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Soft tissue sarcomas of the extremities, the yield of preoperative pathology examinations

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Background: In the work-up of extremity soft tissue sarcomas (STS) a correct histopathological diagnosis is essential before surgical treatment. While open incisional biopsies (IB) have been the golden standard for long, large core needle biopsies (CNB) and even fine needle aspiration (FNA) are increasingly being used to establish a diagnosis. In a nation-wide study in patients that were operated for extremity STS, the preoperative use of IB, CNB and FNA was evaluated and their sensitivity assessed.
Patients and methods: All patients that were operated in the Netherlands between November 2000 untill December 2003 for a newly diagnosed extremity STS were retrieved from the national automated pathological database: PALGA. Biopsies were considered affirmative when it concluded the presence of a mesenchymal malignancy.
Results: In this period, 505 patients in the Netherlands underwent resection of an extremity soft tissue sarcoma in. Definitive surgery was done in 158 patients (31%) without preoperative pathological examination. Of the remaining 347 patients (69%), 319 patients (63% of all patients) had a histological biopsy and/or 99 patients (20% of all patients) a FNA. In patients who were biopsied (n = 319), IB was done more often than CNB (147 vs. 100 patients), while in 72 patients information about the nature of the histopathologic biopsy (CNB or IB) was unclear. An affirmative diagnosis of "mesenchymal malignancy" could be established in 140/147 patients (95%) after IB, in 80/100 patients (80%) after CNB and in 39/99 patients (39%) after FNA. The correct histomorphological tumour type was diagnosed in 80%, 53% and 19% respectively.
Conclusion: In this nationwide study in patients that were recently treated for extremity STS, one third of the patients was operated without preoperative pathological analysis. Although the sensitivity of core needle biopsies is high, open biopsies still have a higher sensitivity and when it comes to a correct histomorphological diagnosis this difference increases. An open incisional biopsy should still be considered the golden standard in the preoperative work-up of extremity STS.

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Intraoperative electron beam radiotherapy combined with dose-reduced external beam radiotherapy is highly effective in limb-sparing treatment of extremity soft tissue sarcomas

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Objective: Management of extremity soft tissue sarcomas has changed dramatically during the past 25 years towards a multimodal approach combining limb-sparing surgery with adjuvant radiotherapy. However, severe side effects resulting in clinically significant limb-function impairment are observed in up to 36% of patients after adequately dosed conventional radiotherapy. We review the results of a treatment strategy combining dose-reduced external beam radiotherapy (EBRT) with intraoperative electron beam radiotherapy (IEORT), which has been implemented in Heidelberg 10 years ago, focussing on local control and the incidence of side-effects.
Patients/Methods: We analyzed the outcome in 153 adult patients treated for extremity soft tissue sarcomas in Heidelberg from June 1991 to June 2004. Median follow up was 48 months. 38% of patients suffered from recurrent, 62% from primary soft tissue sarcomas. Most patients suffered from malign fibrous histiocytomas (35%), liposarcomas (30%) or leiomyosarcomas (10%). Grading distribution was as follows: 57% G3, 35% G2, 8% G1. In 34% of patients the tumors were resected with wide clear margins, 20% with margins below 1 cm (R0); 34% showed microscopic (R1), 12% macroscopic tumor residues (R2). 37% of the treated tumors had a size <5 cm (maximal diameter), 33% of 5–10 cm and 30% were >10 cm. IOERT was delivered via linear accelerator in the operating theater. Electron energies ranged from 8 to 15 MeV. IEORT doses ranged from 10–20 Gy (90% isodose, median 15 Gy) covering the complete tumor bed. Healthy normal tissue was either displaced or covered with appropriately sized lead shields. EBRT was delivered by linear accelerators with 6–23 MV photon energies. 29% of patients had received EBRT preoperatively, 71% received EBRT 2–8 weeks postoperatively. Doses of 39.6–54 Gy (mean 43 Gy) in daily fractions of 1.8–2 Gy were prescribed. CT-based 3D conformal treatment planning was used in all cases. The volume treated included the tumor bed (with surgical clips marking the IOERT-field), plus a wide margin of 5 cm whenever possible.
Results: Our results show an overall 5-year survival rate of 70%. Local control rate after 5 years was 78% and 73% after 10 years, respectively. 5-year distant failure free survival was 53%. 5-year survival rates after R0-resection was 76%, after R1/R2 resection 55% (not statistically significant with p = 0.1). The overall survival rates did not significantly depend on the resection status either. Primary versus recurrent tumor as well as tumor size did not result in essential differences concerning local control rates. Grading, however proved to be of significant prognostic impact on overall survival, but not on local control rates. Overall 5-year survival was better in patients after R0 or R1-resection versus R2 resection though (78% versus 45%, p = 0.01). The applied IEORT dose resulted in a statistically significant difference: 5-year local control after IEORT dose below 15 Gy was 62%, above 15 Gy was 75% (p = 0.008). Acute complications were observed in 28% of patients (89% CTC 1 or 2, 11% CTC3), mainly including wound-healing disturbances, skin damage and seromas. 5 patients had to undergo resurgery. Late effects were scored according to LENT-SOMA scale and were observed in 19% of patients (95% grade 1 or 2), with lymphedema, nerve lesions and contractures due to fibrosis being prevalent. Overall 90% of patients alive 5 years after IEORT showed no significant impairment of limb function in daily life activities.
Conclusions: IEORT represents an excellent method to reduce EBRT in multimodal limb-sparing treatment of extremity soft tissue sarcomas. Radiation induced side effects are low, while an excellent local control rate is preserved.

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The Rotterdam Experience of 217 TNF-based Isolated Limb Perfusions (ILP) for advanced Soft Tissue Sarcomas (STS): long-term follow up, prognostic factors and subgroup analysis

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Background: Extensive and mutilating surgery is often required for locally advanced Soft Tissue Sarcoma (STS) of the limb. As it has become apparent that amputation for STS does not improve survival rates, the interest in limb-preserving approaches has increased. Isolated Limb Perfusion (ILP) with TNF and Melphalan is successful in providing local tumour control and enables limb-preserving surgery in a majority of cases. Here we report on the mature largest single-institution experience with 217 consecutive ILPs for STS of the extremity.
Methods: Prospectively maintained database at a tertiary referral centre. From July 1991 – July 2003, 217 ILPs were performed in 197 patients with locally advanced STS of the extremity. ILPs were performed at mild hyperthermic conditions with 1–4 mg of TNF and 10–13 mg/L limb-volume Melphalan (M) for leg and arm perfusions respectively. We studied the outcome of the patients and performed an analysis to identify prognostic factors for response, disease control and survival after ILP.
Results: Overall response rate was 75%. Limb salvage was achieved in 87% of the perfused limbs and local control could be obtained in 74%. Median survival post-ILP was 57 months and prognostic factors for survival were Trojani grade of the tumour and ILP for single vs. multiple STS. The procedure could be performed safely with a peri-operative mortality of 0.5% in all patients with no age-limit (median age 54 years, range 12–91). Systemic and locoregional toxicity were modest and easily manageable. Limb salvage percentages in subgroups of patients with systemic metastases, multiple sarcomas in the limb and recurrences in previously irradiated areas were all highly positive (97%, 82% and 65% respectively).
Conclusion: TNF+M-based ILP can provide limb salvage in a significant percentage of patients with locally advanced STS and has therefore gained a permanent place in the multimodality treatment of STS.

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Prognostic indicators of locoregional and systemic recurrences after sentinel lymph node biopsy in patients with cutaneous melanomas

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Summary/Objective: Although the sentinel node (SN) technique is widely used, there is no evidence that the SN procedure in melanoma patients influences survival. The objective of this study was to investigate the prognostic value of the SN status, especially in terms of disease-free survival (DFS) and overall survival (OS) and to evaluate locoregional control after the SN procedure.