

European Musculo-Skeletal Oncology Society

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EMSOS was founded in 1987 and its 100 members have since then convened annually. The prime purpose is to encourage mutual collaboration between different specialists involved in the treatment of musculo-skeletal tumors.

This is a representative selection of abstracts at the Prague meeting. Papers also given at the Scandinavian Sarcoma Group meeting this year (pp 55–72, this issue) are not included.

Long term results of allogenic bone transplantation

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We have performed allogenic bone transplantation since 1960 and report two groups of patients,

Giant cell tumor. Of 111 patients, 36 were reconstructed with massive osteoarticular grafts. There were 4 failures due to infection, 2 of these patients had had previous surgery elsewhere. Successful allograft replacement was performed for the acetabulum, upper and lower femur, proximal and distal tibia with a follow-up to 20 years.

Knee tumors. Resection and arthrodesis with allograft replacement was performed in 54 patients of whom 39 had an osteosarcoma. Graft union required a stable osteosynthesis. Complications including infection, failure of osteosynthesis, and pseudarthrosis were common. In cases with a favourable outcome this limb salvaging procedure is a definite solution well accepted by most of our patients.

Allograft reconstruction in bone tumor surgery

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We have followed 171 allograft reconstructions for more than 1 year and made the following observations.

Knee arthrodesis (46). 1 infection, 6 fractures and 16 delayed unions. There were 3 major reoperations. 36 patients had satisfactory (excellent or good) result.

Hip arthrodesis (11). 6 delayed union with 2 major and 1 minor reoperation. 8 patients had satisfactory result.

Intercalary reconstruction (36). 3 infections, 9 fractures and 17 non-unions. A reoperation was performed in 18 patients.

Segmental reconstruction, VF+A (28). 1 infection and 7 fractures. 3 patients were reoperated.

Osteoarticular reconstruction (35). 10 fractures and 10 delayed unions. 12 patients were reoperated.

Composite allografts (6 hips). No reoperations and excellent results in all cases.

Pelvic reconstructions (9). 1 infection and 3 instabilities, 6 patients had an excellent result.

In conclusion we had the best results with arthrodesis and recommend a combination with a vascularized fibula for intercalary grafts. The best indication for an osteoarticular graft seems to be the elbow, wrist and hip.

Fractures in massive allograft reconstruction in bone tumors

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From 1984 to 1992, 123 patients with musculo-skeletal primary tumors of the limbs were treated by resection and allograft reconstruction. The average bone resection length was 13 (8–22) cm. Postoperative chemotherapy was given in 113 cases. A fracture of the allograft occurred in 25 cases after average 23 (7–90) months

3 recent cases have not been treated. In 8 cases the fractures healed with no weight bearing or with cast immobilization. 7 cases underwent surgery without graft removal and 7 cases (5 osteoarticular) had graft removal and different reconstructions. All cases treated without surgery achieved good or excellent function as also 4 of 7 patients who had salvage surgery for their allograft. In patients with the graft removed, 3

had good or excellent results. In conclusion, allograft fracture is a frequent complication, that requires surgery in 2/3 of the patients, ending in failure in 1/3 of the cases.

Vascularized fibula autograft in skeletal reconstruction after bone tumor resection

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We report our experience with 65 patients treated with a vascularized fibular transfer after excision of a malignant bone tumor of a limb 1988–1993. We used a vascularized fibula to bridge a skeletal defect greater than 8 centimeters, particularly in poorly vascularized or infected beds, or when bone healing could be delayed by chemotherapy. In the upper limb the fibula transfer was used as the only means of skeletal reconstruction, while in lower limbs it was mostly supplemented with a non vascularized massive allograft. A VFA was used as a primary reconstruction in 48 cases and as a secondary salvage procedure in 17 cases.

54 patients have a follow up longer than 1 year. Interval until union of the VFA ranged between 2 and 5 months. Complications were: 4 displaced fractures and 1 non union which were successfully dealt with a new osteosynthesis; 1 infection and 2 bone metastasis in the same limb, at a more proximal site, which were treated by amputation.

We prefer a vascularized fibula combined with a massive allograft for reconstructions of the lower limb: in the early phase of healing the allograft protects the VFA against the risk of displaced fracture while fusion and hypertrophy occur. Rapid union of the osteotomy allows early joint motion. The hypertrophied VFA can then support the allograft during the late phase of creeping substitution.

DNA content of soft tissue sarcomas

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To determine the DNA content in soft tissue sarcomas we have used cytofluorometry, a technique which combines the sensitivity of DNA-binding fluorochromes, such as propidium iodide, with the direct observation of individual cells. In 48 cases of soft tissue sarcomas 18 were diploid, 6 polyploid and 24 aneuploid. A diploid pattern was observed in 5 low grade (LG) and 13 high grade (HG) sarcomas. A polyploid pattern was found in 6 HG sarcomas. An aneuploid pattern was present in 23 HG and 1 LG sarcoma. Our data show that diploidy may be found in highly aggressive tumor types, such as synovial sarcoma and small round cell tumors, whose subtle genetic abnormalities are not detected by the analysis of

DNA content; the prognostic value of ploidy depends on the histologic type.

DNA ploidy and prognosis in soft tissue tumors

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We performed image cytometric DNA analysis on Feulgenstained sections (10 µm) of 118 benign, 38 semimalignant (or questionable malignant) and 375 malignant soft tissue tumors of various types. No DNA stemline aneuploidy (DNA-Index > 1.2;) was found in the 118 benign tumors. All 20 cases of aggressive fibromatosis were DNA-peridiploid (DI ≤ 1.2), whereas aneuploidy was found in 1 of 10 dermatofibrosarcomas and in 2 of 3 atypical fibrosarcomas.

Round cell sarcomas (72), synovial sarcomas, Ewing's sarcomas, and PNETs, were characterized by a minor aneuploidy rate (maximum 30%), in contradiction to their high malignancy. In contrast, alveolar rhabdomyosarcomas were characterized by a high aneuploidy rate (11/13) with typically tetraploid DNA indexes, which may even serve as a differential diagnostic criterium. Embryonal rhabdomyosarcomas showed a lower rate aneuploidy (16/29). Neuroblastomas were predominantly aneuploid (17/24) with typical DNA indexes in the triploid range.

The group of soft tissue sarcomas common above the third decade were characterized by a close correlation between cytologic grading of malignancy, and DNA stemline aneuploidy plus single cell aneuploidy. As far as we can judge today, in this group of sarcomas DNA cytometry will be of practical value only in grade I tumors where the evidence of DNA aneuploidy predicts a less favorable outcome.

Fine needle aspiration biopsy of soft tissue tumors

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We assessed the reliability of fine-needle aspiration biopsy in the diagnosis of soft tissue tumors.

Patients and methods. The cytological diagnosis in 342 patients was compared to the histological diagnosis after open biopsy and/or surgery. 164 lesions proved to be benign and 178 malignant.

Results. Cytology was inconclusive in 42 (12%) of the 342 lesions, 9% of the benign and 15% of the malignant. The cellular material was adequate in 25 of these cases but a definite diagnosis could not be made.

The cytological diagnosis was conclusive in 300 cases. 153 lesions was cytologically diagnosed as benign. This was correct in 164 (95%), but in 7 cases histology revealed sarcoma. Among 147 lesions cytologically assessed as malignant, 144 (98%) proved to be sarcomas.

Regarding the 178 lesions finally diagnosed as soft tissue sarcomas, cytology provided the correct diagnosis in 144 (81%). In 27, cytology was inconclusive, necessitating open biopsy and in 7 cases, the cytological diagnosis was incorrectly benign.

In conclusion, we obtained sufficient material for cytological diagnosis in 88% and, among these, the diagnosis was correct in 97%.

Evaluation of lipomas by magnetic resonance imaging

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Introduction. We evaluated the diagnostic value of MRI for suspected lipomas.

Materials and methods. 43 patients with lipomatous tumors greater than 4 cm were examined with MR. and categorized as: lipoma, lipoma with components of other tissues, or expected malignancy. 13 tumors were subcutaneous and 30 subfascial.

The signals on T1 and T2-weighted sequences, together with demarcation and homogeneity of the tumor, were noted. Histologic evaluation was performed in all tumors after incision biopsy or surgical removal.

Results. Based on MRI, 26 lipomas, 8 atypical lipomas and 9 malignant tumors were identified. Histologic evaluation confirmed the MRI findings with regards to the 26 lipomas. The atypical lipomas contained areas of myxoid, or connective tissue, and one was an angiolipoma. The 9 malignant tumors were liposarcomas.

Conclusion. By MRI it seems possible to distinguish between a lipoma and a sarcoma.

Results of a randomized clinical trial for soft tissue sarcomas of the extremities

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After treatment of the primary tumor, 76 patients with soft tissue sarcomas of the extremities were randomized; 32 patients were given adriamycin (total dose 450 mg/m²).

At a medium follow-up of 106 (71–134) months, 18 of 32 are without disease in the chemotherapy group, versus 14 of 44 in the control group. The actuarial disease-free curve shows a highly statistical improvement in patients with chemotherapy (log rank test p 0,015); the overall survival curves also showed a better outcome for the chemotherapy group (p 0,06).

Adjuvant chemotherapy seems to increase disease-free survival in STS; evaluation of results in trials for STS needs a long follow-up (in our study 5 patients relapsed more than 5 years from treatment). In the future trials should be performed with more consistent and homogeneous groups of patients for evaluation of the efficacy of adjuvant chemotherapy in STS.

Resection of pulmonary metastases in soft tissue sarcomas

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We treated 60 patients with thoracotomy and resection for pulmonary metastases from soft tissue sarcomas. The medium disease-free interval was 28 months; 43 patients had monolateral metastases, and 17 bilateral. Contemporary bilateral resection of pulmonary metastases was performed in 1 patient. 14 patients were operated more than once. At medium follow-up of 5 (1–13) years, 21 patients were still alive; 11 of these without sign of disease. The most important prognostic factor was a disease-free interval of almost 2 years (p 0.009).

We recommend surgical resection of pulmonary metastases in patients with soft tissue sarcomas.

Prognostic factors in synovial sarcoma

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We reviewed all our synovial sarcomas to evaluate if there are subsets of patients with different prognosis.

Patients and methods. In 60 synovial sarcomas treated at our institution various prognostic factors were evaluated. The mean age was 40 (9–76) years, 14 patients were in their first two decades. 56 tumors were located in the extremities. The mean size of the tumors was 7.5 (1–30) cm. The duration of symptoms ranged from 1–120 months.

A 4-grade histologic malignancy scale was used; all but one tumor were grade III–IV (high-grade). All patients were surgically treated. 47 patients had primary limb salvage. Postoperative adjuvant treatment was given to 24 patients. All patients were followed for a minimum of 2 years.

Results. At follow-up 28 of the patients had a tumor related death. The strongest prognostic predictors were age and size of the tumor. Of 14 patients below 21 years of age at the time of operation, 11 are alive with no evidence of disease as are 21 of 29 patients with tumors 5 cm or smaller.

Conclusion. Young patients with small synovial sarcoma seem to have the best prognosis. We question whether these young patients would benefit from adjuvant chemotherapy.

Synovial sarcoma. Histopathological and clinical considerations

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We reviewed 65 patients with synovial sarcoma. The mean age was 35 (7–64) years. The minimum follow-up was 5 years, average 10 years. In univariate analysis parameters like age, sex, mitotic index, percent of glandularity, necrosis and cellular atypia did not seem significant, while increasing tumor volume and histological subtype (monophasic showed a worse outcome) correlated with the outcome.

Immunohistological detection of growth factors and receptors in osteosarcomas and Ewing's sarcomas—implications for the autocrine hypothesis of growth regulation

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We investigated the immunohistochemical expression and localization of EGF, TGF α , EGF-r as well as PDGF, PDGF-r and IGF1-r in 17 samples of Ewing's sarcoma and 44 samples of osteosarcoma using a slightly modified APAAP-method on frozen sections. Semiquantitatively assessed, results were:

	Osteosarcoma	Ewing
EGF and EGF-r	40	5
PDGF and PDGF-r	17	4
both pairs	15	1
TGF α	20	10
TGF α and EGF-r	19	5
IGF1-r	35	15

Areas with chondroblastic differentiation showed an only weak or negative reaction for all antibodies tested. In Ewing's sarcoma EGF and EGF-r immunoreactivity was mostly weak. The almost consistent expression of EGF and EGF-r in osteosarcomas suggests an involvement of this factor in growth regulation. Particular growth factors operate at different points of the cell cycle and a concerted action of a number of factors might be needed for stimulation of proliferation. The high incidence of simultaneous expression of growth factors and receptors in osteosarcomas indicates an autocrine mechanism of growth regulation. The striking difference in the expression of these factors in Ewing's sarcomas in contrast to the findings in osteosarcomas underlines the different tumor biology of these entities

Molecular and cytogenetic analysis of a myxoid chondrosarcoma

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We performed cytogenetic and molecular genetic analyses on the myxoid chondrosarcoma cell line 105KC, which had a diploid and an aneuploid clone, and on its clonal derivative 105AJ and 3 subclones, which all had del(9)(p22-pter) as the only cytogenetic change. FISH on 105KC showed one chromosome 9 to be normal and one involved in multiple rearrangements. In 105AJ and its subclones Southern blot analysis showed loss of the interferone genes, localized on 9p21-22, and western blot and activity analyses of these also showed absence of methylthioadenosine phosphorylase. These studies in conjunction with other reports on chondrosarcoma suggest that 9p aberrations are involved in the development of these tumors

Detection of the 11;22 chromosome translocation in Ewing's sarcoma and PNET using reverse-transcriptase-PCR

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We used a reverse-transcriptase-based PCR-assay for detection and characterization of fusion transcripts involved in t(11;22) translocation. In cell lines of Ewing's sarcoma and PNET three types of chimaeric transcripts were found: type I, 324 bp; type II, 390 bp and type III in four different variants, so far. These transcripts show major sequence variations.

Analysis of 21 tissue samples of either the primary biopsy or the post-chemotherapeutic resection specimens of unkaryotyped Ewing's sarcomas and 2 of PNETs revealed a type I chimaeric transcript in 6, type II transcript in 4 and type III transcript in 5 cases. The two PNETs showed both type I transcripts.

Thus reverse-transcriptase-PCR provides a rapid and apparently sensitive method to demonstrate specific fusion transcripts in these tumors.

Infected reconstruction after tumor resection Two stage treatment using antibiotic-loaded cement

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We managed 12 cases of deep infected reconstructions after wide excision for tumor by a two-stage revision

The first stage included a complete surgical debridement, removal of all implants, reconstruction with an antibiotic loaded cement spacer, and systemic antibiotherapy for several months. All infections healed and 6 patients have so far undergone the second stage with the cement spacer replaced by a classical and more lasting reconstruction without any infection.

Conclusion. The two stage procedure seems to be reliable for limb salvage in infected massive reconstructions, especially with multiresistant germs.

Social outcome of young adults after surviving malignancy with special reference to osteosarcoma

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We studied the late consequences of cancer treatment and compared whether the pre- or postpubertal status at the time of cancer diagnosis has an effect on the education, employment,

living arrangement, fertility and offspring. We interviewed 94 survivors in whom the neoplasia had been diagnosed between 1–14 years (44 ALL, and 10 Wilms tumor) or between 15–25 years (19 osteosarcoma, and 21 testis cancer). 69 siblings or friends of the same age were controls.

We found that prepubertal cancer impaired the social outcome. The female patients had better interpersonal relationships than the male ones. Osteosarcoma patients had, however, educated most actively, even more than the peers.

Skip metastases in Ewing's sarcoma

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Skip metastases in Ewing's sarcoma are extremely rare; We present 14 such patients managed with a combined neoadjuvant treatment protocol and surgery; the resection included the primary tumor and the skip lesion. The clinical data did not differ between patients with skips and those without. Most skip lesions were located distally to the primary tumor and all were diagnosed by MRI and confirmed by macroscopy and microscopy. The detection of the skip lesion influenced profoundly the surgical treatment, but had no prognostic importance. 2 patients developed distant metastases, but no local recurrences. 12 patients remained disease free (follow-up 7–54 months). We recommend MRI of the involved bone and adjacent joints in Ewing's sarcoma to detect skip lesions.