P=0.05$), quality of margins (adequate surgery 24% vs. marginal surgery 47%, $P<0.001$); intralesional operations are excluded from this series. Histopathology is stratified in four categories that can actually influence the treatment schedule: low grade, spindle cell type high grade, small blue cell, miscellaneous sarcomas of different or unclear histogenesis. The size is detailed in different definitions of small or large, in a site–size relationship which may be useful in surgical practice, with no prognostic purposes. Finally, the adequacy of a surgical treatment is evaluated and discussed by the quality of surgical margins, defined according to the concept of compartment. A surgical indication rationale is, therefore, proposed taking into account the above-mentioned parameters and conclusive points of discussion.
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INTRODUCTION

FOR MOST malignant solid tumours the surgical treatment is well defined as regards procedure and indications, according to the stage of disease. In contrast, the surgeon who operates on soft tissue sarcoma (STS) has the impression that any surgical procedure depends on his personal skill and choice. There are detailed descriptions available for the main operations, but they have not been assimilated by general surgical practice and there is not a widely accepted and well-defined indication-rationale. The features of the primary lesion, the several histopathological subtypes, the ubiquitary location, and the frequent previous inadequate treatments, lead to an endless number of clinico-pathological combinations and any operation seems to be tailored for each specific situation.

The local recurrence rate, as reported in literature (Table 1), ranges from approximately 6 to 40% of total operations performed in major centres [1–9], and a comparison among different procedures is impossible due to the different criteria in selecting patients, performing operations and calculating the real incidence of regional failures. Many surgeons agree that surgical techniques are still far from perfect, nevertheless the actual quality of local control is considered acceptable and all the hopes and responsibilities in improving final results rely on adjuvant treatments. It is proved that patients who develop local recurrence have an inferior survival [10], but it is not clear if it is a direct or indirect effect; however, as a rule, the possibility of curing a malignant solid tumour, which is poorly responsive to other medical or physical treatments, is only possible when the primary lesion is adequately removed by surgery.

The surgical procedures for soft tissue sarcomas range from a simple excision to a major exarticulation, hemipelvectomy or compound operations for large lesions of the trunk, but the choice between a minor or major operation is determined by the extension of the tumour, whereas the amplitude of the operation

Table 1. Local recurrence rate in some large series reported in literature. The distribution by pathological grading, site of the lesions, methods of calculation are so different that comparison of data is, however, arbitrary

Author	Year	No. of cases	% of local recurrences	Median follow-up (months)
Eilber [1]	1984	183	3†	32
Potter [2]	1986	128	9†	38
Karakousis [3]	1986	109	20*	88
Collin [4]	1988	423	34–59*	>120
Sim [5]	1988	788‡	20–70†	?
Li Guo-Hui [6]	1988	313	24†	>120
Bell [7]	1989	100	28†	14
Mandard [8]	1989	109	~40*	>80
Rydholm [9]	1991	119	11†	54
INT §	1992	417	27†31*	84

*Actuarial values. † Crude values. ‡ Reported by single histotypes. § Istituto Nazionale Tumori, Milano.

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is by itself neither a warrant against recurrences nor for improved survival [11].

The success of an operation is, in fact, provided by the quality of surgical margins, which in account are conditioned by other factors: some are objective such as pathological grading of the tumour, clinical features (basically size and site of the primary lesion) and previous unsuccessful treatments; others are subjective and relate to the experience and faculties of the surgeon and institution where the operation is programmed and performed.

The following chapters describe and analyse in detail some parameters which are expected to have an impact on the regional control of disease; each statement is related to literature and based on our experience.

CLINICAL MATERIAL AND METHODS

The material of data and figures which comment our statements is an unselected series of 444 consecutive soft tissue non-metastatic operable sarcomas treated in our institution from 1974 to 1984. Results are evaluated in terms of local recurrence rate, starting from the date of the operation performed in our institution. The parameters analysed were pathological grading, location of primary lesion, previous inadequate surgery and quality of surgical margins. The quality of surgical margins was stratified in marginal (usually followed by radiotherapy) vs. wide/radical. The pathological grading was stratified in low grade (grade 1) and high grade (grade II and III). The site of the lesion was divided in extremity/girdle vs. trunk/head and neck. Table 2 summarises the distribution of the series. 27 (6%) cases were operated with intralesional margins, therefore were excluded because they were never free of disease. Median follow-up was 84 months, median time to death was 28 months and median time to local recurrence was 12 months. Local failure occurred in 113 cases (27% crude value, 31% actuarial risk at 5 years, 39% at 10 years).

The figures of local recurrence-free interval are calculated by the Kaplan–Meier method and the differences between curves by the log-rank test.

Table 2. Distribution of a series of 444 *non-metastatic soft tissue sarcomas operated at Istituto Nazionale Tumori in the period* 1974–1984.

	No. of cases	%
Male	219	49.3
Female	225	50.7
Low grade	148	34.3
High grade	284	65.7
Superior limb	93	26.8
Inferior limb	224	50.5
Trunk, head and neck	127	28.6
No previous surgery	171	38.5
Previous surgery	273	61.5
Intralesional margins	27	6.1
Marginal margins	126	28.4
Wide-radical margins	291	65.5

THE PATHOLOGICAL CLASSIFICATION

STS are histopathologically divided into different subtypes which reflect on epidemiology and natural history, but with a minimal role for the surgical procedure which is conditioned by the site, size and local spread of the primary lesion. The only pathological information which can modify the indication for surgery is the grading, which is documented to be the main significant prognostic factor.

According to this parameter the surgeon should practically recognise at least these four independent pathological entities:

Low grade sarcomas (grade 1)

These include two great histological entities; low grade liposarcomas and desmoid tumours (or aggressive fibromatosis). These tumours, despite the expected good prognosis, are in several instances the most difficult challenge for the surgeon. The site is typically extracompartmental (liposarcomas of the retroperitoneum, abdominal fibromatosis or fibromatosis in the supraclavicular area), the size is sometimes huge, and adjuvant treatments are not always feasible, nor indicated. Considering the low grade of malignancy the first operation is usually non-aggressive, therefore recurrences are frequent and any further conservative excision can hardly improve the quality of margins. There are no practical suggestions for these lesions in their locally advanced phase, but the indication to perform a major exarticulation must be considered before it becomes worthless. Radiation therapy is indicated, but for the crucial locations of these lesions curative doses are rarely delivered in the entire area. Some expectancies on hormonal and chemotherapy are reported for desmoid tumours [12–14].

High grade spindle cell-type sarcomas

Malignant fibrous histocytoma, high grade fibrosarcoma, high grade liposarcoma, synovialsarcoma, malignant hemangiopericytoma, malignant hemangioendothelioma, malignant schwannoma, leiomyosarcoma, polimorphous adult rhabdomyosarcoma, high grade spindle cell sarcoma NAS are the only histotypes which should be included into the group named high grade soft tissue sarcomas. They are subject for clinical investigations at least until a further more effective stratification will define specific entities with a significantly different behaviour and response to surgery and adjuvant treatments. The definitions of surgical adequacy and surgical indications reported in this paper are basically related to this large group.

Small cell sarcomas

The peripheral neuroepithelioma, soft parts Ewing sarcoma, embryonal rhabdomyosarcoma, small cell NAS sarcoma are lesions highly undifferentiated and frequently disseminated with a poor prognosis. In contrast to other groups, these lesions demonstrated a good responsiveness to chemo- and radiation therapy and the surgical treatment has only a role as a diagnostic, adjuvant or palliative procedure [15, 16].

Other rare histotypes

A number of miscellaneous lesions classified under the name of STS have a different or controversial pathological pattern. We propose clear cell sarcoma, alveolar sarcoma, epithelioid sarcoma, osteosarcoma and chondrosarcoma of soft parts, Kaposi's sarcoma. The treatment of such non-homogeneous lesions should be similar to other tumours with equivalent histopathogenesis (clear cell sarcoma is better treated as a malignant melanoma; chondrosarcoma and osteosarcoma should be man-

aged according to the schedule employed for their bony counterpart). Others should be investigated individually and should not be included in clinical trials of STS.

The present series includes only cases of group A (low grade) and group B (high grade). The local recurrence risk at 5 years was 24 vs. 35% for low and high grade, respectively ($P = 0.05$). The curve of local recurrence-free interval is reported in Fig. 1.

THE CLINICAL FEATURE

The size of STS is an important parameter used as a basis for many well-known staging systems [17–19]. It is still debated whether size really has a prognostic value, nevertheless it determinates the surgical management. It is obvious that a small lesion is more easily removed than a large one, but from the surgical point of view lesions of similar size can be regarded as small or large depending on their different location: for practical use we may consider as small those lesions below 8 cm in maximum diameter, located in large muscular compartments (major lodges of the thigh or buttock), below 5 cm when in small compartments (lodges of the leg, arm, scapular girdle, retroperitoneum), and below 3 cm when extra compartmental (i.e. groin, popliteal fossa, axilla, elbow, wrist, knee area, head and neck, neurovascular bundles). Lesions above this size–area ratio are rarely amenable with adequate margins and conservative operation. This definition has no impact as a prognostic factor, but only as a practical stratification for the choice of local treatment.

The site is also a determinant when trying to obtain an adequate local control: almost all the histotypes are ubiquitary and, independently of histology, some anatomical areas allow an easy or difficult (sometimes impossible) achievement of proper margins. Lesions detected in the extremities are usually easier to remove than those located in the trunk and girdles. A suprafascial or completely intramuscular lesion can be better managed than a deep or extramuscular one: for these favourable clinical features a simpler treatment schedule has been suggested in some instances which avoid either preoperative biopsy or postoperative adjuvant radiation therapy [9].

In our series a significant lower recurrence rate was documented for lesions of the extremities (26%) compared with those of the trunk (47%), $P=0.001$ (Fig. 2).

PREVIOUS SURGICAL TREATMENT

In our centre, and similarly in major institutions, 61% of cases were presenting with a recurrent lesion, as a result of a previous

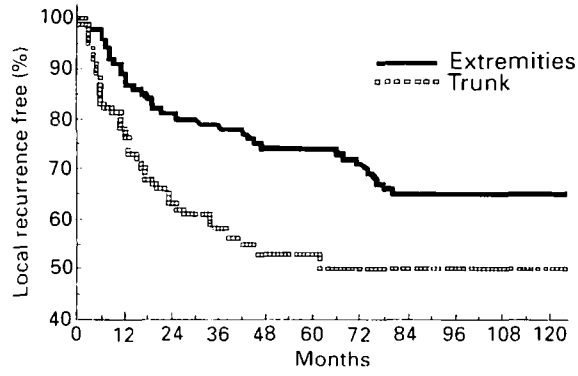

Fig. 2. Local recurrence-free interval by site of the primary lesion: 307 of the extremities or girdles, 110 of the trunk or head and neck (P=0.001).

inadequate surgical treatment. In these cases, the local recurrence rate was higher than in those treated for their primary virgin lesion. This difference was not evident after 5 years (30 vs. 35%, respectively; $P=0.3$) but significantly increased at 7–10 years (32 vs. 43%, respectively; $P=0.05$) (Fig. 3).

THE SURGICAL MARGINS

The quality of the surgical margin is the unique parameter in defining the adequacy of local control of disease. The surgeon is frequently requested to provide a specimen with the tumour surrounded by 2 or 3 cm of normal tissue: when we examine the axial section of one of the largest muscular regions, the proximal thigh (Fig. 4), it is evident that most of any hypothetical lesion located under the superficial fascia cannot be excised with margins thicker than a few mm without reaching an important bone, vessel or nerve, and these structures will never be resected unless directly infiltrated. In our experience, all the deep lesions treated with wide or compartmental resection had macroscopic margins which, in some parts, were less than 1 cm. Enneking, in his historical paper of the innovative staging system [20], introduced the concept of compartment and provided a precise definition of margins: intralesional, marginal, wide and radical, irrespective of the amplitude of the operation. Adequate operations are considered as all those which were not contaminated and with at least wide margins. Marginal operations can be

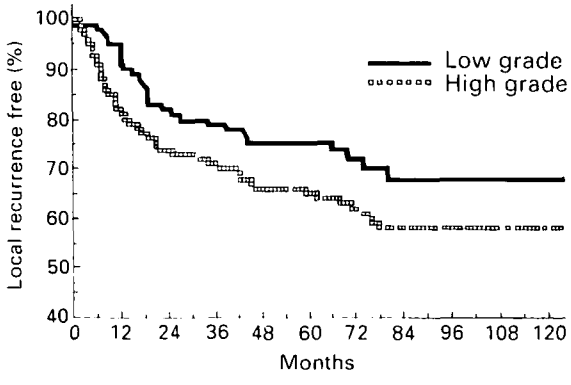

Fig. 1. Local recurrence-free interval by pathological grading: 143 low grade, 274 high grade (P=00.5).

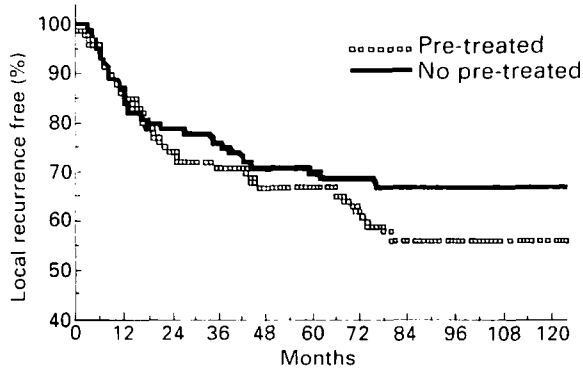

Fig. 3. Local recurrence-free interval by history of previous surgical treatments: 220 cases presented local recurrence at entry, 197 were virgin lesions (P=0.05).

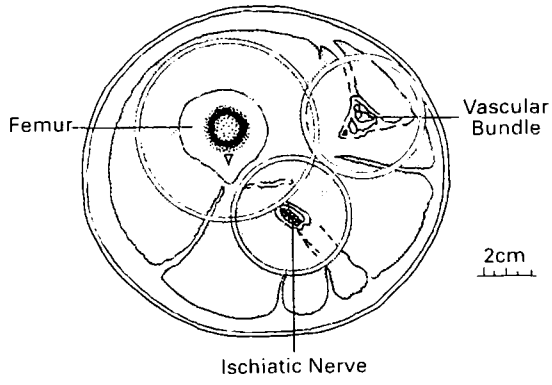

Fig. 4. A schematic of the proximal thigh, where there are the larger muscular lodges. In dotted lines, the area closer than 2 cm to bone, major vessels or nerves. Only lesion growth outside this area can be removed with a surrounding margin, thicker than 2 cm.

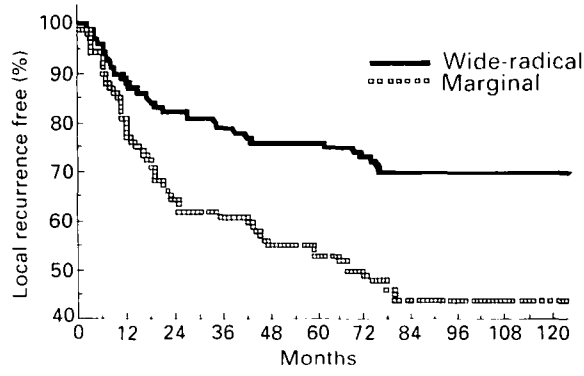

Fig. 5. Local recurrence-free interval by quality of surgical margins: 291 wide or radical, 126 marginal operations ($P < 0.001$).

accepted only when marginality is minimal and when the surgery is followed by radiation therapy. Accordingly, a correct definition of the surgical technique should include the kind of procedure employed together with the information of the quality of margin: for instance, a wide excision is thought to be adequate, whereas a marginal amputation is inadequate. This new glossary is commonly accepted by surgeons and should always be employed in its correct meaning. Moreover, the concept of compartment introduced by Enneking changed the metric evaluation of margins: compartmentectomy is rarely performed in its real meaning [21–22], but the ability to perform a true compartmentectomy resulted in a cultural and technical growth in the surgical practice, and increased the indication to perform adequate limb salvage operations.

A proper definition of margins makes the difference between an adequate or inadequate operation, or between conservative or demolitive surgery, but a compartment delimited by strong fascia sometimes thinner than a few mm is not easily measurable by the pathologists who prefer a metric evaluation of margins reported in cm. Therefore, the surgeon and the pathologist should be contemporarily involved in the assessment of the specimen, and it is important that STS are treated in experienced centres where the quality of surgery is performed at its best, reported with a proper language, following a precise rationale which allows retrospective analysis and comparison with other equivalent experiences.

Our series documented that the quality of margins is highly predictive of the risk of local recurrence: 24 vs. 47% for adequate and marginal operations, respectively ($P < 0.001$). Intralesional operations are excluded (Fig. 5)

THE SURGICAL TECHNIQUE

Conservative and demolitive operations for soft tissue sarcoma are widely described and illustrated in specific literature [23–26]. Most of the lesions are in accordance with the anatomical situations presented in these books and little is left to personal fantasy. Many clinical situations do not fit the typical indication for a specific operation, but it is probable that a similar master procedure combined with others can be applied to that specific case. These reported techniques should be carefully performed from the time of biopsy and first surgical approach.

For large infiltrating lesions the choice between limb salvage surgery and amputation is sometimes crucial, and one should always consider the risk of local failure compared with the level of functional impairment of both the procedures. In the last decade major institutions performed adequate limb sparing operations in many soft tissue lesions, formerly considered inoperable thanks to improved knowledge of surgical anatomy, relationship between wide demolition of muscles, vessels or nerves and related invalidity, and more practice in performing specialised procedures. Major exarticulations, if properly indicated and performed, reduce the risk of local recurrence, but functional impairment is severe, psychological acceptance difficult, and they do not improve survival [11]. Before indicating exarticulation sophisticated procedures must be considered, such as:

—Vascular surgery allows resection of important arteries substituted by prostheses or autologous replacement.

—Synthetic meshes and organic prostheses are now available for replacement of minor or major defects of the abdominal or thoracic wall.

—Plastic surgery can restore the widest skin loss with rotated flaps, or free myocutaneous flaps vascularised by microvascular anastomoses.

SURGICAL INDICATION

The decision to undertake ablative or conservative surgery and the amplitude of the operation itself must be considered in departments with all the above mentioned facilities and with experience on peri-operative adjuvant modalities.

In our institution an indication rationale for typical high grade sarcoma (group B) has been outlined for the more frequent clinical situations encountered, taking into account major parameters leading to increased risk of local failure:

—Pathological grading (the following schedule is only for grade II–III).

—Location: suprafascial, intracompartmental, extracompartmental.

—Size: stratified in small or large according to the site–size ratio reported above in the paragraph on clinical features.

—History of the lesion: already recurrent or pretreated with radiation therapy at entry in our institution.

(a) Intramuscular or superficial (suprafascial) lesion of small size not pretreated or biopsied: punction biopsy (facultative) followed by simple wide resection with a cuff of normal tissue around the mass.

(b) No palpable mass after excisional biopsy or unproper surgery: wide excision or compartmental surgery, according to the size of the scar, previous contamination of

surrounding soft tissue due to haematoma or drainage. Postoperative radiotherapy is indicated if the primary lesion was deep, extramuscular or if the pathological examination reveals residual disease, even if minimal. In other words, radiotherapy can be avoided if the primary lesion was intramuscular, or suprafascial, and when the final operation provided no residual disease in the specimen.

(c) Intracompartmental lesion of small size but already recurrent: wide excision plus radiotherapy or compartmentectomy.

(d) Small lesion in extracompartmental site: if there is no infiltration of major vessels or nerves, wide resection plus radiotherapy. If vessels or nerves are infiltrated the operation must be specifically designed with *en bloc* resection and possibly replacement of the important anatomical structures. RT is always indicated postoperatively; some histotypes like liposarcoma could take advantage also of preoperative RT.

(e) Intracompartmental lesion of any size but recurrent in a previously irradiated area: compartmentectomy. Plastic reconstructive surgery is sometimes demanded in these cases.

(f) Large size primary or recurrent intracompartmental lesion: compartmentectomy. RT will follow or preceed surgery. Exarticulation can be considered in cases of very large lesions when despite correct operative procedures the specimen is expected to be marginal in a large portion, or intralesional. Exarticulation should also be considered for recurrent lesions.

(g) Large lesion extending to more than one compartment or in an extracompartmental area: in these instances important neurovascular or bony structures are usually involved. If the lesion is not recurrent and the technical facilities are sophisticated, the possibility of performing a multicompartmental resection with eventual prosthetic or graft replacement of the resected vessels bone or skin tissues can be considered. Alternatively, and more likely for a recurrent lesion, a preferred choice is exarticulation. Lesions of the trunk are usually inoperable in such circumstances.

(h) Extracompartmental recurrent lesion in irradiated area: exarticulation. Lesions of the trunk are usuallly inoperable in such circumstances.

Preoperative induction chemotherapy can be proposed for high grade lesions within categories d, e, f and g only within a controlled study in centres with that specific experience.

MULTIMODAL PROCEDURES

The employment of adjuvant procedures—radiation and chemotherapy—is considered to be one of the possibilities of improving local control. The role of pre- or postoperative radiotherapy is widely accepted even if evidence for its validity is statistically weak [27–28]. Perioperative chemotherapy also has a potential role in reducing local failure after non-amputative operations [29–31] but, due to the variety and difficulty in reproducing the treatment schedules, patient selection and other biases, the results reported in literature are only effective for the centres where they have been produced. In our experience with 109 cases treated with preoperative intraarterial doxorubicin [32], 46% documented an objective local improvement, but the real change in surgery from amputation to limb salvage was estimated to be around 5%: this numerically small impact on statistics, however, should not ignore the physical and psychological importance of these few conservative-rescued operations. We agree that it is worthless to treat all the patients with complicated and uncomfortable therapies which probably do not improve survival, nevertheless selected cases can take advantage of preoperative induction chemotherapy, those in which a local improvement would enable a reliable limb salvage operation rather than an exarticulation, or considered inoperable for lesions of the trunk.

METASTASECTOMY

A survey on surgery for soft tissue sarcoma should also comment upon the determinant role of lung metastasectomy which since the first experience in the seventies [33–35] is at present the first line treatment for resectable pulmonary lesions. Patients with operable lung metastases can be definitely cured in about 20–30% of cases provided that an adequate local control of primary disease is obtained.

DISCUSSION

In this survey the factors which have been identified as independent causes of local recurrence basically concur with those of prognostic value with regard to survival [10]. The effect of these factors on survival seems to be direct and not mediated by the event of local failure. Therefore, a severe invaliditing operation is not justified in patients who have a poor survival expectancy. Nevertheless, not all the causes of local failures depend on prognostic factors. We recognised other situations which could have increased the risk for local recurrence. These are avoidable causes, and should be regarded before approaching STS or a suspected STS lesion.

—Incomplete preoperative investigations. Preoperative instrumental examinations are frequently very poor especially when a sarcoma is not suspected. The unexpected involvement of vessels, bone, nerves, viscera or a large lesion, or an unexpectedly wide site are the most frequent causes that lead the first operation to be an inadequate and contaminating "shell-out". When a sarcoma is suspected, a needle tru-cut type biopsy, or an open small incisional biopsy is demanded, followed or preceded by computerised topography scan or nuclear magnetic resonance or other informative investigations indicated for lesion of the trunk.

—Underestimation of surgical difficulties. Even after a proper preoperative set-up, the operation itself can be more challenging than expected. The clinical–radiological aspect can give the impression of an easy removal whereas the strong involvement of contiguous structures, usually important vessels or nerves, makes the technique more intricate, and the surgeon must be specially trained to face that situation.

—Poor knowledge or no possibility to perform special procedures. If there is neither the possibility to perform specialised procedures nor to have available meshes and prostheses for tissue replacement, the operation for many lesions would be designed and performed with a lesser quality of margins, or an otherwise avoidable amputation would be performed.

—Obstinate attempt to perform conservative operations. A major exarticulation does not improve significantly the possibility of curing a patient, but where the surgical facilities are highly sophisticated, and where there is cooperation with departments of chemotherapy and radiotherapy, it is sometimes a challenge for the surgeon to perform a limb salvage operation even if the possibilities of performing an adequate operation are really poor. Trust is placed in complementary postoperative

treatment, which, however, should not be a reason for performing improper surgery.

I fully support Enneking's opening to his master treatise [25]:"Management of musculoskeletal tumours requires special knowledge of clinical presentation, methods of clinical assessment, specialised laboratory procedures, sophisticated pathological techniques, orthopaedic oncological surgery, methods of limb and spine reconstruction, adjunctive radiotherapy, adjunctive chemotherapy, physical and psychological rehabilitation, and an understanding of the natural history of the disease and its response to treatment. Since no individual is well versed in all these areas, better care is provided by a team of physicians whose members provide expertise in these diverse fields."

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