Material and Methods: Forty-two patients diagnosed of localized Ewing sarcoma have been recruited. RNA was extracted from peripheral blood samples. RT-PCR was performed according to detect the EWS/FLI1 fusion mRNA.

Results: From forty-two patients, 16 were RT-PCR positive for EWS/FLI1. Nine of these 16 patients (56.25%) showed distant metastatic disease with a median follow-up of 20 months (10–33) and 3 relapsed locally (18.75%). From the 24 patients with no evidence of circulating tumor cells, 5 patients developed metastatic disease (20.8%) with similar follow-up and 2 patients showed local recurrence (8.3%).

Conclusions: These data suggest that the detection fo circulating tumor cells could define a group of patients with a significant higher rate of local failures and/or metastatic spread.

501 POSTER

Growth pattern and development of metastasis in orthotopically transplanted human osteosarcoma xenografts in nude mice

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Purpose: Experimental tumor models which resemble the clinical situation could be valuable in evaluation new treatment strategies in vivo. The aim of the present study was to establish a new human osteosarcoma spontaneous metastasis model using orthotopic transplantation of histologically intact tumor tissue into the tibia of nude mice.

Methods: Subcutaneously growing human osteosarcoma xenografts from the 32nd serial passage was used in the experiment. Solid tumor pieces were implanted into the proximal tibia in 31 nude mice. The animals were sacrificed and autopsied at 2, 4, 6, and 8 weeks after transplantation. The mice were examined macroscopically and microscopically for local tumor growth and metastases.

Results: Intratibial bone tumors were found in all mice at the site of the implantation. The tumors were radiographically and histologically similar to primary human osteosarcoma. Lung metastases were observed in all mice, local and distant lymph node metastases in 15 (48%), and liver metastases in 6 (19%) mice. The microscopic appearance of the metastases was similar to that observed in the donor patient-s tumor, corresponding subcutaneous xenografts and orthotopically transplanted intratibial tumors.

Conclusion: Since local tumor growth were found in all animals and spontaneous metastasis were observed in several mice this model seems suitable for further studies on local tumor growth, formation of metastasis and antitumor therapy.

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Intraoperative radiotherapy (IORT) in soft tissue sarcoma

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Purpose: In high risk patients with soft tissue sarcoma, percutaneous radiotherapy after extremity preserving surgery is the standard treatment. Local control can probably be improved by intraoperative radiotherapy. There is no data available concerning the function of thus treated extremities. The aim of this work was the evaluation of patients with soft tissue sarcomas (STS) of the extremities after IORT with respect especially to local control and function of the extremity.

Methods: From 1986–1996, 23 patients (T1: 6x, T2: 17x; recurences: 11x) were irradiated intraoperatively (12–15 Gy) and postoperatively (40–60 Gy). The course of disease was evaluated retrospectively by interviews of the patients, their relatives and treating physicians as well as evaluation of radiotherapeutical and surgical files. The function of the extremity was analysed by a standardised questionnaire and examination.

Results: Local control was obtained in 18 of 23 patients (78%). Survival rate was 65% (15/23 patients) after a mean observation period of 36 months (1–72). 7 of 20 patients who were initially free of distant metastases, developed distant disease. Of 15 patients alive, 11 patients revealed excellent function of the extremity or had only minor functional deficits.

Conclusion: The addition of intraoperative radiotherapy to routine treatment in high risk patients with STS of the extremity achieved 78% local tumour control during a mean of 36 months observation time. Compared to historical data, this could point towards improved local control. The functional result was excellent with no or minor deficits in 11 of 15 patients alive.

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Morbidity of a combined modality therapy of intra-arterial doxorubicin, neoadjuvant radiotherapy and surgery for locally advanced high grade soft tissue sarcomas (STS) of the extremities

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Intra-arterial doxorubicin, neoadjuvant radiotherapy, and surgery was introduced as limb-saving treatment for "unresectable" high grade STS of the extremities.

Patients and Methods: Between 1982–1986 11 pts, 9 ♂ and 2 ♀, median age 52 (range 24–70) yrs, with "unresectable" grade III STS of the extremities were treated by preoperative i.a. infusion of doxorubicin for 3 consecutive days (daily dose 20 mg/m^2). Within 24 hours after infusion preoperative XRT of the compartment (10 × 350 cGy) started. After chemo-radiotherapy the tumor was resected. Non-radical resections received 20–30 Gy XRT (9 pts).

Results: No local recurrences (median fu 110); pulmonary met's in 5 pts (45%). Local skin toxicity due to doxorubicin in 3 pts (27%). Preoperative 35 Gy XRT was well tolerated. Limb-saving treatment in 10 pts (91%); in 1 an exarticulation of the hip had to be performed. Three of the 5 longterm survivors (fu > 10 yrs) developed a severe fibrosis of the affected limb (60%). Two severe longterm complications: a stress fracture of the affected femur (91 months), and a severe radiation-induced motor and sensory neuropathy of the sciatic nerve.

Conclusion: The longterm results show a limb-saving rate of 91%, without increasing the risk of a local recurrence. Especially the longterm morbidity is extremely high (60%). This combination therapy should therefore no longer be advocated.

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Conservative possibilities of treatment in sarcoma of the limbs

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The study underlines the value of neoadjuvant and postoperative chemotherapy in the aim to realize a successful conservative surgery in locally-advanced sarcoma (LAS) of the limbs.

From oct. 1990 to dec. 1996 we treated 165 non metastatic sarcoma of the limbs: 96 osteo and chondrosarcoma (OS) and 69 soft tissue sarcoma (STS). From 165, 97 cases with LAS received after biopsy 3–4 courses of neoadjuvant chemotherapy with CIVADIC. 92% of all cases were submitted to conservative surgery: extensive bone surgery, with bone grafts or articulation prosthesis in OS; wide excision in 48% and marginal surgery in 45% of STS. Postoperative chemotherapy 6–8 courses with cisplatinum, farmorubicin in OS (CDDP 100 mg/m^2, farmorubicin 70 mg/m^2) and CIVADIC (cyclophosphamide 500 mg/m^2, vincristine 1 mg/m^2, farmorubicin 70 mg/m^2, DTIC 250 mg/m^2/day × 2), alternating with CIVADACT (actinomycin D 500 γ/day × 3) in STS. The tolerance to chemotherapy was good with mild manageable side-effects. In the cases with marginal surgery, compartimental radiotherapy was performed with 50 Gy plus local boost. The median follow-up was 4 years. The disease free survival was 8–24 months.

In conclusion, even in the LAS of the limbs complex treatment chemo-radiotherapy makes possible a conservative surgery with good, long lasting results.

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Neoadjuvant long-term continuous intra-arterial chemotherapy of soft tissue sarcomas

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Purpose: The efficacy of preoperative long-term continuous intra-arterial infusions of cisplatin (CDDP)+adriamycin (ADR) was investigated.

Methods: 26 patients (15 M., 11 F, mean age 40 years) with soft tissue sarcomas of the extremities (15 synovial sarcomas, 8 malignant fibrous histiocytomas, 3 nonclassified sarcomas) were included in this study. All patients had extracompartmental lesions, tumor size >8 sm, volume >100 sm^3. The schedule of chemotherapy consisted of a 5-day